

EP-001

Acute Lymphoblastic Leukaemia

EVALUATING IRON OVERLOAD AT THE END OF THERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

The aim of this study is to determine the hepatic iron overload by using R2 MRI and to evaluate the influence of hepatic iron overload on liver function tests in children with acute lymphoblastic leukemia (ALL).

Methods

Medical charts of 30 patients (19 boys, 11 girls) with diagnosis of ALL were recorded. Age at diagnosis and at the time of R2 MR, risk group of ALL, treatment protocol, amount of transfused blood products were noted from the patients' records. Serum iron parameters, TORCH and hepatitis markers at the end of the therapy were noted from patients' records. We performed R2 MRI study in the first 3 months after therapy to evaluate the liver iron burden. We repeated serum iron, serum ferritin, serum transferrin and total iron binding capacity between 12 to 18 months after the end of the treatment in patients having high ferritin.

Results

Twenty patients were in standard risk group, 8 patients were in intermediate risk group, 8 patients were in high risk group. There was no patient having severe hepatic iron overload. Eight (27,5%) patients had mild and 1 (3,4%) patient had moderate iron overload. High Risk Group had the highest number of red blood cell products. Iron overload was higher in patients having more than 100 ml/kg red blood cell products. Transferrin saturation, ferritin levels and amount of transfusions per year were positively correlated with the amount of liver iron overload. Repeated ferritin measurements between 12 to 18 months after the cessation of the therapy were found to be statistically decreased in patients with high ferritin levels. No abnormal liver function tests were found.

Conclusions

30.9% of our patients had mild-moderate iron overload at the end of therapy. There was no correlation between liver iron overload and liver function tests. Control measurements of ferritin between 12 to 18 months after the cessation of therapy were significantly decreased.

EP-002

Acute Lymphoblastic Leukaemia

LOW DOSE RASBURICASE FOR TREATMENT AND PREVENTION OF TUMOUR LYSIS SYNDROME IN ACUTE LYMPHOBLASTIC LEUKEMIA: SINGLE CENTRE EXPERIENCE

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Objectives

Tumour lysis syndrome (TLS) is an oncological emergency that requires early recognition and intervention. Rasburicase is used widely for both prevention and treatment of TLS at a dose of 0.15-0.2mg/kg/day for 5-7 days. Due to financial constraints, it is difficult to administer rasburicase in the prescribed dose. We observed the effect of single dose of rasburicase (0.1-0.2 mg/kg) used at our center in management of TLS

Methods

A retrospective analysis of ALL/Lymphoma patients who had features of TLS from Jan 2006 -Jan 2014 was done. Biochemical markers were analyzed before and after rasburicase administration

Results

34 patients suffering from ALL/Lymphoma developed features of TLS during the study period. Rasburicase was used only in 17 children because of financial constraints. 13 out of 17 patients had ongoing TLS at admission and 4 developed it after chemotherapy was started. Age range 0.8 to 15 years

Dose range (weight based) 0.1mg/kg to 0.2mg/kg.

Range of Uric acid 4.8mg/dl to 12.6mg/dl.

Range of Creatinine 0.3mg/dl to 1.5mg/dl

Baseline median UA and creatinine levels were 8.9mg/dl and 0.8 respectively. Median serum UA levels 6, 12, 24 hours after rasburicase administration were 8.4, 5.5, 2.4mg/dl. All patients had a significant reduction in uric acid levels on the first day, and creatinine, phosphate, and potassium reduced proportionately as well.

Only 1 patient had to undergo hemodialysis of all the patients who were given rasburicase, due to rising creatinine.

However 4 patients had to undergo hemodialysis in whom rasburicase could not be given.

Conclusions

Financial constraints in developing countries poses a great challenge in management of cancer cure and there is a pressing need to develop cost efficacious yet effective modalities of treatment. Our study suggests that a single dose rasburicase is effective in managing TLS. It effectively reduces the need for renal replacement therapy

EP-003

Acute Lymphoblastic Leukaemia

COMPARATIVE ANALYSIS OF HDAC 2,4,5,7,8,AND 9 M-RNA EXPRESSION LEVELS IN PEDIATRIC ACUTE LEUKEMIA PATIENTS IN BEFORE AND AFTER CHEMOTHERAPY COMPARE TO HEALTHY CONTROLS

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Objectives

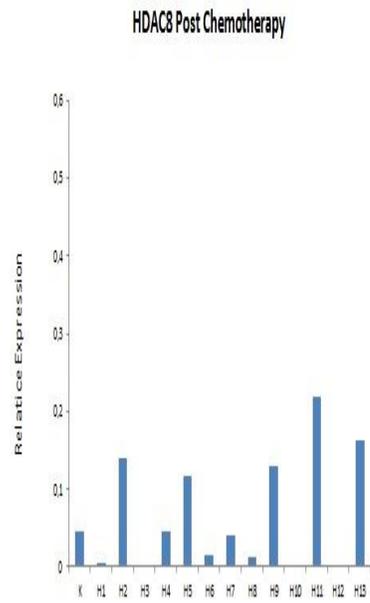
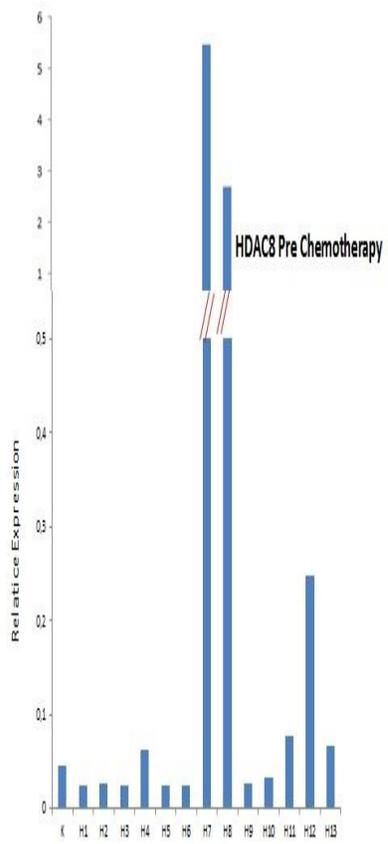
HDACs are involved in both nucleosomal changes chromatin structure remodeling, important in gene transcription and oncogenesis regulation. Mutations and abnormal expression of HDAC have been observed in types of cancers, including haematological malignancies. This study aims evaluating mRNA expression of HDACs (2,8,4,5,7,9) in childhood leukemia samples pre-postchemotherapy.

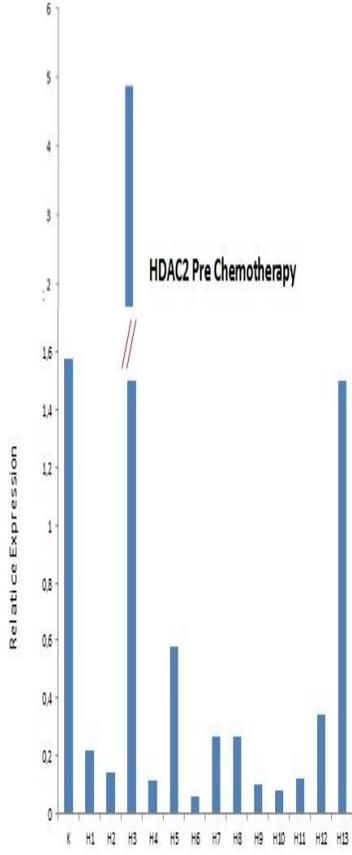
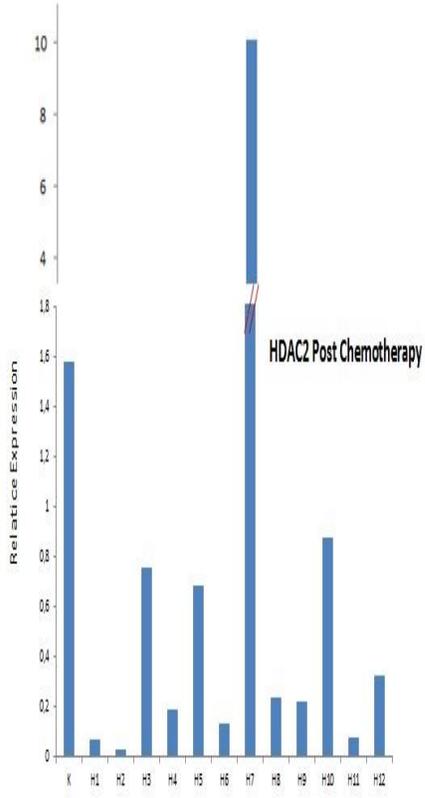
Methods

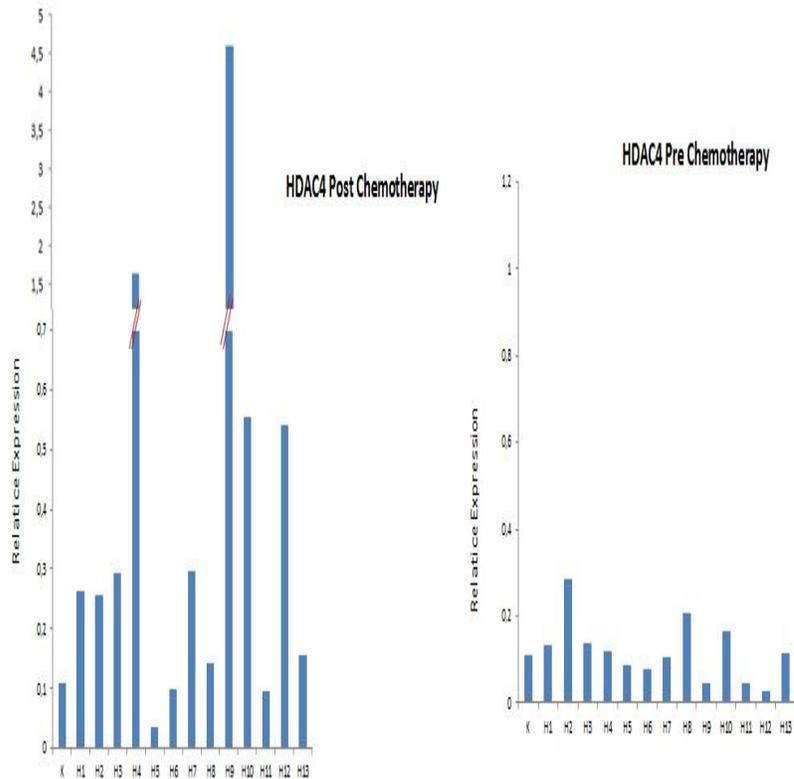
The study population consists of 13 patients 1 to 15 years old, admitted to hospital with a diagnosis of acute leukemia. RNA isolation was performed using RNA isolation kit. Expression data was analyzed using Relative Basic Quantification software provided with LightCycler 480 II.

Sex	Age	Diagnosis	Karyotype
M	1y	Pre B-ALL	tri 4,10,14,17,21
F	3y	ALL	Normal Karyotype (46,XX)
M	3y	ALL	Normal Karyotype (46,XY)
F	2y	CALLA+ALL	Normal Karyotype (46,XX)
F	9y	T-ALL	AML relapse
F	16y	My+ Pre B hücreli ALL	Relapse, chimerism, t(9;22) + CNS relapse- 2 HKHN -2 KI
M	6y	my+Pre-B-ALL	Normal Karyotype (46,XY), t(12:21)
M	5y	Pre B-ALL	Normal Karyotype (46,XY), t(9;22)
F	6y	Pre B-ALL	Normal Karyotype (46,XX), t(4:11)
F	8y	AML-M3	t(15:17)
M	6y	AML-M3-APL	t(15:17)
M	9y	AML	ex t(9;22), t(8:21) –molecular relapse

Results







Interestingly our results indicate differing levels of HDACs expression amongs patients while controls remain relatively consistant. Pre-posttherapy samples of HDAC2 showed lower levels of expression when compared to controls except for two patients. We observed dramatic increases in posttherapy samples are opposed to pretherapy samples for HDAC4 expression. HDAC8 showed great variants in expression both for pre-post samples. HDAC5 expression were high compared to controls for pre therapy samples and decreased to control levels in postsamples. HDAC7 expression demonstrated that no significant changes in either preor postsample, except for one patient. We observed low levels of HDAC9 expression in samples at both experimental time points. One patient diagnosed with My+PreBcell ALL, with t(9;22), CNS relapse and two bone marrow transplants showed unusually high HDAC7 expression in the pretherapy sample. Another patient who had high levels of HDAC4, relapsed and died duringtreatment. One preBcell ALL patient showing MLL translocation had high levels of HDAC2. While another preB-cell ALL patient with normal karyotype showed high HDAC2 expression in posttherapy high HDAC8 expression pretherapy samples. Lastly a PreBcell ALL patient with t(12;21) showed high HDAC8 expression in pretherapy.

Conclusions

Some studies have been conducted in haematological malignancies for HDAC expression. In this study we analyzed expression changes of HDAC2,4,5,7,8,and9 in pediatric leukemia samples pre-post therapy. We found HDAC4,5and9 expression changes are important in pediatric leukemia since these genes have a role in cell differentiation, angiogenesis and regulation pathways.

EP-004

Acute Lymphoblastic Leukaemia

REDUCING SIDE EFFECTS OF SEVERE ASPARAGINASE REACTIONS

(ANAPHYLAXIS): A POSSIBLE ROLE FOR USE OF METHYLENE BLUE AFTER GIVING EPINEPHRINE TO QUICKLY REDUCE ANGIOEDEMA AND HYPOTENSION

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Objectives

L-asparaginase is an effective drug for acute lymphoblastic leukemia and lymphoma with a safety profile which includes severe allergic reactions. These usually occur after repeat dosing and are associated with life-threatening symptoms including angioedema (hives, lip, mouth and throat swelling, hoarseness, wheezing, and difficulty breathing) and hypotension. Anaphylaxis treatment currently involves administration of epinephrine then other supportive measures. To more rapidly reduce reaction severity, we have started using an additional measure, methylene blue, which inhibits angioedema and hypotension.

Methods

In 2014, review of literature shows many papers supporting use of methylene blue to treat anaphylaxis; methylene blue inhibits guanylyl cyclase and nitric oxide associated vasopermeability. Methylene is commercially supplied as 100 mg blue liquid in 10 mL vials containing 10 mg/mL. Each vial costs about \$11 US. Recommended dose is 2mg/kg and is given as a rapid iv bolus over 1-2 minutes. Timing is after the epinephrine is given.

Results

Input from pediatric oncologists, nursing, pharmacy, and Emergency Department resulted in improved pathways of care for reactions to L-asparaginase. These are now characterized as 1) skin only (e.g. hives) or 2) more serious in which prompt administration of epinephrine and team care is started. For 'skin only' reactions, no epinephrine is recommended and diphenhydramine (0.5 mg/kg iv), hydrocortisone (1mg/kg iv) and famotidine (1 mg/kg iv) are given. For severe reactions, a methylene blue bolus infusion is given immediately after 0.01 mg/kg IM epinephrine and additional measures are done including albuterol nebulization, oxygen & pulse oximetry, diphenhydramine, hydrocortisone, famotidine, and hospital admission for monitoring via the Emergency Department. We also encourage parents to take a cell phone picture, so future caregivers can better understand the severity of rash and/or lip&face swelling.

Conclusions

Methylene blue is an inexpensive and effective means to ameliorate severe L- asparaginase reactions.

EP-005

Acute Lymphoblastic Leukaemia

DEMOGRAPHICS AND DISEASE RESPONSE EVALUATION IN PEDIATRIC HIGH RISK ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) PATIENTS AT A TERTIARY CARE CENTRE

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Objectives

The main objective of the study is to discuss presentation and outcome of children with acute lymphoblastic leukemia (ALL).

Methods

We present a retrospective study, looking at demographics and outcome of children with ALL presented to the hematology and oncology department of the children's hospital Lahore between January 2009 and December 2009. Children with Bone Marrow biopsy proven ALL were included and data regarding age, gender, risk categorization and outcome were recorded and analyzed. Children were stratified as high risk who were <2 and >9 years of age, BFM-risk factor 1.2 or above, CNS disease and mediastinal mass on presentation. Lahore Group Protocol for acute lymphoblastic Leukemia LALL01(BFM and UKALLXI based) was used for treatment.

Results

A total of 198 patients were included. Seventy percent were males. Majority 141(66.6%) were between 2-8.9 years of age while 44(22.2%) patients were of 9 years and above. One hundred and sixteen (60%) had high risk disease and only 55(27%) with standard risk. Initial WBC was >100,000/mm³ in 35 (17.6%), 50,000-100,000/mm³ in 14 (7%) and 47 (23.7%) had 10,000-50,000/mm³. BFM risk factor was 1.2 and above in 66 (33.3%), 14(7%) patients had CNS disease and 5% mediastinal mass on presentation. Seventy eight (40%) patients had completed treatment, 44(22.2%) left against medical advice and 38(19.1%) died. Twenty nine (14.6%) had relapse and among them 76% relapsed while on treatment.

Conclusions

High risk disease is the most common presentation of ALL in children at our centre with initial High WBC count, massive organomegaly and male predominance. Abandonment is another major factor affecting the overall survival rate .However overall survival is almost 50% in our treated patients.

EP-006

Acute Lymphoblastic Leukaemia

SAFETY OF NALBUPHINE ON NEURAL TISSUES IN THE RATS AND ITS EFFICACY IN THE TREATMENT OF ACUTE HERPETIC PAIN IN PEDIATRIC WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

Acute lymphoblastic leukemia (ALL) was previously shown to cause severe impairment in the immunity and in turn makes children more susceptible for viral infection especially herpes zoster that is manifested by severe pain. The main purpose of this study was to evaluate: firstly, the safety of nalbuphine experimentally on the neural tissues of the rats and secondly, the efficacy of the caudal injection of nalbuphine with minimal dose of oral paracetamol as an analgesic in pediatric patients with ALL suffering from acute herpetic pain.

Methods

Two studies were performed. **In Study 1**, Evaluation the safety of nalbuphine HCl on neural tissues experimentally in rats. The treated groups were injected with nalbuphine (0.5, 1, 2, 4 and 5 mg/kg) intrathecally each after one day for 14 days. The longitudinal section of the cerebellum and transverse section of spinal cord excised from each animal for histological examination.

In Study 2. The study was conducted on 30 children. Nalbuphine was injected caudally in dose of 5 mg, each dose every 48 h for a period of 14 days, and paracetamol was administrated in dose of 7.5 mg/kg once every 4 hours,

Results

The results revealed that nalbuphine showed no pathological changes in both cerebellum and spinal cord. On the other hand, the protective effect of nalbuphine with minimal dose of paracetamol was associated with a significant analgesic effect in ALL children. Its analgesic effect was assessed by facial pain scale (FPS), behavioral pain assessment (BPA) with motor block effect assessed by Bromage score.

Conclusions

These findings show that nalbuphine caudally injected induced proper analgesic effect with minimal dose of paracetamol in acute herpetic pain in pediatric patient with ALL.

EP-007

Acute Lymphoblastic Leukaemia

TOXICITY DURING HIGH DOSES OF METHOTREXATE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

Intensification of systemic chemotherapy with inclusion of high doses methotrexate(MTX) has contributed to the improvement of event free survival in children acute lymphoblastic leukemia (ALL) and has helped to reduce cranial radiation for mostly patient. Despite this benefit, this agent might cause serious toxicity, even life treating events during the treatment. Because of that, prediction, early detection and management of toxic effects during therapy with high doses of MTX is still great challenge for every pediatric oncologist. The aim of our study was to evaluate the incidence of toxic effects of chemotherapy with high doses MTX (5g/m²) and to compare them with toxicity during application of lower doses MTX(2g/m²)

Methods

Retrospective record review was done in 77 children with standard risk ALL treated in our department. Forty five of them were treated with 5g/m² and 32 of them were treated with 2g/m²(historic group). Toxicity was registered according the protocol for acute toxicity, part of the ALL BFM 95 protocol.

Results

Toxicity of high doses MTX was predominant in the group treated with 5g/m². Most significant toxic effects were hepatotoxicity 77% versus 25%(p=0.000013), oral mucositis 35.56% versus 18.75% (p=0.023) and myelosupresion. Anemia gradus 3 was present in 37.78% versus 6.25%, trombopenia gr 3 in 28.8% versus 12.5% and patient of the study group have experienced more episodes of neutropenia 99 versus 32. Bacterial and viral infections were predominant in the study group due to severe myelosupresion.

Conclusions

In our study toxic effects were more common in the study group due to application of higher doses MTX. Variations in toxicity between the patients in the study group are probably due to the genetic differences in the drug metabolism. Current researches are dedicated on discovering markers which will be able to predict the risk for appearance of MTX toxicity

EP-008

Acute Lymphoblastic Leukaemia

MOLECULAR CYTOGENETIC ABNORMALITIES IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA—EXPERIENCE FROM A TERTIARY CARE CENTER IN NORTH INDIA

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Objectives

The aim of the study was to determine the frequency of cytogenetic abnormalities in childhood ALL patients coming to tertiary care hospital in developing country.

Methods

Retrospective study (2013- 2014). Inclusion criteria - 61 ALL patients in our follow-up, Age < 16 yrs of age. Multiplex reverse transcriptase polymerase chain reaction (Multiplex RT PCR) analysis and conventional cytogenetic were performed to detect the chromosomal abnormalities

Results

Cytogenetic analysis was done in 40 of 61 children with ALL, in rest could not be done in view of financial constraint. Twenty (17 B cells, 3 T cells) had normal cytogenetic. Twenty of them had clonal chromosomal abnormalities. Numerical imbalances consisted of hypodiploid (< 46 chromosomes, no cases), hyperdiploid (> 47 chromosomes, 14 cases out of which 13 were B cell ALL and 1 was T cell ALL) and pseudodiploidy (46 chromosomes, 6 cases, All were B cell ALL). Chromosomal translocations detected by Multiplex RT PCR were observed in 9 patients. Five children had t(9:22) and 4 had t(12:21) positivity. MLL rearrangement was present in 1 infant. Complex cytogenetic were seen in 3 children. Ten out of 61 children relapsed, on BFM 95 protocol. In 6 cytogenetics could not be done, 2 had normal cytogenetics, 1 had t(12:21) (Standard risk) and 1 had t(9:22) (High risk).

Conclusions

In 1/3rd (20/61) cytogenetics could not be performed and so complete risk stratification was hindered. Six children relapsed and cytogenetics was not known which can be confounding factor for risk stratification, management and prognosis and should be aimed in every patient.

EP-009

Acute Lymphoblastic Leukaemia

MTOR RELATED PROTEIN EXPRESSION IN CHILDHOOD ALL

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Objectives

Improvement of treatment of childhood ALL may depend on the development of targeted therapies. mTOR kinase, a central mediator of several signaling pathways, has recently attracted remarkable attention as a potential target in pediatric ALL. However, limited data exists about the activity of mTOR.

Methods

In the present study, the amount of mTOR activity dependent phospho-proteins was characterized by ELISA in human leukemia cell lines and in lymphoblasts from childhood ALL patients (n=49). Expression was measured before and during chemotherapy and at relapses. Leukemia cell lines exhibited increased mTOR activity, indicated by phospho-S6 ribosomal protein (p-S6) and phosphorylated eukaryotic initiation factor 4E binding protein (p-4EBP1). Elevated p-4EBP1 protein levels were detected in ALL samples at diagnosis; efficacy of chemotherapy was followed by the decrease of mTOR activity dependent protein phosphorylation. Optical density (OD) for p-4EBP1 (ELISA) was significantly higher in patients with poor prognosis at diagnosis, and in the samples of relapsed patients.

Results

Our results suggest that measuring mTOR activity related phospho-proteins such as p-4EBP1 by ELISA may help to identify patients with poor prognosis before treatment, and to detect early relapses.

Conclusions

Determining mTOR activity in leukemic cells may also be a useful tool for selecting patients who may benefit from future rapalog treatments.

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EP-010

Acute Lymphoblastic Leukaemia

ANALYSIS OF ADVERSE EVENTS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA (ALL) TREATED WITH PROTOCOL ALL IC BFM 2002 – SINGLE-CENTRE RETROSPECTIVE STUDY

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Objectives

The aim of this study was a retrospective analysis of adverse events in children with ALL treated with protocol ALL IC BFM 2002 between 2002 and 2013 at our department.

Methods

According to ALL IC BFM 2002 criteria 196 patients (90 girls, 106 boys) 1-18 years of age (med. 5.04 yrs) were classified to SR- 56 (29%), IR- 73 (37%) or HR- 66 (34%) group. Remission on time was achieved by 190 (97%) patients. At a median follow-up was 70,9 months (range: 19.8-128.5 months). Results of the treatment were analysed as pEFS and pRFS.

Results

Among adverse events 26 (13.3%) relapses were observed within 1.1-69.5 months (med. 23.5 months) from the diagnosis. There were 9 (34.6%) very early, 5 (19.2%) early and 12 (46.2%) late relapses: 12 (46.1%) in BM (SR: 4, IR: 3, HR:5), 4 (15.4%) in CNS (SR: 1, IR:1 HR:2), 1 (3.8%) in testis (HR), 1 (3.8%) in mediastinum (HR) and 8 (30.8%) mixed relapses: 6 BM-CNS (SR: 1, IR: 3, HR: 2), 1 CNS-testicular (IR) and 1 BM-CNS-abdominal (SR). There were 26 (13.3%) deaths: 1 (3.8%) early death; 14 (53.8%) due to treatment complications (9 in I CR (IR: 2, HR: 7), 5 in II CR (IR:2, HR:3)), 10 (38.5%) due to leukaemia relapse/progression (SR:3, IR:2, HR:5), 1 (3.8%) in car accident. 159 patients are in I CR 159 (81.1%) and 11 in II CR (5.6%).

Conclusions

An analysis has shown that BM, CNS and mixed relapses were seen in high proportion of patients from SR and IR groups. High rate of deaths (mainly in HR group of patients) was noticed due to treatment complications.

EP-011

Acute Lymphoblastic Leukaemia

CLINICO-HEMATOLOGICAL PROFILE OF ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN: AN EXPERIENCE FROM JAMMU (INDIA)

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Objectives

To study the clinico-haematological profile of children presenting with ALL.

Methods

All the children hospitalized with ALL in the Department of Pediatrics, Government Medical College, Jammu during a period of 6 years were included in this retrospective study and their clinical and hematological profile was analyzed in detail.

Results

A total of 62 patients were diagnosed as ALL with male to female ratio of 2.4:1. Majority (77.4%) of children with ALL were less than 10 years of age. Out of 62 patients of ALL, 51 were ALL-L1, 10 ALL-L2 and 1 ALL-L3. 43 ALL-L1 and 5 ALL-L2 patients were less than 10 years of age. Fever, pallor, bleeding manifestations, hepato-splenomegaly, lymphadenopathy, generalized weakness, weight loss and bone pains were present in 65%, 61%, 55%, 53%, 45%, 24%, 21% and 19% respectively. 73% of ALL patients had hemoglobin less than 6 gm% while 20% and 7% had hemoglobin of 6-10gm% and more than 10 gm% respectively. 45% of these patients had decreased and 16% had increased Mean Cell Volume and Mean Cell Hemoglobin. Increased total leucocyte counts between 10000-50000 /dl were seen in 37% patients, while counts more than 50000 /dl were seen in 35% of patients. Leucopenia was seen in 24% of patients and rest had normal counts. 89% patients had thrombocytopenia. 48% had lymphoblasts and 5% had atypical cells in their peripheral blood films.

Conclusions

We found that in this region ALL-L1 FAB is common under the age of 10 years. Fever, anemia, bleeding manifestations, hepato-splenomegaly and lymphadenopathy were the commonest presenting features. Majority of them had leukocytosis and thrombocytopenia at the time of presentation.

EP-012

Acute Lymphoblastic Leukaemia

BONE MARROW EXPRESSION OF VASCULAR ENDOTHELIAL GROWTH FACTOR, VEGF RECEPTOR-1 AND VEGF RECEPTOR-2 IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

Angiogenesis plays an important role in hematological malignancies. Vascular endothelial growth factor (VEGF) promotes angiogenesis via interaction with VEGF receptors-1 and -2. Blood levels of VEGF and its receptors have shown some prognostic significance in pediatric acute lymphoblastic leukemia (ALL). We assessed the significance of sVEGF and bone marrow (BM) expression of VEGF, VEGFR-1 and VEGFR-2.

Methods

Sixty-six children with newly diagnosed with ALL, 5 children with relapse, and 9 in remission after completion of ALL therapy were prospectively enrolled (2008-2012). Controls included 50 healthy children and 10 normal BM biopsies. sVEGF level was measured at presentation of ALL (new and relapsed), at the time of remission induction, and at the end of ALL therapy. Immunocytochemistry for VEGF, VEGFR-1 and VEGFR-2 was done on BM biopsies at those time points.

Results

Untreated leukemia BM samples (n=43) showed strong VEGF and VEGFR1 expression in >90% of blast cells. Conversely, most normal BM (n=10) had moderate VEGF and VEGFR1 expression in 50-89% of mononuclear cells. VEGFR-2 expression was moderate in leukemic samples, in 50-89% of blast cells, contrasting with normal samples which showed strong VEGFR-2 expression in 50-89% of hematopoietic cells. After remission induction (n=24) and at the end of treatment (n=9), immunocytochemistry results were comparable with BM controls. Median (interquartile range) sVEGF was significantly lower in untreated ALL [15.9ng/ml (8.6-30.4)] and relapsed cases [21.5ng/ml (10.9-36.1)] as compared to controls [50.0ng/ml (30.3-73.6)] and to old ALL cases enrolled after treatment completion [48.0ng/ml (15.8-68.9)], p

Conclusions

BM expression of VEGF and VEGFR-1 is strong in ALL blasts, while VEGFR-2 is mainly expressed by normal mononuclear cells. Overexpression reduces with hematological remission.

EP-013

Acute Lymphoblastic Leukaemia

PREDICTORS OF ACUTE CHEMOTHERAPY-ASSOCIATED TOXICITY IN CHILDREN WITH ALL

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Objectives

Success in treating childhood acute lymphoblastic leukemia (ALL) was achieved mainly due to intensification of cytotoxic therapy. We analyzed possible predictors of acute chemotherapy-associated toxicity in this population.

Methods

In this short study, we reviewed the medical records of children at the age of 1-18 years who were diagnosed with ALL and treated according to ALLIC BFM 2002 protocol at two academic medical centers from December 2002 to May 2010. Clinical and biological characteristics, disease characteristics at diagnosis and intensity of the chemotherapy of the patients were analyzed as the possible predictors of toxicity.

Results

The retrospective study included 123 patients with ALL at the average age of 7.11 years (median 5.5 years) and toxicity data. 98.35% of the patients had at least one toxic complication during the treatment. Age ($p = 0.973$), sex ($p=0.847$), body mass index ($p=0.994$), initial leukocyte count ($p=0.979$), organomegaly ($p=0.894$) and CNS status ($p=0.608$) at diagnosis, immunophenotypic ($p=0.929$), molecular ($p=0.994$), and cytogenetic ($p=0.908$) features of leukemia were not associated with higher toxicity. Presence of central venous catheter was not associated with total toxicity as well as the infections as the most common complication ($p=0.056$, $p=0.181$). Dose-intensity of the chemotherapy was only associated with higher incidence of the entire toxicity ($p=0.047$), particularly infections ($p<0.001$). Cycles of chemotherapy in high-risk patient group (HR) with high-dose of cytarabine and methotrexate were significantly associated with higher toxicity ($p<0.001$).

Conclusions

In our sample, we have shown that the intensity of chemotherapy was the only predictor of chemotherapy-associated toxicity and that the patients in the high-risk group with most intense chemotherapy have higher rates of total toxicity, particularly infections. This group of patients requires increased intensive supportive care.

EP-014

Acute Lymphoblastic Leukaemia

CORRELATION BETWEEN DIAGNOSIS DELAY AND RISK STRATIFICATION OF B-PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN

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Objectives

To understand the correlation of diagnosis delay with the risk stratification of B-precursor ALL in children.

Methods

Fifty eight patients diagnosed as precursor B ALL from 2008 to 2011 in Pediatric Department, RSUP Dr. Sardjito, Yogyakarta, Indonesia were observed.

Results

Among 58 medical record analyzed, 46 patients were classified as standard risk ALL and 12 patients were classified as high risk ALL. The mean of diagnosis delay was 58 days.

Analysis using mean of delay as cut-off showed no significant correlation ($p = 0.3$), but the odd ratio was 1.99 (CI = 0.55-7.22).

Conclusions

There is 2 times increased risk to become high risk ALL after 58 days of delay. Further study with bigger sample size should be conducted to confirm the result.

EP-015

Acute Lymphoblastic Leukaemia

PREVALENCE OF CMV INFECTION IN ALL PATIENTS

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Objectives

CMV is an opportunistic infection that may be lethal in immunocompromized patients

Methods

All ALL patients who were admitted in Bahrami Hospital(TUMS), Tehran, Iran between March 2011 and March 2013 were prospectively followed. Eligible patients had a previous diagnosis of ALL and had been treated with UK-ALL-X protocol.

Only patients who were at least one year post-induction chemotherapy were included. None of the patients received hematopoietic SCT. Patients with a positive result for CMV viremia according to a (PCR) *and* with clinical or other laboratory findings suggestive of CMV disease were treated with oral valganciclovir (10 mg/kg twice daily) for 6 weeks. After discharge from the hospital, the first follow up was at 2 weeks after completion of the 6-week course of treatment. Four weeks after completion of treatment, patients were re-evaluated for clinical improvement and repeat PCR. CMV serology was performed at the time of initial diagnosis of CMV infection. Patients with viremia but without evidence of CMV disease did not receive treatment; these patients were followed closely

A Chi-square test (with Fisher's exact test when needed) was used to compare proportions between groups. A p value of <0.05 was considered statistically significant.

Results

Total of 171 patients (males: 49.1%) with a median (range) age of 8 (2-17)years were included. Median(range) values for Hb, WBC, platelets, ALT, and AST were 9.8(7.9-13.6)g/dL, 4.7(1.5-11.2)x10⁹/L, 235(36.8-470)x10⁹/L, 32(10-133)U/L, and 33(15-83)U/L, respectively. Two (1.2%) patients had hepatosplenomegaly. A total of 10 (6.4%) patients had CMV viremia (p = 1.00). Males and females comprised 3 and 7 of the 10 viremic patients, respectively (p = 0.33).

Conclusions

In this study Anti-CMV IgM sensitivity was 100% and its specificity 98.77, and PPV=83.3. It is suitable test for screening and detect the infection.

EP-016

Acute Lymphoblastic Leukaemia

**EARLY COMPLICATIONS AND OUTCOME OF CHILDREN WITH LEUKEMIC
HYPERLEUKOCYTOSIS: EXPERIENCE FROM A DEVELOPING COUNTRY**

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Objectives

We studied the presenting clinical and laboratory features, early complications, and outcome of children with acute leukemia and hyperleukocytosis who were diagnosed and treated in two medical centers of Karachi between January 2009 and December 2013.

Methods

This was a descriptive, observational, non-interventional, retrospective analysis.

Results

Hyperleukocytosis was found in 146 (17.9%) out of 812 patients diagnosed as acute leukemia, precursor T cell ALL in 77 (52.7%), precursor B cell ALL in 61 (41.8%), acute myeloid leukemia in 5 (3.4%) and chronic myeloid leukemia in 3 (2.1%). Age group was 1-5 years in 61 patients (41.8%) and above 10 years in 56 (38.4%), more common among males 111 (76.0%). Half, 72 (49.3%) had symptoms for >30 days. Seventeen patients (11.6%) had CNS involvement. Therapeutic interventions were hydration/allopurinol in 138 (94.5%) patients. Leukapheresis was done in 4 patients, one of whom expired. Median hemoglobin was 7.35 g/dL (range 2.0 g/dL to 13.1 g/dL). Median total leukocyte count was 181.0 x10⁹ /L (range 102 x10⁹/L to 782 x10⁹/L). Median platelet count was 30 x10⁹/L (range 5 x10⁹/L to 558 x10⁹/L). Median LDH was 3184 IU/L (range 520 IU/L to 26024 IU/L). Median uric acid was 5.98 mg/dL (range 1.5 mg/dL to 43.4 mg/dL). Median phosphate was 4.3 mg/dL (range 0.9 mg/dL to 16.6 mg/dL). BCR ABL translocation was positive in 14 patients (9.6%). 30 patients (20.5%) expired after their first admission. The major cause of death was infection in 10 (30%), respiratory complication with infection in 7 (23.3%), CNS with respiratory complications and infection in 3 (10%), only renal complication in 2 (6.6%).

Conclusions

Early death and complications can be prevented by early referrals, timely and appropriate antibiotics, management of tumor lysis syndrome, timely use of ICU modalities and leukapheresis whenever required.

EP-017

Acute Lymphoblastic Leukaemia

NON-CODING RNAs: A NEW FIELD IN THE PHARMACOGENETICS OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

Acute lymphoblastic leukemia (ALL) treatment can produce severe toxicity. In the last years, pharmacogenetic studies have been performed in order to search for markers of toxicity in pediatric ALL. However, up to date, *TPMT* is the only marker in ALL with clinical guidelines for drug dosing.

The majority of the studies by now have focused in coding regions (1.5% of the entire genome). A promising field in pharmacogenetics are regions that do not codify proteins but may have a regulatory function, such as non-coding RNAs (ncRNAs).

Alterations in the ncRNA expression or in their function have been associated with drug response in different cancers. These alterations in ncRNAs could be due to genetic polymorphisms.

The aim of the present study was to evaluate whether polymorphisms in ncRNAs lead to drug response.

Methods

We analyzed blood samples from pediatric B-cell ALL patients during complete remission treated with the LAL/SHOP protocol. We selected all the SNPs described in pre-miRNAs with a MAF > 1% and SNPs in long non coding RNAs (lncRNAs) dysregulated in cancer, using the VeraCode GoldenGate Genotyping assay from Illumina.

Results

In a preliminary study including 46 SNPs in miRNAs and 152 patients, we found for the first time an association between polymorphisms in mir-300 and mir-453 and toxicity in B-ALL.

Taking into account these results, we have extended the study increasing the number of patients and SNPs to a total of 362 SNPs: 235 in 222 pre-miRNAs and 127 in 16 lncRNAs.

We have obtained very promising results.

Conclusions

Genetic variants in ncRNAs could be new toxicity markers in the treatment of pediatric ALL. This project was supported by RETICS (RD/12/0036/0060), UPV/EHU (UFI 11/35) and Basque Government (IT661-13, SAI10/03, and 2006111015).

EP-018

Acute Lymphoblastic Leukaemia

NEW SUSCEPTIBILITY MARKERS IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: NON CODING RNAS

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Objectives

Evidence for an inherited genetic risk for pediatric acute lymphoblastic leukemia (ALL) has been provided in several studies. Most of them focused on coding regions. However, those regions represent only 1.5% of the entire genome.

The expression of non coding RNAs (ncRNAs), specifically microRNAs (miRNAs) and long non coding RNAs (lncRNAs), has been shown to be dysregulated in ALL, suggesting that they may have a role in ALL risk. Changes in ncRNA function may occur through genetic variants.

Therefore, the aim of this study was to evaluate whether polymorphisms in ncRNA contribute to a predisposition for childhood ALL.

Methods

We analyzed blood samples of B-cell ALL patients during complete remission and healthy controls. For the study, we selected all the SNPs described in pre-miRNAs with a MAF > 1% and SNPs in dysregulated lncRNA in cancer, using the VeraCode GoldenGate Genotyping assay from Illumina.

Results

In a preliminary study of 213 patients and 387 healthy controls and 46 SNPs in miRNAs we found for the first time an association between polymorphisms in mir-499, mir-449b and mir-612 and susceptibility in B-ALL. Taking into account these results, we have increased the number of patients to 317 and the number of SNPs to 362. We selected 235 SNPs in 222 pre-miRNAs genes, and 127 SNPs that cover 16 long-non coding RNAs.

Conclusions

Our results suggest that SNPs in non-coding RNAs may affect B-ALL susceptibility and may represent novel markers of B-ALL susceptibility.

This project was supported by RETICS (RD12/0036/0060), UPV/EHU (UFI 11/35) and Basque Government (IT661-13, S-PE12UN060).

EP-019

Acute Lymphoblastic Leukaemia

THERAPEUTIC POTENTIAL OF DASATINIB AGAINST BCR-ABL1-NEGATIVE ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

Src has recently been suggested to be a therapeutic target in both BCR-ABL1-positive and negative acute lymphoblastic leukemia (ALL). To investigate therapeutic potential of Src-inhibition, the effects of dasatinib on survival of BCR-ABL1-negative ALL cells were studied.

Methods

Cytotoxicity of imatinib or dasatinib in childhood ALL clinical samples (n = 15, including 2 BCR-ABL1-positive) and cell lines (n = 7, including 1 BCR-ABL1-positive) was studied by the WST-8 assay. In the clinical samples, the ALL cells were defined to be sensitive if % survival of cells after 4 days incubation with 10 μ M of the drug was lower than 30%. The expression of pSrc or pAkt was analyzed by the phosflow assay. The combination effects of dasatinib and anti-leukemia drugs were evaluated by the improved isobologram assay.

Results

In the clinical ALL samples, 3 (20%) or 7 (46.7%) were sensitive to imatinib or dasatinib, respectively. Two BCR-ABL1-positive clinical samples were sensitive to both drugs. The 6 BCR-ABL1-negative ALL cell lines responded to dasatinib with IC50 values varied from 6.1 nM to >1 μ M. None of BCR-ABL1-negative cell lines responded to imatinib. Dasatinib reduced pSrc expression, followed by subsequent decrease pAkt in ALL cells. The levels of reduction of pSrc or pAkt did not correlate with dasatinib-sensitivity among ALL cell lines. Among anti-leukemia drugs, clofarabine showed the synergistic effects with dasatinib in several different concentration ratios in dasatinib-sensitive YCUB-8 cells.

Conclusions

Dasatinib is suggested to have the therapeutic role in some BCR-ABL1-negative ALL. The combination use with other drugs such as clofarabine might enhance the anti-ALL effects of dasatinib.

EP-020

Acute Lymphoblastic Leukaemia

A PROSPECTIVE RANDOMIZED TRIAL OF L- ASPARAGINASE VERSUS PREDNISOLONE IN PREVENTION OF TUMOR LYSIS SYNDROME IN ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS WITH HYPERLEUCOCYTOSIS

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Objectives

Patients with Acute Leukaemia presenting with hyperleucocytosis develop life threatening complications. Although, leukapheresis has been the standard of care for prevention of these complications, it is expensive and not widely available . Rapid cytoreduction in these patients using steroids significantly increases the risk of tumor lysis syndrome(TLS). In view of the above, there is a need to have a safe and cost effective cytoreductive method for management of hyperleucocytosis with minimal occurrence of TLS. We hypothesize that L-asparaginase causes adequate cytoreduction with minimal TLS as compared to prednisolone in acute leukemia patients with hyperleucocytosis.

Methods

This is a prospective, randomized trial where ALL patients, with hyperleucocytosis(WBC count $>100,000/mm^3$), between age group 1-21 years were randomized to receive either L-asparaginase(10,000IU/m² on alternate days) or Prednisolone(40 mg/m²/day). The medications were continued till WBCs $< 25,000/mm^3$ or 120hrs after enrollment whichever was earlier. If there was less than 50% fall in blood counts after 72 hours of study, patients were taken off study.All patients received standard TLS prophylaxis measures. Primary outcome variables were incidence of laboratory/clinical TLS and secondary outcome variable was rate of cytoreduction.

Results

Amongst 97 patients included, 49 were randomized to receive L-Asparaginase and 48 received Prednisolone. The median age is 9 years (1- 21 years). Median WBC count at presentation is 253000/mm³ (100- 694 x 10³).While 14 /49 patients in L-Asparaginase arm developed Laboratory TLS, the same was noted in 22/48 patients who received prednisolone (p=0.887). One patient in prednisolone arm developed clinical TLS while none was noted in the other group. At 48 hours 31/48 patients in Prednisolone arm achieved adequate cytoreduction (WBC $< 50\%$ from baseline) compared to 24/49 in L-Asparaginase arm

Conclusions

Interim analysis of our study does not show any difference in the incidence of laboratory TLS between L-Asparaginase or Prednisolone in ALL patients with hyperleucocytosis

EP-021

Acute Lymphoblastic Leukaemia

BASAL CELL CARCINOMA AFTER TREATMENT OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA AND CONCISE REVIEW OF THE LITERATURE

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Objectives

The cumulative incidence of secondary malignancies related to treatment of childhood ALL have been reported to be 1-10% depending on the differences in anti-leukemic treatment and follow-up duration. Herein, we report two patients who developed basal cell carcinoma (BCC) within the previous radiation field of pediatric ALL treatment and review of the literature on BCC following childhood leukemia.

Methods

A computerized literature search of electronic databases-Medline and Embase identified all published studies on the subject from the start date of the database to February 2014. The general search structure for electronic databases was (childhood or synonyms) AND (basal cell carcinoma) AND (secondary). The patients with a primary diagnosis of leukemia were included into the literature review after electronic search.

Results

Case 1 is a 29 year-old woman who developed BCC of the scalp 17 years after the successful treatment of childhood ALL. The patient was diagnosed as having B-cell ALL at the age of 12 years and was treated with chemotherapy, intrathecal treatment and 2400 cGy prophylactic cranial radiotherapy for 15 days. She developed BCC at the age of 29 years. Case 2 presented with hyperpigmented macule of 3 cm diameter at the age of 31 years-old, with a latency period of 17 years after initial diagnosis of ALL. She has previously received prophylactic cranial radiation during treatment for leukemia. The pathological evaluation confirmed BCC. In the literature there are 42 patients who developed BCC subsequent to leukemia treatment. Besides, among CCSS data 213 of 13,132 childhood malignancies developed BCC, subsequently, including leukemia as primary malignancy.

Conclusions

Basal cell carcinoma as a secondary malignancy following ALL is rare, but may occur more often among patients who have previously received radiation therapy.

EP-022

Acute Lymphoblastic Leukaemia

PHARMACOLOGICAL EFFECT OF EZH2 INHIBITOR IN PEDIATRIC T-CELL ACUTE LYMPHOBLASTIC LEUKAEMIA.

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Objectives

Polycomb group (PcG) proteins are highly conserved epigenetic effectors that maintain the silenced state of genes involved in critical biological processes. Evidence suggests that over-expression of the histone methyl transferase Enhancer of Zeste Homologue 2 (EZH2) is strongly associated with haematologic cancer progression and poor outcome. 3-Deazaneplanocin (DZNep) is the first molecular inhibitor of EZH2. We have studied pharmacological effect between DZNep and a conventional chemotherapeutic agent Daunoblastina (DNB) in pediatric T-cell Acute Lymphoblastic Leukaemia (T-ALL).

Methods

Jurkat cell line and blast cells of pediatric T-ALL were grown in RPMI and treated with DNB and DZNep, single and in combination to 24h, 48h and 72h. Cell viability was analyzed by MTT and Trypan blue assay. Apoptotic cell death and cell cycle were analyzed by Annexin-V-FITC staining and PI fluorescence. EZH2, Bcl-2 and Procaspase 8 were analyzed by western blotting assay.

Results

Our data evidenced a synergistic effect ($CI_{50}/48h = 0.88$ and $CI_{50}/72h = 0.80$ Biosoft CalcuSyn software) on Jurkat growth inhibition by DNB/DZNep with about a 50% decrease of the sub-G0/G1 peak, presumably due to apoptosis, and a parallel increase of cells in G2/M phase. These results were confirmed by annexin analysis with an increase (26%) of early apoptosis. Moreover, we have found a 60% and 40% decrease of procaspase 8 expression in single treatment with DZNep and in combination with DNB, respectively. Therefore we observed a complete decrease of Bcl-2 protein respect to single treatment with DNB. Samples treated with DNB/DZNep evidenced an inhibition of EZH2.

Conclusions

EZH2 inhibition may offer the opportunity of a novel treatment approach that could be considered in combination with conventional chemotherapy to eradicate ALL stem cells. A better understanding of the complex epigenetic regulatory network controlling EZH2 expression and target genes would facilitate the design of novel therapeutic interventions.

EP-023

Acute Lymphoblastic Leukaemia

FURTHER UNRAVELING OF CHILDHOOD LEUKEMIA GENETIC BOTTLENECK PHENOMENON RELATED TO TEL-AML1: THE POSTULATION BY A MATHEMATICAL MODEL

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Objectives

Childhood leukemia prevention.

Methods

We did comprehensive browsing of articles in leading leukemia research journals, on the etiology of childhood leukemia and we constructed our own view on leukemia bottleneck etiology.

Results

TEL-AML1(ETV6-RUNX1) is formed prenatally in 1% of newborns. But only one child out of a hundred children born with this gene develops leukemia (bottleneck phenomenon). In other words, out of a hundred children born with TEL-AML1 only one child is at risk for leukemia development which means that TEL-AML1 is inevitable, but not sufficient for overt leukemia. There is a stringent requirement for a second genetic abnormality for leukemia development. In most cases of TEL-AML1⁺ leukemia, translocation t(12;21) is complemented with loss of normal TEL gene, not involved in the translocation, on contralateral 12p. The loss of normal TEL gene, i.e. loss of heterozygosity (LOH) at 12p occurs postnatally during mitotic proliferation of TEL-AML1⁺ cell in mitotic crossing over(MCO) process. MCO is very rare event with a frequency rate of 10⁻⁶ in a 10 kb region. Since minimally deleted regions always affect at least some part of the TEL transcriptional framework, follows that reported frequency of ~10⁻⁶ MCO in a 10 kb locus are valid for MCO frequency at 12p in naïve TEL-AML1⁺ cells.

Conclusions

The exploration and identification of environmental exposure(s) that cause proliferation of TEL-AML1⁺ cell in which approximately 10⁶ mitoses are generated to cause 12pLOH i.e. TEL deletion, and/or introduction of mitotic crossing over inhibitors may contribute to childhood leukemia prevention.

EP-024

Acute Lymphoblastic Leukaemia

ANALYSIS OF PROGNOSTIC RISK FACTORS FOR PEDIATRIC ACUTE LEUKEMIA WITH FUNGEMIA

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Objectives

To investigate the epidemiology of fungemia and provide evidence for clinical therapy.

Methods

A retrospective survey was done with the 42 cases of fungemia in our hospital from Jan 2002 to Jan 2011

Results

40 cases candida fungemia accounted for 95.2% in 42 fungemia. The main pathogen agent was non-Candida albicans in candida fungemia, which were candida albicans(14.3%), candida parapsilosis(38.1%), candida glabrata(35.7%), candida tropicalis(2.4%). 11 ineffective cases accounted for 26.2%. Multiple-factor analysis showed that neutropenia time>7 days, antibiotic using time>7 days and fungal infection history correlated with bad prognosis. Our study also showed that chemotherapy regimens including hormone, combining with other organs fungal infection and non-Candida albicans were risk factors of bad prognosis.

Conclusions

The main pathogen agent of fungemia is candida, especially non-Candida albicans. Neutropenia time>7 days, antibiotic using time>7 days and fungal infection history correlate with bad prognosis.

EP-025

Acute Lymphoblastic Leukaemia

NEUROLOGIC COMPLICATIONS DUE TO CHEMOTHERAPY IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS TREATED WITH ALL IC BFM 2009 – SINGLE CENTER EXPERIENCE

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Objectives

This study presents retrospective analyses of 8 acute lymphoblastic leukemia (ALL) patients who developed neurologic complications due to chemotherapy.

Methods

From April 2010 up to February 2014 the diagnosis of ALL was established in 63 patients. Among them, 8 patients (12.7%), whose age ranged between 14 months and 9 years, developed 11 complications. Diagnosis was made upon following procedures: computed tomography (CT) - 7 patients, magnetic resonance images (MRI) - 3 patients, EEG - 8 patients, lumbar puncture (LP)- 2 patients, MTHFR c677T mutation – 1 patient and biochemical analysis including the screening for hemostasis performed in all patients.

Results

The most common clinical manifestation was seizure, which occurred in 5 patients (6 episodes). Sagittal sinus thrombosis was diagnosed in one of them. Acute encephalopathy was noticed in two patients, in two year old boy during the induction treatment and in three year old girl due to hypoglycemia provoked with 6-mercaptopurine during maintenance therapy. Posterior reversible encephalopathy syndrome was diagnosed in one girl with acute onset of hemiparesis. The most peculiar complication was observed in two year old boy who developed persistent chemical arachnoiditis after the first lumbar puncture. During the maintenance therapy, after the 5th prophylactic lumbar puncture, acute ataxia with right sided hemiparesis has occurred. CT scan showed multifocal parenchymal calcifications, and MRI confirmed the presence of calcifications with massive edema in basal ganglia. After the investigations (homozygous for c677t MTHFR mutation) we concluded that this was the case of methotrexate toxicity. Complete recovery was achieved in 6 patients (75%) and two patients (25%) developed neurologic sequels (delayed speech development and mild hemiparesis).

Conclusions

Neurologic complications due to chemotherapy in ALL patients are not rare. By better diagnosis, close follow-up and effective treatment of underlying causes the morbidities and mortalities of these complications can be decreased.

EP-026

Acute Lymphoblastic Leukaemia

CNS COMPLICATIONS IN CHILDHOOD LEUKEMIA: ROLE OF MRI IN DIAGNOSIS AND MANAGEMENT

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Objectives

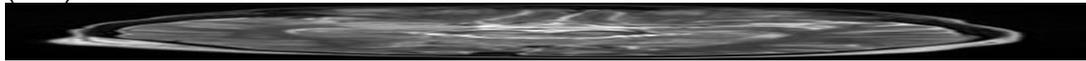
To illustrate the MRI patterns of various CNS complications in Childhood Leukemia.

Methods

MRI studies of 16 children with acute leukemia who presented with seizures, altered sensorium or focal neurological deficits were reviewed. The children were divided into two categories; the first group included the children who had complications related to leukemia and second group therapy related complications.

Results

Of the 16 children, 6 children had complications directly related to leukemia which included leukemic infiltration (n=1), microinfarcts (n=1), stroke (n=2), cortical venous thrombosis (n=1), limbic encephalitis as a paraneoplastic manifestation (n=1). The second group included chemotherapy induced leucoencephalopathy (n=2), vasculitis (n=1), posterior reversible encephalopathy syndrome (n=2), infections (n=4), thrombotic microangiopathy (n=1).



Conclusions

A wide range of abnormalities affect the brain and central nervous system in a leukemic child and MRI plays a substantial role in early diagnosis and management of these conditions.

EP-027

Acute Lymphoblastic Leukaemia

INDUCTION RELATED MORTALITY AND MORBIDITY IN CHILDREN TREATED WITH ACUTE LYMPHOBLASTIC LEUKAEMIA: SINGLE CENTER EXPERIENCE FROM A LOWER MIDDLE INCOME COUNTRY

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Objectives

Outcome during induction phase of therapy (IP) for acute lymphoblastic leukemia (ALL) is reduced to 1-2% in developed countries. But in resource poor settings, morbidity and mortality during IP are still very high. Main objective of this study was to review the outcomes of children with ALL during IP who were treated at Shaukat Khanum Memorial Cancer Hospital Lahore.

Methods

Medical records of all newly diagnosed childhood ALL patients during Jan 2011 to June 2013 were retrospectively reviewed from their first clinic visits till the start of consolidation, abandonment or death. Patients' characteristics and details about diagnosis, chemotherapy, course of illness, re-evaluation bone marrow morphology and complications of therapy were recorded. For those who died, cause of death was assessed by thorough data review.

Results

Of 162 cases reviewed, median age at presentation was 3 years with male to female ratio of 1.7:1. Precursor B ALL was diagnosed in 91% whereas 8% patients had precursor T disease. Bulk disease was present in 40% cases. Standard (84%) and high risk (16%) patients were treated with 3 and 4 drugs induction respectively. Mortality rate during IP was 19% (n=29). Cause of death was attributed to infectious etiology in all patients and 79% (n=23) deaths occurred during or after 4th week of IP. Hypocellular marrow was reported in 57% of patients assessed at day 8 /15 (n=17). Of those successfully completing IP (n=123), common reasons for admission were febrile neutropenia, diarrhea, oral mucositis, pneumonia and sepsis. Severe malnutrition and bulk disease were found to be statistically significant factors with p-values of 0.021 and 0.001 respectively.

Conclusions

Infection was the commonest cause for morbidity and mortality in IP of ALL therapy. Better infection control strategies and supportive care can improve outcome. Nutritional rehabilitation of severely malnourished children and chemotherapy modifications during IP may be other considerations.

EP-028

Acute Lymphoblastic Leukaemia

EXPRESSION OF CD133-2, AS A PROSPECTIVE MARKER, PREDICTING MINIMAL RESIDUAL DISEASE(MRD) LEVEL AT DAY 15, IN CHILDREN WITH CD45-DIM B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL)

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Objectives

To address predictive value of CD133-2 receptor expression on CD45-dim B-ALL cells at initial diagnosis, in the context of minimal residual disease monitoring at day 15 in children with B-ALL.

Methods

Nine newly diagnosed children with CD45-dim B-ALL were assessed for MRD levels on the day 15 of remission induction. We arbitrarily assigned the patients to either relatively 'high or low CD133-2' groups based on percentage of CD133-2 positive events at initial diagnosis. Phenotyping was performed in agreement with ALL-ICBFM-2009 recommendations using 4-color flow cytometry, with an acquisition number of at least 300.000 nucleated cells per tube and MRD of 30 cellular events was considered as positive.

Results

Among study subjects there were four males and five females with an average age of 3.1 (95%CI: 1.9 – 4.3). Median percentage of CD133-2 positive cells in 'low CD133-2' group were defined as 0.8% (Interquartile range (IQR): 0,115 – 1.70) and as 42.85% (IQR: 29,01 – 70) in 'high CD133-2' group gated on CD19+ ALL cells. Comparison between these groups revealed statistically significant difference in minimal residual disease levels at day 15 ($p=0.02$); Median percentage of MRD in 'high CD133-2' group was 1.75% (IQR: 1.18 – 6.6), while a median of 0.04% of residual leukemic cells (IQR: 0.04 – 0.08) was observed in 'low CD133-2' group. Correlation analyses revealed significant positive correlation between CD133-2 and CD45 receptor expression (Mean Fluorescent Intensity) at diagnosis ($r^2= 0.86$; $p=0.029$). Percentage of CD133-2 positive B-ALL cells also positively correlated with leukocyte count at initial diagnosis ($r^2= 0.83$; $p=0.04$)

Conclusions

Study showed that, CD133-2 receptor expression at initial diagnosis might be exercised as a surrogate marker to predict MRD levels at day 15 in children with CD45-dim B-ALL, although further, larger cohort studies are needed to address this question.

EP-029

Acute Lymphoblastic Leukaemia

ASSOCIATION BETWEEN IMMUNOPHENOTYPING AND PROGNOSIS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

Acute lymphoblastic leukemia (ALL) is the most common malignancy in childhood. Immunophenotyping has become important for determining the subgroups of ALL. We aimed to determine the features of subgroups according to immunophenotype, the correlation between clinical and other laboratory and their effects on prognosis retrospectively.

Methods

Sixty-six males and forty females receiving TR-ALL 2000 BFM between 2008-2012 were included in the study.

Results

The mean age was 5.9±3.8 years. The distribution was; 1% pro-B, 44% common B, 38% pre-B, 7.5% pre-T, 5.5% cortical T and 4% mature T. Pre-B ALL had a higher rate compared to literature. Male gender was dominant in T cell ALL when compared with B cell ALL group. T cell ALL was seen more frequent in group with patients older than 6 years of age. Leukocyte count higher than 20000/mm³ at diagnosis was more common in T cell ALL group. Lymphadenopathy larger than 2 cm was more common in T cell ALL group when compared with common B and pre-B cell groups. Mediastinal involvement was high in T cell ALL when compared with common B cell group. Co-expression was found in 20 cases with no statistical difference in subgroups. CD33 was determined as the most common marker showing co-expression. No negative effect related with myeloid antigen co-expression in terms of clinical and medical prognosis was found. Overall relapse rate was 13.6%. Death rate was 41.7% and 2.6% in relapse and non-relapse groups respectively. WBC count, organomegaly, lymphadenopathy, prednisone response in day 8, marrow in day 15, relapse and risk subgroups had significant impact on overall survival. WBC count higher than 20x10⁹L was the only factor influencing the survival by multivariate analysis.

Conclusions

Immunophenotyping by flow cytometry is of importance in the diagnosis of ALL, in determining of the immunophenotype subgroups and risk groups and in planning of the therapy.

EP-030

Acute Lymphoblastic Leukaemia

IMPROVED OUTCOME FOR CHILDREN AND ADOLESCENT WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN THE LAST DECADE: A REPORT FROM THE SLOVAK REPUBLIC

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Objectives

To analyze event-free (EFS) and overall survival (OS) among children and adolescents with acute lymphoblastic leukemia (ALL) treated with International BFM Intercontinental trial (ALL IC 2002) therapy in the Slovak Republic between 2002 and 2012.

Methods

In total, 280 children and adolescent age 1 to 18 years were treated with ALL IC BFM 2002 based therapy from 2002 to 2012, which was divided into two periods. During 2002-2007, when patients were actively enrolled in the ALL IC-BFM 2002 trial, and during 2008-2012 when the trial was closed and patients were treated with the same therapy without randomization.

Results

Five-year EFS and OS rates were 79% (+/- 2.6%) and 86% (+/- 2.1%), respectively, similar to results obtained in the ALL-BFM 95 trial, which was the basis for ALL IC BFM 2002 therapy. The EFS ($p < 0.003$) and OS ($p < 0.009$) were significantly better than the prior Slovak experience in 1997-2001. Survival improved in standard and intermediate risk groups, including males and females; those age 1 to 6 years, and older; in those with B-cell or T-cell immunophenotype, and is also excellent for those with ETV6/RUNX1 translocation and hyperdiploidy and with good response in peripheral blood on day 8 and in bone marrow on day 15 and 33. The rate of death in induction, cumulative incidence of death in complete remission and of relapse decreased. However, outcome was suboptimal for patients in the high risk group.

Conclusions

Current EFS and OS rates for children and adolescents with ALL in the Slovak Republic now approach those obtained in Western Europe as a result of clinical trial participation, and gaining clinical experience with intensive BFM type treatment.

EP-031

Acute Lymphoblastic Leukaemia

HIGH-HYPERDIPLOIDY AND FAVORABLE PROGNOSIS IN B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

High hyperdiploidy (HeH) (51-67 chromosomes), in pediatric B-cell precursor acute lymphoblastic leukemia (ALL) is generally associated with favorable prognosis. We performed a retrospective analysis of B-ALL patients with HeH who were treated in our department in the last 5 years and their cytogenetic analysis was available.

Methods

Pretreatment bone marrow samples were cultured and analyzed by standard cytogenetic methods. A total of 20 children (11 girls and 9 boys) displayed G-banded karyotypes with 51-67 chromosomes who were also informative for molecular studies, were included for analysis.

Results

The most frequently gained chromosomes were X (100%), 21 (95%), 14 (55,5%), 17 (55,5%), 6 (50%), 4 (38,8%), 18 (38,8%) and 10 (38,8%). Triple trisomy (+4, +10,+17) were identified in 33,33% cases. The triple trisomy-positive cases had a median of 57 chromosomes (range, 51-65), whereas the negative cases had a median of 54 chromosomes (range, 51-57). Translocation-positive high hyperdiploidy (t-HeH) was identified in only 2 cases with t(12;21). None of the HeH cases had evidence of extramedullary (central nervous system, mediastinal mass or testes) leukemia at diagnosis. Median age at diagnosis was 4.7 years (range: 1.5-13 years). Median WBCx10⁹/L was 2.100 (range: 1200-17000). Only 3 cases were stratified as high-risk patients because they were prednisone poor responders and their minimal residual disease (MRD) in bone marrow on day 15 was LOG-1 but on day 33 they all achieved complete remission with MRD of LOG-4. All patients are in continuous complete remission with event-free and overall survival of 100%.

Conclusions

Our results are consistent with literature that HeH is the largest cytogenetic subgroup in childhood B-cell ALL and is associated with other favorable clinical features. The impact of triple trisomy (+4, +10,+17) in the context of high hyperdiploidy warrants further investigation.

EP-032

Acute Lymphoblastic Leukaemia

RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA – A SINGLE CENTER EXPERIENCE FROM A DEVELOPING WORLD

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Objectives

Data about relapsed ALL is lacking from developing world. Here, we have analysed our centre's relapsed ALL data to see its pattern and treatment outcomes

Methods

Retrospective data analysis was done among ALL patients from 2005-2013, treated on a modified UK-ALL XI protocol. Relapse defined as presence of >25% blast cells in bone marrow (BM), or on histology, or cytological documentation of blasts in extra-medullary (EM) sites after achievement of complete remission. Based on the time of relapse, they were categorized as very early (within 18 months from diagnosis), Early (after 18 months but within 6 months of completion of therapy) and late (more than 6 months of completion of therapy)

Results

41 (11.6%) patients relapsed among the 353 ALL patients. Median age was 4 years (range 0.16-20). Male preponderance (66%) seen. Majority of them (80%) were of B cell type. Among them one case had CNS disease at diagnosis and 5 of them presented with initial high TLC. Molecular work up showed BCR-ABL n=4, TEL-AML n=4, MLL n=2, Hyperdiploidy, n=2. 16 (34%) and 11 (27%) respectively had isolated BM and CNS relapses. One each had testicular and ocular relapse. 6 (15%) had combined BM and CNS relapse and 6 (15%) had combined BM and testicular relapse. 56%-very early, 26.8%-early and 17%-late relapses. 33 out of 41 opted for therapy and were treated on BFM-REZ 96 protocol. 16 patients are alive at a median follow up of 0.65 years (0.1-4.3 years). Our relapse rates were 11.6% and 2nd CR was achieved in 70%. 12 died (5-sepsis, 3-refractory disease, 4-second relapse). 27% patients were lost to follow up or died of sepsis. 2 year OS 51.7 ± 11.4%, 2 year EFS 27.2 ± 8.9%

Conclusions

It is feasible to treat children with relapsed ALL in the developing world but sepsis treatment abandonment are barriers to improving survival

EP-033

Acute Lymphoblastic Leukaemia

INCIDENCE OF HYPERGLYCEMIA DURING REMISSION INDUCTION CHEMOTHERAPY FOR PAEDIATRIC ALL, A HOSPITAL BASED STUDY

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Objectives

To see incidence of hyperglycemia during remission induction phase of chemotherapy treatment in case of ALL in children

Methods

Prospective observational study. About 50 newly diagnosed ALL patients age range of 1 to 15 years were studied. Study period was 6 months. Hyperglycemia was defined as > 2 random glucose determines of >200 mg/dl during the first 28 days of induction phase chemotherapy.

Results

Out of 50 patients, only 4 (8%) developed hyperglycemia during remission induction. No significant differences was noticed between two groups (hyperglycemic group, non hyperglycemic group) regarding age distribution ($P > 0.05$) and body weight ($P > 0.05$). Hyperglycemia mostly experienced during second week (75% patient) and third week (25% patient). This condition persists <7 days in 75% patients and > 7-days in 25% patients.

Conclusions

Around 8% ALL Patients during induction remission phase of chemotherapy experienced hyperglycemia. They recover when drugs like L -asparaginase, corticosteroid are withdrawn. These patients had no longer long term adverse effects.

EP-034

Acute Lymphoblastic Leukaemia

OUTCOME AND PROGNOSTIC FACTORS FOR TEL-AML1 POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA IN KOREAN CHILDREN: A SINGLE INSTITUTION STUDY

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Objectives

The *TEL-AML1* fusion is the most frequent genetic abnormality in children with acute lymphoblastic leukemia (ALL), and is associated with a favorable outcome. However, its incidence differs according to patient ethnicity, and its prognostic relevance may also differ.

Methods

In this study, we studied the outcome and prognostic features of 50 patients with *TEL-AML1* (M:29 F:21) who were diagnosed at the Department of Pediatrics, The Catholic University of Korea from May, 2005 to June, 2011. Independent variables studied included patient age and WBC count at diagnosis, minimal residual disease positivity at the end of remission induction (MRD), and cytogenetic features including presence of complex karyotype, or additional 12p translocations or inversions besides *TEL-AML1* (12p abnormalities).

Results

Median patient age at diagnosis was 4.5 years (range: 1.8-13.6), with only 4 patients (8%) diagnosed above the age of 10 years. Median WBC count at diagnosis was 11,500 (range: 1,000-134,580). A complex karyotype was found frequently at diagnosis (24/50, 48%). Eight patients relapsed (16%) at a median of 27.4 months from diagnosis (range: 18.3-39.3), including 7 with BM, and 1 patient with isolated CNS relapse. Five-year event-free survival was 84.0±5.2%. All 7 patients with BM relapse received allogeneic transplant; all 7 subsequently relapsed and died of disease progression. Five year overall survival was 74.8±12.3%. In univariate study, WBC count ≥ 50,000 ($P=0.024$), MRD at end of induction ($P=0.029$), and 12p abnormalities ($P=0.001$) predicted relapse. In multivariate study, only 12p abnormalities was a significant factor for relapse ($P=0.011$).

Conclusions

A significant portion of our *TEL-AML1* cohort relapsed. Of note, relapses occurred relatively early after diagnosis, in contrast to Western studies which reported a tendency for late relapses. Considering the extremely poor prognosis once relapse occurs, studies should be undertaken to clarify additional genetic lesions in *TEL-AML1* patients that predict a poor prognosis.

EP-035

Acute Lymphoblastic Leukaemia

CLINICAL SIGNIFICANCE OF DYNAMIC MONITORING MINIMAL RESIDUAL DISEASE IN CHILDHOOD B LINEAGE ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

To study the clinical significance of dynamic monitoring minimal residual disease(MRD)using flow cytometric detection of abnormal immunophenotype in childhood B lineage acute lymphoblastic leukemia. **Methods**

134 patients were enrolled in the research from January 2005 to December 2011. MRD targets were filtered preliminarily by flow cytometry, and then were dynamic monitored at specified time. The overall treatment plan is reference to Shanghai Children's Leukemia Cooperative Group protocol. Divided the patients into low?middle and high risk groups depends on risk factors including day 35 and 55MRD level.All datas were analyzed by SPSS 16.0.

Results

In this study,49 patients belonged to low risk(36.6%),46 patients to middle risk(34.3%)and 39 to higher risk(29.1%),Five year EFS was $85.60\pm 5.0\%$, $69.2\pm 7.2\%$, $63.0\pm 7.0\%$,respectively. There were significant statistic differences between low and high risk groups ($P=0.024$).128 patients achieved complete remission after induction therapy, with a 5-year event-free survival (EFS) $73.4\pm 3.9\%$. 109 patients with MRD targets, 25 patients without, 5-year EFS were $77\pm 4.1\%$? $56.7\pm 10.5\%$, respectively. Univariate analysis confirmed that MRD target were significantly different in both groups ($P=0.019$). MRD detection at day 35: MRD?0.01% were 77 patients with a 5 year relapse free survival(RFS) $80\pm 5.5\%$, MRD?0.01% were 21 cases with a 5-year RFS of $60\pm 12.1\%$ ($P=0.036$). 21 patients with MRD?0.01% at day 35 while 18 turn to normal at day 55(85.7%), 2 relapsed ,3 still abnormal, all of them relapsed. There were significant statistic differences in two groups ($P=0.008$).

Conclusions

The prognosis of low risk patients were significant better than middle and high risk group patients. 5 year EFS of ALL patients with MRD markers was higher than those without MRD marker. There is an important clinical significance for dynamic monitoring MRD to adjust the treatment timely. MRD on day 35 and 55 were important prognostic factors for ALL patients. The prognosis for MRD continued positive is poor.

EP-036

Acute Lymphoblastic Leukaemia

PROGNOSTIC FACTORS AND TREATMENT OUTCOME OF THE PEDIATRIC INTERMEDIATE AND HIGH RISK T-LYMPHOBLASTIC LYMPHOMA/LEUKEMIA-A REVIEW OF 30 CASES

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Objectives

To evaluate the prognostic factors and the therapeutic effectiveness of 30 cases of pediatric intermediate risk (IR) and high risk (HR) T-LBL/ALL treated with three various chemotherapeutic regimens including Sums lymphoblastic lymphoma-08, GZ2002 ALL and GD2008 ALL.

Methods

30 patients in our department from 2002 to 2012 were retrospectively studied. Evaluate patients' 3-year overall survival (OS) rate, 3-year event-free survival (EFS) rate, recurrence rate and mortality rate with Kaplan-Meier analysis; compare inner-group patients' OS and EFS difference and survival curve with Log-Rank test, all data was processed by SPSS 17.0.

Results

Among the 30 cases, OS and EFS for MLL gene negative cases (n=26) and MLL gene positive cases (n=4) were 52.5% vs 0% and 45.6% vs 0%, respectively; while for cases whose LDH level \leq 400U/L at first visit (n=22) and whose LDH level $>$ 400U/L (n=8), OS and EFS were 57.5% vs 31.7% and 35% vs 31%, respectively. Among 25 T-ALL cases, OS and EFS for prednisone good response (PGR) (n=16) and prednisone poor response (PPR) (n=8) cases were both 57.5% vs 32.5%; while on day 33 of induction chemotherapy, OS and EFS for M1 (n=23) and M2 (n=2) cases were 50.4% vs 0% and 44.3% vs 0%, respectively. For cases classified as IR (n=12) and HR (n=18), OS and EFS were 54.5% vs 36.5% and 43.6% vs 36.5%, respectively. After a median follow-up of 36.4 months (3~108 months), OS and EFS were 46.7% and 42.1%, respectively.

Conclusions

MLL gene positive, LDH level \geq 400U/L at first visit, PPR and bone marrow shows no remission on day 33 of induction chemotherapy, the higher the risk degree, all these are poor prognostic factors resulting in lower survival rate. Successfully screening the risk factors is benefit for designing the prognostic analytical model and choosing the optimal solutions for the patients.

EP-037

Acute Lymphoblastic Leukaemia

IMMUNOGENICITY OF INTRAVENOUS ASPARAGINASE ERWINIA CHRYSANTHEMI IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA OR LYMPHOBLASTIC LYMPHOMA

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Objectives

L-asparaginase (ASNase) is an important component of multiagent chemotherapy for pediatric acute lymphoblastic leukemia (ALL). Like other large proteins, ASNases can induce a host response, stimulating development of anti-ASNase antibodies. Implications of immunogenicity on the therapy can range from no effect to alterations in pharmacokinetics (PK), efficacy, and/or safety profiles. The objective of this analysis was to characterize the immunogenicity profile of ALL patients receiving *Erwinia* ASNase following hypersensitivity to *Escherichia coli*-derived ASNase.

Methods

Patients received *Erwinia* ASNase 25,000 IU/m² intravenously 3 times weekly in combination with chemotherapy. Serum samples for antibody testing were collected at trough ASNase activity levels (predose and 48 hours postdose 5), and were evaluated for antidrug antibody (ADA) with a screening assay (ELISA) and a confirmatory assay (competitive inhibition). Samples positive in the confirmatory assay were tested for neutralizing antibodies (NABs).

Results

Thirty patients aged 1–17 years (mean 7.9 years) were enrolled, and 16 completed the study; 12 discontinued due to adverse events. Most patients were male (63.3%) and had precursor-B-cell ALL (76.7%). Seven patients screened positive for ADA (ADA+); 4 were confirmed positive. None of the confirmed ADA+ patients tested positive for NABs. Comparison of PK between the ADA+ and ADA negative (ADA-) patients was limited by the fact that only 2 PK samples were taken after patients became antibody positive and the trough asparaginase activity levels were low. Ten patients experienced hypersensitivity reactions during the study; 7 were ADA- and 3 were ADA+. Six of the ADA- and 3 ADA+ patients discontinued following the hypersensitivity reaction; the fourth ADA+ patient did not experience a hypersensitivity reaction but refused further treatment.

Conclusions

In ADA+ patients the presence of anti-*Erwinia* ASNase antibodies was commonly associated with hypersensitivity reactions, although many patients who experienced hypersensitivity reactions did not have anti-*Erwinia* ASNase antibodies.

Study funded by Jazz Pharmaceuticals plc or its subsidiaries.

EP-038

Acute Lymphoblastic Leukaemia

THE 14-BASE PAIR DEL-DEL GENOTYPE OF THE HLA-G 3' UNTRANSLATED REGION IS ASSOCIATED WITH PEDIATRIC T- CELL LYMPHOBLASTIC LEUKEMIA

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Objectives

HLA-G antigen modulates the immune response in health and disease and the presence of polymorphic sites at the 3'untranslated region (UTR) of the gene seems to be involved in antigen expression. In cancer, HLA-G expression has been associated with worse outcome, but lesser is known in leukemia. We investigated the genetic variability of a *HLA-G* gene segment in children with T lineage acute lymphoblastic leukemia (T-ALL) as a possible prognostic marker.

Methods

47 T-ALL children referred to the Pediatric Oncology at the Instituto de Medicina Integral Professor Fernando Figueira, in Recife, Northeastern of Brazil, were studied. At diagnosis, blast bone marrow was characterized by morphology and immunophenotyping and minimal residual disease (MRD) was investigated using flow cytometry in Day 19 and 49.

Polymorphic sites at the *HLA-G* 3'UTR were determined by *in vitro* gene amplification and sequencing. Allele and genotype frequencies were estimated by Genepop software, and compared with data from 91 healthy children using Prism software.

Results

Children were 8.6±4.7 years and the proportion of boys:girls was 3. Twelve of 47 died, 6 within 30 days. MRD was measured in 16 children, from which 6 presented values above 1% of blast in Day 19, none was positive in Day 49. The *HLA-G* 3'UTR 14-base pair (bp) DEL-DEL genotype ($P=0.051$; OR=2.4) were overrepresented in T-ALL children, and 14-bp INS-INS ($P=0.030$; OR=0.4) underrepresented. Comparing the 12 children who died with the 35 alive, proportion of complete remission (6/12 x 34/35 cases) and relapse (4/12 x 0/35) were different. There were no differences on age ($P=0.961$), leucocyte counting (211,300±73,930 x 171,000±30,370; $P=0.464$), presence of mediastinal mass or hepatic and spleen enlargement ($P=1.00$). The 14-bp DEL-DEL genotype frequency was also the same in both groups.

Conclusions

The *HLA-G* 3'UTR 14-bp DEL-DEL genotype was associated with T-ALL in children, but not with the disease outcome.

EP-039

Acute Lymphoblastic Leukaemia

END OF INDUCTION THERAPY OUTCOMES OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN ETHIOPIA

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Objectives

We examined the data on induction therapy for acute lymphoblastic leukemia (ALL) in children at Tikur Anbessa Hospital in order to determine the outcome and variables determining it.

Methods

All children presenting with new or relapsed ALL were included in this examination between April 2013 and February 2014. Those with incomplete records were excluded.

Results

Fifty nine evaluable children (ages 1.5 to 14 years, median 7.0 years) with ALL received induction chemotherapy on 67 occasions (55 newly diagnosed and 12 relapsed ALL.) At the end of induction, 35 patients were alive, 19 patients died, and 14 patients abandoned (52, 31, and 17% respectively). Mortality and abandonment rates for those on 3-drug induction (n=40) were 18 and 22%, respectively, with 60% of the patients being alive at the end of induction. Mortality rate was 41% and abandonment rate was 18% for those receiving 4-drug induction (n=27) with 41% of the patents alive at the end of induction. Among high risk ALL patients (n=42), survival, mortality and abandonment rates for all patients were 51, 30, and 17%; for those receiving 3-drug induction(n=15) were 73, 13, and 13%; and for those receiving 4-drug induction (n=27) were 41, 41, and 18%, respectively. Infection and bleeding were the primary reason for mortality with similar rates in all groups (average 58% for infection and 27% for bleeding.) Socioeconomical constraints and hopelessness were the primary reasons for abandonment and this was somehow higher among those considered standard risk ALL (28%.)

Conclusions

Intensive chemotherapy leads to significantly lower survival rates in children with ALL in Ethiopia. These observations underline the importance of making an honest assessment of the settings and ascertainment of proper supportive care when making therapeutic decisions in low and middle income countries.

EP-040

Acute Lymphoblastic Leukaemia

CLINICAL ANALYSIS OF THREE CASES OF FUNGAL ESOPHAGITIS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

To summarize the experience of diagnosis and treatment of fungal esophagitis in children with acute lymphoblastic leukemia (ALL).

Methods

Retrospectively reviewed the clinical manifestations, diagnosis and treatment of fungal esophagitis in three children with acute lymphoblastic leukemia during chemotherapy.

Results

Three patients with ALL had symptoms of epigastric pain, vomit or discomfort of the precordial area during and after chemotherapy. They were diagnosed fungal esophagitis by gastroscopy. One case had fever and neutropenia. The regimen for chemotherapy in all patients included dexamethasone. All cases were given antifungal drugs including fluconazole, micafungin and itraconazole for two to four weeks. They all recovered based on endoscopy results.

Conclusions

Gastroscopy can be performed to make diagnosis of fungal esophagitis when ALL patients have symptom of epigastric pain or discomfort of the precordial during chemotherapy.

Gastroscopy can be a useful way to find out the site of fungal infection when patient is febrile and neutropenic. Antifungal drugs are effective for fungal esophagitis.

EP-041

Acute Lymphoblastic Leukaemia

FLOWCYTOMETRIC PATTERN AND PROGNOSTIC SIGNIFICANCE OF CELL SURFACE PHENOTYPE IN ACUTE LYMPHOBLASTIC LEUKEMIA IN PAEDIATRIC PATIENTS-A RETROSPECTIVE ANALYSIS AT A REGIONAL CANCER CENTRE IN KASHMIR, INDIA

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Objectives

Acute lymphoblastic leukemia (ALL) is a heterogeneous disease with biologically and clinically distinct subsets. The immunophenotype of leukemic cells at diagnosis reflects the level of differentiation achieved by the clone. Aim of the study was to review the flowcytometric pattern of ALL and its prognostic significance in paediatric patients.

Methods

This retrospective study was carried out at the Department of Medical and Paediatric Oncology, Regional Cancer Centre, Sher-i-Kashmir Institute Of Medical Sciences, Srinagar, Jammu and Kashmir, India. The clinical, hematological and flowcytometric data of the patients was reviewed over a four years period from January 2009 to December 2012.

Results

Out of 167 ALL patients registered during the study period, 118 (70.65%) were paediatric patients and 49 (29.35%) were adult ALL. Flowcytometry was available in 109 (92.37%) children with ALL. There were 68 male and 50 female children (M:F, 1.3:1). B-cell ALL constituted 67.25% and T-cell ALL were 29.64%. Early pre B cell was common (54.7%) followed by pre B cell (40.2%) and mature B cell (6.1%) among B cell phenotype. In T cell phenotype, mature T cell was common (88.3%) followed by pre T cell ALL (11.7%). Mixed phenotype ALL was present in 3.11%. CALLA positivity was present in 67.33% and 3.4% were ph+ve ALL. Early Pre B cell ALL had favourable prognosis with complete response rate of 67.33%, followed by Pre B cell ALL (64.22%). In T cell ALL mature T cell had complete response rate of 13.66% followed by pre T cell ALL 3.4%. Treatment failure rates were higher in T cell type ALL (75.23%) compared to B cell phenotype (33.23%).

Conclusions

Immunophenotyping plays a central role in the determination of clinically relevant subsets. Although intensive therapy may blur some prognostic distinctions, consideration of toxicity/efficacy ratios and the persistence of definable high-risk groups requires the continued use of immunophenotyping in the diagnosis and classification of ALL.

EP-042

Acute Lymphoblastic Leukaemia

SUCCESSFUL TREATMENT WITH DASATINIB IN A CASE OF RELAPSED ALL WITH NOVEL ATF7IP-PDGFRB FUSION GENE.

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Objectives

BCR-ABL1 positive acute lymphoblastic leukemia (ALL) has poor response and prognosis for conventional chemotherapy, however outcome can be improved with the addition of first and second generation tyrosine kinase inhibitors. Recently, new high risk subtypes of BCR-ABL1 negative ALL were identified which have similar expression profile to BCR-ABL1 positive ALL and have genetic alterations that activate kinase signaling including rearrangement of platelet derived growth factor receptor β (PDGFRB). We report the first patient of ALL with ATF7IP-PDGFRB who received allogeneic stem cell transplantation (allo-SCT) and treatment with dasatinib.

Methods

A 11-year-old boy who achieved first complete remission (CR) by conventional chemotherapy suffered from first bone marrow (BM) relapse of B cell precursor ALL during maintenance therapy. Chromosomal karyotype analysis of relapsed blast cells showed 45,XY,t(5;12)(q33;p13),-7. Using samples at relapse, we performed the mRNA sequence analysis and the in vitro drug testing with the WST-8 assay.

Results

The mRNA sequence analysis identified an in-frame transcript fusing exon 13 of ATF7IP with exon 11 of PDGFRB. Furthermore, the in vitro drug testing revealed sensitivity to dasatinib. REZ-BFM style chemotherapy could not provide a reasonable efficacy. We therefore altered to ECM therapy (etoposide, cytarabine, mitoxantrone), and as a result, second hematological-CR was achieved after 2 cycles of the therapy. ATF7IP-PDGFRB was still detectable in BM by reverse transcription polymerase chain reaction (RT-PCR). Subsequently we performed allo-SCT with 1 HLA-DR allele mismatched cord blood. His neutrophil recovered at day25, and BM showed 99% donor type at day30. Treatment with dasatinib was started from day 62 against positive ATF7IP-PDGFRB in BM at day30 and day61. ATF7IP-PDGFRB in BM decreased after dasatinib and finally became undetectable by RT-PCR at day 146.

Conclusions

Dasatinib may be effective for relapsed ALL with PDGFRB rearrangement.

EP-043

Acute Lymphoblastic Leukaemia

**PHILADELPHIA POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN:
EXPERIENCE FROM A SINGLE CENTRE IN INDIA**

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Objectives

Philadelphia Positive Acute Lymphoblastic Leukemia (Ph+ve ALL) is an aggressive disease with poor prognosis in children. Our objective was to determine the outcome of the Ph+ve ALL in childhood from Northern India.

Methods

Sixty one cases of pediatric acute lymphoblastic leukemia were studied retrospectively.

Results

Ph+ve ALL was found in five cases (8.2%). Of the 5 patients, three were male and two were female with a median age of 10 years (range, 6 months to 12 years). Four were treated on BFM-95 protocol and one on UKALLXI protocol. Imatinib mesylate (375 mg/m²) was started daily at the time of diagnosis. All went in remission and later achieved complete molecular remission. However during maintenance therapy 3 patients started having rising value of quantitative BCR-ABL values at 18 months, 25 months and 31 months from diagnosis. As all these 3 children had no siblings and no matched unrelated donor was available so in these three Imatinib was stopped and after taking informed consent of parents Dasatinib was started at a dose of 100 mg/m²/day in two divided doses and maintenance therapy of oral 6-Mercaptopurine and Methotrexate was continued. All these 3 patients achieved reduction in BCR-ABL quantitative PCR after 3 months and molecular remission after 6 to 9 months after starting dasatinib. One patient stopped Dasatinib after 8 months on its own and started on herbal medicine, is in molecular remission. One had isolated CNS relapse. Rest two patients are on Imatinib and in molecular remission. Two patients on Dasatinib had acquired WHIM syndrome during therapy and one patient on Imatinib had fracture, excessive callus formation and mal-union of humerus. Four patients had growth delay with short statured for their age.

Conclusions

Dasatinib is a useful alternative drug for Imatinib resistant Ph+ve ALL. Side effects need to be monitored carefully while patients on Dasatinib or Imatinib.

EP-044

Acute Lymphoblastic Leukaemia

COLLABORATION AMONG DIFFERENT ONCOLOGY CENTERS IN A MIDDLE INCOME COUNTRY CAN IMPROVE RISK STRATIFICATION IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

Acute lymphoblastic leukemia (ALL) is the most common cancer in childhood. Optimally, treatment strategies differ among different risk cases. The Children Cancer Center of Lebanon at American University of Beirut offers to all newly diagnosed Lebanese children with ALL the chance to get risk-specific treatment by providing analysis of bone marrow (BM) flow cytometry, molecular and cytogenetic testing free-of-charge. Costs were covered through fund raising at the national level.

Methods

We identified ALL patients younger than 18 years, diagnosed between 04/2002 and 12/2012; retrospective chart review was conducted to collect patients' laboratory data. This review included Lebanese patients newly diagnosed with ALL and treated at Lebanese hospitals.

Results

338 patients were identified (191(57%) males); 9(2.6%) patients were <1 year of age, 254 were between 1-10 years, and 75(22%) ≥10 years; initial WBC was ≥50,000 in 80(23.6%) patients, 82.5% had B-lineage and 17.5% had T-lineage ALL; DNA index was ≥1.16 in 18.5%. Metaphase cytogenetics revealed normal karyotype in 50%, >50 chromosomes in 10%, 47-50 chromosomes in 8% and <46 chromosomes in 3%. The rest failed cytogenetic testing. Molecular studies (RT-PCR) were done for 242 patients; 18% had t(12:21), 6.5% had t(1:19), 2% had t(9:22), and 3% had t(4:11).

Conclusions

The high karyotype failure rate is attributed to the long waiting time between BM performance and delivery to cytogenetics lab. Our future plans include performing Day 15 MRD studies for all patients as well as the use of a uniform treatment protocol. Offering free-of-charge examination of BM for Lebanese pediatric ALL patients was important for risk stratification of patients in order to offer them risk-adapted therapy, thus the best chance of cure. Our experience can serve as a good model for other middle and low-income countries for collaboration, implementing uniform treatment protocols and hopefully improving survival of children with ALL.

EP-045

Acute Lymphoblastic Leukaemia

TREATMENT RELATED DEATH IN RELAPSED CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

Patients with relapsed acute lymphoblastic leukemia (ALL) are more susceptible to the adverse effects of leukemia therapy both because of the accumulation of organ specific toxicities and the intensity of the relapse treatment. In addition, a higher proportion of patients undergo stem cell transplantation (SCT) in second complete remission (CR2), where prolonged severe immunosuppression and graft-versus-host disease (GVHD) further increase the risk of life threatening events. The aims of this study were to investigate the incidence and risk factors for treatment related deaths (TRDs) in patients with relapsed childhood ALL.

Methods

In this retrospective population-based study we analyzed data on all children that relapsed after common upfront treatment according to the Nordic Society of Paediatric Haematology and Oncology (NOPHO) ALL-92 and ALL-2000 protocols. All patients had pre-B or T-cell immunophenotype and were >1 years and <15 years at diagnosis but those undergoing SCT in first complete remission were excluded from the study. Patient data was exported from the NOPHO ALL registry but in case of incomplete registration requests were sent to treating clinics,

Results

We identified 50 patients with TRDs among the 485 patients that were included in the study (10.3%). Eleven patients died before reaching CR2, 15 in CR2 treated with chemotherapy only and 24 patients after undergoing SCT in CR2. Infections were the most common cause of death, 35 of 50 (70%). Independent risk factors for TRDs were high risk clinical profile at relapse and unfavorable cytogenetics but we did not find any significant gender or age differences.

Conclusions

Treatment related deaths are approximately three times as common during relapse treatment than during primary treatment. Infections are the most common reason for TRDs. Patients stratified as high risk at relapse and patients with unfavorable cytogenetics should be monitored closely and treated promptly for suspected infections.

EP-046

Acute Lymphoblastic Leukaemia

ENDOCRINE SIDE EFFECTS AFTER CHEMOTHERAPY IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

Focus on long-term side-effects after cancer therapy in childhood has become of the crucial importance. The exposure of chemotherapy at young ages has increased vulnerability to long-term treatment induced sequelae. Also contribution of radiation may increase adverse sequelae.

Methods

We aimed to evaluate endocrine side effects in 41 patients (M/F=20/21) with acute lymphoblastic leukemia (ALL) being followed-up 1-5 years after treatment. Patients were screened for endocrine side effects, growth, blood glucose metabolism, lipid metabolism abnormalities, sexual development, thyroid metabolism, bone mineral density and adrenal insufficiency.

Results

Mean age of the patients were 10±3,1 years . In 35 of 41 (85,3%) patients at least one endocrine complication was detected. One patient's (2,4%) height was under 3 percentile, 12 (29,3%) patients were obese. Forteen (34,1%) patients had insuline resistance. Three (7,3%) patients had IGF levels under -2 SDS, two (4,9%) patients had high FSH-LH levels. One (2,4%) patient had subclinical hypothyroidy, one (2,4%) patient had positive thyroid antibodies. Twenty (48,9%) patients had low levels of cortisol. Six (14,6%) patients had subclinical D vitamine deficiency, two (4,9%) patients had subclinical hyperparathyroidy, three (7,3%) patients had isolated hypercalcemia. Only insulin resistance rate was higher in patient who were applied RT than those who weren't applied RT.

Conclusions

In this study endocrine side effects were seen in the two years after therapy. The patients who were applied chemotherapy and RT for ALL treatment, should be followed-up closely for endocrinological side effects, and early diagnosis and treatment should be performed for endocrinological diseases which may develop later in life.

EP-047

Acute Lymphoblastic Leukaemia

INTERACTION MODEL BETWEEN NATURAL KILLES CELLS AND LEUKEMIC CELLS: FIRTS GOALS AND PRELIMINARIES DATA

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Objectives

Acute Leukaemia is the most common malignant pathology. Contemporary chemotherapy protocols achieve 75% overall survival; this results did not improve during the last several years. A new treatment approach is represented by the anti-tumor immune mediated inherent alloreactivity of NK cells (NKc). We need to know more about the role of the interaction between NKc and leukemic cells; about this we started a prospective trial in October of 2012 to clarify it. The trial's goals are: describe the match or mismatch NKc receptors (KIR) with leukemic cells, the cytotoxicity, the role of serum cytokines and the progress in transplant patients.

Methods

Preliminaries results are presented in this review. We included 20 acute lymphoblastic or mieloblastic leukaemia from October 2012 till January 2014, and One patient was excluded because refused to sing the consents. We collected data from 13 boys and eight girls, the median was 6 years old (age range from 1 to 13 years old). At the same time we stored sera and leukemic cells previous treatment.

Results

We got a 78,9% of free event survival and only a 10,5% of mortality. The sample has three children with ALM M7, thirteen B ALL and three T ALL. We transplanted six of them, watching disparities around 0 to 8 in KIR receptors.

Conclusions

In conclusion, We show that the AB genotype was the most common genotype in relapsed patients. The next steps in the study are: test the cytotoxicity in the complete remission patient at the end of treatments and link these results with KIR and HLA genotype.

EP-048

Acute Lymphoblastic Leukaemia

GENE EXPRESSION OF MULTI DRUG RESISTANCE PROTEIN (MDR-1), MULTI DRUG RELATED PROTEIN (MRP) AND LUNG RESISTANCE PROTEIN (LRP) IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA CASES

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Objectives

Introduction: Approximately 25% of ALL children present with disease recurrence. Treatment failure is due to either pharmacokinetic resistance or cell resistance to antineoplastic drugs.

Aims & Objectives: To study gene expression of Multi drug resistance protein (MDR-1), Multi drug related protein (MRP) and Lung resistance protein (LRP) in pediatric ALL and to correlate it with early response to chemotherapy and other clinical and laboratory variables.

Methods

Prospective study (2013-2014), in which 45 pediatric ALL cases were enrolled. Relative quantification of mRNA of MDR-1, MRP and LRP was done by Real Time PCR assay using SYBR-G dye. A high expression was defined as > 0.5 fold than in control cells.

Results

Of 45 cases, 33 male and 12 female (M:F-2.75:1). Mean age was 5.2 years. Based on TLC and age, 26/45 (58%) were in standard risk, 17/45(38%) intermediate and 2/45 (4%) in high risk category. Only 3/45 (7%) were T-ALL and rest (93%) B-ALL cases. Abnormal cytogenetics was noted in 5/45 (11.0%). Day 14 check marrow status was M1 in 38/45 (84%), M2 4/45 (9%) and M3 3/45 (7%) cases. High expression of MDR-1 and LRP was noted in 10/45 (22%) cases each and MRP in 18/45 (40%) cases. A significant association was noted between slow early response (M2 & M3 status at D14) and four fold or higher LRP gene expression (p<0.05). Only one case had disease relapse and it also had 4 fold high LRP expression.

Conclusions

There were 6 post induction deaths, all sepsis related. In three of them, high expression of LRP gene was noted. A study by ET Valera et al also found a positive association between increased LRP expression and poor event free survival. Larger prospective studies are needed to correlate drug related gene expressions with overall survival/outcome to better understand their clinical relevance.

EP-049

Acute Lymphoblastic Leukaemia

PLATELET MICROPARTICLES IN PEDIATRIC PATIENTS WITH LEUKEMIA AND SOLID TUMORS

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Objectives

The contribution of platelets to the progression of cancer is an emerging area of research interest. Study aim: to assess the level of platelets microparticles (PMPs) in childhood malignancies and its relation to response to therapy.

Methods

A prospective case control study including 25 newly diagnosed patients with malignancy; acute lymphoblastic leukemia (ALL, n=10), acute myeloid leukemia (AML, n=10) and stage IV neuroblastoma (n=5). PMPs were assessed by flow-cytometry at diagnosis and after complete remission/or good partial response and were compared to 25 healthy matched controls.

Results

No significant difference was found in levels of PMPs between patients and control group at diagnosis. No significant difference in median initial or post-induction PMPs between patients with ALL (1.48 (0.62 – 1.87); 2.6 (1.84 – 4.11), AML 1.48 (0.88 – 2.25), 1.84 (1.03 – 2.90) neuroblastoma (1.77 (0.75 – 1.77); 1.76 (1.75 – 2.89)), P=0.595 and 0.232 respectively. There was no significant difference between pre and post induction PMPs in patients with ALL (P=0.401), AML (P=0.482); and a significant rise in PMP was found in patients with neuroblastoma post-induction phase (P=0.026). In ALL group, there was no significant correlation was found between platelets count and in PMPs before (r=.0.443, P=0.2) or after chemotherapy (r=0.236, P=0.511); a significant positive correlation was found between platelets count and PMPs after chemotherapy (r=0.818, P=0.013) in AML group. In neuroblastoma group, both mean platelet count and PMPs level significantly increased after chemotherapy, and significant correlation was found between platelets count and PMPs after chemotherapy (r=0.9, P=0.037). Higher PMPs level at diagnosis was found in the patients who died during the induction phase.

Conclusions

We conclude that platelets microparticles rose after induction phase in children with ALL, AML and neuroblastoma; we suggest interpreting the absolute PMP count with caution in patients with thrombocytopenia and rather use a PMP/platelet count ratio; yet conclusions need to be cautiously interpreted because of the small sample size.

EP-050

Acute Lymphoblastic Leukaemia

ESTABLISHING CLINICAL RESEARCH IN A LIMITED RESOURCE SETTING, "ACUTE LYMPHOBLASTIC LEUKEMIA MODEL"

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Objectives

Establishing research team on Childhood Acute Lymphoblastic Leukemia (ALL) in a limited resource country like Egypt was a challenge. This challenge was increasing with the increase the number of ALL patients it receives every year (average 250 cases).

Methods

Research Department was established in November-2008. I was the first time in Egypt to introduce the concept of forming team for each disease. A multidisplenary team of ALL was formed.

Results

The above mentioned steps had a marvelous impact on childhood ALL. Initially, a genetic epidemiology grant in ALL funded by US-NIH was obtained. Based on the results of this grant we applied to another grant on ' Genome wide Association Study (GWAS) in ALL' to get fund and complete our research to identify the cause of ALL in Egyptian population and successfully obtained 10 million Egyptian pounds. The presence of ALL database and statistical analysis of the survival, allow them to 1- hold collaboration with St Jude Research Hospital in special risk protocol that allow both check quality of flow cytometry results, cytogenetics results so enhance the quality and allow rapid consultation on complicated cases, 2- the presence of hospital based-cancer registry for ALL, 3- Supplying biobank with samples that will help in future research, 4- rapid statistics of the number of relapsed patients and died during induction and in relapse. In addition to Production of patient education booklet as an educational material for their treatment protocol. The future plan to make strategy becomes mandatory: 1- Identifying the genetic causes of relapse, 2- Route-cause analysis for patient died during induction and in complete remission, 3- The plan to make translational research and how to individualize treatment. 4- educate illiterate families and their kids via simple audio-visual materials.

Conclusions

The presence of clinical research has an impact on the childhood ALL patients, staff and the institution.

EP-051

Acute Lymphoblastic Leukaemia

SIGNIFICANCE OF DAY 29 BONE MARROW IN ACUTE LYMPHOBLASTIC LEUKEMIA WITH M1 BONE MARROW AT DAY 8/15 IN ABSENCE OF MRD

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Objectives

Acute lymphoblastic leukemia (ALL) is most common hematological malignancy among pediatric population. Different protocols like UKALL and COG are used for management and all protocols suggest bone marrow biopsy at day 8 or 15 and then at day 29 during induction phase. On day 29 Minimum residual disease (MRD) status is usually advised. Developing countries where facility of MRD is not available patients of ALL are being treated according to these protocols and bone marrow biopsies are advised on both day 8/15 and day 29. Our hypothesis is "if day 8/15 bone marrow is in remission there is no significance of day 29 bone marrow in absence of MRD facility"

Methods

All patients of ALL admitted from Jan 2008 to Dec 2013 and survived during induction were included. Induction therapy according to standard arm of UKALL 2003 was given. Bone marrow biopsy was done on day 8 or 15 depending upon regimen and day 29 in all patients. MRD was not available.

Results

Total 282 patients were included. Male to female ratio was 2:1. Age range from 7 months to 17 years. Seventeen (6%) patients were >10 yrs and 265 (94%) were < 10 years. 30 (10.6%) patients had T cell ALL and 252 (89.4%) had Pre B ALL. Seventeen (6%) patients had M2 bone marrow and 13 (4.6%) had M3 bone marrow on day 8/15 but none of them had residual leukemia on day 29. 252 (89.3%) patients had bone marrow in remission on day 8/15 and none of them had evidence of residual leukemia on day 29 bone marrow.

Conclusions

In absence of MRD facility there is no significance of day 29 bone marrow if day 8/15 bone marrow is in remission.

EP-052

Acute Lymphoblastic Leukaemia

SURVIVAL ANALYSIS OF CHILDREN AND ADOLESCENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA TREATED IN A ONCO HEMATOLOGIC CENTER OF CHILDHOOD - CETOHI FROM BRAZIL

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BACKGROUND: In a public institution children with de novo acute lymphoblastic leukemia were treated from January 2000 to December 2012, according to Brazilian Childhood Cooperative Group-Protocol (GBTLI) ALL-99 and Berlin-Frankfurt-Munich (BFM) protocol ALL-95/02.

AIM: Evaluate the experience with these protocols and the treatment results according to the risk groups.

METHODS: children aged 0 to 18 years old were stratified into 2 risk groups: low and high-risk group.

RESULTS: One hundred and ninety nine children entered the study (male-female ratio was 1.48:1, the average age was 7 years and 7 months and the median age was 6 years and 4 months). 111 (62,92%) children were in the low risk, 68 (37,07%) in the high-risk group. The overall complete remission rate was 88,26%. Twenty-one (12,35%) children died in induction and 04 were non-responders. The 5-year overall survival for all patients was 61,5%, in the low risk group 70,10% and in the high-risk group 52,7% the average age of follow was 6 years and 2 months. The median of follow-up was 6 years and 5 months. From the 179 patients 110 (61,5%) are still in their first complete clinical remission and other 07 children are alive after relapse. In 22,3% of the patients have relapsed. The 5-year disease-free survival for all patients was 51,5%, in the low risk group 73,1% and in the high-risk group 55,5%.

CONCLUSION: The treatment outcome of children with acute lymphoblastic leukemia improved remarkably over the last decade. 61,5% of children suffering from acute lymphoblastic leukemia could be cured with the GBTLI-ALL 99 and BFM-ALL 95/02 protocol. The results of the patients of this public institution were comparable with the results achieved by other services in Brazil and other countries.

EP-053

Acute Lymphoblastic Leukaemia

THREE CASES OF CHILDHOOD MATURE B-ACUTE LYMPHOBLASTIC LEUKEMIA WITH NON-L3 MORPHOLOGY AND MLL-AF9

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Objectives

Mature B-ALL is typically associated with FAB-L3 morphology and rearrangement of the *MYC* gene. However, some reports showed that rare ALL cases with non-L3 morphology and *MLL-AF9* chimeric gene can express a mature B-cell immunophenotype and may represent a distinct subset with a mostly rapid and aggressive clinical course. We report 3 such cases of mature B-ALL, and discuss the clinical, genetic, and immunophenotypic features in the context of previously reported cases.

Methods

Patient 1 was a 4-month-old female infant. Patient 2 or 3 was a 15-month-old or a 4-year-old female, respectively. The bone marrow smears at diagnosis showed FAB-L1 morphology in all patients. Immunophenotypically, they were positive for CD10, CD19, CD20(or CD22), HLA-DR, sIgλ, and sIgM. No evidence of *MYC* rearrangement was detected in all cases with FISH analysis. *MLL* rearrangement was detected by FISH and *MLL-AF9* was confirmed by RT-PCR.

Results

They achieved complete remission after conventional chemotherapy and underwent hematopoietic stem cell transplantation as high risk ALL; patient 1 for infantile ALL with *MLL* rearrangement and the others for ALL with *MLL* rearrangement and hyperleukocytosis (WBC at diagnosis $>50 \times 10^9/L$). Patient 2 received bone marrow transplantation from HLA-identical sibling and patient 1 or 3 received cord blood transplantation from 5/6 or 8/8 HLA-matched unrelated donor, respectively. Patients 1 and 2 have maintained complete remission for more than 6 years since transplantation. Patient 3 remains in complete remission at 6 months after initial diagnosis.

Conclusions

In previous reports, survival of patients with ALL characterized by mature B immunophenotype, non-L3 morphology and *MLL-AF9* is poor, especially after relapse. Accumulation of cases with such features will further clarify clinical significance of the unique phenotype in childhood ALL.

EP-054

Acute Lymphoblastic Leukaemia

RETROSPECTIVE ANALYSIS OF A COHORT OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) CASES FROM SINGLE TERTIARY CARE CENTER IN INDIA

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Objectives

Pediatric ALL is characterized by varied clinical presentation with recurrent numerical and structural chromosomal abnormalities, which are thought to be specifically associated with diagnosis, risk stratification, treatment response and prognosis.

Methods

Children (upto 18yrs) diagnosed with ALL over a period of 7yrs (Jan 2006-Dec 2013) were analyzed retrospectively.

Results

A total of 61 (53 B cell, 8 Tcell)patients were evaluated. Mean age at presentation was 7.2 yrs (1 yrs - 18 yrs). M:F was 2:1. National Cancer Institute risk stratification was standard in 35, high 23 and very high in 3 patients. 35 were treated on BFM 95 protocol and 26 on UK ALL XI protocol. 8 were lost to follow up (LTFU) at a median of 12 months (1 to 29 months) and 1 refused treatment after relapse.

As on 31st Dec 2013, 52 patients were evaluated for final outcome analysis. 12 are alive on various phases of chemotherapy after a mean follow up of 21.4 months; 38 are alive and completed treatment after a mean follow up of 49 months. 10 relapsed at median of 34 months (12 - 57 months). Those who relapsed 4 were very early, 2 early and 4 were late relapse. Except 1 who was standard risk, all relapses were in high or very high risk (BCR-ABL) category. All were started on relapse protocol (ALL REZ BFM 95/96). 1 refused treatment, 4 given chemotherapy, 3 underwent bone marrow transplant (allogenic) and are alive on follow up and 2 expired. For the entire cohort event free survival (EFS) was 70% and overall survival (OS) was 81% at 35 months mean follow up.

Conclusions

Cytogenetics studies could not be done in significant number of patients due to resource constraints. There were a significant number of LTFU patients that needs to be addressed in LMIC setting.

EP-055

Acute Lymphoblastic Leukaemia

SOMATIC NT5C2 MUTATIONS IN CHINESE PATIENTS WITH RELAPSED PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

Children with relapsed acute lymphoblastic leukemia (ALL) carry poor prognosis owing to intrinsic drug resistance. However the biological pathways that mediate chemotherapy resistance remain unknown. Relapse-specific mutations of *NT5C2* gene have recently been identified in childhood ALL. The aim of the present study was to investigate the frequency and clinical impact of *NT5C2* mutations in Chinese pediatric patients with relapsed ALL.

Methods

This study enrolled 58 patients with relapsed ALL which included 15 T cell ALL and 43 B-precursor ALL. We sequenced the exon 9, 13, 15, and 16 of the *NT5C2* gene.

Results

The R367Q mutation was detected in 2/15 (7.5%) relapsed T cell ALL patients. A novel mutation (H352D) which mapped to the active site of the *NT5C2* enzyme was detected in 1/43 (2.3%) relapsed B-precursor ALL patient. All the mutations were heterozygous and located in exon 13. Clinically, all patients carrying *NT5C2* mutations relapsed early, within 36 months after initial diagnosis, although the difference was not significant ($P=0.150$).

Conclusions

These findings suggest that *NT5C2* mutation is a recurrent event in ALL. The novel H352D mutation expands the mutation spectrum of *NT5C2*.

Acknowledgments

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EP-056

Acute Lymphoblastic Leukaemia

UNUSUAL MANIFESTATIONS OF NON SINOPULMONARY FUNGAL INFECTIONS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

Fungal infections causes significant morbidity & mortality, increasing economic and Psychological burden in acute lymphoblastic Leukemia children.

we described different types of non sinopulmonary fungal infections and their outcome in ALL children

Methods

Identified 4 interesting cases of ALL children with different types of fungal infection manifesting in different forms.

Results

A 10 years boy with CALLA positive B cell ALL, in week 4 of Induction presented with 3cm hyperpigmented lesion over medial aspect of Right foot. He had pancytopenia. Lesion was not responding to antibiotics and antifungals , requiring debridement and been identified as *Exserohilum Rostratum* in fungal culture.

Lesion resolved after 4 weeks of Iv amphotericin B and Debridement.

Case 2: Unusal Fungal infections in well child should raised the suspicion of malignancy. A 3.5 years boy presented with fever of 7 days ,was initially managed as Enteric fever with iv antibiotics. An abscess at cannula site noticed, culture grew *Rhizopus Aerialis* . CBP revealed hb of 8.5 gm% and WBC 3800, Lymphocytes of 74%, platelets were 1.8 lakhs. Bone marrow Aspiration confirmed CALLA Positive B ALL. He responded to Amphotericin B.

Case 3: A 5 Years boy ,with CALLA Positive ALL standard risk , on Induction presented with history of right eye swelling and chemosis. Even by week 4 of induction had neutropenia of 544 cells. Right eye Vitreous biopsy done , had endophthalmitis. Intravitreal amphotericin given. Culture of Vitreal fluid Isolated *Aspergillus fumigatus*. Antifungals given for 8 weeks to control fungal infection.

Case 4: 13 years girl with CALLA positive, CNS negative standard count and genetics ALL, on consolidation developed skin fungal infection in axilla which has been identified as mucormycosis, She required debridement of skin lesion along with 6 weeks of Iv liposomal amphotericin B.

Conclusions

Awareness & early recognition of different fungal infections in ALL children is important to prevent mortality and morbidity

EP-057

Acute Lymphoblastic Leukaemia

PEG ASPARGINASE INDUCED SUPERIOR SAGITAL SINUS THROMBOSIS: IN ACUTE LYMPHOBLASTIC LEUKEMIA CHILDREN - A REPORT OF 2 CASES

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Objectives

To identify the cause of cerebral sinovenous thrombosis (CSVST) in 2 children on induction therapy for acute leukemia

Methods

Two children identified to have CSVST out of 178 ALL's treated from October 2008 to December 2013. 18 received pegasparginase and remaining L asparaginase.

Results

Case 1: a 2.6 years standard risk ALL boy developed left focal tonic-clonic seizure evolving into status epilepticus & left hemiparesis, 3 days in to consolidation, 2 weeks post second dose of pegasparginase. Induction given using dexamethasone, vincristine, peg-asparaginase and intrathecal methotrexate. He had CSVST, predominantly on right side in MRI brain. Started on low-molecular weight heparin (LMWH) and levetiracetam. Left hemiparesis improved and was fully ambulatory within 1 week. Consolidation chemotherapy continued smoothly with the concomitant use of LMWH. Intrathecal methotrexate has been omitted temporarily, which was subsequently restarted. He was continued on LMWH for 6 months until post reinduction where pegasparginase is part of schedule. His repeat MR angiogram revealed partial recanalization. His thrombophilia work up initially showed low protein S and antithrombin III which became normal 6 months post CSVST. Parents procoagulant work up was completely normal.

Case 2: 3.4 years girl presented with status epilepticus with left hemiparesis in week 4 of induction, 2 weeks after first dose of pegasparginase. Had similar course as case 1 except requiring 2 antiepileptics to control seizures. And also normal thrombophilia work up even at the time of episode. Low molecular weight heparin continued in similar fashion till reinduction.

Both of them showed good response to therapy without any residual neurological disability.

Conclusions

Both cases illustrate strong correlation between rare thrombotic complication, CSVST and hypercoagulable status secondary to combination of asparaginase and corticosteroid. Early and vigilant recognition and prompt anticoagulation prevents further neurological damage.

EP-058

Acute Lymphoblastic Leukaemia

LIPID PROFILE BEFORE AND AFTER INDUCTION CHEMOTHERAPY IN BANGLADESHI CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

To evaluate the changes in lipid profile after L- asparaginase and after completion of induction chemotherapy.

Methods

This was an observational analytic study carried out from March to November 2013 in the department of Pediatric Hematology and Oncology, BSMMU, with a view to evaluate the changes in lipid profile due to induction chemotherapy (Protocol UKALL 2003 modified). 35 newly diagnosed children with ALL age range 3-15 years were included in the study . Fasting (8-12 hours) serum total cholesterol, TG, HDL, LDL, fasting blood glucose, ALT, creatinine were done before treatment, after completion of asparaginase and after induction completed. Risk stratification of the patients was done by age, report of CBC and bone marrow examination.

Results

The mean (\pm SD) age of 30 children of this study was 6.07 ± 2.95 years, 66.7% were in the age group ≤ 6 years and 66.7% were male. In the current study before treatment mean total cholesterol, TG, HDL and LDL values were 158.40 ± 42.70 , 184.47 ± 65.32 , 19.93 ± 10.85 , 101.20 ± 35.01 mg/dl. After completion of L-asparaginase, TG, LDL declined significantly and HDL increased significantly. After completion of induction chemotherapy the mean values of total cholesterol, HDL LDL level increased to 195.43 ± 36.58 ($P=0.003$), 50.20 ± 19.59 ($P=0.001$) and 116.70 ± 27.59 ($P=0.186$) respectively, but TG decreased to 140.93 ± 62.80 ($P= 0.060$). It was also observed that those patients who received dexamethasone $10\text{mg}/\text{m}^2$ had significantly increased cholesterol level in comparison to those received it $6\text{mg}/\text{m}^2$.

Conclusions

After induction chemotherapy total cholesterol, HDL and LDL level increased and TG level decreased. Increased cholesterol value was probably due to steroid rather than L- asparaginase.

EP-059

Acute Lymphoblastic Leukaemia

RHINOCEREBRAL MUCORMYCOSES IN CHILD WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

Mucormycosis is rare fungal disease, affecting immunocompromised patients. Rhinocerebral mucormycosis is most common form and has very high mortality rate.

Methods

Here, we present a case of rhinocerebral mucormycosis in pediatric acute lymphoblastic leukemia patient (ALL).

Results

A 2.5-year-old girl diagnosed with ALL presented with febrile neutropenia for the third time during induction phase. First and second line antibiotics were introduced without success. Dark discoloration of hard palate and periorbital edema were noted. Caspofungin was administered due to suspicion of aspergillosis (positive serum galactomannan assay). Due to aggravation of general condition, patient was transferred to PICU. Two days later, dark discoloration of skin was noted at the base of nose. Endocranial CT revealed hyperdense fluid in paranasal sinuses and in nasal cavity. Endoscopic examination of nasal cavity revealed perforation of nasal septum and necrosis of maxillary and ethmoidal sinuses. On 9th day of infection colloid dispersion of amphotericin B was introduced to therapy due to suspicion of mucormycosis. Tissue samples that were taken for histopathology and cultures confirmed diagnosis. Progression of local findings and deterioration of general condition continued and led to respiratory failure. Local surgical intervention was considered but was not performed due to progression of process on cerebral parenchyma as seen on MRI. Patient developed pulmonary hemorrhage and ARDS which led to fatal outcome on 17th day of infection.

Conclusions

Late recognition, aggressiveness of infection and inability to perform radical surgical debridement has led to fatal outcome. This was the first case of mucormycosis at our institution. Rhinocerebral mucormycosis is rare, rapidly progressing disease with high mortality rate. Early diagnosis, resolution of predisposing factors, aggressive surgical intervention and timely use of adequate antifungal agents are cornerstones of successful treatment. Nevertheless, mortality is still high and further efforts must be made to improve outcome of mucormycosis.

EP-060

Acute Lymphoblastic Leukaemia

**METHYLENETETRAHYDROFOLATEREDUCTASE AND GLUTATHIONE S
TRANSFERASE GENE POLYMORPHISMS IN SECONDARY LEUKEMIA**

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Objectives

Therapy-induced leukemia is well-known clinical syndrome occurring as a late complication in patients treated with cytotoxic therapy. We herein present results of analysis of common gene polymorphisms in methylenetetrahydrofolatereductase (MTHFR) and glutathione S transferase (GST) genes in a 10-year-old boy who developed rare type of cancer, acute biphenotypic leukemia, six years after treatment of acute lymphoblastic leukemia.

Methods

We studied *MTHFR* C677T and A1298C and *GSTA1*, *GSTM1*, *GSTT1*, *GSTP1* and *GSTO2* gene polymorphisms to assess role of heritable factors in development of this rare type of childhood secondary leukemia.

Results

Analysis of *MTHFR* gene polymorphisms showed that the patient is homozygous for 677TT and heterozygous for A1298C, which results in lower enzyme activity. Among GST genotypes tested, lower expression *GSTA1*B* gene variant together with homozygous deletion of *GSTM1* was found. Absence of *GSTM1* protein as well as down-regulated *GSTA1* expression and activity could result in lower detoxification potential towards anticancer drugs.

Conclusions

Analysis of *MTHFR* gene polymorphisms showed that the patient is homozygous for 677TT and heterozygous for A1298C, which results in lower enzyme activity. This could confer to increased risk for development of secondary malignancy in several ways. Our results are in accordance with higher frequency of *GSTM1 null* genotype in secondary hematologic malignancies of patients after treatment with cyclophosphamide. It seems reasonable to assume that *GSTM1 null* and lower activity *GSTA1*B/A* genotype resulted in enhanced chemotherapy induced oxidative DNA damage, which could lead to mutations and secondary leukemia.

EP-061

Acute Lymphoblastic Leukaemia

EXPRESSION OF BID, BAK AND BCL-XL IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

The quantitative determination of the expression levels of anti-apoptotic **BCL-XL**, and pro-apoptotic molecules **BAK** and **BID** in bone marrow (BM) of children with acute lymphoblastic leukemia (ALL) at diagnosis and in remission and of children with Solid Tumours (ST) without bone marrow involvement.

Methods

Twenty eight children (15 boys, median age 7,68±1,06 years) with ALL (23 ?-ALL, 5 T ALL), 25 children at diagnosis (ALLd), 23 after remission was achieved (ALLr), and 38 with Solid Tumors at diagnosis without bone marrow involvement, were studied. Total RNA was isolated from bone marrow mononuclear cells. The mRNA levels corresponding to BCL-XL, BAK, and BID were quantified by real-time polymerase chain reaction (PCR) analysis using GAPDH as normaliser. All reactions were performed in duplicates. For quantification of the genes a standard curve was made by serial dilutions of a reference line cDNA (Tanoue).

Results

The expression levels of anti-apoptotic **BCL-XL** were determined significant higher in ALL blasts at diagnosis compared with remission (ALLdvsALLr:3,16vs0,97, $p=0,00001$), as well as with ST (ALLdvsST:3,16vs0,64, $p=0,000000013$). The expression levels of **BID** were determined low at diagnosis of ALL and high enough in remission with statistically significant difference (ALLdvsALLr:4,57vs18,07, $p=0,000001$), result which is in accordance with its apoptotic role. High levels were also observed in ST without BM involvement (ALLdvsST:4,57vs10,329, $p=0,003$). Concerning the expression of apoptotic **BAK** gene, the levels were found statistically significant higher at ALLd compared with ALL in remission (ALLdvsALLr:4,73vs1,84, $p=0,001$). Similar high levels were determined in Solid Tumors with statistically significant differences compared with ALLr (STvsALLr:5,44vs1,844, $p=0,011$).

Conclusions

The over-expression of **BCL-XL** at ALL diagnosis seems to be suppressed by the induction treatment and remission achievement. The expression of **BID** is amplified in remission as a pro-apoptotic molecule stimulating apoptosis. The role of ??? levels at diagnosis and remission in respect to its pro-apoptotic function warrants further investigation

EP-062

Acute Lymphoblastic Leukaemia

DO TRAUMATIC LUMBAR PUNCTURES LEAD TO GREATER RELAPSES IN ACUTE LYMPHOBLASTIC LEUKEMIA? OUTCOME FOR A SINGLE CENTER IN INDIA

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Objectives

The thorn in the success story of treatment in acute lymphoblastic leukemia (ALL) remains relapse. 10-15% patients relapse despite risk adapted therapy. This study was done to address whether traumatic lumbar punctures (TLP) contribute to relapse.

Methods

All children treated for ALL between January 2010 and December 2012 were analyzed. TLP's at diagnosis and subsequently during therapy were evaluated with outcome.

Results

310 children were treated as per UKALL 2003 protocol. Median age: 5 years (1-13). First diagnostic lumbar puncture results- 274: CNS1; 8: CNS3; 28: TLP. TLP patients got 2 extra intrathecal (IT) methotrexate during induction. Overall, 28 (9.0%) have relapsed, with 12 (3.9%) having CNS relapse. 4 patients with a TLP relapsed (2: CNS). A TLP at diagnosis did not correlate with an increased incidence of overall relapse [p=0.966] or CNS relapse [p=0.296]. There was no significant difference in overall Survival (OS) and event free survival (EFS) in children with CNS1 & TLP (OS: 80.2% & 75%; EFS: 70.3% and 64.3%). A total of 3823 IT's were administered. The rate of traumatic LP was 10% (383/3823). Average number of TLP per child was 1.2 (0-7). A receiver operator characteristic curve was generated for prediction of relapse based on TLPs during entire treatment. This offered poor sensitivity [AUC CI: 0.48-0.71]. There were 12 CNS relapses, 6 being asymptomatic and detected on routine CSF examination. These were confirmed by cell count and flow cytometry.

Conclusions

Traumatic LP at diagnosis is not associated with an increased risk of relapse. Possibly, the extra intrathecal ameliorated the effect of TLP. Having more than one traumatic LP during treatment does not increase the risk of a relapse. However, routine CSF malignant cytology surveillance has a role in detecting CNS relapse before the onset of symptoms.

EP-063

Acute Lymphoblastic Leukaemia

CLINICO-HAEMATOLOGICAL PROFILE AND OUTCOME OF ACUTE LYMPHOBLASTIC LEUKEMIA: DEVELOPING COUNTRY EXPERIENCE

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Objectives

Acute lymphoblastic leukemia(ALL)is the most common hematolymphoid malignancy in children.With the advent of new chemotherapeutic protocols and good supportive care,it is highly curable.Aim of this study is to give a comprehensive overview of clinical,haematological presentation,events during therapy,outcome and other significant problems occurred in patients with ALL,as data is lacking from developing country.

Methods

Retrospective data analysis of 174 patients of ALL over a period of 3years(2009-2012),treated and followed at our centre.Infants were treated with interinfant ALL2006 protocol and others with HongKong Singapore(HKSG)1997 protocol.

Results

174 children of age group 3months to 15years were analysed.Median age was 5years.5(2.8%)children were infants.There was male preponderance(66.6%).Majority of them(89.6%)were of Bcell type.Clinically,168(96.5%)patients had fever,54(31%)joint pain,26(14.9%)bleeding manifestations,17(9.7%)pallor and 7(4%) abdominal distension.At diagnosis 60(34%)patients had high WBC count $>50,000/\text{mm}^3$,144(82%) Hemoglobin $<7\text{gm/dl}$ and 107(61.4%) platelet count $<50,000/\text{mm}^3$.12/156(7.6%)patients had CNS disease at diagnosis.Cytogenetic and molecular analysis showed 22-diploidy,23-ETV6/RUNX1,14-tetrasomy21,13-trisomy(12,4,10,17),11-t(1,19),7-hyperdiploidy,6-trisomy-tetrasomy(4,10,11),4-t(9,11),4-t(4,11),3-TCR β translocation,3-9p21 del,1-BCR/ABL,1-monosomy9,30-normal cytogenetics.14/174 children received steroids for few days just prior to diagnosis.According to risk stratification 48(28%) fall in Standard risk,117(67%) Intermediate risk,and 9(5%) High risk.Out of 174children,132 achieved complete remission(CR),2 had resistant disease.Of remaining 40 patients;9-self referral to other hospital,8-loss to follow up,9-refused treatment,14-expired in induction.CNS events occur in 21/148(14%) patients;4-PRES,3-stroke,6-convulsion,1-vitreous hemorrhage,2-CNSgranuloma,3-superior sagittal sinus thrombosis,2-methotrexate toxicity.21/132(16%)patients relapsed among 132 patients of ALL who achieved CR.17(80%) were Bcell type and 4(20%)were Tcell type.72% had very early,14% had early and late relapse each.Nature of relapse was isolated BM in 10(47.6%),BM & CNS in 10(47.6%),CNS & orbit in 1(4.7%).

Conclusions

Most common type of ALL was preB type.Most patients who received steroid prior to diagnosis,resulted in delay in diagnosis and impaired prognostication,therefore it requires better awareness among doctors regarding use of steroids.Cytological analysis reveals that tetrasomy21 and trisomies are most common followed by ETV6/RUNX1.CNS complications are frequent events during ALL therapy and require rapid detection and prompt treatment to limit permanent damage.

EP-064

Acute Lymphoblastic Leukaemia

THE OUTCOME OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA IN PATIENTS WHO PRESENTED WITH HYPERLEUKOCYTOSIS

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Objectives

The patients who have hyperleukocytosis at diagnosis of pediatric acute lymphoblastic leukemia (ALL) constitute 5-22% of patients. Our knowledge about the management of these patients is limited.

Methods

In our retrospective study, 101 patients between 1986-2013, who presented with hyperleukocytosis at diagnosis of ALL were included.

Results

Of the cohort, 40 received St Jude Total XI(Group 1), 46 received Total XIII(Group 2) and 15 received Total XV protocols(Group 3). The median age at diagnosis was 84 months (2-192). All patients received iv alkaline hydration, at least twice of the daily fluid maintenance. Patients were initiated methylprednisolone(MPZ, 0.5-1 mg/kg/day), and if no decrease in WBC in 12-24 hours, vincristine was administered. Cytoreductive treatments such as, leukopheresis and exchange transfusions were applied to symptomatic patients in Group 1 and 2. Cytoreductive treatments were applied in 2 patients(5%) in Group 1, 3 of (6.5%) Group 2. In Group 3, all patients except one who were unresponsive to MPZ and vincristine doses were treated with leukopheresis. In Group 3, leukopheresis was applied in 4(26.6%) of the patients. Eight patients from Group 3 received rasburicase. Of the patients in Group 1 and 2, 9 (%10.4) developed either ICB or pulmonary leukostasis. Five-year EFS in Group 1 and 2 46.2±9.3% and 65±9.8%, respectively (p=0.03). Five-year OS in Group 1 and 2 are 36.6±8% and 65± 8% (p=0.05). Four patients from Group 1 (10%) and 6 (13%) from Group 2 deceased during induction treatment. No death during induction observed in Group 3.

Conclusions

Initiation of lower dose and sequential chemotherapy seems to be rational instead of initiation of all treatment protocol at the same time. In our current practice, we apply cytoreductive treatments more oftenly and early mortalities and morbidities are lesser in this type of approach.

EP-065

Acute Lymphoblastic Leukaemia

L-ASPARAGINASE INDIVIDUALIZED DOSING AND SWITCHING IN ACUTE LYMPHOBLASTIC LEUKEMIA: A NUMBER NEEDED TO TREAT ANALYSIS

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Objectives

L-asparaginase is an important component of chemotherapy for pediatric acute lymphoblastic leukemia (ALL). Five-year event-free survival (EFS) in a recent published study (Vrooman 2013 JCO) was significantly higher with newly-diagnosed ALL patients randomized to individualized dosing (ID) – initial dose of 12,500 IU/m², with adjustments to maintain nadir serum asparaginase activity (NSAA) within 0.1–0.14 IU/mL – vs fixed-dose (FD) (25,000 IU/m²) *Escherichia coli* L-asparaginase (EC-Asnase). Our objective was to compare the number needed to treat (NNT) associated with ID vs FD treatment strategies.

Methods

NNT was calculated as the reciprocal of the absolute risk reduction (1/ARR), where ARR equals control minus experimental event rates. We compared the NNT to prevent one event (relapse or death) with ID vs FD. We also calculated the NNT for switching asparaginase preparations because of silent inactivation (SI), defined as ID patients with NSAA <0.1 IU/mL on successive determinations despite dose adjustment or when coupled with EC-Asnase antibody positivity. NNTs were compared with those for other pediatric oncology interventions by conducting a literature search to identify randomized controlled trials (RCTs) of other interventions in pediatric hematologic and solid malignancies reported in the past 10 years.

Results

Five-year EFS for FD and ID groups was 82% and 90%, respectively (NNT=13 for ID vs FD). FD patients with levels <0.1 IU/mL who never switched preparations had a 5-year EFS of 76% vs 95% for ID patients who switched preparation for SI (NNT=5 for ID with switch for SI vs FD with no switch). Five RCTs in ALL and other pediatric cancers had outcome measures with NNTs ranging from 4 to 50.

Conclusions

These NNT values for ID and for switching asparaginase preparations based on evidence of SI resemble those for well-accepted oncology treatments, highlighting the value of monitoring to prospectively identify suboptimal asparaginase activity and SI.

Analysis funded by Jazz Pharmaceuticals plc or its subsidiaries.

EP-066

Acute Lymphoblastic Leukaemia

A NEW TRANSCRIPT OF GNAO1 IN CHILDHOOD ALL

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Objectives

To Research the transcription methods of GNAO1 in Childhood ALL tumor cells.

Methods

GNAO1 mutations were found in 16 cases of childhood ALL tumor cells in whole exome sequencing, but in the course of the experiment transcripts that had been reported couldn't be cloned, so there might be a new GNAO1 transcript variant in childhood ALL tumor cells. Designed the gene-specific primers(GSP) of GNAO1, used RNA of TEL-AML1-positive children to reverse transcription and PCR by SMARTer RACE cDNA amplification kit, then obtained the complete sequence of the new GNAO1 transcript by sequencing.

Results

Used SMARTer RACE cDNA amplification kit and obtained the first strand reaction product according to experimental corresponding steps. After prepared Master Mix, added the first strand reaction product and the mixture of RACE universal primers(UPM), GSP1, GSP2, and GSP1 and GSP2 of relevant control samples in 0.5ml PCR tubes, after PCR amplification specific bands were obtained. The PCR product were processed by gel extraction , cloning and transformation in plasmid, then delivery the plasmid genome sequence for sequencing, the complete sequence of the new GNAO1 transcript was obtained. There were complete UPM sequence at 5'-end, complete UPM sequence and poly A at 3'-end. The new GNAO1 transcript had 7 exons, exon1 and exon2 were not reported yet. The new exon1 located between exon2 and exon3 from GNAO1-001 and GNAO1-002 transcript, the new exon2 located between exon3 and exon4 from GNAO1-001 and GNAO1-002 transcript, new exon3~exon7 were corresponding to exon4~exon8 from GNAO1-002 transcript.

Conclusions

A new transcription method of GNAO1 exists in Childhood ALL tumor cells.

EP-067

Acute Lymphoblastic Leukaemia

THE ANALYSIS OF THERAPEUTIC EFFECT OF HIGH DOSE OF CYTARABINE PLUS L-ASPARAGINASE IN CHILDREN OF ACUTE LYMPHOBLASTIC LEUKEMIA WITH MRD

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Objectives

To analyze the therapeutic effect and safety of high dose of Cytarabine combined with L-Asparaginase in minimal residual disease (MRD) of childhood acute lymphoblastic leukemia (ALL).

Methods

Four color fluorescence antibody labeling method was used to monitor the dynamic changes of the MRD in children with ALL. Total 21 cases of patients (17 cases of high risk, 1 case of moderate risk, 3 cases of low rise) were considered MRD positive after remission, including 13 male cases and 8 female cases with average age 81.38 months, ranging from 9-156 months. All patients were treated with combination chemotherapy (Cytarabine 2g/m², d1-2, etoposide 100mg/m², d3-5, L-Asparaginase 25000u/m², d6, dexamethasone 10mg/m², d1-6). The efficacy, survival time and adverse events of all patients were statistically analyzed using SPSS 19.0.

Results

The levels of MRD of 21 patients were tested after one month chemotherapy, while 17 of which turned negative and 4 of which decreased yet still positive. The patients were followed up to Dec 2013, 5 of who relapsed and 3 died. The recurrence rate was 23.80%, and the 4 years probability of an event-free survival and the overall survival were 77.6% and 80.4% respectively.

The dose-limiting toxicity includes grade 0 to 3 diarrhea and nausea; grade 2-4 neutropenia associated with fever, 2 cases with grade 2 liver function damage. There were not treatment-related deaths.

Conclusions

It is showed that high dose of Cytarabine combined with L-Asparaginase can effectively improve the prognosis of childhood ALL with positive MRD. The adverse events could be well tolerated.

EP-068

Acute Lymphoblastic Leukaemia

A RARE COMPLICATION OF DASANITIB IN A REFRACTORY-IMITANIB-RESISTANT ACUTE LYMPHOBLASTIC LEUKEMIA CASE: HEMORRHAGIC CYSTITIS AND COLITIS

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Objectives

Dasanitib is a new generation tyrosine kinase inhibitor used in high risk childhood acute lymphoblastic leukemia (ALL) cases having Philadelphia chromosome with BCR-ABL fusion gene. In literature side effects associated with Dasanitib treatment commonly reported in adults. In this case report, a 7 year-old child diagnosed with refractory-imitanib-resistant acute lymphoblastic leukemia presented with hemorrhagic cystitis and colitis after Dasanitib treatment.

Methods

7 year old child diagnosed with ALL resistant to imitanib treatment was enrolled to Dasanitib therapy.

Results

48 hours after initiating Dasanitib therapy hemorrhagic diarrhea was started. Stool culture result was negative in terms of pathogen agents. Hemoglobin levels were detected as 6 gr/dl, Dasanitib therapy was stopped and steroid treatment was started. Hematological parameters and clinical status were improved 48 hours after cessation of Dasanitib therapy therefore low dose Dasanitib was restarted. During the follow up period blastic white cell counts were decreased progressively and dosage of Dasanitib was increased. Dysuria presented with massive haematuria was developed after adjustment of dosage. Renal functions was normal and thrombocytopenia or coagulopathy were not defined. Urinary system ultrasonography and urine sample results were normal. Patency of urinary system tract was ensured by catheterization of bladder and haematuria was improved completely after 2 days discontinuation of Dasanitib treatment.

Conclusions

Dasanitib is a new tyrosine kinase inhibitor and useful in cases resistant to imitanib treatment for acute lymphoblastic leukemia. Gastrointestinal system side effects associated with Dasanitib treatment are related with infiltration of T cells on epithelial surfaces. The beneficial effects of steroid treatment against to side effects of Dasanitib maybe considered as a result of T cell activation. Although imitanib is a substrate of p glycoprotein dasanitib is not, so this property of Dasanitib is an important factor about development of drug resistance in terms of kinases family. Clinicians should be keep in mind the potential side effects of Dasanitib when its usage is essential.

EP-069

Acute Lymphoblastic Leukaemia

THE EXPRESSION AND SIGNIFICANCE OF TLR-4 AND BCL-XL IN CHILDREN WITH ACUTE LEUKEMIA

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Objectives

To examine the expressions of TLR-4 and Bcl-xL in bone marrow cells in children with acute leukemia (AL) and to detect a relationship with the classification, clinical features, therapeutic effects and prognosis of AL.

Methods

Using the SABC method of immunohistochemical staining, expressions of TLR-4 and Bcl-xL in the bone marrow cells of 76 cases with AL were detected.

Results

The expressions of TLR-4 and Bcl-xL in the initial treatment, refractory relapse and relief groups were obviously higher than that in the control group ($P < 0.05$).

There was no significant difference in the expression of TLR-4 and Bcl-xL between the acute lymphoblastic leukemia (ALL) and acute nonlymphoblastic leukemia (ANLL) groups

($t = 1.023, t = 1.037; P > 0.05$). The expressions of TLR-4 and Bcl-xL in the complete

remission (CR) group were lower than that in the initial treatment group

($t = 3.577, t = 3.895; P < 0.05$). The expression of TLR-4 in the refractory relapse group was higher than that in the initial treatment group ($t = 3.921, P < 0.05$). However, high expression of Bcl-xL occurred both in the initial treatment group and the refractory relapse group,

and there was no significant difference ($t = 0.916, P > 0.05$). Pearson rank correlation analysis indicated that there was a positive correlation between the expression of TLR-4 and Bcl-xL ($r = 0.653, P < 0.05$). Statistical analysis showed that the CR rates in patients with negative expression of TLR-4 and Bcl-xL were remarkably higher than that with positive TLR-4 and Bcl-xL expression ($P < 0.05$).

Conclusions

Expressions of both TLR-4 and Bcl-xL play a role in onset, progression and prognosis of AL, and the two may act synergistically in the onset and development of AL.

EP-070

Acute Lymphoblastic Leukaemia

OUTCOME OF RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA WITH MODIFIED ALL-REZ BFM 96 PROTOCOL IN CHINA

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Objectives

Acute lymphoblastic leukemia (ALL) is the commonest childhood malignancy and modern treatment has achieved steady improvement with long-term survival up to 80%.

Nevertheless, approximately 20% of patients would experience relapse of the disease which remains the major cause of treatment failure.

Methods

We started a new relapsed acute lymphoblastic leukemia (ALL) treatment protocol based on modified ALL-REZ BFM 96 protocol aiming at improving the treatment outcome in Chinese children. All patients with first relapse of childhood ALL from 2003 to 2012 were included. Patients were stratified into four risk groups (S1, S2, S3, and S4) and the treatment consisted of intensive chemotherapy followed by allogeneic hematopoietic stem cell transplantation (HSCT) if indicated.

Results

Thirty-nine patients were recruited and median age at diagnosis of ALL was 6.2 (range 4.5–14) years. The median time from initial diagnosis to relapse was 2.5 (range, 0.6–5.2) years. The risk group (standard risk group, intermediate group and high risk) rates with initial diagnosed patients were 28.2%, 35.9% and 35.9%. Nineteen patients (48.7%) achieved second complete remission (CR2). CR2 rates for S1, S2, S3, and S4 groups were 100%, 81.2%, 33%, and 15.4%, respectively. Five-year overall survival (OS) was 30.8%. OS for S1, S2, S3 and S4 patients were respectively 100%, 56%, 11%, and 7.7%.

Conclusions

We should be alert on the standard risk group patients with initial diagnosis. The relapse of children with relapsed ALL of S1 and S2 risk groups could be well treated with intensified treatment protocol. HSCT could improve the survival rates with S2 group. The S3 and S4 group needs more innovative approach to improve treatment outcome.

EP-071

Bone Tumours

SURVIVAL IN PEDIATRIC PATIENTS WITH OSTEOSARCOMA: RESULTS FROM THE PEDIATRIC HEMATOLOGY AND ONCOLOGY GROUP OF TOLUCA VALLEY MÉXICO

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Objectives

The objective of this study was to assess the survival of pediatric patients with osteosarcoma treated at two hospitals in the Toluca Valley, Mexico, as well as the factors relating to this

Methods

Is a study of course clinical and prognosis of patients with diagnosis of osteosarcoma, evaluating characteristics demographic clinical, paraclinical of disease, and factors of risk, as well as clinical features time survival, medical treatment and surgical as well as possible factors related to this type. We used Kaplan-Meier analysis

Results

In the period from March 1999 to March 2014 diagnostic osteosarcoma in 30 patients, with age from 3 to 16 years, 60% male, the most frequent site was followed by proximal humerus distal femur 85% with metastatic disease at diagnosis, being only 4 patients candidates for preservation of limb. Five patients died early. Survival in patients with metastatic disease was 25% at 12 months and disease not metastatic from 45% to 36 months. All patients received neoadjuvant chemotherapy with doxorubicin and cyclophosphamide and etoposide adjuvant cisplatin. Only one patient with disease not metastatic to the diagnosis was also mifamurtida.

Conclusions

Advances in chemotherapy treatment as well as the use of biological therapies have achieved a significant increase in survival in pediatric patients with osteosarcoma, however in developing countries, the late diagnostic decrease exponentially the survival, due mainly to high tumor burden in the diagnosis limiting access to the limb preservation surgery as well as the use of biological therapies. We are carrying out training to staff of first contact for the early detection of cancer in childhood, whose impact on survival will be measurable in some years.

EP-072

Bone Tumours

ICE REGIMEN FOR RELAPSED/REFRACTORY BONE AND SOFT TISSUE SARCOMAS

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Objectives

Patients with recurrent or refractory sarcoma have dismal prognosis. In this study response to treatment and outcome of children with recurrent/refractory sarcoma who were treated with ICE regimen were retrospectively evaluated.

Methods

Patients with relapsed/recurrent bone and soft tissue sarcoma treated with ICE regimen were selected and their demographic and clinical characteristics and treatment results were analyzed. ICE regimen was given as ifosfamide (3gr/m²/day on day 1-2), carboplatin (450 mg/m²/day on day 1) and etoposide (100mg/m²/day on day 1-3).

Results

66 patients (45 boys and 21 girls) were evaluable for response to treatment. Median age at diagnosis was 8,3 (ranged 0.5-17.2). Tumor types were rhabdomyosarcoma (n=26), Ewing sarcoma (n=21), osteosarcoma (n=11), pPNET (n=7) and undifferentiated sarcoma (n=1). Total 44% of patients had metastatic disease at diagnosis. ICE regimen was given median 6.3 months after diagnosis due to relapsed/refractory disease. Patients received median 5 cycles (ranged 1-9). The ORR was 58% (complete response: 28%, very good partial response: 3%, partial response: 12% and stable disease: 15%). Median duration of response and OS after ICE were 8.2 months and 25.8 months. Two-year EFS and OS rates were 27% and 63%. OS rates were significantly increased in responders (97% vs. 67%, p<0.0001). 1-yr EFS rates for rhabdomyosarcoma, Ewing sarcoma, osteosarcoma and pPNET were 54%, 17%, 43% and 27% (p=0.04).

Conclusions

The treatment of relapsed or refractory sarcomas remains challenging. The ORR and OS rates were significantly improved in patients with response to treatment or rhabdomyosarcoma after ICE regimen. The results showed ICE is valuable therapeutic option for relapsed/refractory sarcomas.

EP-073

Bone Tumours

SYSTEMIC AND REGIONAL HEMODYNAMICS IN CHILDREN AND ADOLESCENTS WITH BONE SARCOMAS

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Objectives

To study the hemodynamic of lower extremities taking into account of cardiac output and volume of tumors in patients with bones sarcomas.

Methods

Analysis of data obtained during of the initial ultrasound examination of the 49 patients aged 8-18 years with morphologically proven bone sarcomas lower extremities was performed. Were estimated: cardiac output (CO), volume of blood flow in main femoral artery (Q ml/min), indices - resistance and pulsation (RI, PI), as well as size of their percentage deviations for the affected limb compared with the contralateral (%Q, %RI, %PI).

Results

In system 'organism-tumor' were noted the change in cardiac output with increasing tumor volume ($r = 0.41$; $p < 0.05$), so-called 'systemic effects of the tumor' on the background of the interdependence of volume blood flow in the main artery of the affected and healthy limbs ($r = 0.68$; $p < 0.05$). Herewith a negative correlation between index value of %Q and blood flow to the healthy limb - Q ($r = -0.42$; $p < 0.05$), is confirmation, that one of component of hemodynamic changes there is redistributive blood flow. Was established the correlation volume of malignancies and %RI, %PI ($r = 0.35-0.38$; $p < 0.05$) too. That is, there has been a decrease in regional vascular tone in affected limbs.

Conclusions

Pathological mechanisms of hemodynamic support of affected limb may include systemic increase in CO, regional changes in vascular tone and against this background - the redistribution of certain volumes of blood from healthy to affected limb.

EP-074

Bone Tumours

IS THERE A ROLE FOR THROMBOPROPHYLAXIS IN PEDIATRIC SARCOMA PATIENTS? A LITERATURE REVIEW FOCUSING ON EPIDEMIOLOGY, RISK FACTORS AND OUTCOMES OF THROMBOEMBOLISM IN SARCOMA PATIENTS

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Objectives

Thromboembolism (TE) is a common complication of cancer in children, including those with sarcoma. TE causes significant morbidity and mortality in this patient population. Currently thromboprophylaxis is not recommended for pediatric sarcoma patients (PSP). We reviewed literature to describe epidemiology, risk factors and outcomes of TE in PSP and to evaluate thromboprophylaxis practices in PSP.

Methods

English language articles were searched on PUBMED using terms "sarcoma & thrombosis" and "sarcoma & thromboembolism" for time period between 1995 and 2013. Studies describing epidemiology, risk factors, outcomes and/or thromboprophylaxis in PSP or adult sarcoma patients (ASP) and TE were reviewed. Case reports were excluded.

Results

Among four reviewed studies, the average incidence of TE in PSP was 14% (7-16%), which is 3.5 fold higher than described in adults (4%). Audino (2013) described lower incidence (3%) in PSP, however it was limited to inpatients.

Central venous catheter (CVC) dysfunction is the only statistically significant risk factor described for PSP (Athale, 2007), while trend towards clinical significance has been described for metastatic disease (Paz-Priel, 2007). Important adult risk factor of hip/thigh disease has not been studied in PSP.

TE-related mortality, though infrequent, is reported. Significant morbidities include CVC removal, recurrent TE, post-thrombotic syndrome and delay in cancer treatment.

Nowak-Gottl (1999) used 6-12 weeks of low molecular weight heparin thromboprophylaxis in children with bone sarcomas (n=75); none developed TE. However, this study lacked a control group. A recent survey of oncologists, including medical and surgical, was published by Crocco (2013) describing use of mechanical and/or chemical prophylaxis by 43% of respondents.

Conclusions

Incidence of TE in PSP is higher than ASP, despite age and lifestyle related risk factors. Yet, thromboprophylaxis is recommended for ASP post-definitive surgery. Evidence for thromboprophylaxis in PSP is very limited, hence larger studies are urgently required to define the role and timing thromboprophylaxis in select PSP.

EP-075

Bone Tumours

SKIP METASTASES IN OSTEOSARCOMA: THE ST. JUDE CHILDREN'S RESEARCH HOSPITAL EXPERIENCE

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Objectives

The presence of synchronous regional bone metastases (known as “skip” metastases) in osteosarcoma has historically been associated with poor clinical outcome. This study describes our experience with osteosarcoma and skip metastases over a 27-year period.

Methods

A retrospective review was conducted of patients treated at St. Jude Children's Research Hospital with newly diagnosed osteosarcoma between January 1986 and December 2013, with radiographic and/or histopathological evidence of skip metastasis. Data evaluated included clinical characteristics, surgical and medical treatments, histologic response, and clinical outcomes. Event-free survival (EFS) and overall survival (OS) were estimated, and clinical and pathologic factors were correlated with outcome.

Results

Skip metastases were identified in 12/382 patients (3.1%). Median age was 13.3 years (range 6.2–19 years). 6 patients presented with additional metastatic sites (5 with pulmonary nodules, 1 with a locoregional lymph node). Of 11 patients that received neoadjuvant chemotherapy and were evaluable for histologic response, 6 patients (54.5%) had a good response of greater than 90% necrosis. 7 (56.3%) developed recurrences (6 with lung nodules, 1 with local/lung disease). The one with local relapse had positive margins at the site of the skip metastasis. 6 patients were alive with median follow-up time of 58.7 months (range 4-132 months), 2 with active disease. 5 year EFS was 36.7% (SE 14.6%) and OS was 50% (SE 15.8%). Tumor necrosis greater than 90% approached significance for OS (p=0.06). 4 patients without other metastatic sites at diagnosis were alive, compared to 2 who presented with pulmonary nodules; sample size was not large enough to determine a difference between these groups.

Conclusions

Skip metastases occur rarely in osteosarcoma. Outcomes may be suboptimal compared to localized osteosarcoma without skip lesions, even in the absence of other disease sites. Histologic response to chemotherapy may still predict likelihood of survival in this unique subset of patients.

EP-076

Bone Tumours

PROPOSAL FOR FUNCTIONAL REHABILITATION PHYSICAL THERAPY IN A PATIENT UNDERGOING TOTAL INTERNAL HEMIPELVECTOMY TYPE IV

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Objectives

Malignant primary bone tumors are rare . It mainly affects children and young adults , and may occur anywhere in the body. With the emergence of more effective drugs in the treatment and technical improvement of surgeons , internal hemipelvectomies (IH) with surgical removal of the hemipelvis or part of it , preserving more of the limb were conducted generating a challenge rehabilitation of patients. IH consists of resection of bone and affected tissues of the pelvic girdle with limb salvage, as Enneking classification.

Demonstrate the functional outcome after rehabilitation for total IH type IV.

Methods

On the first postoperative physical therapy evaluation is performed considering muscular strength, range motion , lung capacity , sitting balance , and posture in bed vascularity . Directed global cinesioterapia , changing positions , balance training in the sitting position , kinetic respiratory maneuvers and positioning of the affected limb . After discharge the patient is referred for outpatient physiotherapy where the following aspects are evaluated: muscular strength , range of motion , balance , proprioception , gait. After an evaluation is performed global cinesioterapia , stretching, strengthening , Russian current , gait training with or without support , partial and full weight bearing , workout static and dynamic balance with and without support , partial and full weight bearing , balance training static on a limb.

Results

On average after 8 months of physical therapy patient ambulation with support of crutches and has excellent balance without support any type of prosthesis or arthrodesis to reconstruct the pelvis ,the extensive fibrosis, allows the patient do weight bearing on the affected limb , despite the shortening.

Conclusions

The functional outcome in patients with total internal hemipelvectomy through a specific and intense physical therapy rehabilitation can positively influence the quality of life .

EP-077

Bone Tumours

RESULTS WITH AN INTENSIVE CHEMOTHERAPY REGIMEN WITHOUT METHOTREXATE FOR THE TREATMENT OF PEDIATRIC HIGH-GRADE OSTEOSARCOMA. EXPERIENCE AT THE INSTITUTO NACIONAL DE PEDIATRÍA, MÉXICO

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Objectives

In Mexico, pediatric high-grade osteosarcoma (HGO) occupies the fifth place of all pediatric cancers, representing the 4.4%. It presents with a high incidence of metastatic pulmonary disease and large primary tumor volume at diagnosis resulting in poor survival.

We described the results from a recent cohort treated with a systemic chemotherapy regimen without methotrexate at the Instituto Nacional de Pediatría, Mexico City.

Methods

A retrospective, longitudinal and clinical study was performed from January 2005 to January 2012. Fifty-five patients younger than 18 years with extremity HGO and no prior chemotherapy treatment were included. All patients received a chemotherapy regimen without methotrexate based on a 10-week neoadjuvant chemotherapy regimen (6-courses) with cisplatin 120mg/m² plus doxorubicin 75mg/m², and a 15-week adjuvant treatment (5-courses) of cyclophosphamide 1800mg/m² by course given in two therapeutic arms, with a 9000 mg/m² total dose for non metastatic patients, and a gradually climbed doses by course up to 12,000 mg/m² for metastatic or bad responders patients, both arms plus etoposide 900mg/m² by course.

Results

Pulmonary metastases presented in 58.2% at diagnosis. Osteoblastic histology prevailed; 36.4% underwent amputation procedure and 15 (27%) limb disarticulation; 22% had limb-sparing surgery. Only 18.2% were good responder patients to neoadjuvant-chemotherapy. Five-year overall survival (OS) for non-metastatic patients was 70% and 35% for metastatic patients (p=0.016). Five-year event-free survival (EFS) for non-metastatic was 65% and 30% for metastatic patients (p=0.032). Five-year OS for good responders was 80% and 50% for bad responders (p=0.009). No important toxicity and no second malignancies were reported at this point of the follow up.

Conclusions

This intensive and short chemotherapy regimen without methotrexate, with relatively few adverse events, improved outcome in OS mainly, and was able to achieve similar outcomes in EFS as the most current series reporting 3-year EFS from 60% to 70% for patients with localized, extremity osteosarcoma.

EP-078

Bone Tumours

LONG TERM FOLLOW UP OF EWING SARCOMA PATIENTS: THE MEMORIAL SLOAN KETTERING EXPERIENCE

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Objectives

We aimed to determine long-term overall survival (OS) and characterize second malignant neoplasms (SMN) for a cohort of 305 patients diagnosed with Ewing Sarcoma (ES) and treated at a single institution from 1974 through 2012.

Methods

We performed a retrospective chart review on eligible ES patients. IRB approval was obtained prior to review. Individuals were excluded if they were not at least 6 months off therapy at time of review, or if they had not received >70% of their chemotherapy at MSKCC. Overall survival with 95% confidence intervals (CI) was assessed with Kaplan-Meier estimates and Cox proportional hazards regression. Cause-specific mortality was evaluated with the cumulative incidence function accounting for competing risks.

Results

We assessed outcomes in 305 patients (40.3% female; 12% racial/ethnic minorities) treated consecutively from 1974 to 2012. Primary site was bone in 78.4%, soft tissue in 21.6%. Median age at diagnosis was 16 years (range, 0.3 to 40); median interval from cancer diagnosis to last contact was 7.8 years (range, 1.3 to 37.2). Relapses occurred in 110 patients (36%); 93% occurred within 5 years of diagnosis. There were a total of 23 SMNs (9 MDS-AML, 6 solid tumors, 3 melanomas, and 3 non-melanoma skin cancers). Five-year OS was 65% (95% CI: 60%-70%). There were 80 deaths related to relapsed/progressed ES and the cumulative incidence of death due to ES at 5 years was 25%; 32 deaths were due to other causes. In multivariable model, racial/ethnic minority ES patients were 2.3-times more likely to have poor OS than white non-Hispanic patients (95% CI: 1.1-1.7). Older age at diagnosis was also associated with poor OS (for every 10 years increase in age, hazard ratio=1.4; 95% CI: 1.1-1.7).

Conclusions

Overall survival and SMN risk remains suboptimal for patients with Ewing Sarcoma, highlighting the need for new targeted therapeutics.

EP-079

Bone Tumours

ZOLEDRONIC ACID FOR THE TREATMENT OF CHILDREN WITH REFACTORY GIANT CELL TUMOR OF THE JAW

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Objectives

No approved systemic therapies currently exist for the treatment of pediatric giant cell tumor of the jaw (GCT)/central giant cell granuloma. Although the bisphosphonate zoledronic acid (ZA) has been used with success in adults, its use in pediatrics has been limited due to concern for effects on bone health and growth arrest. We review the outcome of pediatric GCT treated with ZA at our institution.

Methods

Data were collected by retrospective chart review of patients with GCT treated with ZA at Children's Hospital Los Angeles between January 2006 and December 2013. 4 mg/m² (4 mg max dose) ZA was administered intravenously every 4 weeks.

Results

Four patients (3 females, 1 male) between the ages of 3 months and 15 years were treated with ZA. Patient A was a 3 month old female with incompletely resected maxillary GCT. She received ZA as primary treatment due to unacceptable risk of interferon treatment, and achieved tumor remission after 4 courses. She is in remission one year following therapy. Patient B and C received ZA as second-line therapy for recurrence after surgical resection and interferon therapy. The recurrent lesion was surgically resected followed by 3 courses of ZA. While Patient B is disease free for four years, Patient C developed a local tumor recurrence two years after treatment, which was successfully resected. Patient D had an underlying diagnosis of osteoglophosis dwarfism and had refractory GCT resulting in administration of multiple regimens, including ZA. She experienced disease progression following 6 courses. Side effects of ZA included flu-like symptoms, electrolyte abnormalities including hypocalcemia and hypophosphotemia which were mild and asymptomatic. No effect on projected anthropometric growth parameters was noted.

Conclusions

Our results demonstrate that therapy with ZA is a reasonable and well-tolerated option for children with relapsed or refractory GCT, though larger studies are needed to demonstrate efficacy.

EP-080

Bone Tumours

PREDICTORS OF INFECTION IN PROXIMAL TIBIA ALLOGRAFT AND ALLOGRAFT-PROSTHESIS COMPOSITE RECONSTRUCTIONS

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Objectives

Reconstruction of the proximal tibia after wide resection is challenging. Advocates argue advantages to include bone preservation, biological reconstruction that facilitates reattachment of the extensor mechanism and other soft-tissue structures, metallic prosthesis use delay, and distal femoral growth plate preservation. Complications are numerous, infection being the most common. It is believed that infection correlates with the poor soft-tissue coverage seen in this area. This investigation evaluates our experience with 32 patients, analyzing incidence and management of infection.

Methods

32 patients(17 males, 15 females), average age 13 years old(2-18) who underwent 33 allograft proximal tibia reconstructions were evaluated for occurrence of infection. Potential predictors of infection categorized as pre and perioperative factors were analyzed in terms of risk for developing allograft infection.

Results

Twenty-three patients had Osteosarcoma and the the remaining 9 patients had Ewings sarcoma. Most reconstructions(21) were osteoarticular allografts. Fifty percent of patients had flap coverage at the index procedure. Allograft survival rate was 73% at 4.6 years. Allograft infection rate was 15%. Two patients were converted to a metallic endoprosthesis, 2 to a new allograft, and 1 to a knee disarticulation. Most common complications were wound dehiscence(48%), non-unions (33%) and allograft fractures (24%). No predictors of infection could be identified. A trend of lower WBC was noted in patients who developed infections; however not statistically significant. All patients who developed infections had a previous wound dehiscence. 56% of wound dehiscences had a positive bacterial culture. However, only 30% progressed to allograft infection.

Conclusions

Despite being unable to identify predictors of infection, we recommend nutritional and immunological optimization of patients before surgery and a low threshold for flap coverage at the index surgery. Wound dehiscence is a common complication for which aggressive surgical treatment is recommended to avoid progression to allograft infection. Allograft infection reduction rate as high as 25% can be attained with this approach.

EP-081

Bone Tumours

USE OF MIFAMURTIDE AND STEROID IN A PATIENT WITH OSTEOSARCOMA AND CHRONIC RENAL FAILURE SECONDARY TO CISPLATIN

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Objectives

A case report of 13-year-old boy with non-metastatic osteoblastic osteosarcoma is presented.

Methods

Patient presented May 2011 referring pain at right leg, secondary to contusion, not responding to analgesics, increased extremity volume and claudication. Tumoral lesion at right tibia on X-ray; Computed Tomography (CT) and Magnetic Resonance Image (MRI) showed an 11x5x6cm lesion, involving adipose tissue and adjacent muscles, thoracic CT was negative for metastasis. Bone scan showed a single focal well delimited concentrate augmentation at proximal metaphysic area. Chemotherapy with cisplatin 120mg/m² plus doxorubicin 25mg/m² for 3 days, alternating with cisplatin 120mg/m².

Results

After 5th cycle presents severe emesis, dehydration and acute renal failure (ARF), creatinine 8.8mg/dl, BUN 114, urea 243.9mg/dl, oliguria; uremic encephalopathy. Partial improvement: creatinine 13.3mg/dl, BUN 92, urea 196mg/dl. Steroid pulses initiated continuing with prednisone as maintenance. Renal ultrasound showed bilateral glomerulonephritis. Bilateral renal scan reveals deficient renographic curves in 3 phases, mainly excretory, high depth activity suggesting chronic renal failure (CRF): right kidney 47% function and effective renal plasma flow (ERPF) 54.63 while left kidney 53% function and ERPF 51.46. After 3 months creatinine 5.3mg/dl. Chemotherapy continued without cisplatin and with steroids. CT showed tumor 6x4x4cm, limb salvage November 2011. Adjuvant cycles with cyclophosphamide-escalated from 300mg/m² up to 650mg/m² and etoposide 200mg/m², for 8 cycles. Mifamurtide 2mg/m² initiated one month after surgery, total 48 doses, 15 doses while steroid treatment. Vigilance started February 2013. Last thoracic CT and bone scan negatives with a follow up of 14 months.

Conclusions

Cisplatin is a highly effective chemotherapeutic agent. One of its limiting side effects is nephrotoxicity that may lead to CRF. As reported by Venkatakrishnan et al, mild-moderate renal impairment does not alter the clinical pharmacokinetics or pharmacodynamics of mifamurtide; no dose modifications appear necessary for these patients, in this case the steroids also seem not interact with mifamurtide.

EP-082

Bone Tumours

A NEW META-ANALYSIS IN MDM2 SHOWS NO ASSOCIATION BETWEEN rs2279744 AND rs1690916 AND RISK OF OSTEOSARCOMA: CRITICAL STUDY

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Objectives

A recent systematic review on osteosarcoma concluded that two murine double minute 2 (*MDM2*) polymorphisms, rs2279744 and rs1690916, had an impact on disease risk. However, we and other authors have detected several weaknesses in the study such as inaccuracies in the analyses performed.

Therefore, the aim of the present study was to analyze whether *MDM2* polymorphisms increased the risk of osteosarcoma.

Methods

First, we studied the effect of rs2279744 and rs1690916 on two different osteosarcoma populations from Spain (n=113) and Slovenia (n=58) and their corresponding controls (n=166 and n=91; respectively). Second, we performed a meta-analysis with all the studies performed so far, including the two previous populations.

Results

The results in the two populations analyzed and the meta-analysis allowed to conclude that the two *MDM2* polymorphisms analyzed do not statistically increase the risk of osteosarcoma, in contrast to the previous meta-analyses. Data about the discussion of our results compared to the previous meta-analysis will be also shown.

Conclusions

The *MDM2* polymorphisms rs2279744 and rs1690916 do not increase the risk of osteosarcoma.

This project was supported by RETICS (RD12/0036/0060), UPV/EHU (UFI 11/35) and Basque Government (IT661-13).

EP-083

Bone Tumours

NON CODING RNAS AS NEW MARKERS OF SUSCEPTIBILITY TO OSTEOSARCOMA

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Objectives

Osteosarcoma is the most common primary malignant bone cancer in children and young adults. Susceptibility to osteosarcoma is due to complex and multiple genetic factors. Non coding RNAs (ncRNAs), specifically long non coding RNAs (lncRNAs) and microRNAs (miRNAs), have been shown to be deregulated in diverse kinds of cancers, including osteosarcoma, showing their importance in the disease. Alterations in the ncRNA expression levels or in their function can be attributed to genetic polymorphisms. In fact, a recent study has found association between a polymorphism in miR-34b and osteosarcoma risk. The aim of this study was to evaluate the role of ncRNAs-related SNPs in susceptibility to osteosarcoma.

Methods

We analyzed blood samples from 122 osteosarcoma patients from two different populations, Spain (n=77) and Slovenia (n=45) and their corresponding controls (n=321 and n=96, respectively). In total, 235 SNPs in 222 miRNAs and 127 SNPs in 16 lncRNAs were genotyped by using the VeraCode GoldenGate Genotyping Assay from Illumina.

Results

Previous results from our group showed that SNPs in processing genes and miRNAs were associated with the risk of osteosarcoma. Therefore we decided to extend the study analyzing two different populations and increasing the number of samples and polymorphisms. Our preliminary results show that polymorphisms in ncRNAs are associated with osteosarcoma. These results are being confirmed.

Conclusions

Our results suggest that SNPs in non coding RNAs may affect osteosarcoma susceptibility. This project was supported by RETICS (RD12/0036/0060), UPV/EHU (UFI 11/35) and Basque Government (IT661-13).

EP-084

Bone Tumours

RADIOFREQUENCY ABLATION FOR EPIPHYSEAL CHONDROBLASTOMAS IN CHILDREN – EMERGENCE OF A NEW MODALITY OF TREATMENT

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Objectives

Chondroblastoma are treated by curettage and bone grafting with risk of injury to articular surface or growth plate. Minimally invasive technique like percutaneous radiofrequency ablation (RFA) has been attempted as an alternative to surgical interventions. Present study was done to demonstrate the safety and efficacy of RFA as an novel alternative to surgery in chondroblastomas. We also evaluated the functional and Oncological outcomes.

Methods

Between January 2010 and January 2014, we treated 8 cases of chondroblastomas with RFA. All were males with a mean age of 17.5 years (range 13-21 years). All cases were primary with involvement of proximal femur in 3 cases, proximal tibia in 3 and proximal humerus & distal femur in 1 case each. The procedure was done with computed tomography guidance. Lesion was biopsied, confirmed on frozen and then treated with RFA in the same setting. The Clinical symptoms, range of movements, radiographs and MSTS score were assessed before, 24 hours, 6 weeks and then every 3 months after the procedure

Results

Significant relief of symptoms was noted on the immediate post procedure day in all patients after a single session of RFA. No patient required a repeat procedure or surgical curettage. All the patients had complete relief of symptoms with no need of any medical assistance at first follow up (6 weeks). All patients are available for final evaluation with a median follow up of 28 months (range, 3 to 50 months). There was no recurrence or treatment related complications. All patients returned to the pre disease activity level with average MSTS Score of 29 at last follow-up.

Conclusions

Percutaneous RFA is safe, effective, less morbid and minimally invasive alternative to surgery for the management of epiphyseal chondroblastoma of the extremity

EP-085

Bone Tumours

ONCOLOGICAL OUTCOME OF PEDIATRIC EXTREMITY SKELETAL CHONDROSARCOMAS AT A TERTIARY SARCOMA TREATMENT CENTRE

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Objectives

Chondrosarcoma is the third most common primary bone tumour with late recurrences leading to 10-year survival rates below 50%. They are uncommon in children (<10%). Present study was done to analyse the outcomes of chondrosarcoma in pediatric population

Methods

Between 2001 and 2010, 372 cases of musculoskeletal chondrosarcoma were treated. Ten of these patients (2.6%) were under 21 years and were included in this study. All patients underwent pre surgical staging. The site of disease was humerus in 4, pelvis in 3, and one each in tibia, clavicle, scapula and femur. 7 patients had primary disease and 3 secondary (enchondromatosis 1; multiple osteochondroma 2). The mean duration of follow up was 35 months (range 6 months – 84 months).

Results

Of 10 cases, 1 was metastatic at presentation,(lungs) and Two had pathological fracture. Nine had limb salvage and 1 had amputation. Margins were free in 8, microscopic positive in 2. The final histopathology was mesenchymal chondrosarcoma in 1, de differentiated chondrosarcoma in 2, clear cell in 1, grade II chondrosarcoma in 5 and grade III chondrosarcoma in one patient. Both patients with de differentiated chondrosarcoma received adjuvant chemotherapy. 1 patient is loss to follow up and 6 patients are alive and disease free. Three patinet developed distant metastasis and scummed to disease.

Conclusions

Chondrosarcomas are rare in pediatric population accounting for 2.6% of all chondrosarcomas in our hospital. Surgical resection with wide margins is the treatment of choice. De differentiated and mesenchymal subtypes are associated with poorer prognosis.

EP-086

Bone Tumours

NON OPERATIVE MANAGEMENT OF ANEURYSMAL BONE CYST WITH PERCUTANEOUS SCLEROSANT INJECTIONS IN CHILDREN – EARLY RESULTS FROM A PROSPECTIVE OBSERVATIONAL STUDY

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Objectives

To evaluate the results of treating primary aneurysmal bone cysts (ABC) with intralesional sclerosant injections.

Methods

Between February 2010 and November 2013 we treated all primary aneurysmal bone cysts with serial intralesional sclerosant injections. 25 such lesions were treated (femur/2, tibia/6, pelvis/7, fibula/3, humerus/2, hand/2 and ulna, scapula and clavicle/1 each). The median follow up was 16.3 months. All cases had a diagnostic biopsy. There were 12 females and 13 males. Age ranged from 1 – 17 years (median 11.2 years). Polidocanol was injected percutaneously into the lesion under image guidance as an outpatient procedure. Healing was assessed by serial radiographs and symptomatic improvement as observed by the patient. Opacification of the lesion with an increase in cortical thickening was taken as evidence of healing. Injections were repeated (maximum 4) at an interval of 6 to 8 weeks if the lesion did not show evidence of healing.

Results

All but 2 of the lesions showed evidence of healing. One lesion in the periacetabular area showed no evidence of healing after 3 injections and was operated with curettage and bone grafting. Another proximal humerus lesion failed to heal with injection and subsequently underwent surgery. A 1 year old child needed surgery subsequently because of a progressive varus deformity developing at the site of the lesion. 14 cases healed with a single injection, 2 had 2 injections, 4 had 3 injections and 1 had 4 injections and 1 required 4 injections and a session of angioembolisation. The first evidence of radiologic healing was seen from 6 to 24 weeks (median 12 weeks). There were no complications.

Conclusions

Though a longer follow up is mandated to rule out development of recurrence, early results for this inexpensive, non invasive method of managing aneurysmal bone cysts are promising

EP-087

Bone Tumours

MIFAMURTIDE (L-MTP-PE) IN CHILDREN WITH OSTEOSARCOMA: THE TURKISH EXPERIENCE

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Objectives

Mifamurtide (liposomal muramyl tripeptide), activates macrophages, provides antitumor effect in lungs. Mifamurtide+chemotherapy improved survival in nonmetastatic osteosarcoma patients, in phase III study. After EMA approved mifamurtide for nonmetastatic osteosarcoma, it could be used off-label by the approval of the Ministry of Health on a patient basis, in Turkey. This multicentric study aims to evaluate the demographic characteristics, adverse effects, outcome of adding mifamurtide to chemotherapy in children with osteosarcoma in Turkey.

Methods

From September 2011-February 2014, in 40 nonmetastatic, 3 metastatic(after metastasectomy) osteosarcoma patients, mifamurtide was added to chemotherapy after surgery in 7 centers in Turkey. Chemotherapy regimens used were epirubicin/ifosfamide/cisplatin in 21(Istanbul University Oncology Institute-IUOI) and other in 22 (MayoPilotII, EURAMOS, ICE etc.). Mifamurtide was given i.v.2 mg/m², twice weekly for 12 weeks, followed by once weekly for 24 weeks.

Results

Median age was 13 years(4-17 years). Total of 1296 doses of mifamurtide were administered, with no major side effects. Chills, fever initially were frequent. Median follow-up time for all was 15 months (3-57mo.).For nonmetastatic patients 2 year EFS was 76 %, OS 83 %. Fifteen/40(38 %) nonmetastatic patients completed mifamurtide, all have no evidence of disease (NED) at median 17,5 mo. (12-29 mo.); 4 relapsed at median 14 months(11-17), 1 died, 3 AWD; 21 continue treatment. 2/3 metastatic patients died (28, 57 months). When 20 nonmetastatic patients from center IUOI were compared with the historical control receiving same chemotherapy, the median FU was 14 mo (4-57), 2 had relapsed at present, whereas 33/94 of the historical cases had relapsed at median 9 months (1-40).

Conclusions

In this multicentric study, mifamurtide could be administered safely with no major side effects. The experience with mifamurtide in patients with nonmetastatic osteosarcoma is promising; a longer follow up is needed to make further conclusions for survival benefit.

EP-088

Bone Tumours

POLYLACTIDE BIOABSORBABLE STRUTS FOR CHEST WALL RECONSTRUCTION IN A PEDIATRIC PATIENT

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Objectives

Chest wall reconstruction following pediatric tumor resection is challenging. Children have unique characteristics related to growth and prosthetic material for reconstruction must be chosen carefully. Poly-L-Lactide (PLA), a bioabsorbable prosthetic material, has been used in the plate form for reconstruction following tumor resection in children. Recently developed PLA struts have been successfully used to reconstruct pediatric chest wall deformities. This is the first description of the use of PLA rib struts to reconstruct chest wall defects after a pediatric chest wall tumor resection.

Methods

We present the case of a 15 year-old female that presented with right-sided back pain due to a 8 x 5cm chest wall mass that was confirmed as Ewing's Sarcoma of the eighth rib. The patient elected for a surgical resection of her tumor.

Via a right posterior thoracotomy, chest wall resection of the 7th to 9th ribs was performed. Reconstruction was performed using PLA rib replacement struts. For each resected rib, the replacement strut was sutured to the transverse process of the spine posteriorly and the bony component of the native rib anteriorly. Two additional struts were placed vertically in the posterior-lateral and antero-medial axillary lines. The five struts used (2 vertical and 3 horizontal) were not connected to each other so that the vertical struts join the normal ribs above and below the defect and allow for synchronized vertical rib movement. A 28Fr chest tube was placed in the tenth intercostal space.

Results

The patient made an uneventful recovery and was discharged home with all drains removed by the seventh post-operative day. The patient at 3 months follow-up has a stable chest wall with symmetrical appearance.

Conclusions

Poly-L-Lactide rib struts are a stable and physiologically advantageous method of reconstructing the chest wall after malignant tumor resection. Bioabsorbability is particularly advantageous to the growing pediatric chest wall.

EP-089

Bone Tumours

OSTEOSARCOMA OF THE SKULL: CASE REPORT AND REVIEW OF LITERATURE

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Objectives

Osteosarcoma of the skull is very rare as a primary tumor and represents 1-2% of tumors of the skull. Due to the rarity of this tumor, we present a case of primary osteosarcoma of the skull and a review of cases reported in the literature to date.

Methods

We describe a young with primary osteosarcoma of the skull. Clinical presentation, histological features and clinical outcome were examined. A PubMed/Medline search was performed to collect all cases of primary osteosarcoma of the skull.

Results

A man of 17 years old, with a history of 5 months with a painless growing mass parieto-occipital, headache and nausea. Skull radiography evidenced a large lesion with sun radiating pattern. The initial MRI shows a mass of 18 x 15 cm with periosteal reaction and infiltrates adjacent brain parenchyma. The pathology evidences a osteogenic sarcoma. No distant lesion was evident. We started neoadjuvant chemotherapy (CT) with ifosfamide, vincristine, adriamycin and methotrexate, for 14 weeks, showing a poor tumor response. We performed a left parieto-temporo-occipital craniectomy and en bloc resection of bone tumor. Histopathology confirmed the finding of osteosarcoma with cerebral parenchymal infiltration and committed edges. He presented a favorable postoperative course continuing with chemotherapy and radiotherapy. The patient had progression of disease and died after 15 months of diagnosis. There are at least 12 pediatric cases of osteosarcoma of the skull described in the literature from clinical case reports or small series. Due to the rarity of the disease there are no large prospective studies of this entity.

Conclusions

The skull osteosarcoma is a rare tumor, hard to manage and worse prognosis. The surgery with negative margins of the primary lesion is the most important prognostic. Chemotherapy (adjuvant and neoadjuvant) may increase survival. There are few reported cases of pediatric osteosarcoma of the skull, which makes the characterization of this entity and possible therapeutic strategies.

EP-090

Bone Tumours

ROLE OF FDG-PET SCANS IN THE EVALUATION OF BONE SARCOMAS IN CHILDREN AND YOUNG ADULTS

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Objectives

18-fluorodeoxy-glucose positron emission tomography (PET) is recommended for initial bone sarcoma workup by the COG and the NCCN. Compared to conventional imaging (X-Ray/bone Scan/CT/MRI) PET has been shown to be superior in detecting soft tissue metastases and bone scan-negative skeletal metastases, but insensitive for small lung metastases. The detection of occult metastases or incorrect identification of metastases may change treatment decisions. Our objective was to describe our institution's experience of PET scanning in evaluation of primary and relapsed bone sarcoma in children and young adults.

Methods

We retrospectively evaluated the PET/CT and conventional imaging (MRI, CT chest, Bone scan) findings of 20 patients (12 male, age 6-30 years) with primary or relapsed bone sarcoma diagnosed over the past 5 years at our center. Lung metastases <5 mm in size were excluded. Nine patients had Osteosarcoma (5 metastatic) and 11 had Ewing sarcoma (5 metastatic). A total of 30 PET scans and 48 lesions met inclusion criteria.

Results

The sensitivity/specificity for detection of the bone primary were 100%/98%. The overall sensitivity/ specificity for detection of any metastases was 71%/88%. Three confirmed lung metastases > 5mm, 1liver metastasis >1cm and 2 bone lesions, both in the skull were PET negative (Figure1). Four lesions (3 lung,1 bone) were infectious but PET positive. The positive/negative predictive value (PPV/NPV) for any metastatic bone tumor was 75%/87%. Sensitivity/specificity/PPV/NPV(%) was 63/92/67/91 for lung metastases > 5mm, 67/94/80/93 for all bone lesions and 100/96/80/100 for non-skull bony lesions (Figure 2).

Figure 1: Metastatic Lesions in Sarcoma **Not** Detected by PET

Patient	PET	MRI	CT	Bone Scan
1	Vertebrae, Lung	Vertebrae, Skull	Vertebrae, Lung	Vertebrae, Skull
2	<u>Humerus</u>	<u>Humerus</u> , Skull	Skull	<u>Humerus</u> , Skull
3	Femur	Femur	Femur, Liver	Femur
4	<u>Humerus</u>	<u>Humerus</u>	Lung	<u>Humerus</u>
5	femur	Femur	Lung	Femur
6	Femur	Femur	Lung	Femur

Figure 2. PET Scans in detecting metastatic lesions from bone sarcoma

Type of metastatic lesion	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Lung metastases > 5mm	63	92	67	91
Bone metastases	66	94	80	93
Non skull bone metastases	100	96	80	100
Any metastases	71	88	75	87

Conclusions

In our cohort, PET was a useful adjunct but could not replace conventional imaging in the diagnosis and staging of bone sarcoma. In some cases PET alone would have missed metastases or under-staged disease influencing treatment decisions. More studies are needed to evaluate its role in diagnosis and staging of bone sarcomas in children and young adults.

EP-091

Bone Tumours

ORAL VP 16 IN RELAPSED/REFRACTORY EWING SARCOMA: THE EXPERIENCE OF FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI, MILAN

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Objectives

To evaluate the efficacy of low dose oral VP 16 in relapsed/refractory Ewing sarcoma, secondarily to evaluate its toxicity.

Methods

Records of all patients treated between 1989 and 2012 for relapsed/refractory Ewing sarcoma who received oral VP 16 in our department were analyzed. The dose was 20 mg/m²/day for 21 consecutive days every 28 days. The response was evaluated, whenever possible, after 2 cycles according to RECIST criteria.

Results

Forty-three/55 received at least 2 cycles, 9/55 suspended treatment before 2 cycles due to rapidly progressing disease. At diagnosis the median age was 14, 26/55 were metastatic. All patients received intensive poly-chemotherapy program including VP 16 iv in first (n=52) or second line (n=3). Twenty-one/55 received myeloablative regimen with PBSC rescue, 1 allogeneic transplantation. Oral VP 16 was prescribed in II, III, IV line in 18,25,12 patients respectively. Total number of cycles administered was 233, median 3, mean 4 (range 1-14). Forty-one/55 were evaluable according to RECIST criteria. 11 responses (9 PR, 1 VGPR, 1 CR) and 9 stabilizations were recorded with a mean response duration of 7 months. Hematological toxicity G3/G4 (160/233 evaluable cycles) was recorded in 15%, 16%, 11% of cycles for hemoglobin, leukocyte and platelets respectively. 2 responsive patients decided voluntarily to stop the therapy due to gastritis G2. Of note are 5 cases of pneumonia and one HZV reactivation. We recorded 2 secondary leukemia in patients who received 12 and 14 cycles.

Conclusions

Low dose oral VP 16 may be suitable in a palliative setting with acceptable toxicity, further conclusion for the efficacy warrants a prospective study. The risk of secondary leukemia is in line with that reported in literature.

EP-092

Bone Tumours

POOLED SHRNA SCREEN TO IDENTIFY TUMOUR CELL SPECIFIC THERAPEUTIC TARGETS IN EWING SARCOMA

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Objectives

To improve prognosis and reduce treatment toxicity for Ewing sarcoma patients, novel therapeutic targets and treatment approaches are needed. The Ewing sarcoma EWS-FLI fusion protein provides a unique tumour-cell specific target in principle, but effective targeting remains an unsolved challenge. An identification of proteins synthetic lethal to EWS-FLI expression may not alone present an alternative approach towards tumour-cell specific targeting, but further promote the understanding of EWS-FLI oncogenic transformation. Objective therefore is to identify such proteins.

Methods

shRNA technology provides a functional, i.e. loss-of-function, approach to the identification of survival-indispensable proteins, i.e. potential molecular targets. Recent advances in pooled screening approaches combined with next-generation sequencing facilitate large-scale screens. Applying this technology to an A673 Ewing sarcoma cell line model with stable knockdown of endogenous EWS-FLI or control (EWS-FLI off/on) we aim to identify novel tumour-cell specific targets synthetic lethal to EWS-FLI expression.

Results

Stable shRNA transduction of A673 cells was established and optimized for the GIPZ shRNAmir lentiviral system (ThermoScientific). The multiplicity-of-infection was adjusted to 0.3 to achieve integration of 1 shRNA per cell. Sufficient target knockdown by single-copy shRNA integration was confirmed at mRNA and protein levels using LaminA/C, EG5 or non-silencing-control shRNA sequences. Defined test pools of these shRNAs were utilized to confirm DNA recovery and PCR amplification of shRNA sequences. A probe-based real-time-PCR was developed to quantify shRNAs recovered from the defined pools to thereby simulate and validate the established pooled screening protocol in principle.

Conclusions

We established a pooled shRNA screening protocol in an Ewing sarcoma cell line model in presence/absence of EWS-FLI. The subsequent shRNA screen can contribute to the identification of novel tumour-cell specific targets and the understanding of EWS-FLI oncogenic function.

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EP-093

Bone Tumours

INTRAMEDULLARY EXTENSION IN PERIOSTEAL OSTEOSARCOMA – DOES IT PORTEND AGGRESSIVE BIOLOGY?

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Objectives

To evaluate if intramedullary extension in periosteal osteosarcoma was indicative of more aggressive biological behaviour in terms of poorer overall survival.

Methods

A retrospective analysis of 18 cases of periosteal osteosarcoma treated between January 2001 and December 2010 was carried out. There were 12 males and 6 females. The mean age at presentation was 16.3 years (range 5-26 years). Tibia and femur were the most common sites (seen in 8 patients each). Sixteen of 18 patients received chemotherapy, 16 had limb sparing resection, one had an amputation and one had rotationplasty.

Results

Surgical margins were free in all patients. On histopathology, intramedullary involvement was found in 7 patients (44%). All patients were available for follow up. The median follow up was 61 months (range 18- 130 months). Pulmonary metastasis subsequently occurred in 4 cases (22%). Intramedullary involvement was seen in 3 of these 4 cases. Fourteen patients are currently alive and continuously disease free. The median follow up of survivors was 82 months (30-130 months). Disease free survival at 5 years was 77.8% and overall survival was 83.3%. Patients without marrow involvement had a better overall survival at 5 years as compared to patients with marrow involvement (90% vs 75%), $p = 0.23$.

Conclusions

Intramedullary involvement may suggest more aggressive disease biology in these intermediate grade tumors. The difference in our study was not statistically significant but this could be a reflection of the small numbers.

EP-094

Bone Tumours

CHEMOTHERAPY INDUCED NECROSIS AS A PROGNOSTIC MARKER IN OSTEOSARCOMA DO WE NEED TO RAISE THE BAR?

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Objectives

Study co relation between chemotherapy induced percentage necrosis and overall survival (OS).

Methods

192 consecutive patients of non metastatic osteosarcoma were analysed. Patients underwent appropriate surgical resection after receiving neoadjuvant chemotherapy. Excised specimen was analysed for chemotherapy induced percentage necrosis. Patients were divided based on the percentage necrosis as <90 %, 90 – 99 % and 100%.

Results

Necrosis was available in 184 patients. 77 had < 90 % necrosis, 63 had 90 – 99 % necrosis and 44 had 100 % necrosis. 187 of these patients were available for follow up. Currently 85 patients are alive (follow up range 31 to 88 months, median 49 months). The OS of all patients was 47 % at 5 years. There was no difference in OS in groups when traditional cut-off “< / > 90 %” necrosis was used (46 % and 32 % for < 90 % necrosis and > 90 % necrosis respectively - p = 0.139). When we changed the cut-off to “< / = 100 %” necrosis OS was 41 % and 73 % for < 100 % necrosis and = 100 % necrosis respectively (p = 0.001).

Conclusions

Our data suggests that the traditional cut off “< / > 90 %” necrosis may not be a true representation of poor and good responders. It may be better to stratify patients as < / = 100 % necrosis, both for prognosis and in trials evaluating post surgery chemotherapy change.

EP-095

Bone Tumours

CHEMOTHERAPY INDUCED NECROSIS AS A PROGNOSTIC MARKER IN EWING SARCOMA DO WE NEED TO RAISE THE BAR?

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Objectives

Study co relation between chemotherapy induced percentage necrosis and overall survival (OS).

Methods

94 consecutive patients of non metastatic Ewing sarcoma were analysed. Patients underwent appropriate surgical resection after receiving neoadjuvant chemotherapy. Excised specimen was analysed for chemotherapy induced percentage necrosis. Patients were divided based on the percentage necrosis as <90 %, 90 – 99 % and 100%. 23 patients received adjuvant radiotherapy.

Results

Necrosis was available in 80 patients. 25 had < 90 % necrosis, 18 had 90 – 99 % necrosis and 37 had 100 % necrosis. All patients were available for follow up. Currently 62 patients are alive (follow up range 33 to 90 months, median 61 months). The OS of all patients was 68 % at 5 years. There was no difference in OS in <90 % and 90 – 99 % groups (51 % and 61 % for < 90 % necrosis and 90 – 99 % necrosis respectively - p = 0. 641). On comparing the 90 – 99 % necrosis and = 100 % necrosis groups, OS was 61 % and 87 % for 90 – 99 % necrosis and = 100 % necrosis respectively (p = 0.041).

Conclusions

Our data suggests that the traditional cut off “< / > 90 %” necrosis may not be a true representation of poor and good responders as the 90 – 99 % necrosis group behaves similar to the < 90 % necrosis group. It may be better to stratify patients as < / = 100 % necrosis, both for prognosis and while evaluating for decisions related to treatment.

EP-096

Bone Tumours

OUTCOME OF CHILDHOOD EWING SARCOMA FAMILY TUMOURS TREATED WITH TWO CONSECUTIVE PROTOCOLS: A 15 YEAR EXPERIENCE AT UNIVERSITY MALAYA MEDICAL CENTRE, KUALA LUMPUR

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Objectives

Review of demographic data, clinical features and treatment outcome of patients with Ewing Sarcoma Family Tumours (ESFT) from 1998 till 2013 in University Malaya Medical Centre (UMMC).

Methods

Retrospective analysis of medical records of all patients diagnosed with ESFT aged less than 18 years treated on two consecutive chemotherapeutic regimens from 1998 to 2013. MKSCC P6 protocol from 1998 to 2008 and subsequently Euro-Ewing99 protocol from 2009 onwards were used in the unit.

Results

26 patients (M:F=1:1.3) were seen in the 15 years study period. Ten (35%) presented with metastatic disease (lung = 2, bone = 2, bone marrow = 3, combined =3). The sites of primary tumour were: appendicular skeleton=9; axial skeleton=6 ; extra-osseous =5; ribs=3 and skull=3. 22 patients (85%) had gross total resection (GTR) a median time of 6 months after initiation of therapy. With a median follow-up time of 4.5 years, the combined overall survival rate for both treatment arms was 46% (localized disease, 47% and metastatic disease, 44%). 10 relapses occurred with median time of 11 months (range: 7-48 months) mainly in long bones and one had refractory disease. Relapse rate in our patients with ESFT was 50% in metastatic disease and 35% in those with localized disease. All relapsed patients died within 8 months (mean 4.5 months) despite of various salvage therapies. There were 2 induction toxic deaths in Euro-Ewing protocol. Most common side effects observed were septic shock and tubulopathy. 1 patient defaulted follow-up and hence, the disease status is uncertain.

Conclusions

In our cohort, overall survival rate was 46% in 26 consecutive patients treated on two multi-modal protocols. Relapse was seen in both local and metastatic patients and occurring within one year post-treatment. Relapse of Ewing sarcoma is associated with a dismal prognosis despite various salvage therapies.

EP-097

Bone Tumours

EVALUATION OF OVERALL SURVIVAL (OS) AND EVENT-FREE SURVIVAL (EFS) OF PAEDIATRIC SARCOMA PATIENTS - WEST OF SCOTLAND EXPERIENCE

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Objectives

To evaluate OS and EFS of paediatric sarcoma patients with an interest in comparing metastatic cases with non-metastatic cases, and compiling statistics on treatment methods.

Methods

Retrospective observational study of sarcoma patients identified from unit database. These contained information about diagnosis, treatment, prognostic indicators, and outcomes for each patient.

Results

56 patients, 2001-2008.

Osteosarcoma: 11 patients, 7 males, age range: 4-16; median = 10; OS = 64%, EFS = 55%; Primary site of disease: Femur (47%), Tibia (41%), Humerus (5.5%), Scapula (5.5%), Other (1%); Metastatic Rate = 27% (OS = 0%).

Ewing sarcoma: 24 patients, 10 males, age range: 1-16, median = 12; OS = 71%, EFS = 58%; Primary site of disease: Pelvis (29%), Femur (22%), Paraspinal (16%), Chest Wall (10%), Tibia (10%); Metastatic Rate = 21% (OS = 40%; EFS = 40%);

Alveolar rhabdomyosarcoma: 10 patients; OS = 80%, EFS = 60%; Metastatic Rate = 20% (OS = 100%; EFS = 100%).

Embryonal rhabdomyosarcoma: 11 patients; OS = 73%, EFS = 73%; Metastatic Rate = 0%.

Conclusions

Our results reflect access to an experienced and innovative paediatric sarcoma service with close links to a National Sarcoma Multidisciplinary Team. The data falls in line with other studies in terms of age of onset, location of primary tumour, metastatic rate, site of metastases, and prognosis for all cancer types. Limb salvage surgery is greatly favoured over amputation for both osteosarcoma and Ewing sarcoma. Females have a more favourable prognosis in osteosarcoma and a slightly poorer prognosis in Ewing sarcoma. Our overall survival rates are currently better than the UK-wide statistic for three of the four tumours examined.

EP-098

Bone Tumours

PROGNOSTIC IMPACT OF THE EXPRESSION PROFILE OF THE HYPOXIA RELATED GENES CA9, CA12, HIF1A, HIF2A, SCL2A1 AND VEGF IN OSTEOSARCOMA AND EWING SARCOMA

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Objectives

Osteosarcoma (OS) and Ewing sarcoma (ES) are the most common primary malignant bone tumors in children and adolescents. Hypoxia related genes had shown important prognostic markers and have been associated with radio- and chemoresistance in different human cancers, but few studies have been conducted in primary bone cancers. The aim of this study was to analyze the expression profile of hypoxia related genes in these tumors.

Methods

We analyzed the gene expression profile of hypoxia related genes *CA9*, *CA12*, *HIF1A*, *HIF2A*, *SCL2A1* and *VEGF* in consecutive microdissected samples of osteosarcoma (n=32) and Ewing sarcoma (n=16) at diagnosis by RT-qPCR using TaqMan probes by the $2^{-\Delta\Delta Ct}$ method. Mann-Whitney test was used to assess the correlation between gene expression and clinical/biological variables. Event-free survival was analyzed by Kaplan-Meier plots and log-rank test.

Results

Patients with osteosarcoma presented higher levels of *HIF1A* (+2.97-fold, P = 0.001) when compared with Ewing sarcoma. In osteosarcoma it was found a significant association between lower degrees of tumor necrosis post neoadjuvant chemotherapy (Huvos scores I/II) had higher expression levels of *VEGF* (+ 3.36-fold, P = 0.022) and *SCL2A1* (+2.97-fold, P = 0.011). In patients with Ewing sarcoma, *HIF1A* gene expression levels higher than median had a significant higher 5 years event free survival (100% versus 37.5%, P = 0.022)

Conclusions

Our data suggest a prognostic impact of the hypoxia related genes in pediatric osteosarcoma e Ewing sarcoma. Functional studies and analysis of a great number of cases is necessary to confirm these findings

EP-099

Bone Tumours

OSTEOSARCOMA IN CHILDREN UNDER 8 YEARS OF AGE. A 28-YEAR EXPERIENCE AT A SINGLE INSTITUTION

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Objectives

Osteosarcoma is the most common malignant bone tumor in children and adolescents. Prognosis in children under 10 years of age is dismal. We describe herein the treatment and outcome of patients under 8 years of age with osteosarcoma.

Methods

We reviewed the cases of children under 8 years of age, treated for osteosarcoma at the National Institute of Pediatrics in Mexico City, between 1985 and 2013.

Results

There were 29 patients with a median age of 7 years. Most common primary site was femur (51%), followed by humerus (20%), tibia (13%), fibula, cranium, and axial skeleton. Most common histologic type was osteoblastic.

All patients received neoadjuvant chemotherapy according to national protocol at the time of diagnosis.

Surgery for primary tumor included limb-salvage or wide local excision in 10 patients, and 14 amputations. Five patients did not accept radical surgery when proposed.

Despite multimodal therapy and successful complete surgical resection, 13 patients remain alive, while 16 children died.

Conclusions

Patients under 8 years of age with diagnosis of osteosarcoma carry a dismal prognosis. They seem to have a higher rate of chemo-resistant tumors. Newer treatment strategies, possibly including tailored treatment are needed for this group of patients.

EP-100

Bone Tumours

PROGNOSTIC FACTORS IN CHILDHOOD OSTEOSARCOMA: A 15-YEAR SINGLE INSTITUTION EXPERIENCE IN PERU

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Objectives

To determine the prognostic factors that influence survival of pediatric patients with high-grade osteosarcoma of the extremities.

Methods

A retrospective analysis of all patients with osteosarcoma of the extremities treated at Rebagliati Hospital from January 1998 to December 2013 was performed. Patient's sex, age, primary tumor site, serum alkaline phosphatase and lactate dehydrogenase level, distant metastasis at onset, presence of pathological fracture, histological response and type of surgery were analyzed. Overall survival (OS) and event-free survival (EFS) was determined by Kaplan-Meier method.

Results

Seventy-three patients with high grade osteosarcoma of extremities were identified, with a median age of 14 years (range, 5-17 years). The most common site of primary tumor was distal femur (45,2%). Twenty-seven patients (37%) had metastatic disease at onset. In the localized group, 22 of 46 patients had conservative surgery (43,5%). The type of surgery (conservative vs radical) in these patients did not affect survival ($p=0,65$). All patients received neoadjuvant and adjuvant chemotherapy. A raised serum alkaline phosphatase ($p=0,027$) and poor histological response to chemotherapy (necrosis less than 90%) ($p<0.001$) showed significant correlation with worse prognosis. Age, histological subtype, pathological fracture and site of primary tumor did not affect survival. Five-year estimates of OS and EFS were $64,5\pm 8,1\%$ and $48,5\pm 8,7\%$ for patients in the localized group, respectively. Five-year estimates of OS and EFS were $16,2\pm 7,9\%$ and $14,4\pm 7,3\%$ for patients in the metastatic group, respectively. The median of follow-up was 30 months (1.5-152).

Conclusions

A raised serum alkaline phosphatase and poor histological response to chemotherapy were associated to a worse prognosis in patients with high grade osteosarcoma. . There is a need for improving stratification and intensifying treatment, especially in patients with metastatic disease.

EP-101

Bone Tumours

CLINICAL OUTCOME, TOXICITY AND SURVIVAL OF PATIENTS WITH EWING SARCOMA TREATED WITH THE NATIONAL PROTOCOL AT THE NATIONAL INSTITUTE OF PEDIATRICS IN MEXICO

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Objectives

To analyze the survival of patients with Ewing Sarcoma (ES) treated with a National Treatment protocol at a single institution.

Methods

We included all consecutive patients with ES from January 2007 to January 2012. Tumor work-up consisted in evaluation of the primary site with MRI, high resolution CT lung, bone marrow biopsy and PETCT. Patients received treatment with Vincristine (2mg/m² for 1 day), Doxorubicin (conventional 25 mg/m² for 3 days or pegylated 50 mg/m² for 1 day) and Cyclophosphamide (2.1gr/m² for 2 days) alternated with Ifosfamide (2gr/m² for 5 days) and Etoposide (100mg/m² for 5 days). The number of courses was established according to the presence of metastases and the complete resection of the tumor.

Results

We studied 24 patients (median age 9.4 years), 62.5% were male. The mean time between onset of symptoms and start of treatment was 4.4 months. The presentation was 54% axial and 24% had metastatic disease. 50% of patients were treated with conventional doxorubicin and 50% with pegylated doxorubicin. 136 cycles of chemotherapy were administered, presenting toxicity in 58% of them. Overall survival was 70% in patients with localized and 45% for patients with metastatic disease (P =0.05). Survival in patients with axial disease was 50% vs.75% with extra-axial location (P =0.05). 9 patients died, 5 (55%) due to toxicity and 4 (44%) due to progression of the tumor. 4 patients with metastatic disease underwent autologous hematopoietic stem cell transplantation with a survival of 50%.

Conclusions

The National Treatment Protocol is well tolerated in patients with ES, with a similar survival reported internationally. Despite of this the survival for patients with metastatic disease is low. There is a need to explore and/or expand other therapeutic options including stem cell transplant as a consolidation alternative proceeding chemotherapy with new agents and/or combinations of therapy including radiotherapy.

EP-102

Bone Tumours

OSTEOSARCOMAS OF THE MANDIBLE (MOS): MULTIDISCIPLINARY MANAGEMENT. A COOPERATIVE STUDY OF THE GSF-GETO, RARE CANCER NETWORK, GETTEC/REFCOR AND SFCE: FOCUSING ON PATIENTS

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Objectives

MOS is exceptional in children and adolescents.

Methods

Retrospective study conducted of all cases of MOS diagnosed in France between 1973 and 2010, aiming to determine the impact of chemotherapy, radiation therapy and surgery on outcomes and to identify prognostic factors. This report focusses on patients <18 years old.

Results

In 111 patients, 13 (14%), were less than 18 years old (median age 14 years-old (range 7-18)). 5 were males; In 6 patients MOS was a second or even third primary malignancies; 4 with previous history of head and neck cancer treated by radiotherapy; 3 with Li Fraumeni syndrome.

TNM staging was 12 T1, 1 T2 and 13 N0M0.

Pathological WHO grades were 12 high and one low.

Neoadjuvant chemotherapy including high-dose Methotrexate, Ifosfamide/Etoposide, Doxorubicin, Cisplatin was carried out in 12.

One patient had progression during first line therapy, no surgery and died.

Surgery was carried out for 12 pts. Resections were 7 R0, 4 R1 and 1R2; histological response was poor (>10% viable tumor cells in resected specimen) in 7 patients, good in 4 and not known in 1 case.

Post operative chemotherapy was performed in 10 patients and post op radiotherapy for 2.

At last follow up, 4 are alive in CR1 (1-7 yrs after) and 9 patients experienced an event: 1 death from primary progression, one alive with disease, 3 relapses local and metastatique (3 alive), and 4 metachronous osteosarcomas, 3 in pts with Li Fraumeni syndrome.

For the entire cohort, wide surgery with clear margins was the strongest prognostic factor.

Neoadjuvant chemotherapy improved disease-free and metastatic-free survival.

Conclusions

MOS remains a rare and highly malignant tumor demanding aggressive therapy. Surgery is the mainstay of treatment, and margins are the most important factor for local control and survival.

EP-103

Brain Tumours

MEDULLOBLASTOMA BELOW THE AGE OF 3 YEARS: TREATMENT AND PROGNOSTIC FACTORS

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Objectives

To investigate the treatment end-results of medulloblastoma under 3 years old and determine the factors affecting its prognosis.

Methods

Twenty five children below the age of 3 years were treated at Children's Cancer Hospital_Egypt during the period from July 2007 and Oct 2013. Gross total resection was performed in 15 children (60%), subtotal excision in 9 children (36%) and biopsy in one patient. Seventeen children (68%) were non-metastatic, while 8 (32%) metastatic M₁₋₃. Eight out of the 11 (44%) children received infantile medulloblastoma chemotherapy protocol, while the other 14 (56%) received other chemotherapy protocols. All 8 metastatic children received craniospinal irradiation (CSI). Nine out of the M₀ patients received posterior fossa (PF) irradiation, while the other 8 received CSI at age of 3 years.

Results

The 4 year OS for non-metastatic was 78.4±11.6% and 22.9 ± 19.7% for M children. The EFS for nonmetastatic was 61.1±14.3 % and 15.0±13.8 % respectively. The infantile chemotherapy protocol in M₀ patients led to 4-year OS of 63.6± 17.7% compared to 55.6 ± 24.8% for other protocols. The OS for CSI was 88.9 ± 10.5% compared to 75.9 ± 10.5% for conformal PF irradiation. OS of GTR and less than GTR is 83.3 ± 18.2% , 75.3 ± 28.6% respectively. Two patients of the CSI group developed CNS relapse and other two patients had spinal relapse. No relapse in patients who received PF irradiation. None of these detected differences were statistically significant. All children tolerated treatment with minimal immediate toxicity and late effects with more aggressive treatment.

Conclusions

Non metastatic status in Medulloblastoma below the age of 3 years carry out better OAS and EFS than metastatic category irrespective to the treatment protocol

EP-104

Brain Tumours

HISTONE DEACETYLASE INHIBITOR PCI-24781 SHOWS INHIBITION OF CELL PROLIFERATION AND CLONOGENIC SURVIVAL IN PEDIATRIC GLIOBLASTOMA CELLS.

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Objectives

This study aimed to evaluate the therapeutic potential of HDACi PCI-24781 on pediatric GBM lines, SF188 and KNS42 by proliferation and clonogenic survival assays.

Methods

Proliferation assay with Resazurin dye was performed in 96-well plates using 2×10^3 cells per well. Cells were treated with the PCI-24781 with different drug concentrations (of 0.5-16 μ M) for 24-96h. For clonogenic survival assay, cells were seeded into six-well plates with 500 cells per dish. Cells were treated with increasing drug concentrations (0.5-16 μ M). After 72h, culture medium was replaced and the cells were cultured for an additional 10–14 days. Individual colonies (>50 cells per colony) were fixed with methanol, stained with crystal violet and subsequently counted. Statistical analysis was made by One- and Two-way ANOVA and Bonferoni post-hoc.

Results

Both cell lines were sensitive towards PCI-24781 treatment, displaying an inhibition of proliferation after treatment ($P < 0.05$). In SF188 cell line, the strongest effect was observed at the dose of 16 μ M at 96h, when growth inhibition was approximately 93%. The KNS42 cell line showed a time dependent inhibition of proliferation after treatment. The strongest effect was observed at 96h when growth inhibition was approximately 84%. In clonogenic assay, there was no colony formation after treatment, showing a great sensibility of GBM cells for PCI-24781 treatment.

Conclusions

This primary data demonstrates that PCI-24781 can induce inhibition of cell proliferation and clonogenic survival of GBM cells. Additionally it shows the potential of HDACi for the treatment of pediatric GBM. Further experiments will be performed to assess the ability of this HDACi in modulating the cellular response to ionizing radiation.

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EP-105

Brain Tumours

CLIVAL CHORDOMAS IN CHILDHOOD

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Objectives

Clivus chordomas are rare locally aggressive neoplasm of bone treated primarily with surgery. Most series consist small numbers of children and there is no suggested standard treatment algorithm other than total surgery. This series of patients were reviewed for the characteristics and course of disease.

Methods

The files of patients with clivus chordoma who were diagnosed and followed-up between 1987 and 2014 were retrospectively analyzed.

Results

Seven patients were diagnosed and followed-up with the diagnosis of chordoma at clival localization. The median age of 5 girls and 2 boys was 11 years. Symptoms were headache in 3 patients, diplopia in 2 patients, sleep apnea, dysphagia, hemiparesis, motor dysfunction on arm and ataxia each in one patient for median 2.5 months. Patients were followed median 17 months (1-84 months). First medical intervention was surgery in all. Three of five patients, whom had subtotal resection, locally recurred and re-resections were needed. Three patients with recurrent tumors received radiotherapy. Two of them received chemotherapy also (one received VAC regimen and the other ifosfamide, etoposide and imatinib after their 2nd and 5th resections. Third patient refused chemotherapy; he is still alive with progressive brain metastases. First patient who were given VAC regimen died of progressive disease after first course.

Conclusions

Clivus chordoma can be problematic when total resection cannot be achieved. Addition of radiotherapy helps improving disease-free or overall survival. Chemotherapy with ifosfamide and etoposide might have benefit on recurrent tumor. Further research is needed to define the role of chemotherapy and targeted therapies on stabilization or regression of the chordomas.

EP-106

Brain Tumours

PEDIATRIC TECTAL PLATE GLIOMAS

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Objectives

Tectal gliomas are a distinctive form of brain stem tumor which are generally low-grade astrocytomas with an unusually benign behavior. Treatment includes observation of the lesion or shunting and diversion of cerebrospinal fluid (CSF) to relieve associated hydrocephalus. We aimed to investigate the clinical characteristics and management approaches in our patients with tectal plate gliomas.

Methods

Files of children treated at our hospital between 1990 and 2013 with the diagnoses of tectal plate gliomas were reviewed retrospectively for clinical characteristics and treatment results.

Results

We identified 5 girls and a boy with a tectal plate glioma whose ages ranged from 5.5 to 14.5 years (median 7.4). Most common presenting symptoms were headache, vertigo, tremor of the hands and gaze palsies. One patient had findings of neurofibromatosis type 1. Median duration of delay from onset of symptoms to definitive diagnosis was 9 months (2-36 months). In the magnetic resonance images (MRI) the sizes of the primary tumors ranged from 1.7 to 2.5 cm with contrast enhancement in 2 cases. At a median follow-up of 23 months (1.5-120 months) four patients underwent a CSF-diverting procedure in the form of a ventriculoperitoneal shunt or endoscopic third ventriculostomy; one patient underwent tumor resection due to progressive disease in 3 months and one patient was observed with no intervention. Three patients needed at least one more CSF-diverting procedure in the follow-up. Median progression-free follow-up was 7.8 months (1.5-66).

Conclusions

Since the lesions are capable of growth either with, or without, new neurologic symptoms, close follow-up and monitoring are essential to intervene prior to the development of irreversible debilitating neurologic sequelae. Tumor size >2 cm and contrast enhancement on MRI scans might be related to tumor progression. All children with findings of late-onset hydrocephalus should undergo MRI and tectal plate glioma should be considered in the differential diagnosis.

EP-107

Brain Tumours

**UTILITY OF IDH 1 EXPRESSION IN CHILDHOOD AND ADOLESCENT AGE GROUP
GLIOMAS ACROSS NORTHERN INDIA**

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Objectives

Paediatric Gliomas are a heterogeneous group of gliomas encompassing tumors of different histologies. Clinical utility of IDH 1 expression has been well established in adulthood gliomas. However, paediatric data is quite scanty to consider IDH 1 expression as a utility tool in management of paediatric gliomas. Present study is an attempt to reflect and answer this concern.

Methods

A total of 46 cases, with 20 of them being under 10 years, of paediatric gliomas of different histologies were enrolled over a period of 2 years. A parallel arm with 154 cases was constituted for adulthood gliomas. Age of patients ranged from 1 to 16 years (mean 8.2 years). There were 18 cases of pilocytic astrocytomas, 16 ependymomas, and 4 each mixed gliomas and oligodendrogliomas. Most common site of involvement was fronto-temporal followed by parieto-occipital and posterior fossa. Increased intracranial tension accompanied by varying degrees of motor paralysis was the most common clinical feature, with duration ranging from 1 to 15 months. All cases were looked for IDH1 expression as per protocol.

Results

Of 46 cases, IDH1 expression was present in 8 cases only, 4 oligoastrocytomas and 2 cases of diffuse astrocytoma and oligodendroglioma each. 6 of them showed WHO grade II, while 2 grade III. Regarding age distribution, 6 of the positive cases were over 10 years (75 %). In the parallel arm too, involving adults, 60% positive cases were seen in early to mid adulthood (<40 years). This comparison was statistically significant. The accompanying parameters viz. site, symptoms, duration, nucleo-cytoplasmic expression were in concordance in both groups.

Conclusions

To conclude, it can be emphasized that utility of IDH 1 expression in early childhood gliomas is limited, however early adolescent age groups and beyond have shown concordant results. It can be considered as a diagnostic tool for gliomas presenting in older pediatric population.

EP-108

Brain Tumours

COMBINED MULTIPLE CHEMOTHERAPY AND POSTERIOR FOSSA RADIOTHERAPY IN INFANTS WITH NONMETASTATIC MEDULLOBLASTOMA

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Objectives

New radiotherapy modalities, 3D-conformal radiation therapy (CRT) and IMRT allow to include the radiotherapy in the treatment of patient younger than 36m with medulloblastoma. The aim is to evaluate the results of a protocol with chemotherapy and 3D-CRT/IMRT in infants nonmetastatic medulloblastoma.

Methods

From October 2002 to December 2012, 25 infants patients with medulloblastoma were treated in our institution, 8 metastatic; 15 of 17 nonmetastatic patients were evaluable for this study. Median age at diagnosis was 12.3 (3,1-30,6) months. After initial surgery, children received 5 cycles of induction chemotherapy, including Vincristine (0.05mg/k/d1,8,15), Cisplatin (3.5mg/k/d1), Cyclophosphamide (30mg/k/d2,3), Etoposide (4mg/k/d2,3), followed by maintenance chemotherapy: Carboplatin (18mg/k/d1), Vincristine (0.05mg/k/d1, 28), Cyclophosphamide (50mg/k/d28), and Etoposide (1,6 mg/k/d2-14; 29-43 orally). Patient with gross residual tumor received HD metotrexate during induction. Posterior fossa 3D-CRT or bed tumor IMRT with/without Temozolamide was indicated after induction or when achieved 18 months old (54/55.8Gy)

Results

The histological subtypes were: 4p classic medulloblastoma, 10p desmoplastic/nodular, 1 extensive nodularity. Four patients had gross residual tumor. Thirteen patients received 3D-CRT/IMRT. The median time from resection to radiotherapy was 7,1m(5,4-25,3). The median age of 3D-CRT/IMRT was 30,2m(18,4-48,4). Two pt did not receive CRT, 1 died in induction and 1 was extensive nodularity. The median follow up was 52,7m(5,9-137). The 5 year event-free survival and overall survival probabilities were 70,9% and 78,7% respectively. Four pt relapsed, 1 supratentorial metastasis, 1 intraventricular relapse, 1 leptomeningeal dissemination and 1 in spinal space. Median time from diagnosis to relapse was 21m(5,1-21,5).

Conclusions

The results obtained in this particular group of patients are very encouraging, considering similar result in group of patients more 36m old with the use of craneoespinal radiotherapy.

EP-109

Brain Tumours

RESPONSE TO INTRAVENTRICULAR TOPOTECAN (ITV), ORAL TEMOZOLAMIDE AND ETOPOSIDE IN CHILDREN WITH RELAPSED MEDULLOBLASTOMA: A MONO-INSTITUTIONAL EXPERIENCE

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Objectives

Patients with relapsed medulloblastoma are unlikely to be cured. New effective treatment strategies are needed.

Methods

We retrospectively reviewed 9 cases of relapsed medulloblastoma between Jun 2011 - Oct 2013, treated with palliative care criteria with IVT 0.4mg/dose, temozolamide 160mg/m²/day orally d1-5/28d and etoposide 50mg/m²/day orally d1-14/28 d. Ommaya reservoir was implanted. IVT was administrated twice a week for 3m; weekly for others 3m and twice a month since that. Surgery was performed when only one site was affected or to improve patient symptoms. Response was assessed by MRI every 3m.

At initial diagnosis the median age was 76m (31-108). Six were standard-risk and 2p were high risk. They received Craniospinal radiotherapy 2340/3600cGy respectively and 5400/5580cGy respectively in posterior fossa. It was followed by adjuvant chemotherapy using Cisplatin, Vincristine, Lomustine and/or cyclophosphamide (adaptive COG strategy). One was younger than 36m and was treated with baby protocol including posterior fossa radiotherapy. At relapse the median age was 117m (82-131). Median time from diagnosis to relapse was 23m (18-47). Five had isolated intraventricular relapse, 2 had leptomeningeal dissemination and 2 had extra-axial supratentorial meningeal metastasis.

Results

Four underwent surgical resection (2p gross resection and 2p subtotal resection). Evaluable tumor was seen in 7p. Responses to chemotherapy were seen in all cases, 1p complete remission, 5p with partial response and 1p stable disease with a median follow up of 11m (4-27). Eight remain alive: 6 without progression. Two showed MRI progression (12m and 13m). One relapsed and died, 13m and 27m respectively. The treatment was well-tolerated. Grade 3 thrombocytopenia was observed in 2p, leading to 25% decrease of temozolamide.

Conclusions

The combination of ITV, oral Temozolamide and Etoposide produces objective responses with minimal toxicity in children with relapsed medulloblastoma. This strategy allows our pt to live as normal as possible their residual life.

EP-110

Brain Tumours

TREATMENT STRATEGY IN CHILDREN WITH SUPRATENTORIAL HIGH-GRADE GLIOMAS

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Objectives

The aim of our non-randomised study was to evaluate results of treatment and analyze prognostic factors in patients with supratentorial high-grade gliomas.

Methods

From 1991 to 2005, we treated 43 pts, median age 11 (range 3 to 18 years). Gross total resection was performed in 8 pts, subtotal in 8 pts, and partial in 27 pts. Anaplastic astrocytoma (AA) was found in 35 pts and glioblastoma multiforme (GBM) in 8 pts. After surgery, patients were treated with local radiotherapy to the primary site (range 55-60 Gy) and chemotherapy. Chemotherapy regimens were: Vcr, CCNU (Group 1) in 10 pts; 8/1 regimen (Group 2) in 15 pts and Vcr, CCNU, CDDP (Group 3) in 18 pts.

Results

During the 10 to 216 months follow-up period, 5-year overall survival was 42,1%. Significant prognostic factors were: pathohistological type (AA vs. GBM) and extent of surgery. There were no significant differences between chemotherapy regimens (Group 1 vs. 2 & 3 and Group 2 vs. 3).

Conclusions

Pathohistological type and extent of tumor resection are predictors of better prognosis. Among the chemotherapy regimens applied, there was no difference in overall survival.

EP-111

Brain Tumours

PROTEOMICS CHANGES AFTER INHIBITION OF SP1 TRANSCRIPTION FACTOR BY TETRA-METHYL NORDIHYDROGUAIARETIC ACID IN GLIOBLASTOMA CELLS

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Objectives

Tetra-methyl nordihydroguaiaretic acid (M4N), is a global transcriptional repressor of genes dependent on the Sp1 transcription factor that affects apoptosis, drug resistance, proliferation responsive genes, and radiation resistance. Recently, we have demonstrated the antineoplastic effects of M4N, it induced apoptosis, acted synergistically with chemoradiotherapy and deregulated the Sp1-dependent genes *Survivin* and *Cdk1* in glioblastoma (GBM) cells. However, the global impact of Sp1 inhibition by M4N on transcriptome and proteome of these cells is unknown.

Methods

The GBM cell lines SF188, KNS-42, U87MG and T98G were treated with 20 and 40 µM of M4N for 48h. Cell proliferation was assayed using XTT[®] test. Protein extracts were obtained for western blot assays and labeled with isobaric tags for relative and absolute quantitation (iTRAQ) technology. An off line strong cation exchange chromatography (SCX) and on line reverse phase LC coupled to ESI-Q-TOF-MS were used to identify peptides and determinate proteins differentially expressed. Statistical analysis was performed using Scaffold software.

Results

M4N treatment reduced proliferation and deregulated the protein expression of Survivin and CDK1 in all cell lines investigated. The quantitative proteomic analysis identified about 100 proteins with at least 2 peptides identified and 95% protein identification probability in both cell lines. Thirteen and six proteins were deregulated after M4N treatment in SF188 and U87 cells, respectively. Gene ontology analysis demonstrated that all the deregulated proteins by M4N participate of important cell metabolic processes, such as carbohydrate metabolism.

Conclusions

We found evidence that Sp-1 inhibition by M4N treatment altered significantly the expression of proteins related with metabolic processes in GBM cells. Further studies will investigate the molecular changes of M4N-treated GBM cells, mainly in transcriptomic field in order to achieve a better understanding of Sp1 inhibition and provide new insight into GBM biology. Financial support: FAPESP Process number 2012/16889-4 and 2012/16888-8.

EP-112

Brain Tumours

CHEMOTHERAPY FOR IRRESECTABLE LOW GRADE GLIOMAS IN A UNIVERSITY-BASED COMBINED NEURO-ONCOLOGY SERVICE IN SOUTH AFRICA

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Objectives

To assess the role of chemotherapy in the management of low grade gliomas by the combined neuro-oncology services of the University of Cape Town.

Methods

A retrospective analysis was performed on the folders of patients diagnosed at the Red Cross Children's Hospital and Groote Schuur Hospital between 2001 and 2013.

Results

There were 60 children, aged 0.41 to 13.75 years [median 5.38]. Forty six tumours (77%) were WHO grade I, and 14 were WHO grade II, including 7 fibrillary astrocytomas, 4 pilomyxoid astrocytomas and one pleomorphic xanthoastrocytoma. The commonest sites were cerebellum (30%), hypothalamus (20%), cerebrum (15%) and optic tract (12%). Fourteen patients were managed expectantly, including 5 of the 8 with neurocutaneous syndromes. Thirty two patients underwent surgery at diagnosis in the form of debulking or gross total resection, and 11 patients required surgery for recurrence or progression. Fifteen patients (25%) received radiotherapy; 5 of them as first line treatment. Thirteen patients with irresectable disease (median age 2.67) were treated with chemotherapy; 11 of them with vincristine and carboplatin as the first line regimen. Eleven of these tumours (84.6%) involved the optic tracts or the hypothalamus; ten were juvenile pilocytic astrocytomas and 3 were pilomyxoid astrocytomas. One patient progressed, three showed stable disease and nine responded, reducing in volume by 40-93% (median 68%). Estimated 5-year Overall Survival (OS) was 89.2% for the whole group; 92.3% for WHO I tumours and 74.2% for WHO II tumours. Estimated 5-year Progression Free survival (PFS) for the whole group was 53.5%. The patients treated with chemotherapy had an OS of 100% and a PFS of 33%.

Conclusions

Chemotherapy is a vital part of the multidisciplinary management of low grade gliomas in low and middle income settings.

EP-113

Brain Tumours

GLIOBLASTOMA MULTIFORME A SINGLE INSTITUTION EXPERIENCE AT BELO HORIZONTE/BRAZIL

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Objectives

The goal of this study was to determine the epidemiology, clinical presentation and treatment outcome of pediatric Glioblastoma Multiforme in a single center institution

Methods

Clinical data of 108 patients under 18 years of age with brain tumors from December 2000 to December 2012 were reviewed in Santa Casa de Belo Horizonte/Minas Gerais-Brazil .

Results

Six patients (5.5%) had the diagnosis of Glioblastoma Multiforme (5 female and 1 male), with average age of 6.2 years were analyzed (range 4-12 years). During diagnosis 4 patients had Supratentorial tumors and 2 posterior fossa tumor. The most common signs and symptoms were associated with intracranial hypertension in five patients (Headache, somnolence, vomit, papilledema). Three patients had seizures and hemiparesis. One patient presented with posterior fossa tumor (brainstem) had paralysis of multiple cranial pairs, intracranial hypertension and ataxia. Partial resection was performed in five patients and one (brainstem) stereotatic biopsy. All patients were treated with radiotherapy and 3 associated with chemotherapy, just one patient use Temozolamide and survival seven months. Median of Overall survival was 5.2 months (range 6-12 months), all children died due to disease progression

Conclusions

Glioblastoma occurs rarely in pediatric patients (0.6-7.9% of all glioblastomas). Symptom duration is about 3-5 months prior to diagnosis with a dismal prognosis. Glioblastomas have a tendency to recur and disseminate despite treatment with surgery, chemotherapy, and radiation. The poor outcomes seen with this tumor suggest that the optimal treatment strategy has yet to be elucidated and much work needs to be done.

EP-114

Brain Tumours

BRAIN TUMORS IN A SINGLE-CENTER: EXPERIENCE DURING 12 YEARS AT BELO HORIZONTE/BRAZIL

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Objectives

The goal of this study was to determine the epidemiology, clinical presentation, associated factors, pathological pictures, and treatment outcome of pediatric brain tumors in a single center institution.

Methods

Clinical data of 108 patients under 18 years of age with brain tumors from December 2000 to December 2012 were reviewed in Santa Casa de Belo Horizonte/Minas Gerais-Brazil.

Results

One hundred and eight children (58 female, 50 male) with the median age of 7.2 years were analyzed. During diagnosis 64 (60%) patients with intracranial hypertension and 21 (20%) with seizures. 55 (51%) patients with posterior fossa tumor (21 with medulloblastoma and 20 with brain stem tumors), Supratentorial tumors was present in 51 (47%) children with 24 (47%) were low grade gliomas. Six (5%) patients with glioblastoma multiforme, but four were supratentorial none alive. Total resection was performed in 40 (48%) patients, parcial resection in 35 (40%) and 5 (6%) stereotatic biopsy. Fifty-five (51%) patients were alive without tumor, 35 (32%) died due to tumor progression or infections and 8 (7%) lost of segment.

Conclusions

In a single center institution with limited resources, most patients died with tumor progression or infections. So it's necessary to improve the supportive care and development of new treatment strategies to increase overall survival.

EP-115

Brain Tumours

WEEKLY VINBLASTINE IN PEDIATRIC LOW GRADE GLIOMAS

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Objectives

To assess the efficacy and toxicity of weekly vinblastine in low grade gliomas of children.

Methods

We conducted a prospective study involving children treated for incompletely resected or unresectable low-grade glioma (LGG). Vinblastine (6 mg/m²) was administered weekly until progressive disease, unacceptable toxicity, or a maximum of 2 years of therapy.

Results

Thirty-two patients (median age, 7.5 years, sex ratio 0.73) were enrolled on to this study. The response rate was 46%. After a median follow up of 52 months (range 12-78 months), overall survival was 96% at 3 years and 93% at 5 years, progression-free survival is 82% at 3 years and 62% at 5 years. Toxicity was 6% mostly hematologic, and manageable.

Conclusions

The low-grade gliomas are a chronic disease, treatment should be less aggressive as possible. Vinblastine is an effective therapeutic, with a good tolerability, ease of use and low cost, would be an interesting alternative in our country and could be used as first line.

EP-116

Brain Tumours

MULTIDISCIPLINARY APPROACH AND VISUAL ACUITY IN TREATED CASES OF OPTIC PATHWAY GLIOMAS

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Objectives

Within pediatric brain tumors, optic pathway gliomas (OPG) are a specific group that requires special handling. We review our experience in therapy response and visual prognosis of OPG.

Methods

Review of low grade gliomas (LGG) with involvement of visual pathway in the last 10 years (2004-2014). We analyzed epidemiological, clinical, radiological and histological data at diagnosis and follow-up, focusing in multidisciplinary approach, therapies, and visual acuity at diagnosis and evolution.

Results

Among 29 LGG patients referred to the Pediatric Oncology Unit, 10 had involvement of the optic pathway at the time of diagnosis (5 men/ 5 women). The average age was 5.0 years (4.5 months-9 years). In 5 cases the presence of neurofibromatosis 1 was confirmed. Only one patient had isolated unilateral optic nerve involvement and most had regional CNS extension. Initial biopsy was performed on 3 patients and 1 after progression. MRI characteristics were analyzed. Different specialists were involved in their management (pediatric oncologist, neurologist, neuroradiologist, geneticist, radiotherapist, neurosurgeon, endocrinologist, ophthalmologist, otolaryngologist, nephrologist): 8 in 4 cases, 7 in 3, 6 in 2 and 5 in 1. Treatments administered were chemotherapy (9), radiotherapy (3) and surgery (3). Mean follow-up was 48 months. Two patients died due to tumor progression (one had oligodendroglioma with spinal dissemination). Visual acuity on follow up was highly impaired in 2, slightly impaired in 3, stable in the rest but one that improved after chemotherapy.

Conclusions

Despite advances in brain tumors, management of optic pathway gliomas remains a challenge. Although vital prognosis can be favorable nowadays, there is still lack of consensus regarding therapies. As poor visual outcomes occur in many cases, a close follow-up is important with precise visual assessments. Management in multidisciplinary teams remains essential for optimal care of these patients.

EP-117

Brain Tumours

GLIOBLASTOMA MULTIFORME: REHABILITATION OF A CASE

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Objectives

Glioblastoma multiforme is a grade IV astrocytoma and represents about 7 % of intracranial tumors in childhood.

Methods

Patient 18 years old, female, admitted on 11/01/2013 with headache, vomiting and paralysis in the right arm 15 days ago, she developed right facial paralysis and mild dysphagia, FOIS 5 (Functional Oral Intake Scale).

The functional classification was based on KPS 80% (Karnofsky Performance Status) and Scale Independence in Activities of Daily Living Katz scoring 0 (ADL-Katz).

MRI of brain: "solid-cystic lesion with central necrosis, perilesional hematoma, measuring 6,4x5,8x5,7 cm, the left frontal region, compressing the pre central gyrus and diverting the midline to right".

Made frontal parietal craniotomy, subtotal resection, the patient developed cerebral edema, done dural repair and cranial bone was placed in the subcutaneous tissue of the abdomen.

Results

In intensive care unit, Glasgow 3T without sedation, KPS 20 and ADL-Katz 6

The rehabilitation care were: 1. Nutrition: Enteral nutrition, pasty, bland, general support and supplements; 2. Physiotherapy: motor and respiratory kinesiotherapy, workout sitting posture, balance, orthostatic and functional neuro electrostimulation; 3. Speech Therapy: passive and active orofacial exercises, cold thermal stimulation, workout swallowing and breathing for decannulation of tracheostomy; 4. Occupational therapy: guidance for positioning, treatment adherence, encouragement of self-esteem and relationships, use of adapted recreational activities and expressive activity.

Outside hospital after 22 days with Functional Independence Measure (FIM) 28.57%. Made 3D radiotherapy (60 G) with temozolomide (75mg/m²/day). Currently FOIS 7, KPS 80%, FIM 88.09% and ADL-Katz scoring 3.

Last MRI: stable disease. Currently, using temodal (150-200mg/m²/day, 5 days, 6 cycles).

Cranioplasty scheduled for 07/04/2014.

Conclusions

Although we know that potentially all malignant gliomas will recidivate, it is clear in this case that patients may benefit from surgery, radiotherapy, chemotherapy and of a good rehabilitation work.

EP-118

Brain Tumours

ANTITUMOR ACTIVITY OF AMG900 ALONE OR IN COMBINATION WITH HISTONE DEACETYLASE INHIBITOR SAHA ON MEDULLOBLASTOMA CELL LINES

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Objectives

Medulloblastoma (MB) is the most common malignant childhood brain tumor. Aurora kinases are essential for cell division and are primarily active during mitosis. Following their identification as potential targets for cancer chemotherapy, many Aurora kinase inhibitors have been discovered, and are currently under development. Recently, the combination of aurora kinases inhibitors (iAURK) with histone deacetylase inhibitors (iHDAC) has shown potential antitumor effects and had significant biological effects in preclinical cancer models. To evaluate the effects of the pan-aurora kinases inhibitor AMG 900 alone or in combination with the histone deacetylase inhibitor SaHa on pediatric MB cell lines UW402 and UW473.

Methods

Cell proliferation, clonogenic, apoptosis and qRT-PCR assays were performed in triplicate.

Results

AMG 900 caused the inhibition of cell proliferation, diminution of clonogenic capacity and increased the apoptosis rate in both cell lines ($p < 0.05$). The IC₅₀ values were 183,16 nM and 242,16 nM for UW473 and UW402 cells, respectively.

A synergistic effect in the AMG900-SaHa combination was evidenced on the inhibition of cell proliferation in both cell lines, especially in sequential drug treatment. Moreover, the combination of these drugs reached 100% of the inhibition in colony formation (synergistic effect). The treatment with AMG900 increased the p21 and GDF15 expression, but did not alter the TP53 one in the cell lines.

Conclusions

These results showed that the inhibition of aurora kinases by AMG 900 leads to antineoplastic effects on pediatric MB cell lines and its combination with iHDAC has promising effects in the treatment of this tumor.

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EP-119

Brain Tumours

THE HERBY STUDY: A PHASE II OPEN LABEL, RANDOMIZED, MULTICENTER STUDY OF BEVACIZUMAB-BASED THERAPY IN PEDIATRIC PATIENTS WITH NEWLY DIAGNOSED HIGH-GRADE GLIOMA (HGG)

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On behalf of the European Innovative Therapies for Children with Cancer (ITCC) Consortium, The European Society of Paediatric Oncology (SIOP-E) Brain Tumour Group, and the Australian Children's Cancer Trials Group

Objectives

Despite recent therapeutic advances, outcomes in pediatric HGG remain poor. A phase I study (Glade-Bender et al., *J Clin Oncol.* 2008) indicated that bevacizumab is well tolerated in children with refractory solid tumors and yielded pharmacokinetic data that support further studies of bevacizumab in childhood cancer.

Methods

A total of 120 eligible patients aged 3 to 18 years with newly diagnosed, localized supratentorial or infratentorial cerebellar or peduncular, histologically confirmed World Health Organization grade 3 or 4 HGG (central independent histologic confirmation) will be randomized to 6 weeks of concomitant temozolomide and local radiotherapy, followed by a 4-week temozolomide treatment break and 48 weeks of adjuvant temozolomide ± bevacizumab every other week. Children aged 6 months to 3 years are included in a young patient cohort; at relapse these patients will receive temozolomide and bevacizumab without radiotherapy. All patients/parents provided written informed consent per the local institutional review boards. The primary end point is event-free survival, defined as the time to earliest occurrence of tumor progression/recurrence (by central independent assessment per Response Assessment in Neuro-Oncology criteria), secondary malignancy, or death. Secondary end points include overall survival, response rate, safety, feasibility, and tolerability. All randomized patients will be followed for ≥3 years. A futility analysis will be performed after the first 60 randomized patients have been followed for 1 year; the primary analysis will be performed after all patients have been followed for 1 year. Updated analyses will be performed 3 years after the last patient has been randomized. **Results**

HERBY is being conducted at 87 clinical sites in 15 countries. The first patient was randomized in October 2011. Among 118 patients screened to date, 79 have been randomized, and 1 has been enrolled in the young patient cohort.

Conclusions

Completion of the study is expected in 2016.

EP-120

Brain Tumours

PEDIATRIC MALIGNANT BRAIN TUMORS TREATED WITH BEVACIZUMAB

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Objectives

Bevacizumab is a humanized monoclonal antibody that recognizes and blocks vascular endothelial growth factor. It has been evaluated in malignant brain tumors in children. We report our experience with bevacizumab in these tumors in our pediatric oncology unit.

Methods

A retrospective study in all patients with malignant brain tumors treated with bevacizumab between May of 2010 and February of 2014 was undertaken. Bevacizumab was administered at a dose of 10 mg/m² q2wk along with chemotherapy (Irinotecan) until progression.

Results

16 patients diagnosed with malignant brain tumors and treated with bevacizumab from 2010 to 2014 are presented. 5 DIPG (5) patients were treated at diagnosis right after radiation therapy. All other patients were treated at relapse or progression: Ganglioglioma (4), Anaplastic ependymoma (2), medulloblastoma (2), PNET (1), Oligodendrogliomatosis (1) and atypical teratoid rhabdoid tumor (1). The mean age at diagnosis was 6.2 years old [0.8-18.8]. Treatment was administered for a mean time of 8.1 months [1-18]. It was quite well tolerated with minimal toxicity (bleeding or wound healing problems), leading to temporarily treatment interruption in three patients. Treatment was stopped in one patient because of parental decision. At the present time: 1 patient continues in complete remission (6.3%), 3 patients have stable disease (18.7%), 2 patients are alive with tumor progression (12.5%) and 10 died with tumor progression (62.5%). Two of them had severe complications (high blood pressure and massive stroke) which may have accelerated death within the context of tumor progression.

Conclusions

Bevacizumab is a well tolerated drug and it can be used in combination with other antineoplastics stabilizing the tumor growth. Our results are likely to be influenced by the use of this drug as a second line in patients with progression of the disease and worse basal status.

EP-121

Brain Tumours

CLINICAL EXPERIENCE WITH NIMOTUZUMAB IN CHILDREN DIAGNOSED WITH DIFFUSE INTRINSIC PONTINE GLIOMA (DIPG)

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Objectives

Nimotuzumab is a humanized monoclonal antibody that targets the epidermal growth factor receptor (EGFR). It has been evaluated in malignant brain tumors in children. Our experience with nimotuzumab in DIPG is presented.

Methods

A retrospective study of patients with DIPG diagnosed and treated with Nimotuzumab between March of 2011 and March of 2014 at our unit was undertaken. Nimotuzumab was administered at a dose of 150 mg/m² weekly during Radiotherapy (six weeks) and q2weeks thereafter until tumor progression or toxicity.

Results

We took care of 8 patients diagnosed with DIPG and treated with nimotuzumab over three years. Five were girls. The mean age was 7.6 years (range 1.9-18.8). All of them received nimotuzumab in combination with radiotherapy. Seven patients received also vinorelbine during and after of radiotherapy. Five patients were treated also with bevacizumab, and six patients received also Dexamethasone. Nimotuzumab was administered for 1,5-17 months (mean: 3 months). Nimotuzumab was well tolerated in all cases. Mean follow up was 7.5 months (5-30). Half of patients (4) have died, two have progressive disease and two of them have stable disease.

Conclusions

DIPG has a poor prognosis. Radiation Therapy (IMRT) is the standard treatment upon diagnosis. Nimotuzumab is a recombinant monoclonal IgG antibody that recognizes human EGFR, blocks the binding of its ligands and leads to the inhibition of cell proliferation and pro-apoptotic signals and a decrease in vascular endothelial growth factor (VEGF) production. Nimotuzumab represents a new tool for treating DIPG along with radiation therapy. It has proved to be no less effective than chemotherapy, it can be administered along with other drugs and it has no toxicity in this group of patients.

EP-122

Brain Tumours

NIMOTUZUMAB EXPERIENCE IN PEDIATRIC HIGH-GRADE GLIAL TUMOURS

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Objectives

Nimotuzumab (NMZ) which is a monoclonal antibody against E-GFR on tumor cells becomes widespreadly used in pediatric oncology. In this study we shared our experience with nimotuzumab in high-grade gliomas.

Methods

We used nimotuzumab (150 mg/m²/w) in combination with vinorelbine (VNR) in 5 DIPG, one glioblastoma multiforme and one recurrent anaplastic ependymoma. In DIPG group median age was 9 years-old (3.5-17), there were 4 female and 1 male. Diagnosis of DIPG was made with MRG in 4 cases, except one who have had biopsy.

Results

All were irradiated after diagnosis. TMZ was used in 4 out 5 patients, prior to NMZ-VNR, with 2-10 courses starting at irradiation. Upon clinical or radiological progression, NMZ-VNR combination was started at median 7 (3-13) months. Median time of NMZ-VNR use was 6 months (1.5-15). One patient did not receive TMZ, but still on NMZ-VNR. She is alive for 17 months. Three out of other 4 patients died of progressive disease, but one with biopsy-proven disease is still alive for 30 months.

We have also used NMZ-VNR in a patient with GBM who have been treated with surgery and irradiation plus TMZ, but progressed at 13 months. Use of NMZ-VNR combination for 4 months unfortunately failed to stop progression in this patient.

Last patient was an anaplastic ependymoma who relapsed 2 years after inial diagnosis. After second surgery NMZ-VNR combination was started at 27 months. During 9 month-use of this combination she stayed progression-free, however she later progressed and died of disease.

Conclusions

Nimotuzumab was very well tolerated. Nimotuzumab plus vinorelbine combination seems to have some benefit in high-grade gliomas. Our results with two patients are encouraging. In children, we need to have more clinical trials with these targeted therapies of high-grade gliomas or recurrent gliomas.

EP-123

Brain Tumours

PINEALOBLASTOMAS

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Objectives

Pinealoblastomas (PBL) are rare tumors of the central nervous system and more common in children. The objective of this study is to evaluate the demographic data and outcome of children with PBL in a single center.

Methods

Files of children diagnosed with pinealoblastoma in the Istanbul University, Oncology Institute were evaluated retrospectively for demographic data, treatment and long term outcome.

Results

During 1990-2012, 6 children (3 male, 3 female) with a median age of 6 years (2 years- 14 years), were diagnosed with pinealoblastoma, in the Istanbul University, Oncology Institute. At the same time interval 494 patients <19 years old were diagnosed with malignant central nervous system (CNS) tumors in the same center, thus pinealoblastomas constituted 1.2 % of all CNS tumors. Three had subtotal resection and three underwent a biopsy. At diagnosis, one had spinal seeding both in MRI and cerebrospinal fluid cytology. All recieved craniospinal radiotherapy and chemotherapy, the patient <3 years old recieved neoadjuvant chemotherapy first. The median follow up is 5 years (1-9.5 years). Two patients are alive for 5 and 9.5 years. One has just had a total thyroidectomy for papillary thyroid cancer as a second malignancy at 9.5 years. All others have died at a median of 2.7 years due to progressive disease.

Conclusions

In conclusion, PBL are aggressive tumors necessitating intensive treatment strategies including surgery, craniospinal radiotherapy and chemotherapy. Patients should be folowed up for long term side effects such as second malignancies.

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NEUROCOGNITIVE EVALUATION OF LONG TERM SURVIVORS WITH ATYPICAL TERATOID RHABDOID TUMOR (ATRT): THE CANADIAN REGISTRY EXPERIENCE

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Objectives

Because ATRT is a rare disease of infancy carrying grim prognosis, focus on long term outcome, especially neurocognitive remain very limited. With new era of multimodality therapy, some patients are now long term survivors.

Methods

We reviewed the neuropsychological(NP) status of the survivors from the Canadian ATRT registry.

Results

Among patients diagnosed between 1995-2012, 16/72 were survivors(22%). Formal NP assessments were available in 8 patients. Five patients could not be tested (3 too young, 1 blind significantly impaired, 1 lost to follow up). Additionally 1 patient was in special education class(grade 12), one received educational assistance(grade 8), one met academic expectation(grade 4).

For the 8 patients with comprehensive NP, median age at diagnosis was 28.8 months(11.2-60.7). Four tumors were infratentorial and 3 were metastatic. Four patients underwent complete resection. All patients received post operative sequential high dose chemotherapy(Caroplatin/Thiotepa). Five patients received intrathecal chemotherapy. Two patients underwent radiation(1focal, 1CSI). Median age at time of NP was 7.3 years(3.9-9.28). Full Scale Intellectual Quotient(FSIQ) ranged from 60 to 119(median=71). Simple expressive and receptive language appeared relatively preserved(low average to superior). Three most recently diagnosed patients (median time assessment post diagnosis 2.6 years (2.6-4.7)) had average to high average scores for FSIQ, academic and visual spatial skills, visual and verbal memory. Four other diagnosed earlier tested at a median time of 5.1 years(3.3-8.3) post-diagnosis had FSIQ ranging from 60 to 71(median=68) and one patient with preexisting genetic syndromic condition was extremely low functioning(FSIQ<50). Approximately 50% of their scores were in the impaired range.

Conclusions

Whether these findings suggest further decline overtime or reflect improvement in overall management of these recently diagnosed patients remain unclear. Nevertheless this cohort of infants appears significantly impaired at school age despite the absence of systematic radiotherapy. Larger series focusing on neurocognition are definitely needed before embracing adjuvant radiotherapy as standard of care.

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Brain Tumours

**LATE MORBIDITY IN LONG-TERM SURVIVORS OF CHILDHOOD BRAIN TUMORS:A
NATIONWIDE REGISTRY- BASED STUDY IN FINLAND**

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Objectives

The population of long-term survivors of childhood brain tumors (BT) is growing and the follow-up of survivors should be organized in a structured way. Most of the earlier research on the morbidity of BT survivors has suffered from small sample sizes. On the other hand, larger studies are often based on self-reporting with a possibility for recall and selection bias.

Methods

All patients diagnosed with a neuroepithelial BT at age 0-15 years in Finland between 1970 and 2004 were identified from the Finnish Cancer Registry, and their new diagnoses (≥ 5 years after cancer diagnosis) were assessed using the Hospital Discharge Registry containing data on hospitalizations and outpatient visits in specialist health care. Siblings of the BT patients were identified as controls of the patients via Population Registry.

Results

The 5-year survivors of childhood BT had a significantly increased hazard ratio for endocrine diseases (HR 14.7), mental and behavioral disorders (HR 1.8), mental retardation/disorders of psychological development (HR 16.6), diseases of the nervous system (HR 9.8), disorders of vision and hearing (HR 10.5), and diseases of the circulatory system (HR 2.7) compared with the sibling control group. Most of the outcomes also had an increasing prevalence up to 10 or 30 years after primary diagnosis. Irradiation treatment did not explain all the excess of morbidity, Survivors of embryonal tumors had kidney problems more than the other groups. Female survivors had higher hazard ratios for mental and circulatory problems compared with siblings than had the male survivors.

Conclusions

Systematic long term follow-up and supportive measures are essential due to numerous late effects among childhood brain tumor survivors. Even health related quality of life of survivors might improve if late sequelae were recognized and taken care of adequately.

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Brain Tumours

ENERGY EXPENDITURE IN WHITE ADIPOSE TISSUE IS ACTIVATED IN RESPONSE TO BRAIN TUMOUR GROWTH

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Objectives

Brain tumours are the most common solid tumours in children. The PI3K pathway is frequently activated during tumourigenesis through deletion of the tumour suppressor phosphatase and tensin homolog (PTEN). In contrast, this same pathway may also be inhibited by increased PTEN expression in adipose tissue resulting in an increase in uncoupling protein (UCP) 1 expression and metabolic protection from tumourigenesis. This intrinsic protection is thought to arise from interscapular brown adipose tissue (iBAT) but may also occur through 'beiging' of inguinal white adipose tissue (iWAT). The aim of this study was to see if an association existed between UCP1 expression in adipose tissue and paediatric brain tumour growth through elevated PTEN levels.

Methods

Two types of medulloblastoma (WNT (n=3) and group 4 (n=5)) and ependymoma (n=3) tumour cells were orthotopically xenografted into mice. iBAT and iWAT samples were extracted from tumour and non-tumour bearing mice (n=5) to examine UCP1 and PTEN expression through QRT-PCR and Western blotting. Haematoxylin and eosin staining and UCP1 antibody immunohistochemistry (IHC) was also used to determine each BAT depot. Thermogenic activity of the adipose tissue was indirectly measured by thermal imaging of mice.

Results

iWAT from ependymoma tumour-bearing mice had evidence of beiging and increased UCP1 abundance through histology and IHC, while UCP1 expression in iBAT remained high in all mice. An increase in UCP1 gene expression and thermogenesis was observed in mice with spinal metastasis. PTEN expression did not relate to UCP1 expression.

Conclusions

Our data indicated mice implanted with aggressive tumours had increased UCP1 in iWAT. Though PTEN is not involved, other pathways like the β -adrenoceptor pathway should be explored due to its association with tumourigenesis and UCP1 expression in WAT. In conclusion, this pilot study suggests rapidly growing and metastatic brain tumours may stimulate metabolic protection via an increase UCP1 expression in iWAT.

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Brain Tumours

NO IMPACT OF HIGH DOSE CHEMOTHERAPY REGIMEN IN CHILDREN WITH HIGH RISK CNS TUMORS

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Objectives

It is unclear whether any specific high dose chemotherapy (HDC) regimen for autologous stem-cell rescue (ASCR) in children with high-risk or recurrent CNS tumors is superior. This study evaluates the outcome of different HDC regimens in children with CNS tumors.

Methods

Clinical characteristics, outcome and toxicity in children with high-risk CNS tumors treated from 1995 with HDC followed by ASCR were retrospectively reviewed. Primary endpoints were overall survival (OS) and event free survival (EFS). Toxicity was a secondary endpoint.

Results

Fifty-nine patients (22 males) with a median age of 5 (range, 1-18) were evaluated. Diagnoses were: medulloblastoma (34), CNS-PNET (10), high-grade glioma (6), ATRT (4), and other (5). Location was infratentorial in 71% of them. Disease status prior to HDC was: complete remission (CR) 25, non-CR 34. HDC regimen was: busulfan/melphalan (20); busulfan/thiotepa (16); carboplatin/etoposide/thiotepa (4), HD-thiotepa (3), tandem-HDC (5), and other (10). Median number of CD34x10⁶/Kg was 5.15 (range, 0.9-48). Median days of admission were 19 (range, 10-50). Seventy-one percent of the patients developed mucositis (38% grade IV) and 31% engraftment syndrome. Transplant-related mortality was 4±2%. At 5 years OS and EFS were 27±8% and 21±7% respectively. Five-year OS was 48±11%, 12±11%, and 28±12%, for patients receiving busulfan/melphalan, thiotepa-containing regimens, and other HDC-regimens respectively (p=0.4). Five-year EFS was 34±12%, 10±8%, and 28±12%, for patients receiving busulfan/melphalan, thiotepa-containing regimens, and other HDC-regimens respectively (p=0.6). Patients in CR prior to HDC achieved a 5-year EFS of 44±11% vs. 7±6% for those not in CR (p=0.02).

Conclusions

Although HDC with ASCR was well tolerated, and has been incorporated to our routine practice, overall results remain disappointing. No single HDC regimen showed superiority in children with high-risk CNS tumors. Disease status prior HDC remains the strongest predictor of survival.

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FOLLOW-UP STUDY OF INTELLECTUAL FUNCTIONING IN CHILDREN TREATED FOR A BRAIN TUMOR

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Objectives

Below average intellectual functioning, with performance IQ more affected than verbal IQ, is a well-known finding in children treated for a brain tumor. However, most studies are cross-sectional, making it difficult to evaluate the evolution of intellectual functioning and to disentangle tumor specific from treatment factors. In the present study we investigated the evolution of IQ performance between two time-points (at diagnosis and after treatment).

Methods

A total of 24 children diagnosed with a brain tumor at the University Hospitals Leuven were tested twice with the age-appropriate Wechsler scale. The first assessment was conducted as soon as possible after diagnosis and before initiation of chemo- and/or radiotherapy. The second assessment was performed 2-3 years after diagnosis. Mean age at diagnosis was 9.42 years. Localization was infratentorial in 63%; 25% of children were diagnosed with medulloblastoma. 21% received ventricular drainage and 71% underwent surgery before baseline testing. 67% underwent cranial irradiation during their treatment.

Results

At baseline, total IQ and performance IQ were significantly below the normative average ($t=-3.38$, $p=0.003$ and $t=-4.18$, $p<0.0001$). Performance IQ was significantly lower than verbal IQ ($t=-3.00$, $p=0.006$). A similar pattern was found at the second assessment. A repeated measures analysis with tumor type as between factor and the use of radiotherapy as covariate demonstrated a significant interaction effect for the difference score ($F=4,50$, $p=0.046$). The discrepancy between verbal and performance IQ increased with 9.5 IQ points over time for children with medulloblastoma.

Conclusions

Our results demonstrated a discrepant intelligence profile already present in newly diagnosed children. This pattern remained present 2-3 years after diagnosis but the discrepancy became more pronounced in children with medulloblastoma. More specific neuropsychological testing at diagnosis is recommended to refine the cognitive profile and larger groups are needed to evaluate more potential predictors of cognitive outcome in children treated for a brain tumor.

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STAT3 SIGNALING: A CRITICAL TARGET AMONG RESVERATROL-INHIBITED SIGNAL TRANSDUCTION PATHWAYS IN HUMAN MEDULLOBLASTOMA CELLS

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Objectives

Medulloblastoma is the most frequent brain malignancy in childhood and characterized with rapid growth, earlier intracranial dissemination and frequent recurrence. Although the combination of operation with craniospinal radiation and/or multi-agent chemotherapy have been adapted in clinical settings, the outcome of medulloblastomas remains poor due to the difficulty in removing the tumor radically and the side-effects of conventional adjuvant therapies. Several signaling pathways are activated in medulloblastomas and play pivotal roles in the tumor development and progression. Resveratrol, a non-toxic polyphenol compound, possesses multifaceted biological activities and shows inhibitory effects on medulloblastoma cells. However, the underlying anti-medulloblastoma mechanism(s) of resveratrol remains unclear. This study aims to address this issue.

Methods

The influences of resveratrol in the statuses of cancer-associated pathways mediated by Wnt, Notch, NF- κ B, Sonic hedgehog/SHH and STAT3 of medulloblastoma UW228-2 and UW228-3 cells were analyzed by multiple experimental approaches.

Results

Resveratrol suppresses Wnt, Notch, Sonic hedgehog/SHH and STAT3 activations as well as the expression of their downstream genes. NF- κ B signaling is enhanced by resveratrol and its selective inhibition directly commits resveratrol-treated cells to apoptosis without induction of differentiation. Selective inhibition of Wnt, Notch or Sonic hedgehog/SHH activation has little effect on the growth of medulloblastoma cells. A single dose of AG490 effectively inhibits STAT3 activation and leads the treated cells to growth arrest and apoptosis.

Conclusions

Multiple cancer-associated signaling pathways are concurrently inhibited by resveratrol, of which STAT3 inactivation is the critical event because of the importance of this signaling in the survival of medulloblastoma cells. STAT3 signaling can be regarded as the molecular target and resveratrol as a promising agent in the management of medulloblastomas.

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OMEGA-3 FATTY ACIDS INHIBIT MEDULLOBLASTOMA GROWTH IN VITRO AND IN VIVO

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Objectives

Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are omega-3 fatty acids with antitumoral effects in several cancer types. DHA also protects neural cells from apoptosis and is of importance in the maintenance of normal brain development and function including cognitive functions.

Medulloblastoma, the most common malignant brain tumor of childhood is a highly invasive embryonal tumor arising in the cerebellum or brainstem . Multimodal treatment is necessary including surgery, radiotherapy and chemotherapy. However, treatment often results in significant neurological sequelae and the risk of resistant relapses is significant. The neuroprotective and antitumoral properties of omega-3 could therefore be of great benefit

Methods

Cytotoxic activity of DHA and EPA was studied in cell viability assays in a panel of medulloblastoma cell lines. The molecular mechanisms were characterized using cell- and molecular biology techniques. Mice with human medulloblastoma xenografts were treated with omega-3 fatty acids prophylactically and therapeutically while tumor growth was monitored.

Results

DHA and EPA induced medulloblastoma cell toxicity with IC₅₀ values ranging from 1.9 to 68 μM in six medulloblastoma cell lines. DHA inhibited the prostaglandin E2 production, indicating a possible mechanism of action. *In vivo*, omega-3 supplementation resulted in significantly delayed establishment of xenograft tumors and significant inhibition of tumor growth when established tumors were treated. The *in vivo* treatment was non-toxic.

Conclusions

Medulloblastoma cells are highly sensitive to omega-3 induced toxicity both *in vitro* and *in vivo*. DHA/EPA are therefore good candidates for improving current therapy by acting as both "sword and shield" by killing off cancer cells while protecting healthy neurons from therapy-induced toxicity promoting cognitive function in survivors. Thus, omega-3 has the potential of a tumor growth inhibitor as well as that of reducing sequelae.

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TUMOR HISTOLOGY ACCORDING TO TUMOR LOCATION IN CHILDHOOD CENTRAL NERVOUS SYSTEM TUMORS: SINGLE CENTER STUDY

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Objectives

central nervous system tumors account for second most common childhood malignancies and the first cause of mortality in children with cancer. Patients received multimodality treatments according to the pathology of their tumor. In this area, improving treatment modalities can lead to increase the survival rate of patients.

by this study, we examined the pathologic types of childhood brain tumors based on tumor location in patients who referred to MAHAK's Pediatric Cancer Treatment and Research Center (MPCTRC) in Tehran, Iran for treatment.

Methods

A retrospective review of all children less than 15 years old with a CNS histologically proven tumor, who presented to MPCTRC from April 2007 to April 2010, was performed. Data was analyzed by SPSS version 19 .

Results

There were 198 (124 boys) children eligible for the study. The majority of the tumors were infratentorial (n=134), supratentorial (n=60) and spinal (n=4). the mean age per tumor location was 6.33 ± 4.08 years for supratentorial, 5.96 ± 3.41 years for infratentorial, and 7.75 ± 4.99 years for spinal tumors. Tumor histology according to infratentorial location was as: medulloblastoma (49.26%), low grade glioma (23.16%), high grade glioma (15.65%), ependymoma (10.43%), AT/RT and Germ cell tumor 0.75% respectively. according to supratentorial location, there were low grade glioma (34.97%), high grade glioma (31.6%), ependymoma (10.09%), PNET (13.33%), AT/RT (3.33%) and Germ Cell tumor, Craniopharyngioma, Primary CNS malignant lymphoma, histiocytosis 1.67% respectively. At the time of this analysis, there were 82 (41.4 %) deaths, and 11 (5.6 %) lost for follow-up.

Conclusions

In this hospital base study, the rate of commonest types of CNS tumors were similar to other reports. these data can be as a benchmark for increasing our understanding of childhood CNS tumors in Iran.

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SMALL MOLECULE TOLFENAMIC ACID INHIBITS MARKERS OF ANGIOGENESIS IN MEDULLOBLASTOMA CELLS VIA TARGETING SPECIFICITY PROTEIN TRANSCRIPTION FACTORS

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Objectives

Medulloblastoma (MB) requires aggressive multimodality therapy. Survivors frequently suffer numerous long-term side-effects from such therapy. The objective of this study was to explore novel strategies for enhancing and optimizing the therapeutic effects of current MB treatments. Specificity protein (Sp) transcription factors (Sp1 and Sp3) are known to regulate survivin, an inhibitor of apoptosis protein associated with a poor prognosis and resistance to treatment. Sp proteins also modulate the expression of vascular epithelial growth factor (VEGF) and regulate angiogenesis. Small molecule tolfenamic acid (TA) inhibits MB cell proliferation and tumor growth in mice xenografts by targeting Sp proteins and survivin. We evaluated the effect of TA on the expression of VEGF and VEGFR1 and compared it with the changes in the key transcription factors, Sp1, Sp3, HIF-1 α , and ERK1/2 phosphorylation and microRNAs, miR20a and miR27a (regulators of Sp1 repressors).

Methods

Human MB cell lines, DAOY and D283, were treated with vehicle (DMSO) or TA (10-100 μ M) and cell viability was monitored at 24-72 hours post-treatment using a CellTiterGlo kit. Mithramycin A (10-100nM) was used in some control experiments. The expression of Sp1, Sp3, survivin, ERK1/2, pERK1/2 and actin were determined by Western blot analysis and microRNA expression was measured using TaqMan small RNA assays.

Results

TA caused a dose and time-dependent inhibition (15 μ g/ml: ~50% at 48 hours) of cell viability and decreased the expression of Sp1, Sp3, survivin, VEGF, VEGFR1 and total/phospho ERK1/2. TA (15 μ g/ml: 48 hours) caused ~40% decrease in the expression of miR20a and miR27a.

Conclusions

These results demonstrate that TA targets key regulators of MB tumor growth mediated via Sp proteins-associated molecular mechanisms, including the candidates involved in angiogenesis. Further research will focus on epidemiological studies to evaluate the association of Sp proteins in MB, along with dedicated molecular profiling to better understand the underlying mechanisms.

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INTRAOPERATIVE MRI FACILITATES AGGRESSIVE BRAIN TUMOR RESECTIONS IN INFANTS, CHILDREN AND ADOLESCENTS

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Objectives

The prognosis for children with operable brain tumors correlates to the degree of resection, regardless of benign versus malignant histology. The use of adjuvant chemotherapy and/or radiation therapy is critical, but initial tumor resection remains paramount. The application of diagnostic quality intraoperative magnetic resonance imaging (iMRI) has been recently introduced to pediatric neurosurgery. We have designed and implemented a unique IMRIS iMRI operating room suite whose mobile, ceiling-mounted, 1.5 Tesla Siemens magnet glides from a diagnostic suite to the operative suite. We present our first 200+ consecutive iMRI brain tumor resections.

Methods

In February 2007, we dedicated an iMRI operating room suite housing MRI-compatible anesthesia equipment, standard operating room equipment (intraoperative neuro-navigation and mobile operating microscopes) and robust safety protocols. The iMRI room is engaged for epilepsy and Chiari surgery, vascular malformations and brain tumor resections.

Results

We employed the iMRI operating room for 207 tumor extirpation cases over a 7 year period. Patients ranged in age from infancy to late adolescence, with a mean age of 9 years. Posterior fossa tumors accounted for 41% of the resections. Low-grade neoplasms represented 67%. There were an average of 1.2 intraoperative MRI scans per procedure, with a mean scan time of 37 minutes. Intraoperative scanning prompted additional tumor resection in 43% of cases. There were no iMRI-related complications, no increased incidence of infection (one patient) and no anesthesia problems. The next day re-operation rate (going back to neurosurgery the next day due to unseen, unresected tumor) was zero.

Conclusions

iMRI facilitates aggressive brain tumor resection in infants, children and adolescents with a low complication rate. The technology is safe and has resulted in no unanticipated 'go back' reoperations the next day as had historically occurred in our prior non-iMRI cases. iMRI during tumor resection surgery has become standard practice at our institution.

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INTRATHECAL-/INTRAVENTRICULAR-METHOTREXATE IN CHILDREN WITH CNS TUMORS: AN EXPERIENCE OF A SINGLE INSTITUTE

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Objectives

Intrathecal- and intraventricular-chemotherapies using methotrexate (IT-MTX and IV-MTX) are powerful tools controlling CNS leukemia and IT-MTX is standard treatment. However, as for these procedures, leukoencephalopathy is concerned about in combination with radiation therapy in CNS tumors. The aim of this study is to exam the incidence of leukoencephalopathy correlating with IT-/IV- MTX.

Methods

We retrospectively reviewed the medical records of pediatric patients with CNS tumors treated with IT-/IV-MTX in our institute since 2006 till 2012.

Results

36 patients, aged 0 to 26 years, were treated with IT-/IV-MTX. 13 patients were diagnosed with germ cell tumor, 16 medulloblastoma, 5 ependyoma and 1 AT/RT. MTX (8 to 12 mg) was given via lumber puncture (IT-MTX) in a single does and 1.5 to 3 mg of MTX was given via Ommaya reservoir (IV-MTX) for a single or three to four consecutive days. 29 newly diagnosed patients received IT-MTX in combination with systemic chemotherapy with (n=20) or without (n=9) radiotherapy: mainly, 24Gy local irradiation for germinoma and 50-55Gy local and 18-24Gy craniospinal irradiation for medulloblastoma. 12 patients with relapsed tumors received IT-/IV-MTX in combination with radiotherapy (n=9). At present, 31 patients survive for 5 to 96 months. Four patients received more than 10 courses of IT-/IV-MTX and two of them developed asymptomatic leukoencephalopathy. These two patients received IT/IV MTX for recurrent diseases after 1st. line treatment with irradiation and systemic chemotherapy.

Conclusions

In this study, development of leukoencephalopathy was limited to patients with recurrent diseases. In newly diagnosed patients, IT/IV MTX seems to be the treatment that should be developed in future.

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A RETROSPECTIVE MULTICENTER ANALYSIS OF CHILDREN WITH LOW GRADE GLIOMAS - RESULTS OF THE JAPANESE PEDIATRIC BRAIN TUMOR CONSORTIUM

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Objectives

We retrospectively investigated long-term history of children with low-grade gliomas (LGGs) diagnosed at 27 centers in Japan from 1998 to 2013.

Methods

219 children (mean age 5.9 years (range: one month-15 years), tumor location: cerebrum 46, cerebellum 57, optic pathway/thalamus 87, midbrain 4, others 25) were assessed. In 67 patients tumors were totally removed. Histological WHO grading was grade I in 144 (pilocytic astrocytoma (A)128), grade II in 51(diffuse A 20, pilomixoid A 11) and LGG, NOS in 18. In six patients histological examinations were not done.

Results

Initially, 99 received chemotherapies and 24 received radiotherapy. The patients were followed for median of 35 months (one-190 months) from diagnosis. At present 93 patients have been in complete remission and 117 in stable disease, but recurrence have been observed in 83 among them. Seven patients died of diseases. In one of them, malignant transformation of the disease was observed 9 years after diagnosis. For all LGG 15-year OS and PFS were 94.5±2.6% and 43.0±5.2%. 10-year OS and PFS of PA, DA, and LGG, NOS were 95.1±3.3% and 38.2±6.4%, 70.6±20.8% and 50.7±12.9%, 100% and 72.7±17.7%, respectively. Among PA, 10-year PFS of optic pathway was inferior to that of cerebellum (18.4±7.0vs.60.3±9.0%). In patients with residual tumor after surgery, 10 year PFS was 33.7±6.2%, which was worse than that in patients whose tumors were totally removed (66.1±8.8%). There were no patients suffering recurrence 7.9 years after diagnosis. As the sequelae, epilepsy, hydrocephalus and lost vision were seen. 31 have some endocrinal problems (26 need therapy) and 28 need some support for living. One had second malignancy.

Conclusions

LGGs especially PA have clinically benign appearance and the incidence of malignant

transformation was low. Pathologic diagnosis, tumor location and resection extent influence the outcome of the disease. We also need to follow the late effect sequel.

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Brain Tumours

MEDULLOBLASTOMA AND RISK OF PERI HIPPOCAMPAL DISEASE PROGRESSION

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Objectives

To report the natural history of medulloblastoma (MB) with incidence of hippocampal area metastases.

Methods

Children treated for high-risk (HR) MB (majority included in PNET HR+ 5) and for metastasis at time of relapse were reviewed for distribution of metastatic location. Axial post-contrast MRIs, and central review reports were used to identify metastasis and hippocampus. Clinical and radiographic were analyzed in term of nodular or leptomeningeal infiltration and distance to peri hippocampal and hippocampal region divided in three groups of MTS: hippocampal (H-MTS), near hippocampal (1-10 mm from hippocampus; NH-MTS), at distance (AD-MTS). We divided the hippocampal area into the anterior and the posterior area.

Results

51 patients were analyzed: 33 initially HR-MB (iMB) and 19 at time of relapse (ToR) (1 HR with spinal location at diagnosis and treated with craniospinal irradiation (CSI) at 23.4 Gy and 18 low risk at diagnosis). In iMB group, 16 (48%) had sustentorial metastases at diagnosis: 4 intra lateral ventricular nodules, 1 leptomeningitis infiltration, 2 metastasis NH-MTS, 9 AD-MTS including 4 with V3 infiltration. On the 19 patients in ToR group, 12 developed a sustentorial location: 6 with intra lateral ventricular nodules, 2 in NH-MTS (included the HR patient with leptomeningitis infiltration), 1 in contact with hippocampal area and 3 in AD-MTS. In NH MTS, only 3/10 were near to anterior area.

Conclusions

These results underline that in high risk MB and in patients with relapse after low risk, 50% and 60% respectively developed sustentorial location. No metastasis underwent into hippocampal area. 12% at diagnostic and 15% after progression presented metastases near to hippocampal area. This study is still on going to define a sub- group of patients with low risk of hippocampal progression to propose partially hippocampal-avoidance CSI.

EP-137

Brain Tumours

EPENDYMOMA TREATED IN A MULTI-DISCIPLINARY CLINIC SETTING IN SOUTH AFRICA

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Objectives

To review the demographics and outcomes of Paediatric ependymoma patients referred to the combined paediatric neuro-oncology services of the University of Cape Town.

Methods

A retrospective analysis was performed on all children aged 13 years or less diagnosed with ependymoma at the Red Cross Children's Hospital (RCCH) and Groote Schuur Hospital (GSH) between 1980 and 2013.

Results

59 children were seen aged between 1 and 13 years with a median of 6 years. 4 patients had no data available and were excluded from the analysis.

44 patients(80%) had brain tumours, of which 32(73%) were infratentorial, 11(25%) were supratentorial and one was not known. 8 patients(15%) had spinal tumours. 34(63%) patients had localised disease, 10 patients(18%) had advanced or metastatic disease and 11 patients had no staging information.

25 patients(45%) had a gross total resection of tumour, 15 patients(27%) had a subtotal resection and 7 patients(13%) had biopsy only. In the remainder of patients, extent of surgery was not documented.

10 patients(18%) received chemotherapy and 42 patients(76%) received radiotherapy, of which 18(43%) received craniospinal radiotherapy and 4(9%) received proton therapy.

Estimated relapse free survival(RFS) of all patients was 54.8% and overall survival(OS) was 65%.(n= 53) For brain tumours only (n=43) RFS was 50%.

For grade 2 tumours(n=36) RFS was 47.25%, whereas for anaplastic tumours(n=11) RFS was 62.5%. For infratentorial tumours(n=28) RFS was 51.8% and for supratentorial(n=5) tumours it was 37.9%. For patients treated between 2001 and 2010 only, 5 year OS was 75.3%.

Conclusions

Management of ependymoma is difficult and best done by a multi-disciplinary team even in a resource-constricted environment. Management strategies have evolved over the 33 years of study and outcomes have improved.

EP-138

Brain Tumours

QUALITATIVE EVALUATION OF OUR CRANIOSPINAL IRRADIATION TECHNIQUE (PLANNING AND SET UP) IN PEDIATRIC PATIENTS WITH MEDULLOBLASTOMA (MB)

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Objectives

Craniospinal irradiation historically became the mainstay of therapy for MB, introduced Cooperative Groups adjuvant chemotherapy in the treatment of MB and leading to improved survival and subsequent reduction of RT dosage in irradiation treatment. To achieve a dose reduction in this kind of treatment offers better neurocognitive results and clinical outcomes in patients with average risk. This concept supports the importance of developing adequate techniques for dose delivery in RT. The purpose of this paper was to document the quality of RT delivered in pediatric patients with MB implementing our technique proposed for our task group.

Methods

We present our technique of planning and patients' set up for MB treatment. 24 pediatric patients with chemotherapy scheme were treated in our department during the period 2009-2012. The mean age was 8 years (3 – 14 yrs.) After surgery, a RT treatment was delivered with 3D conformal RT (CRT). Different devices were used for the patients immobilization. The individual set ups varied in prone or supine according to the patient clinical status. RT dose in critical structures, was recorded in plans for each patient.

Results

These technique allowed us to deliver highly reproducible treatments with a very low rate of relapse, only the 12.5%. As a secondary goal with the immobilization devices, we improved the comfort of patients and reduced the margin of error in the set up of each field.

Conclusions

In the management of pediatric patients with MB, any strategy to reduce RT dose into the craniospinal axis, must include accurate planning verification and the dose delivered in all risk organs and any PTV for each treatment. In our experience with CRT, consistency in the set up each day of treatment is crucial and the proposed technique is a good way to achieve it.

EP-139

Brain Tumours

EVALUATING THE EFFECTS OF TREATMENT BRAIN TUMORS AND INTRACRANIAL DISEASES IN CHILDREN BY ROTATING GAMMA KNIFE (RGK) AT BACH MAI HOSPITAL, VIETNAM

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Purpose:

To assess the effects of treating brain tumors as well as intracranial diseases by rotating gamma knife (RGK) at Bach Mai Hospital, Vietnam.

Methods and Materials:

A prospective clinical interventions in 67 patients (≤ 15 years) were diagnosed with brain tumors or intracranial diseases, treated with rotating gamma knife from July 2007 to July 2013 at Bach Mai Hospital, Vietnam.

Results:

Average age is 10.5 years old. Ages at the time of radiosurgery ranged from 4 (youngest) to 15 (oldest). The male/female ratio: 1,8. In our study, 67 patients including arteriovenous malformations (AVM) 22.4 %, pineal tumors 16.4 %, astrocytoma 7.5%, cavernoma 6.0%; ependynoma 6,0%. Clinical symptoms: headache: 73.1%; nausea, vomiting: 53,7%; convulsions: 25.4%; hemiplegia: 20.9%; cerebellar syndrome: 6%. Tumor location: frontal - temporal sides: 56.5 %; intraventricular 6.0 %; brainstem 7.5 %. The median tumor size was 2.13 ± 1.24 cm (range 0.6–4.1cm). The median prescribed dose was varied (depending on nature and position of the tumor): 14,4Gy; min: 8Gy, max 20Gy. In group arteriovenous malformations and low grade astrocytoma had good response. Craniopharyngiomas had poorly response. So far, 55 patients (82.1%) improved obviously clinical symptoms: reduced headache, nausea, tumor size. 12 patients (17.9%) died due to progressive tumor after treatment.

Conclusions:

Radiosurgery for treating brain tumors and intracranial diseases with Rotating Gamma Knife is safe and effective for children.

EP-140

Brain Tumours

TREATMENT OUTCOME OF CHILDREN WITH MEDULLOBLASTOMA: 20-YEAR EXPERIENCE FROM A SINGLE INSTITUTION IN MALAYSIA

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Objectives

To review outcome of children with medulloblastoma treated at University Malaya Medical Centre (UMMC) from 1994 till 2013.

Methods

Clinical and prognostic indicators of 52 patients with medulloblastoma from 1994 to 2013 were retrospectively analyzed. Children aged more than 3 years were treated on CCG 9892 protocol and for those less than 3 years, UKCCSG CNS 9204 (1994-1996) and Headstart (from 1997 onwards) protocols were used. Risk stratification was based on Chang staging classification.

Results

There were 20 male patients. Median age of diagnosis was 3.5 years(range:0.9-15) and median duration of symptoms was 3 weeks(range:1-20). Vomiting (n=29), headache (n=21), unsteady gait (n=15) and diplopia (n=6) were common presenting symptoms. 15 patients were excluded from the review; 5 refused treatment after surgery, 8 defaulted follow-up and 4 transferred to other hospitals. The remaining 37 patients were treated as per protocol based on risk stratification. 43% (n=16) of them had metastatic disease at diagnosis. Post-operative residual tumour >1.5cm² and distant metastasis at presentation were associated with high relapse rate of 71% and 75% respectively. In this cohort, age at diagnosis, gender, duration of presenting symptoms, delayed post-operative imaging and delay in radiotherapy did not significantly influence the outcome. Analysis of histopathological result was excluded due to lack of description details. 57% (n=21) of patients died; 4 related to treatment associated complication and 17 due to disease recurrence or progression. Median time of recurrence was 11 months (range:1-24) and most of them died within 1 year. None of them responded to salvage chemotherapy. 5-year overall survival rate is 39.4% with a median follow-up time of 9 years(range:6-13). Neuro-endocrine abnormalities are commonest long-term side effects.

Conclusions

Our results demonstrate dismal prognosis of medulloblastoma due to advanced stage of disease at diagnosis. High rate of treatment refusal and abandonment were observed in our centre.

EP-141

Brain Tumours

STUDY OF TERT AND MECHANISTICALLY RELATED MOLECULES IN MEDULLOBLASTOMAS

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Objectives

Hotspot activating mutations of the *TERT* promoter region were recently described in several tumor types. These mutations lead to enhanced expression of telomerase, being responsible for telomere maintenance and allowing continuous cell division. Additionally, *ATRX* mutations are an alternative telomere maintenance mechanism, associated with histone H3 mutations, responsible for disrupting the histone code and affecting regulation of transcription. Alternatively affecting histone regulation are *SETD2* inactivating mutations and *SETD2* absence results in microsatellite instability (MSI). Here, we investigated the clinical relevance of these mechanistically related molecules in medulloblastoma.

Methods

A cohort of 113 formalin-fixed paraffin embedded medulloblastoma (aged 1-70 years) was used to investigate hotspot mutations of *TERT* promoter region, *H3F3A* and *HIST1H3B*, using Sanger sequencing. *SETD2* deregulation was analyzed at the protein level by immunohistochemistry. MSI status and 24 MSI target genes were studied by multiplex PCR followed by genotyping

Results

We have successfully sequenced *TERT* in 68 medulloblastoma and identified a total of 18 mutated cases (26.5%). The C228T and C250T mutations were detected, respectively, in 15 and 3 samples. Similarly to previous reports, *TERT* mutations were more frequent in older patients ($p < 0.0001$), being found only in 5 patients younger than 20 years of age. In addition, *TERT* mutated tumors were more frequently recurrent ($p = 0.035$) and *TERT* mutations were significantly enriched in tumors located in the right cerebellar hemisphere ($p = 0.035$). No other clinicopathological data available was found to be statistically significant. No mutations were found on *H3F3A* or on *HIST1H3B*. MSI phenotype was seen in 10% of the analyzed samples. *SETD2* expression is currently under pathological evaluation

Conclusions

TERT promoter mutations are frequent in medulloblastoma and associated with older patients, tumors prone for recurrence and arising in the right cerebellar hemisphere. On the other hand, MSI phenotype and Histone mutations are rare events in medulloblastoma.

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Brain Tumours

MEDULLOBLASTOMA IN CHILDHOOD:TUNISIAN EXPÉRIENCE

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Objectives

Medulloblastoma is the most common brain embryonal tumour in children. The aim of this retrospective study is to evaluate clinical, radiological, therapeutic and prognostic features of this disease.

Methods

Seventy seven children with medulloblastoma were treated in our department between 1994 and 2010, the clinical presentation was dominated by signs of intracranial pressure (80%), gait instability (28.9%) and altered eye movement and diplopia (10.4%). The tumours were located in the fourth ventricle (35%) and vermian (30%). A ventricular shunt before resection was performed to increase intracranial pressure (7%). The resection was complete in 76.6% of patients. Four patients have leptomeningeal dissemination. Sixty eight patients (88%) had postoperative radiotherapy (RT), preceded by an initial chemotherapy (CT) in 25 cases (32.4%), exclusive in 36 cases (46.7%) and followed by CT in 5 cases (6.4%). The average dose to the craniospinal axis was 27.13 Gy (Range, 18 - 36Gy) with a boost to the posterior fossa to a total dose of 49.76 Gy (Range, 50-56 Gy). Exclusive CT was recommended in 9 patients. CT protocols most commonly used were VP16 - carboplatin or BBSFOP.

Results

The median age was 9 years with a sex ratio of 2.2. After a median follow up of 32.7 months, 29 patients (37%) were in complete remission, 46 patients (59%) presented local recurrence that 36 required reoperation and 12 a CT alone. Two patients were lost to follow up after the initial resection.

Conclusions

Medulloblastoma is curable in a significant proportion of patients with average-risk disease at initial diagnosis. The delay in diagnosis and quality of excision remain the most important factors that influence the prognosis.

EP-143

Brain Tumours

RADIATION THERAPY IN THE TREATMENT OF BRAIN-STEM TUMORS IN CHILDREN

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Introduction

Due to their location, tumors of the trunk (TT) present a high surgical risk and the diagnosis is usually made by imaging. In Chile, these cases are treated according to the PINDA Program (national treatment guide for pediatric tumors). All patients receive radiotherapy (RT) after diagnosis. The aim of this study is to evaluate the treatment results for TT at the National Cancer Institute (NCI) between 1993 and 2011.

Patients and Method

A retrospective review of patients diagnosed with TT at NCI was conducted. Patient population, symptoms, treatment received and overall survival are described. Prognostic factors were analyzed.

Results

From November 1993 to December 2011, 70 children were referred for possible RT, 68 of them actually received it. The median age at diagnosis was 7 years old. In March 2014, out of 70 patients, 61 were deceased, all due to disease progression. The median survival of patients who received RT (68 patients) was 11,1 months from the end of treatment; the survival rates at 1, 2, 3 and 5 years was 48 %, 16 %, 15 % and 15% respectively. Univariate analysis showed that survival was affected by the MRN high resolution imaging ($p = 0.08$, HR 1,64) and by the diffuse tumor pattern ($p = 0.025$, HR 1,14). Multivariate analysis showed survival is affected by the MRN high resolution imaging ($p = 0.011$, HR 2,56) and a higher dose of RT protector ($p = 0.017$, HR 0,87).

Conclusions

The poor results obtained in the treatment of TT with RT at the INC are similar to those reported by other centers. Further explorations regarding other treatment options based on combined therapy using RT are needed.

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Brain Tumours

PRE-RADIATION CHEMOTHERAPY IMPROVES SURVIVAL IN PEDIATRIC DIFFUSE INTRINSIC PONTINE GLIOMAS (DIPG)

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Objectives

The median survival rarely exceeds 9 months after standard treatment of DIPG by focal radiotherapy. The BSG 98 protocol was a prospective trial of frontline chemotherapy aimed at delaying radiation until time of clinical progression. As OS results were encouraging (*Frappaz Neuro Oncology 2008*), this protocol was proposed as a routine in our cancer center for further DIPG patients who did not participate to another prospective study. The current abstract deals with this new cohort.

Methods

Protocol consisted of frontline chemotherapy. Each cycle included three courses delivered monthly ; the first course was nitrosourea-cisplatin, and the second and third were high-dose methotrexate. Standard radiotherapy was delivered either at time of progression or electively after 12 month. A contemporary comparison cohort of 9 patients who received any experimental treatment that contained at least local radiation therapy served as controls. The initial and 3 monthly MRI were retrospectively centrally reviewed by a specialized neuro-radiologist who confirmed diagnosis of DIPG according to published criteria.

Results

From 15/09/2004 to 14/01/2013: 16 patients were treated according to BSG 98 protocol. Two patients underwent one cycle; 2 patients two cycles; one patient three cycles; nine patients four cycles and one patient was going on his third cycle (not finished yet). Three patients experienced severe iatrogenic infections, and ten patients required platelet transfusions. Median survival increased significantly in patients treated according to protocol compared to contemporary control (15 months vs 8 months $p=0.029$), median PFS was longer (respectively 8 vs 3 months $p=0.077$) and median radiation free survival was 7 months.

Conclusions

BSG 98 strategy is confirmed as one of the most effective current treatment of DIPG. It may serve as a control arm in randomized trial exploring innovative treatment, and may be proposed to parents and children who are reluctant for biopsy.

EP-145

Brain Tumours

SALVAGE CHEMOTHERAPY WITH BEVACIZUMAB-IRINOTECAN ASSOCIATION IN RECURRENT/REFRACTORY BRAIN TUMORS IN CHILDREN

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Objectives

To date, there is no current standard of care in the treatment of recurrent/refractory brain tumors and the majority of patients succumb to disease. A novel treatment strategy exploring the use of anti-angiogenic agents combined with cytotoxic CHT has been investigating but only few studies are reported. We report a phase II study in a series of consecutive cases with recurrent/refractory brain tumors.

Methods

Eight children (6 males and 2 females), median age at initial diagnosis 114 months, (range 17-240), affected by relapsed medulloblastoma (5pts), glioblastoma (1pt), PNET (1pt), low-grade glioma (1 pt), were treated with bevacizumab and irinotecan association . Five of these also received temozolamide. All pts had received two previous CHT lines. The median age at start of treatment was 143 months (range: 72-300). All pts received treatment as follows: bevacizumab 10 mg/kg i.v. with irinotecan 150 mg/m² i.v. every 2 weeks ± temozolamide 200 mg/m² p.o. daily for five consecutive days every 28 days. In total 117 courses were administered (median/pt:14.6, range 4-44). Two pts are still on treatment.

Results

Two pts (MB) who started treatment after radical surgical re-operation remained in CR respectively for 19 and 14 months. One of these is still on treatment, the other one progressed 6 months after therapy was stopped. Five pts (3 MB, 1 PNET, 1 GB) maintained SD (62%) for a median of 5.4 months (range 2-9). One pt (LGG) obtained a PR after 3 months and he is still on treatment. PFS at 6 months was observed in 5 pts (62%). Treatment was well tolerated with a good quality of life. Toxicity included allergy (1 pt) and grade 3 thrombocytopenia (5 pts).

Conclusions

In our small series of pts, bevacizumab-irinotecan association ± temozolamide showed encouraging results with a low-toxicity. Further studies in a larger population of pediatric pts with brain tumors are needed.

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Brain Tumours

HIF1A IS OVEREXPRESSED IN MEDULLOBLASTOMAS AND ITS INHIBITION IS ABLE IN REDUCE PROLIFERATION AND INCREASE HIF2A AND ATG16L1 METHYLATION LEVELS IN A CELL LINE MODEL

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Objectives

Medulloblastoma (MB) is the most common malignant brain tumor in childhood. Several studies had correlated hypoxia genes to tumor progression and chemo/radioresistance in human cancers but few is known about these genes in MB. The aim of this study was to analyze the expression profile of hypoxia related genes in MB.

Methods

This study evaluated the gene expression profile of the hypoxia related genes *CA9*, *CA12*, *HIF1A*, *HIF2A*, *SCL2A1* and *VEGF* in 38 pediatric medulloblastoma in comparison to those from 7 non-neoplastic fetal cerebellum samples by qRT-PCR using TaqMan probes. Additionally it was analyzed the effect of hypoxia and normoxia level conditions in the pediatric medulloblastoma cell line UW402 in gene expression and the effect of the *HIF1A* silencing by siRNA in cell proliferation (by XTT assay) and methylation levels of 10 genes related to hypoxia and apoptosis by pyrosequencing.

Results

A lower expression level of *CA9* (-4.21-fold, $P = 0.009$), *CA12* (-44.8-fold, $P < 0.001$) and *VEGF* (-5.24-fold, $P = 0.001$) and a higher *HIF1A* expression level (+1.93-fold, $P = 0.022$) was observed in MB samples when compared to fetal non-neoplastic cerebellum when analyzed by Mann-Whitney test. In UW402 cell line, the hypoxia condition resulted in up regulation of the genes *HIF1A*, *VEGF*, *SCL2A1* and *CA9*. After *HIF1A* knockdown (protein silencing efficiency 88% analyzed by Western blot) it was found a decrease of 30% in cell proliferation ($P < 0.05$, One-way ANOVA) and the reduction of the expression of the genes *VEGF*, *SCL2A1* and *CA9*. Inhibition of *HIF1A* caused significant increase in the pattern of methylation of genes *ATG16L1* and *HIF2A*.

Conclusions

Except to *HIF1A* gene, a lower expression of hypoxia related genes was observed in MB when compared to fetal cerebellum. Silencing of *HIF1A* in pediatric MB cell line was able in decrease significantly the cell proliferation, suggesting that *HIF1A* could be a potential therapeutic target gene in MB.

EP-147

Brain Tumours

**EFFECTIVENESS OF TREATMENT OF CHILD SUPRATENTORIAL PRIMITIVE
NEUROECTODERMAL TUMORS**

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Objectives

Supratentorial primitive neuroectodermal tumors in children are relatively rare, and are one of the most malignant brain tumors.

Methods

This work is based on results of retrospective analysis of treatment of 73 children with primitive supratentorial neuroectodermal brain tumors, that have undergone treatment in the Institute during 1995 - 2011. The patients consisted of 43 (58.9%) male and 30 (41.1%) female children, and the mean age at surgery was 5.5 years (range 1 month – 17 years). 24 (32.9%) cases were infants.

Results

Total resection was performed in 48 (65.8%) cases, subtotal in 19 (26.0%) cases and partial in 4 (5.5%) cases. Two children had a biopsy. The operative mortality was 5.5%. In 29 (39.7%) cases tumor was classified as neuroblastoma and in 4 (5.5%) cases - ganglioneuroblastoma. The presence of tumor cells in the CSF was found in 18 (24.7%) cases, metastasis to other parts of the brain diagnosed in 3 (6.8%) cases and metastases in the spinal cord in 5 (6.8%) cases. Extraneural dissemination in two cases. 57 (82.6%) patients underwent chemotherapy, and 39 (56.5%) patients had radiation therapy. Follow-up data from 1 month to 13 years is available for all patients, average survival rate 31.2 months. There was a significant worse survival in younger children, while no significant difference was found in the survival according to patient sex, tumor pathology or the stage of disease at the time of diagnosis.

Conclusions

Complexity of the surgery, application of radiation therapy and chemotherapy affect the survival rate and overall quality of life of the patient. An aggressive surgical approach is associated with postoperative low mortality and long survival. Inclusion in the complex treatment of radiation and chemotherapy prolongs survival.

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Brain Tumours

INTRACRANIAL TUMORS IN NEWBORN BABIES

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Objectives

We report a retrospective study of brain tumors diagnosed during the neonatal period and treated at the Institute of Neurosurgery, NAMS of Ukraine" from 1980 till 2012.

Methods

In 33 years, 15 cases of newborn babies with brain tumors were observed at the Institute of Neurosurgery, which makes 0.3% of all the children with brain tumors treated at the Pediatric department over the above mentioned period. Ten of them were boys (66.7%), and five - girls (33.3%). The histological analysis of the tumor was confirmed in 13 (86.7%) observations. Benign tumors were diagnosed in 6 (46.1%) cases: plexus papilloma — 1, atypical plexus papilloma — 1, hemangiopericytoma — 1, a mature teratoma — 1, and lipomas — 2. Malignant tumors were found in 7 (53.9%) cases: anaplastic astrocytomas — 3, neuroblastoma — 1, an immature teratoma — 1, medulloblastoma — 1 and sPNET — 1. The histostucture was not identified in 2 cases.

Results

In total, 11 patients underwent 13 operations, as tumor removal was complemented by a shunting procedure in two cases. A total tumor removal was performed in 7 patients, a subtotal tumor removal – in 2 cases and a biopsy – in one case. The mortality after the tumor removal was 20%. 7 patients were followed; the average life expectancy was 3.1 years (from 1 to 12 years).

Conclusions

Modern diagnostic techniques make it possible to diagnose the congenital brain tumors at the early stages of life, or prenatally. Though the treatment outcomes and the survival rate remain poor, certain categories of children show a quite satisfactory period of outcome and the quality of life.

EP-149

Brain Tumours

LEPTIN CONCENTRATION AND NUTRITIONAL STATUS IN THE COURSE OF TREATMENT IN CHILDREN WITH BRAIN TUMOURS

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Objectives

The assessment of the nutritional status of children with malignant brain tumours in the course of treatment in correlation with the concentration of leptin

Methods

The study involved 44 children treated for CNS tumours. The body mass index and leptin value were analysed three times: before the beginning of the treatment, during the maintenance treatment and after its completion.

Results

The initial SDS BMI were similar to the control group value of this parameter. The SDS BMI decreased during therapy, but after the completion of the treatment SDS BMI value increased. During the therapy an increase in the concentration of leptin and its decrease after the completion of the therapy was observed.

Conclusions

In children with brain tumours there are quantitative disorders of the nutritional status which correlate with the period of the treatment. The correlation between the concentration of leptin and the nutritional status of children with brain tumours was not confirmed.

EP-150

Brain Tumours

INVESTIGATION OF VDR GENE POLYMORPHISM IN PEDIATRIC PATIENTS WITH BRAIN CANCER

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Objectives

Vitamin D is a steroid in structure. Intracellularly, it bounds to special receptors and plays an important role in cell proliferation and inflammation. In recent years, it is also believed that Vitamin D may play a protective role in some cancer types. Certain regions of the VDR gene may show a genetic difference in structure. The most frequent polymorphisms in this gene are in Taq-1, Fok-1 and Bsm-1 regions. Some cancers are associated with VDR gene polymorphism like colorectal Ca, breast Ca and prostate Ca in adults. Reviewing the medical literature, there has no such a study been done on children so far.

Methods

We investigated the three most common gene polymorphisms in VDR gene in 32 childhood brain tumour and 40 healthy children.

Results

We could't find any relationship between childhood brain tumors and VDR gene polimorphism in these 3 regions.

Conclusions

In children, the relationship of VDR gene polimorphism , D vitamin status and pediatric solid tumours needs to be evaluated with larger series of patients.

EP-151

Brain Tumours

PENCIL BEAM SCANNING PROTON THERAPY WITH AND WITHOUT CONCOMITANT CHEMOTHERAPY FOR CHILDREN WITH ATYPICAL TERATOID/RHABDOID TUMOR: THE PAUL SCHERRER INSTITUTE EXPERIENCE

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Objectives

Atypical teratoid/rhabdoid tumor (ATRT) of the CNS is a rare and extremely aggressive embryonal neoplasm of early childhood. The mean reported survivorship of these young ATRT children ranges from 6 to 11 months. Unlike conventional radiotherapy, proton therapy (PT) allows for optimal dose distributions, with the added benefit of no exit dose. We assessed the clinical results of pencil beam scanning (PBS) PT in the treatment of non-metastatic ATRT patients.

Methods

Fifteen children (male, $n=8$, 53%) were treated with PBS PT between May 2008 and January 2013. Mean age at diagnosis was 17.4 ± 7.0 months. The localization was infratentorial (type A) and supratentorial in 9 and 6 patients, respectively. Gross total resection of the primary tumors was achieved in 7 (47%) patients. The median dose administered focally under sedation was 54 Gy(RBE). All and 7 (47%) patients received pre-PT and concomitant chemotherapy, respectively. Acute toxicity was assessed according to the CTCAE, version 4.0.

Results

After a median follow-up time of 24.5 months (range, 9.7-69.2), 3 (20%), 4 (27%) and 2 (13%) patients presented with local failure (LF), distant brain failure (DBF) and spinal failure (SF), respectively. Combined treatment failures (2 LF and DBF, $n=2$; DBF and SF, $n=1$) were observed in 3 (20%) patients. Six patients died, all of tumor progression. Median overall survival (OS) was not reached. The 2-year local failure, DB progression-free survival and OS rates are 22%, 76.6%, and 72.7%, respectively. Age ($p<0.01$), localization ($p=0.012$) and type of resection ($p=0.067$) were prognosticators for OS. PT was well tolerated. No grade > 2 acute toxicity was observed. One grade 4 and another grade 1 impaired motor function were observed in 2 (13%) patients.

Conclusions

PBS PT is an effective treatment for young children with ATRT. After PT, with or without concomitant chemotherapy, the median OS was not reached in this series. Acute toxicity was manageable.

EP-152

Brain Tumours

LONG-TERM SURVIVAL OF TWO YOUNG CHILDREN WITH RELAPSED ATYPICAL TERATOID/RHABDOID TUMOR

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Objectives

Atypical teratoid/rhabdoid tumor (ATRT) is a highly malignant embryonal central nervous system tumor that primarily occurs in children less than three years of age. Median survival is less than 10 months and approximately three-fourths of patients eventually relapsed despite of aggressive treatment. Treatment options for patients with relapsed disease are particularly limited.

Methods

We conducted a retrospective chart review of two patients treated for relapsed ATRT.

Results

Case 1: The patient was diagnosed with posterior fossa ATRT at the age of three months. The initial treatment consisted of gross total tumor resection and chemotherapy. The patient had local relapse six months after the completion of chemotherapy and underwent gross total tumor resection and four courses of intensive multidrug chemotherapy. The patient is now alive without evidence of disease 10 years after the initial diagnosis.

Case 2: The patient was diagnosed with posterior fossa ATRT at the age of 19 months. The initial treatment consisted of gross total tumor resection and chemotherapy followed by craniospinal irradiation. The patient had metastatic relapse at anterior cranial fossa 12 months after the completion of the treatment. After the subtotal tumor resection, 50 weeks of multidrug chemotherapy was initiated. Stereotactic radiosurgery using Cyberknife was performed for the residual tumor during the chemotherapy. The patient is now alive 4 years after the initial diagnosis.

Conclusions

The prognosis of patients with relapsed ATRT is extremely poor. However, multimodality approach including chemotherapy, surgery and stereotactic radiotherapy may prolong survival and maintains quality of life.

EP-153

Brain Tumours

PRE-IRRADIATION CHEMOTHERAPY FOR CHILDHOOD INTRACRANIAL EPENDYMOMA

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Objectives

Standard therapy for childhood intracranial ependymoma is maximal tumor resection followed by involved-field irradiation. Although not used routinely, chemotherapy has produced objective responses in ependymoma, both at recurrence and in infants. We undertook a clinical trial of pre-irradiation chemotherapy in children with intracranial ependymoma at Kanagawa Children's Medical Center to investigate the potency of pre-irradiation chemotherapy.

Methods

Between 2003 and 2013, 18 children with newly diagnosed ependymoma were treated in our institute. All but 1 patient who could not receive chemotherapy because of severe brainstem compression by tumor were enrolled in the study. All children were with non metastatic ependymoma. The median age was 4 years (0- 10 years). The primary site was infratentorial in 10, supratentorial in 7 patients. Gross total resection (GTR) was achieved in 9 patients, subtotal resection (STR) was achieved in 8 patients. WHO grade II and grade III tumors were 6 and 11, respectively.

Results

All children received chemotherapy (vincristine 1.5 mg/m², etoposide 100 mg/m² x 5 days, cyclophosphamide 1.2 g/m² x 2 days, cisplatin 20 mg/m² x 5 days) following surgery and focal irradiation. Fourteen children completed 4 cycles chemotherapy. The median follow-up was 5 years (range 0.3–11 years). For the entire group, 5 year overall survival (OS) and event-free survival (EFS) was 71.8%, and 47.5 %, respectively. Three patients experienced disease recurrence, and eventually died. The 5 year OS was 100% for grade II and 63.7% for grade III tumors (P=0.303). The 5 year OS was 60.0% for patients who underwent a STR versus 80.0% for those who underwent a GTR (P=0.433).

Conclusions

These results suggest that primary chemotherapy strategies have an important role in the treatment of children with intracranial ependymoma. Patients with STR have inferior outcome despite responses to chemotherapy, and should be considered for second-look surgery prior to irradiation.

EP-154

Brain Tumours

PEDIATRIC EPENDYMOMA: AN ITALIAN SINGLE-INSTITUTION EXPERIENCE

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Objectives

Ependymomas constitute 10% of all primary Central Nervous System tumors in children and have a 5 years progression-free survival (PFS), at best, of 60%. We report on our single-institutional experience.

Methods

All children who had a diagnosis of ependymoma confirmed through central neuropathology review and who attended the Neurosurgery unit at Santobono-Pausilipon Children's Hospital during 2007-2013 were enrolled.

Results

Twenty-seven consecutive children (median age, 3.1 years; range, 0.4-12.4 years) were studied. Male to female ratio was 1:2. Ninety-two percent of the tumors were intracranial, 77% occurred in the posterior fossa (PF). Supratentorial and spinal localizations were associated with age older than 3 years. On imaging ependymomas were heterogeneous containing cysts, calcification, occasional hemorrhage and irregular enhancement. There was no disseminated case at diagnosis. PF Ependymomas were infiltrating the brainstem in 13% of cases and projected to the cerebellopontine angle and upper spinal canal in 35% of cases. Eighty-four percent of children with PF ependymomas received a complete surgical resection. Histopathological variants were: cellular, clear cells, papillary and anaplastic. Following surgery, all but 4 patients received additional therapy: radiotherapy in 50% and chemotherapy in 68% of cases. 5 years PFS was 41% (median PFS, 1.25 years; range, 0.25-8.75 years). PFS for children with supratentorial tumors was slightly better than that for children with PF tumors. There was a correlation between anaplastic histology and a higher rate of disease recurrence (85 vs 46%). Recurrence occurred on tumor bed and in 28% of cases was also metastatic. All patients who received only surgery had progression. Recurrence rate was significantly lower if radiotherapy paired with surgery (5 years PFS, 64%) independently of extent of resection. It seems there was no advantage in PFS in patients who received chemotherapy.

Conclusions

This tumor collection is an useful source for molecular studies aimed to identify genes relevant to recurrence.

EP-155

Epidemiology

**EPIDEMIOLOGY OF CHILDHOOD CANCER IN WESTERN AFRICAN REGION:
ASSESSING GENDER DIFFERENCES**

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Objectives

It is widely believed that male are more susceptible to develop cancer than their female counterparts except some types or sites of cancers. The same also applies to the childhood cancers where there is little difference between male and female globally. Knowing the gender susceptibility can give important clues to the aetiology of cancers. The study seeks to assess if there is any gender difference among children with cancers in Western African region.

Methods

Secondary data analyses were conducted using the Globocan 2012 datasets. The incidences of all childhood cancers excluding non-melanoma skin cancers were analysed. Fifteen countries of the Western African region were examined. Paired data analysis was conducted to determine the differences among male and female cancer patients. The analysis was carried out using Stata / IC 12.1.

Results

The region recorded 18455 new cases in 2012, which is 22% of Africa burden (7837/36428). Males had mean of 692 (305 – 1079 95%CI) and females mean of 538 (229 – 848 95%CI) ; P = 0.0000.

Nigeria had the highest number among both male and female with 1882 and 1631 respectively. Cape Verde had the lowest number of cases.

Conclusions

Western African region had significant gender difference in new cases of childhood cancers. Male are much more than the female unlike what was initially believed or as it is in other regions.

EP-156

Epidemiology

ANALYSIS OF TOTALLY IMPLANTABLE VENOUS ACCESS PORTS IN PAEDIATRIC ONCOLOGY.

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Objectives

Venous access is a challenge in pediatric oncology. In order to overcome this barrier, venous tunneled catheters were created, which is widely used in pediatric and adult patients undergoing chemotherapy. The objective of this study was to evaluate the complications of the totally implantable venous access ports (TIVAP) in pediatric oncology patients.

Methods

We have retrospectively analyzed 71 patients under 16 years old, treated with chemotherapy between January 2009 to December 2010, submitted to TIVAP insertion. We followed a Catheter Protocol, in which contemplated an operation room insertion, manipulation care and control in a specific catheter ambulatory by expert surgeons and nurses. The cases of infection were supervised by the Hospital Infection Control Committee. The patients with suspicion of thrombosis were submitted to a Doppler scan, and in the confirmed cases, the catheter was removed and initiated a thrombolytic therapy.

Results

In 259 pediatric patients with catheter 71 patients had TIVAP. There is no statistically gender difference (35males:36females). Of these, 70 were followed in the catheter ambulatory. Most of them were non-hematological tumors 61 (87.1%), only 9 (12.9%) hematological patients. In 50 patients (71.43%) there were no complications, and the catheter are still in use; 7 (10%) were removed after completed chemotherapy protocol. The complications that caused catheter removal were infection in 6 (8.57%) (bacterial infection in 5 and fungal infection in 1); thrombosis in 2 (2.86%); thrombosis and infection in 1 (1.43%). Four patients (5.71%) died during the treatment with no catheter related complications.

Conclusions

The use of long term catheter, in pediatric oncology, is safe and provide a good adhesion to the treatment. Our results showed a infection rate compared with the literature. It is important o follow up the patients with TIVAP by a specialized team and a catheter ambulatory.

EP-157

Epidemiology

DELAY IN DIAGNOSIS OF CHILDREN TO A THIRD CARE CENTER SPECIALIZED IN PEDIATRIC ONCOLOGY IN MEXICO CITY, A LOW INCOME COUNTRY

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Objectives

In developing countries there is a delay in the referral of patients to specialized medical centers in pediatric cancer treatment thus worsening the prognosis. Aim: To describe the time between the beginning of symptoms and signs of illness and the final definitive diagnosis of cancer.

Methods

Medical records of 456 pediatric patients with cancer treated in the last ten years at the Department of Oncology of Centro Medico Nacional 20 de Noviembre ISSSTE in Mexico city were reviewed.

Results

Diagnosis distribution was similar to the one reported in the literature. 26.5% consulted a medical doctor within the first five days of the first symptom. The average referral from the first doctor to the cancer unit was 105 days, while the delay in the cancer unit to the final diagnosis took 9 more days. The average number of doctors that the patients consulted before the pediatric oncologist was 4.

Conclusions

There is an important delay in the referral of sick children to a cancer center. We must consider a better education of medical and administrative people in order to improve survival.

EP-158

Epidemiology

THE INCIDENCE AND SURVIVAL AMONG ADOLESCENTS WITH CARCINOMA IN ISRAEL DURING THE YEARS 1998 TO 2009

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Objectives

Our goal was to describe adolescent carcinoma incidence and survival in Israel, and to identify demographic and epidemiologic variations among adolescents with carcinoma.

Methods

We used data from the Israel National Cancer Registry in order to examine the incidence and survival of adolescent cancer in Israeli adolescents aged 15-19 years, diagnosed during the years 1998-2009. Cases were analyzed according to sex, ethnicity and compared to the population of children diagnosed before the age of 15 years old. We estimated the survival probability updated to December 2009, and calculated the 5-year survival for new cases until the end of 2004.

Results

Among the 1532 new cases of cancer children between the ages of 15 to 19 years old, 143 adolescents with carcinoma were diagnosed, median age was 17.83 for the Jewish children and 17.32 for the Arab children. Incidence rate was 24.95 per million, 24.6 for the Jewish children and 25.9 for the Arab children. The incidence of children diagnosed before the age of 15 was 5.72 per million. Carcinoma was located to the thyroid gland in 78 cases, testis in 15 cases, nasopharynx in 14 cases, bladder in 9 cases, parotid gland in 8 cases, colon in 6 cases, ovary in 5 cases, unknown primary site in 8 cases. The overall survival at 5 years for the Jewish children was 90.7%, 76.9% for the Arabic population ($P < 0.001$). In comparison with the SEER data the incidence of adolescents with carcinoma was higher in Israel.

Conclusions

This study may add more information for further investigation of the genetic and environmental factors that cause adolescent cancer in Israel. As well as delineate the genetic basis for ethnic origin disparities in survival.

EP-159

Epidemiology

PSYCHOLOGICAL FACTORS MEDIATE THE RELATION BETWEEN PHYSICAL FITNESS AND QUALITY OF LIFE IN CHILDREN WITH CANCER

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Objectives

Children with cancer have a decreased physical fitness and QOL. This study aimed to investigate the relation between physical fitness and QOL, and whether this was mediated by psychological factors.

Methods

These cross-sectional analyses are based on the baseline QLIM (Quality of Life in Motion) study data; a randomized controlled trial evaluating the effects of physical exercise and psychosocial intervention on physical function and fitness among children aged 8-18 years old, during, or no longer than one year post cancer treatment. Data of 68 children (54% boys) aged 12.8 (SD 3.1) years were analysed, of whom 68% were treated for a haematological malignancy. Cardiorespiratory fitness (CRF) was assessed by a maximum cardiopulmonary exercise test. Psychological functioning was assessed by questionnaires (PedsQoL for QOL physical functioning and fatigue; Child Depression Inventory for depressive symptoms and Youth Self Report for behavior problems). Series of linear regression analyses were conducted to examine the association between CRF and QOL, CRF and the mediator variable, and the mediator variable and QOL, controlling for age and sex. The mediation effect was examined using the product of coefficients method, and bootstrapping to calculate 95% confidence intervals.

Results

CRF was positively associated with QOL ($b = 1.33$ 95% CI: 0.88 – 1.77). The association was mediated by fatigue (mediation effect (M): 0.36; 95% CI: 0.11 – 0.79), depressive symptoms (M: 0.22; 95%CI: 0.01 – 0.56) and internalizing behavior problems (M: 0.47; 95% CI: 0.07 – 1.28). The mediation effects accounted for 27%, 26%, and 38%, respectively.

Conclusions

CRF scores are significantly associated with QOL and this association is mediated by fatigue, depression and internalizing behaviour problems. In order to increase QOL in childhood cancer patients, interventions should focus on improving CRF, since this may reduce fatigue, and distress, and improve the QOL. Future longitudinal studies should confirm this finding.

EP-160

Epidemiology

BEYOND BURKITT LYMPHOMA: A WIDE SPECTRUM OF PEDIATRIC MALIGNANCIES ARE CURABLE DESPITE RESOURCE LIMITATIONS IN A PUBLIC TERTIARY HOSPITAL IN LILONGWE, MALAWI

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Objectives

While Burkitt lymphoma (BL) is the most common pediatric malignancy in sub-Saharan Africa, we herein describe our experience treating a variety of childhood cancers in Lilongwe, Malawi.

Methods

We retrospectively analyzed records of pediatric oncology patients between 12/2011 – 6/2013. Diagnosis was usually clinical, however fine needle aspiration +/- biopsy was performed routinely starting in 1/2013. Patients received transport reimbursement plus extensive follow-up counseling.

Results

There were 254 children diagnosed with cancer: 142 males, 112 females. Diagnoses included: 45% lymphoma, 21% Kaposi sarcoma (KS), 18% solid tumors of the abdomen (majority Wilm's tumor), 8% sarcomas, 4% leukemias, and 5% other. There were 21 Hodgkin (17 biopsy-confirmed) and 94 non-Hodgkin lymphomas (NHL). In NHL, 39 had jaw involvement—23 jaw +/- nodes, 7 jaw and abdominal masses, 9 jaw and CNS+ (cranial nerve palsies and/or spinal cord compression). These 39 were probable BL diagnoses; there were also 32 possible BL and 23 other NHL (lymphoblastic lymphoma or diffuse large B-cell lymphoma) based upon pathology and/or clinical characteristics. Seven NHL patients had primary mediastinal mass (probable lymphoblastic lymphoma). Altogether, 97 children presented with an abdominal mass—52 had lymphoma. Pediatric NHL Murphy staging revealed: 27 stage I/II, 49 stage III, and 18 stage IV (CNS+ or presumed bone marrow involvement). 47 patients were HIV+: 43 KS/4 NHL. There were 10 endemic (HIV-negative) KS patients. Overall, 48% completed their treatment regimen and 15% were lost to follow-up. 78 children (31%) achieved 12-month overall survival. Three patients with CNS+ BL achieved 12-month complete remission with dose-modified CHOP chemotherapy plus intrathecal.

Conclusions

BL accounted for 28% of childhood cancers; lymphoma altogether accounted for 45%. The majority of lymphomas (>70%) presented stage III/IV, with abdominal mass as the most common primary site. Prompt diagnosis with careful, but intensive chemotherapy, can result in curative outcomes despite significant resource limitations.

EP-161

Epidemiology

EPIDEMIOLOGY AND SURVIVAL ANALYSIS OF EGYPTIAN CHILDREN WITH SOLID TUMORS (SINGLE CENTER EXPERIENCE)

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Objectives

The total incidence of solid tumors among children is 65.3/million. The overall survival for solid tumors at 5, 10 and 20 years follow-up reaches 80, 79 and 76%, respectively as result of continuing improvement and increasing efficacy of treatment. This study evaluates the clinico-epidemiological aspects and survival analysis of solid tumors among children treated in a single pediatric oncology center over the last 10 years.

Methods

This is a retrospective data analysis of all children with solid tumors who were diagnosed during the period from January 2003 to January 2013 in the Pediatric Oncology Unit, Children's Hospital, Ain Shams University, Cairo, Egypt.

Results

There were 123 patients diagnosed with solid tumors (15% of total patients diagnosed with cancer during same period). They included 56 (45.5%) males and 67 (54.4%) females. The frequency distribution of newly diagnosed patients with solid tumor were heterogenous over period of 10 years being highest in year 2011 and lowest in year 2010. Throughout the 10 years period, excluding CNS tumors, Neuroblastoma was the most common (34.9%), Wilm's tumor(22.7%) came next in frequency, then retinoblastoma(13.8%) , followed by Germ cell tumor (8.9%), hepatoblastoma(6.5%),Osteosarcoma (4%), Ewing sarcoma (3.2%), and Rhabdomyosarcoma(4%).The 1, 5, 7-years overall survival(OS) of patients with solid tumor was 90.3%, 59.7, 55.4 %. Male patients, patients without family history of malignancy, those who were operated upon had significantly higher 1, 5, 7 years OS. The 3 years OS of patients with retinoblastoma was the highest (87%), while those with osteosarcoma had the lowest OS (53.3%).

Conclusions

In our center, the incidence of pediatric solid tumors is rising, and the frequency of the different types varies from year to year; in the past 10 years, the OS rates were improving as a result of implementation of internationally approved optimal treatment regimen based on risk factors and molecular markers.

EP-162

Epidemiology

FACTORS INFLUENCING PARENTAL CONSENT FOR PARTICIPATION IN CLINICAL RESEARCH INVOLVING THEIR CHILDREN IN EGYPT

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Objectives

Factors affecting parents' decision to involve their children in clinical research have not been studied

in all cultural backgrounds. We aimed to explore the attitudes and beliefs influencing parents' decision to involve their children in clinical research in Mansoura, Egypt.

Methods

Study design and sample Parents or legally authorized representatives of children admitted to the inpatient departments of Mansoura University Children's Hospital, Mansoura, Egypt, between January 2009 and December 2011 were eligible for the study. Parents or guardians were approached within 48 hours of the child's admission and were asked to complete a questionnaire exploring factors that would influence their decision to involve their child in clinical research.

Results

Of 523 families approached, 357 filled the questionnaire. Only 98 (27.5%) parents consented to involve their child in clinical research. The children of consenters were significantly older than refusers: 8.6 (SD 7.2) versus 2.6 (SD 1.2) years. Factors favouring consent were: research of benefit to child (84.7%), enough explanation about the benefits (40.8%) and to learn more about child's condition (29.6%). Factors favouring refusal were: use of new drugs or vaccines (89.6%) and invasive procedures (84.2%). Parents' rate of consent was positively correlated with the research being non-invasive and the belief that research was of benefit to their child and negatively correlated with belief that refusal may negatively affect the care provided to their child.

Conclusions

In this hospital in Egypt, minimally invasive research of clear benefit to the child and with a clear explanation of the research process by staff were the most important motives for parental consent to involve their children in clinical research.

EP-163

Epidemiology

PEDIATRIC OSTEOSARCOMA IN NIAMEY: FIRST RESULTS FROM THE NIGER CANCER REGISTRY

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Objectives

Worldwide, an estimated 160 000 children are diagnosed with cancer each year, with an incidence of about 14.9 cases per 100 000 children less than 20 years of age. More than 80% of children with cancer live in developing countries where access to information, early detection and effective treatment and care is often poor. This study aims to investigate the epidemiological characteristics of osteosarcoma in pediatric patients during the past 18 years in Niamey.

Methods

This is a descriptive retrospective study of pediatric osteosarcoma cases, reported between 1992 and 2009 to the Niger Cancer Registry, established in 1992, in the Faculty of Health Sciences at the Abdou Moumouni University in Niamey.

Results

During the study period, 15 children under the age of 15 years were diagnosed with osteosarcoma in Niamey, accounting for 4.5% of all pediatric malignancies collected during this period. Nearly three-quarters of the cases (73.3%) were boys with a male-female ratio of 2.75. The average age of diagnosis was 11.7 ± 2.5 years (range 5-14 years). Nearly 87% of these cases were diagnosed in children aged 10-14 years. The most common sites of osteosarcoma at initial diagnosis were the long bones of the lower limbs. The most prevalent ethnic group was the Djerma-Sonrai.

Conclusions

The most recent estimates of childhood cancer incidence and mortality in the world reveal sharp differences between developed and developing countries possibly related to missed opportunities for early diagnosis and incomplete reporting of childhood cancer in Africa.

EP-164

Epidemiology

PEDIATRIC HODGKIN LYMPHOMA IN MOROCCO

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Objectives

Hodgkin lymphoma (HL) is a rare malignancy in Northern Africa, with an incidence of 1.4 per 100 000 in 2012. It is the 18th most common cancer and the 18th leading cause of cancer-related death in both sexes, with an estimated 3 107 new cases of HL (1 758 men and 1 349 women) and 1 698 deaths from HL in 2012 (GLOBOCAN 2012). The aim of this study is to determine the frequency and the epidemiological characteristics of pediatric Hodgkin lymphoma in Morocco.

Methods

This is a descriptive retrospective analysis of pediatric Hodgkin lymphoma cases, diagnosed and treated at Al Azhar Oncology Center in Rabat between 1994 and 2004.

Results

There were 18 children under the age of 15 years diagnosed with Hodgkin lymphoma at Al Azhar Oncology Center, which was 40.9% of all new cases of pediatric hematologic malignancies and 14.3% of all cancers in children collected during the study period. More than one-half of the cases were boys, with a male-female ratio of 1.25. The average age at diagnosis was 10.7±3.5 years (range 5-14 years). More than two-thirds of the cases were diagnosed in children aged 10-14 years (66.7%), while the highest rates for boys were noted between 5 and 9 years and for girls between 10 and 14 years of age. Among the cases for whom the outcome was known, a 14-year-old girl died during the study period.

Conclusions

Although rare, cancer in children has a substantial impact on public health in Morocco. A national cancer registry will assist in better planning, resource allocation and management including psychosocial support to improve the quality of life of childhood cancer survivors and their families.

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Epidemiology

COLORECTAL CARCINOMA IN PEDIATRIC AGE GROUP- EPIDEMIOLOGICAL PARADIGM

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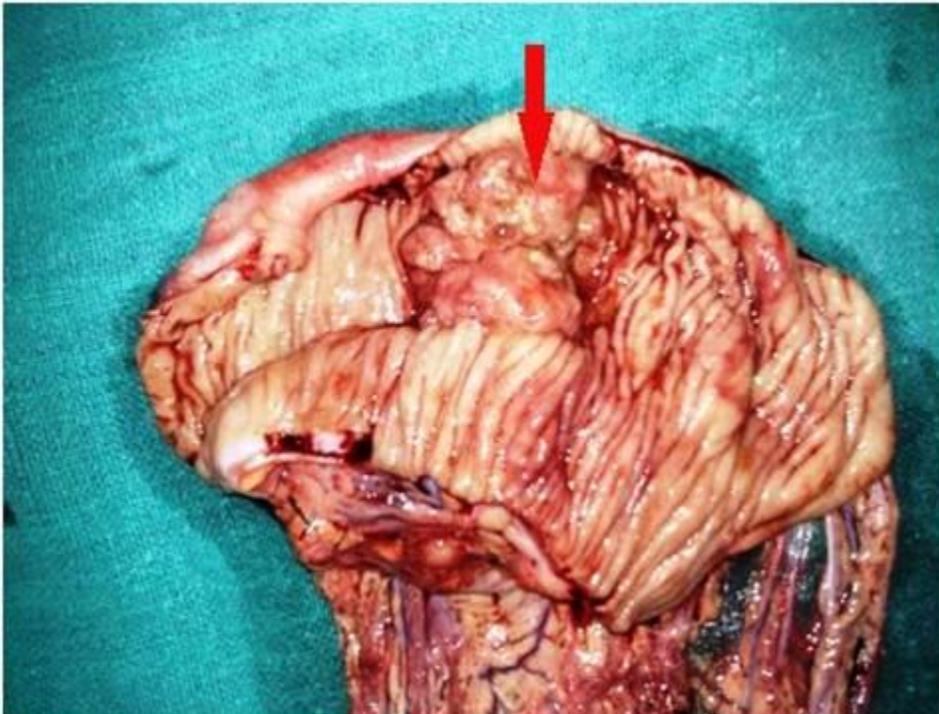
Objectives

Colorectal cancer is a rare disease in pediatric age group with an annual incidence of 1.3 cases per million children. Spectrum of colorectal cancer includes the pediatric population also, which usually presents at advanced stage, unfavorable histology and ultimately poor prognosis. Difficult differential diagnosis, delay in presentation and aggressive biological behavior leads to poor outcome.

Methods

Retrospective analysis of all pediatric colorectal cancer patients presented to Division of Pediatric Surgery between June 2006 to June 2012 were included in the study. A specifically designed audit form was devised to capture all relevant information regarding clinical presentation, pathologic factors, treatment outcome, prognostic factors and follow up.

Results





During the study period of 6 years from June 2006 to June 2012 only 7 cases of pediatric colorectal cancer were reported. Median age was 11.8 years [range, 5-16years]. Five patients presented with features of intestinal obstruction and diagnosed during emergency laparotomy. The most common site of involvement was rectum (59%) & transverse colon being the next most common site (26%). Adenocarcinoma was histological type in all patients. 3 patients died within 2 years of follow-up. Rest 4 patients are receiving treatment and under follow-up.

Conclusions

Colorectal cancer is a rare disease in pediatric age group. Diagnostic dilemma, difficult differential diagnosis, delayed presentation & treatment, advanced stage and poor histological features contributes to the poor prognosis of the disease in pediatric age group as compared to adults. As in adult colorectal cancer; early detection, stage stratification, multidisciplinary treatment plan and participation in prospective clinical trials will help in improving the prognosis & outcome in pediatric patients.

EP-166

Epidemiology

DEMOGRAPHIC, CLINICAL AND SURVIVAL FEATURES OF CHILDHOOD CANCERS IN ISTANBUL UNIVERSITY, ONCOLOGY INSTITUTE (1990-2012)

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Objectives

The aim of this study is to identify demographic, clinical and survival features of childhood cancers admitted to Istanbul University, Oncology Institute, Pediatric Hematology-Oncology in 22 years.

Methods

Charts of patients <19 years admitted (1990-2012) were evaluated retrospectively for age, gender, birth date, date of diagnosis, place of birth/residence, family history, concomitant diseases, primary diagnosis, primary site, stage, presenting symptom and duration, date of the last examination/death. (Istanbul University Cerrahpasa Medical Faculty Clinical Trials, Ethics Committee no. 83045809-3507)

Results

2413 children with cancer were enrolled. Median age was 7 years (3 days-19 yrs). Male:female 1,26. Distribution in age groups were 0-1 years 7,9%; 1-4 years 31,9 %; 5-9 years 24,9%; 10-14 years 26,1%; 15-19 years 9,2%. 5 year survival of all patients 74,4%. Distribution in disease groups were [5 year survival]: Central nervous system (CNS) tumors (n=494) 20,5% [61,0%]; Malign bone tumors (n=367) 15,2% [60,9%]; Lymphoma (n=360) 14,9% [90,7%]; Soft tissue sarcomas (n=317) 13,1% [68,9%]; Retinoblastoma (n=207) 8,6% [94,3%]; Neuroblastoma (n=164) 6,8% [64,6%]; Leukemias (n=133) 5,5% [82,0%]; Germ cell tumors (n=130) 5,4% [89,8%]; Carcinomas (n=129) 5,3% [83,8%]; Renal tumors (n=88) 3,6% [81,9%]; Hepatic tumors (n=24) 1,0% [44,7%]. After 2005, number of patients diagnosed at early stage has increased (p=0,001). In the whole group, the 5 year survival rate was 85,2% in patients diagnosed at an early stage, while the 5 year survival rate in patients with advanced stage disease was 57,0% (p<0,001)

Conclusions

The most common solid tumor, similar to developed countries, was CNS tumors. The frequency of retinoblastoma and bone tumors were high (reference center).. Survival in patients diagnosed at early stage were significantly higher than those with advanced stage, which is promising for the future. Cancer registry in our country has developed in recent years, registries in major centres help to obtain more detailed data on the epidemiology and clinical characteristics of cancer patients which may help organizing health care programs.

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Epidemiology

THE CURRENT STATUS OF FOLLOW-UP SERVICES FOR CHILDHOOD CANCER SURVIVORS IN TURKISH PEDIATRIC ONCOLOGY CENTERS

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Objectives

We aimed to describe survivorship services provided by the Turkish Pediatric Oncology Centers including the extent of services provided, resources and barriers to service development.

Methods

All 31 institutions in Turkey which have a pediatric oncology program were invited to participate this survey in order to define the pediatric cancer survivor services . Participation rate was 100% .

Results

The number of new cancer cases were 50-100 in 52%, and >100 at %13 of the centers. 71% of centers were treating leukemias and solid tumors, others were treating all cancers except for leukemias. Majority (90%) of the institutions reported providing survivorship care. However, survivor follow up services were given within the routine pediatric oncology outpatient clinic practice by the attending pediatric oncology doctors at 96.4 % of the centers. Only one centre reported a survivor clinic with a multidisciplinary team. Pediatric oncology clinics were staffed by: pediatric oncologist (31/31), pediatrician (3/31), oncology fellow (16/31), nurse (6/31), oncology nurse (15/31), social worker (1/31), psychologist (7/31); dietitian (6/31). Nine institutions keep survivors until the age of 18 at the treating institution, 7 centers until they feel ready for transition, and 5 keep them indefinitely. Nine centers reported having a standard follow up guideline, 5 centers reported having a standard clinical assessment form. A copy of care plans were given to survivors in only 5 centers. When a sub-specialists evaluation was needed, this service was provided through consultations at 28 centers (at the same day in 13, with an appointment at another day in 15).The most prevalent barriers were insufficient qualified staff (83%), the lack of dedicated time for program development (72%), lack of physical space (70%), and lack of funding (63%).

Conclusions

Survivorship services needs to be improved in Turkey. Governmental attempts are required to overcome the defined barriers to developing survivorship programs by the institutions.

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Epidemiology

ENVIRONMENTAL HEALTH INDICATORS AND INCIDENCE OF CHILDHOOD CANCER IN PERNAMBUCO, NORTHEASTERN OF BRAZIL: THE ROLE OF URBANIZATION

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Objectives

To evaluate the impact of environmental health indicators on the incidence of childhood cancer in Pernambuco state, Northeastern of Brazil.

Methods

Based on the authorization reports for chemotherapy and radiotherapy authorization for 2009 until 2012 provided by the State Health Secretary of Pernambuco, new cases of childhood cancer (aged under 20 years) were analyzed in terms of gender, age, diagnosis and municipality of origin. Population for 2009 to 2012 was estimated by the whole period based on the official population counting. Health environmental indicators of Driving Force (Gini Index, Population growth rate, Urbanization rate, Human Development Index); Pressure (Number of vehicles, agricultural establishments, extractive and manufacturing industries per capita), and Situational (Basic Health Unit per capita) were provided by official sources. Empirical Bayesian estimator, Moran's global and local index were estimated and multiple regression was used to evaluate association of health indicators and cancer incidence.

Results

We analyzed 1261 new cases of cancer from 19 years and 11 months diagnosed in Pernambuco from 2009 to 2012. The average crude incidence rate was 113 cases per million people, with an increasing rate of 0.44%. The ratio male:female was 1.20, except in children under 1 year. Leukemia/lymphoma predominated with 45.28% of cases, central nervous system tumors corresponded to 16.6%, and the remaining solid tumors accounted for 38.12% of cases. The mean average incidence rate of municipalities grouped in the upper quartile by Bayesian method was 126.11 cases/million, while for counties in the bottom quartile was 65.31 cases/million ($P < 0.000$). Moran's local index identified 14 municipalities with spatial autocorrelation. Bivariate analysis identified positive correlation between cancer and urbanization ($P = 0.018$), confirmed by multiple regression model ($P = 0.010$).

Conclusions

The adjusted average incidence rates of cancer showed grouping of municipalities with high rates in the eastern of state. Habit change due to urbanization might increase exposure to cancer promoting agents; the casual relation, though, is more complex.

EP-169

Epidemiology

EFFECTS OF E-WASTE EXPOSURE ON THE SYNTHESIS OF HEMOGLOBIN IN PRESCHOOL CHILDREN

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Objectives

Guiyu is the major electronic-waste (e-waste) recycling town in China. The primary purpose of this study was to measure the effect of e-waste exposure on the synthesis of hemoglobin (Hb) in preschool children.

Methods

Two hundred and twenty-two children (aged from 3 to 7, exposure group) lived at Guiyu town and 204 children (aged from 3 to 7, control group) lived in a no e-waste polluted town were chosen to test their blood lead, Hb, ferritin, folate, vitamin B₁₂ levels and hemoglobinopathy, then fill the self-questionnaires by their parents.

Results

In order to better access the effect of environmental toxicants on the synthesis of hemoglobin, there were no significant differences in the levels of ferritin, folate, vitamin B₁₂ between exposure and control groups, and all children had been excluded thalassemia. The blood lead levels (BLLs) and rate of BLLs $\geq 10\mu\text{g/dL}$ in exposure group were significantly higher than that in control group (all $P < 0.01$). Three groups were divided according to BLLs (Group A: $< 5.0\mu\text{g/dL}$, Group B: $5.0-9.9\mu\text{g/dL}$, Group C: $\geq 10.0\mu\text{g/dL}$). It can be seen that the levels of Hb were decreased along with elevated BLLs significantly in exposure group ($F=3.52$, $P=0.03$), however, not shown in control group ($F=1.98$, $P=0.14$). Furthermore, the prevalence rate of anemia along with BLLs $\geq 10\mu\text{g/dL}$ in exposure group was significant higher than that in control group (4.0% versus 0.5%, $P < 0.05$), and the prevalence rate of anemia without BLLs $\geq 10\mu\text{g/dL}$ and iron deficiency in exposure group was significant higher than that in control group (6.5% versus 2.0%, $P < 0.05$).

Conclusions

Different from the general environment, the lead exposure in e-waste area might aggravate the inhibition of synthesis of Hb, and other potential e-waste toxicants might also have a responsibility for it.

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Epidemiology

COMPARISON OF RETINOBLASTOMA INCIDENCE AMONG CHILDREN IN THE REPUBLICS OF KYRGYZSTAN AND KAZAKHSTAN

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Objectives

To study descriptive epidemiology of retinoblastoma among children in the Central Asian republics of Kyrgyzstan and Kazakhstan.

Methods

This study covers the period 1997-2006. The data on all registered cases of retinoblastoma were provided by specialized and non-specialized hospitals in both countries. We calculated retinoblastoma incidence rates by age group (0-4, 5-9, 10-14), geographic regions, gender, and ethnicity. We report crude, and age-standardized rates (ASRs), calculated using the world reference population.

Results

On average, annual all types of childhood cancer incidence was 71.8 per one million in Kyrgyzstan and 73.8 in Kazakhstan. During the study period, a total of 106 children under 15 with malignant tumors of the eye were registered in Kazakhstan. This corresponds to 3.6% of registered childhood malignancies in this country. A total of 74 new cases (6.1% of all pediatric malignant tumors) were registered in Kyrgyzstan. Among all childhood cancers, retinoblastoma was the eighth most common malignancy. The average annual crude incidence rates were 2.6 per one million in Kazakhstan (male: 2.8; female: 2.4) and 3.9 (male: 4.1; female: 3.6) in Kyrgyzstan. Incidence rates ranged from 1.8 in 1998 to 4.1 in 1999 and 2005 (Kazakhstan). ASR was higher (8.3) in Kyrgyzstan than in Kazakhstan (7.6) for the age group 0-4years. High incidence rate of retinoblastoma (5.6) was found among those of Uzbek ethnicity compared with other ethnic groups (Kyrgyz: 4.8; Russian: 2.7) in Kyrgyzstan. Incidence rate was slightly higher among those from rural regions than urban regions (RR=0.9, 95% CI 2.7-7.4). No significant difference in retinoblastoma incidence was found for ethnicities in Kazakhstan.

Conclusions

The incidence rates of retinoblastoma in these Central Asian countries are relatively low and comparable to levels of disease in some countries of Asia, Africa, and South America. Our findings support the idea that there is need for population based childhood eye cancer surveillance and etiologic research.

EP-171

Epidemiology

A STUDY ON CANCER INCIDENCE FROM SEVEN MAJOR HOSPITALS IN NEPAL (2003-2010)

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Objectives

This study gives overview to reliable information of the cancer incidence in Nepal for 8 years period from 2003-2010. It helps to make some prevention, control plan and policies to the clinicians, policies makers to give priorities for the cancer prevention and control activities.

Methods

This was descriptive type of study and all cases were collected from medical record section of seven collaborative hospitals for data analysis. A breakdown of the incidence by year, age and gender has been analysed. Age standard incidence of common cancers and age specific rate has been tabulated.

Results

The total 41,713 cases were included in this study to know the burden of cancer patients in 7 major hospitals of Nepal where cancer diagnosed and treated from 2003-2010. In this study Female (53.3%) cases were diagnosed more than males (46.7%). Overall, the most common cancer sites in Males were lung, stomach and leukemia but in Females Cancer of cervix uterus, breast and lung. More cancer cases (67.7%) seen in Female but in Males found 52.5% in the broad age group 35 to 64 years. In young age leukemia and lymphoma were more common replaced by lung, oral and stomach cancer in middle age but in old age lung, stomach cancer were found in males but in females breast cancer in young, cervix uterus cancer in middle and followed by lung cancer in older age.

Conclusions

This type of study is the first time in Nepal to know the burden across a greater proportion of cancer from 7 major hospitals, but the coverage may not represent the whole country. More than 50% cancer patients were diagnosed in BPKM cancer hospital. Population based cancer registry is not yet established so, it is difficult to reflect the burden of cancer.

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Epidemiology

IMPACT, AND MORTALITY TRENDS IN CHILDHOOD CANCER IN MIDWEST OF BRAZIL 1996 TO 2011 , COMPARED WITH SEER DATA (U.S.A.)

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Objectives

There is a global trend of increased incidence and decreased mortality of pediatric tumors. The aim of this study is to analyze the incidence rates and trend in mortality of childhood cancer in Midwest of Brazil and compare the trends with USA (SEER).

Methods

Incidence data were obtained from the Cancer Registry Population-Based Goiânia, Cuiaba, Brasilia and Campo Grande. Mortality data were obtained from the Mortality Information System (DATASUS/ MS). Standardized rates were calculated according to the 2000 U.S. Std Population. To analyze the mortality trend was used the logistic regression model of Poisson from join point software.

Results

Adjusted incidence rates from Midwest region of Brazil for all childhood tumors were about 67.60 per 100,000 in men and 63.58 per 100,000 in women. Mortality was higher in boys (22.19 per 100,000) than in girls (16.26 per 100,000). There was trend in reduction of mortality from childhood cancer in both genders, but not significantly. (Male: 0-19 years: APC: -1.5 (-3.1 to 0.0, p: 0.58). The incidence rates, in U.S.A. were lower than in Brazil. Boys had higher rates (18.2 per 100,000) than in girls (16.1 per 100,000). The mortality rates were 2.6 per 100,000 in boys to 2.2 per 100,000 in girls in the period of 2006 to 2010 in USA. Incidence trends, in USA (SEER) is increasing significantly (APC: 0.6, p<0.5) and the mortality is decreasing (APC: -2.7, p< 0.5).

Conclusions

Trends in mortality for pediatric cancer in the Midwest of Brazil (developing country) is similar to the U.S.A. There was a reduction in mortality, although incidence and mortality rates in Brazil were higher. To analyse incidence trends in Midwest was not possible due to lack a long time series.

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Epidemiology

EPIDEMIOLOGY OF PEDIATRIC MALIGNANCIES IN INDIA

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Objectives

Not much is known regarding the epidemiology of childhood cancers in third world countries. There may be significant differences in the incidence of different malignancies in developing countries due to the different genetic and environmental factors. Data regarding disease pattern is the building block for forming public health strategies in any country. This study attempts to study the epidemiology of childhood malignancies in a third world country

Methods

A retrospective analysis was undertaken using data from a Tertiary Cancer centre in India collected from 1st Jan to 31st Dec 2012. 1445 cases of patients in the age group 0 – 18 years were taken into consideration. The case distribution of individual malignancies was evaluated. We also analysed the age of presentation of individual malignancies.

Results

Hematological malignancies were the most common, with Leukemia forming 32% and Lymphoma 11.7% of the total cases. Among solid tumors the top five were CNS (9.3%), PNET (8.5%), Osteosarcoma (7%), Neuroblastoma (4.8%) and GCT (4.4%). If the occurrence of malignancies is analyzed across different age groups we see that, 22.7% of the Retinoblastomas were found in the 4 to 12 years age group. Similarly for Lung 20 % of the cases were in the 4 to 12 age group and 80% were in the above 12 age group. In case of Colorectal, 5.9% of the cases are in the 0 to 3 age group and 23.5% of cases were in the 4 to 12 group.

Conclusions

The trend in pediatric cancer is different in India than in developed countries with higher rates of PNET and Osteosarcoma and lower rates of CNS malignancies. Public Health programmes and strategies should be framed using country specific epidemiological data, for prevention, early detection and treatment of disease.

EP-174

Epidemiology

CANCER IN EGYPTIAN CHILDREN:EPIDIMIOLOGY AND SURVIVAL INCIDENCE

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Objectives

To report and clarify the prevalence of the different types of malignancy among the Egyptian children as well as the incidence of survival.

Methods

A retrospective study of the incidence of different types of cancer children admitted and treated in the Pediatric Oncology and the Pediatric Surgery Departments of University of Alexandria, Egypt over a period of 20 years was done.

The incidence of the overall 5 years survival was analysed,reported and compared to that of the western countries. The possible causes of low survival were studied and analysed.

Results

A total number of 1277 cases of cancer children had been reported over a period of 20 years in Alexandria University Hospitals,Egypt.They were treated in the Pediatric Oncology and Pediatric Surgery Departments.

The relative incidence was as follows:leukemia 34%,brain tumors 19%,lymphoma 14.5%,bone tumors 11.5%,Wilms tumor 11.5%,Neuroblastoma 8.5%,soft tissue tumors 3%,germ cell tumors 2.5% and liver tumors 1.5%.

The overall five years survival rate was 39.8%,this is much lower when compared to that of the western countries which was proved to be 60-70%.

Conclusions

*Egyptian cancer children have higher incidence of lymphoma than that reported in UK and USA series.They also have higher incidence of Wilms tumor and a lower incidence of soft tissue tumors.

*Cancer children in Egypt have lower incidence of survival compared to that reported in the western countries.

*Among the important causes of this low survival is the delayed presentation and consequently delayed diagnosis and delayed treatment as well as the lack of specialized centers of Pediatric Oncology.

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Epidemiology

DIAGNOSTIC DELAYS IN CHILDHOOD MALIGNANCIES: A HOSPITAL BASED STUDY

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Objectives

Timely diagnosis followed by effective treatment is essential for the management of childhood malignancies. However, diagnosis of childhood tumors often gets delayed, due to non-specificity of early symptoms and rarity of disease. The objective of this study was to investigate the diagnostic process of childhood malignancies with emphasis on the time from the onset of symptoms until the start of treatment.

Methods

This retrospective study was conducted in a tertiary care referral hospital in India. During the study period of Feb 2012-Feb 2014, 57 children were diagnosed as having malignancy. The study chronicled the events from initial symptoms, final diagnosis, treatment and current status of patient and disease. Treatment delay was defined as time from first symptom to the onset of treatment.

Results

Acute lymphoblastic leukemia(ALL) was the commonest malignancy, diagnosed in 22/57(38.6%) children followed by brain tumors (9/57, 15.8%). Rhabdomyosarcoma accounted for 4 patients, while AML, Hodgkin Lymphoma, neuroblastoma, PNET, and Wilms tumor accounted for three patients each. Non-Hodgkin lymphoma and hepatoblastoma were the diagnosis in two children each; Osteosarcoma and langerhan cell histiocytosis contributed one patient each. The median delay in treatment for the entire study group was 15 days (range=4-154days). The median delay among children with ALL was 13(range=4=51) days as compared to 19(range=6-116) days among children with brain tumors (p=0.13). The treatment delay >21 days (three weeks) was associated with poor event-free-survival (Hazard ratio [HR]=8.94; 95%CI=3.17,25.27; p<0.0001). For acute leukemia HR was noted to be 9.31 (95%CI=0.26 to 338.3, p=0.22), while the same for brain tumor was determined to be 34.1(95%CI=2.74,424.3; p=0.006).

Conclusions

The long delay between onset of symptoms and treatment initiation is associated with poor outcome. High index of suspicion, and early initiation of diagnostic tests may aid in an early diagnosis and reduce the time to onset of treatment.

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Epidemiology

A DESCRIPTIVE STUDY ON ESTABLISHING DEDICATED PAEDIATRIC ONCOLOGY SERVICES IN LOW INCOME COUNTRIES: GHANA, SOUTH AFRICA AND UGANDA

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Objectives

This descriptive study evaluated the logistical, clinical, social and educational challenges in establishing paediatric oncology services in Africa.

Methods

A retrospective chart review was conducted of 946 children over an 8, 13 and 24 month period respectively in Kumasi, Ghana; Pietermaritzburg, South Africa and Kampala, Uganda in three newly established dedicated Paediatric Haematology Oncology services. The study was conducted in demographically varied countries to determine the burden of disease, nature of histology, presentation, co-morbidities and the ability to treat children with malignancies. It evaluated infrastructure, services and resources to treat children.

Results

The Kumasi, Pietermaritzburg and Kampala units respectively serviced 5.1 million, 1.1 million and 17.2 million children in their respective catchment areas with a ratio of 550 000 - 17.2 million children per Haematology-Oncology specialist, The most prevalent diagnosis in Ghana and Uganda was Endemic Burkitt's lymphoma whilst in South Africa it was Hodgkin's lymphoma and Nephroblastoma. Stage 4 disease dominated at 65%. All three services had a malnutrition rate of 75%. Ghana had a 0% HIV rate amongst oncology patients whilst in Uganda and South Africa it was 10%. Most HIV cases were haematological malignancies. Malaria was the most common co-morbid disease in the equatorial countries and complicated the treatment of neutropenic fevers. In Pietermaritzburg all children were started on established protocols whereas in Kumasi and Kampala modified protocols were used due to drug unavailability and toxicity. Paediatric services had to compete with adult services for resources.

Conclusions

The burden of disease outweighs current staff and medical resources available to deliver comprehensive services. Various co-morbid diseases prevent the initiation of standard chemotherapy protocols and cause frequent modification of treatment. The treatment goal is mainly palliative. The future training of Paediatric Oncologists should include more interpretive application of standard treatment modalities in regards to co-morbid disease and treatment limitations.

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Epidemiology

MISSING DATA AND SURVIVAL ANALYSIS OF CENTRAL NERVOUS SYSTEM TUMOURS AMONGST CHILDREN AND ADOLESCENTS IN YORKSHIRE, UK, 1990-2009

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Objectives

Severity of cancer at diagnosis is poorly recorded in medical records, often resulting in cases with this missing prognostic factor being excluded from analyses (complete case analysis (CCA)) creating potential bias. We investigated survival trends of central nervous system (CNS) tumours using multiple imputation (MI) to impute missing values of grade and ethnicity.

Methods

Children and adolescents (<30 years) diagnosed with CNS tumours were identified from a population-based cancer register (N=795). Missing values were imputed using logistic regression, with age, sex, diagnosis year, deprivation, relapse and treatment as predictors. We performed 40 imputations; hazard ratios (HR) of Cox regression models were pooled and compared to CCA.

Results

Missing data occurred in 30% of cases. Survival analysis after MI showed a 2-fold increased risk of death for 'other' compared to 'white' ethnicity and an increased risk of death for grade II, III and IV tumours compared to grade I. Survival improved by 4% per year over the study period.

	CCA			MI		
	HR	95%CI	P-value	HR	95%CI	P-value
Year of Diagnosis	1.02	0.99-1.05	0.29	0.96	0.94-0.98	<0.01
Ethnicity						
White	1			1		
Asian	1.33	0.76-2.33	0.32	1.43	0.81-2.50	0.22
Other	2.04	0.94-4.40	0.07	2.22	1.07-4.60	0.03
WHO Grade						
I	1			1		
II	3.66	2.24-5.98	<0.01	3.64	2.46-5.39	<0.01
III	6.93	3.75-12.78	<0.01	6.31	3.89-10.22	<0.01
IV	13.06	7.72-22.07	<0.01	11.02	7.35-16.53	<0.01

*Model was additionally adjusted for age, gender, diagnostic subgroup and socioeconomic status

Effects of ethnicity and grade were similar in CCA, however, improvements over time were not observed. MI reduced standard errors of coefficients by 18% on average compared to CCA.

Conclusions

MI minimised bias and enhanced precision. Survival worsened exponentially with increasing grade of tumour and was poorer for 'other' compared to 'white' ethnicity. Survival improved significantly over the study period; importantly, this effect was not observed using the standard CCA method.

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Epidemiology

CANCER DIAGNOSIS IN ADOLESCENCE IN THE EMERGENCY ROOM AT A NATIONAL INSTITUTE OF HEALTH

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Objectives

In Mexico, the diagnosis of cancer in adolescent is late and it has been associated with a poor prognosis. The aim of our study was to describe the clinical characteristics at the diagnostic in adolescence with cancer.

Methods

We realized a descriptive retrospective study where we included all the patients between 12 and 17 years at the moment of cancer diagnosis from January to December 2013. We analyzed the clinical characteristics stratifying in two groups: patients diagnosed at the emergency room and in the outpatient clinic.

Results

We included 45 patients, 66% were diagnosed with an oncological emergency. The relation male: female was 2.7:1. The main oncological diagnosis was osteosarcoma followed by acute lymphoblastic leukemia and central nervous system tumors. The reason for visiting the emergency room was pain, headache, tumor and pallor. The association between diagnosis in the emergency room and the mortality was not statistically significant.

Conclusions

Adolescents were diagnosed more frequently in the emergency room with advanced stage of disease and the medical urgency. It is relevant to establish an early detection program in this population in order to reduce diagnosis delay.

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Germ Cell Tumours

COMPARISON OF GONADAL AND EXTRAGONADAL, EXTRACRANIALLY LOCALIZED GERM CELL TUMORS IN CHILDREN. MULTICENTER STUDY FROM POLAND.

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Objectives

To compare clinical characteristics, histology and treatment results of gonadal and extragonadal, extracranially localized malignant germ cell tumors (MGCT) in children.

Methods

Retrospective analysis of clinical and histological features with regard to the outcome in two groups of patients: group I with extragonadal (EG) and group II with gonadal (GN) MGCT.

Results

152 patients from 15 Polish Paediatric Oncological Centres, diagnosed between 2008-2013 were evaluated. They were treated according to TGM-95 protocol. 42 /152 were included to group I (EG tumors) and 110/152 to group II (GN tumors). Patients with GN tumors were older (median age 13 years 10 months) than patients with EG tumors (median age 4 years 1 month). In group I the girls predominated (23/19), in group II - the boys (23/87). Size of

tumors was bigger in group I. Evaluation of serum markers indicated increased AFP in 66% from group I and in 82% from group II. Increased HCG was revealed in 23% from group I and in 64% from group II. High levels LDH ($>2x$ normal value) were found in 9% and in 16% adequately.. Uremic acid was increased in 10% vs 28%. 55% of patients from group I and 49% from group II were qualified to high risk group. The most frequently recognized histological types were teratoma and yolk sac tumors (YST) in group I; in group II YST and dysgerminoma/seminoma. Relapses were noted in 2 patients in every group, primary resistance was observed in 2 GN tumors. Third line therapy was used in 6 patients from group I and in 1 from group II. Unsatisfactory outcome was seen in 5 patients.

Conclusions

Some significant differences in clinical and histological features were documented. Further studies are needed to explain if the prognostic factors are the same in gonadal and extragonadal tumors.

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Germ Cell Tumours

TESTICULAR AND PARATESTICULAR TUMORS IN CHILDHOOD AND ADOLESCENCE

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Objectives

Testicular and paratesticular tumors are rare in childhood and have different characteristics from adult counterparts. We reviewed 41-year experience for testicular cancer in children and adolescents in our center.

Methods

Clinical characteristics and outcome of children who were treated between 1973 and 2014 were retrospectively evaluated.

Results

The median age of 149 patients with primary testicular and paratesticular tumors was 2.5 years (ranged 0-17). Histopathological diagnoses were yolk sac tumor (55.7%), teratoma (12.8%), mixed malignant germ cell tumor (7.4%), Leydig cell tumor (3.4%), granulosa cell tumor (0.7%), and paratesticular rhabdomyosarcoma (10.7%). Three patients were diagnosed as primary testicular non-Hodgkin lymphoma and one patient as metastatic paratesticular Wilms tumor. The most common clinical presentation was painless scrotal mass (88%). Initial surgery in 83.2% of patients was radical inguinal orchiectomy. Patients with stage 2 and higher germ cell tumors received BEP regimen (cisplatin 100mg/m²/day on day 1, etoposide 120 mg/m²/day on days 1-3, bleomycin 15 mg/m²/day on day 2). Patients were followed median 25 months (1 day-23.5 year). 5-year EFS and OS for stages 1, 2, 3 and 4 were 86%, 100%, 53%, 75%, and, 100%, 100%, 67%, 63% respectively. Most of the patients with rhabdomyosarcoma (11/16) had stage 1 disease. OS at 5 years was 92% for patients with paratesticular rhabdomyosarcoma.

Conclusions

Most frequent testis tumor is yolk sac tumor in childhood. BEP is effective regimen in testicular germ cell tumors. Stage 1 and 2 tumors have excellent prognosis regardless of histology.

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Germ Cell Tumours

PURE GONADOBLASTOMA WITH KARYOTYPE 46,XX AND XY CHIMERISM NEGATIVE INTO A GIRL - A CASE REPORT

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Objectives

Gonadoblastoma are germ cell tumors intimately mixed with sex-cord stromal in circumscribed nests, usually with hyaline basal membrane and focal or diffuse calcifications. Despite not being metastatic gonadoblastomas tumors, other types of germ cell tumors associated with them can invade the stroma, especially when combined with disgerminomas (50 %) or others.

They usually appear in patients with dysgenetic gonads, phenotypically female with sexual or somatic abnormalities, most often in the karyotype 46XY (96 %), but it has been observed individuals with absence of the Y chromosome (karyotype 46,XX,45,X45, X/46,XX), with structural abnormalities of X, (46,XX,del(11p)) and true hermaphrodites.

Methods

We report a case of an infant with pure gonadoblastoma, female, 8 months old, without gonadal dysgenesis, 46XX karyotype and negative XY chimerism, which was admitted to our hospital with a palpable mass in the pelvis discovered during surgery for correction right inguinal hernia. Alpha-fetoprotein (AFP) and beta-subunit of human chorionic gonadotropin (HCG) were normal. Ultrasonographical examinations revealed a large solid expansive training, adnexal right, heterogeneous, partially accurate and lobulated contour, measuring 7.3 x 3.5 x 5.8 cm, with a volume of 77 cm³. At laparotomy, we found extensive tumor in the left ovary and right ovary tape, performed left salpingo-oophorectomy and biopsy of the right ovary. Histological examination showed gonadoblastoma in the left ovary and absence of neoplasia in other structures analyzed. Immunohistochemical examination with calretinin, CD113 (C-KIT), inhibin and OCT-4 positive, helped to diagnose this gonadoblastoma.

Results

She is currently being followed up with exams ultrasonography and collecting AFP and HCG monthly to control possible relapse.

Conclusions

With this case, literature review was done to discuss treatment approach and additional research.

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Germ Cell Tumours

GERM CELLS INDUCED FROM HUMAN UMBILICAL CORD MESENCHYMAL CELL-DERIVED INDUCED PLURIPOTENT STEM CELLS BY BMP4

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Objectives

To reprogramme the induced pluripotent stem (iPS) cells from Human umbilical cord mesenchymal cells (HuMSCs) and induce the iPS cells into germ cells by BMP4.

Methods

OCT4, SOX2, Klf4, c-myc, Nanog, Lin28 were transfected into HuMSCs with lentivirus to reprogram HuMSCs into iPS cells. Morphological observation, Alkaline Phosphatase staining, karyotype analysis, RT-PCR, immunofluorescence staining, tumor formation in vivo and embryoid body formation in vitro were performed to examine the pluripotency of the iPS cell lines. We then induced one of the iPS cells lines into germ cells by BMP4. Gene expression was measured by qRT-PCR at days 0, 3, 7, 10 and 14. Early-stage germ specific protein VASA and meiosis specific protein SYCP3 were assessed by immunofluorescence staining.

Results

We obtained two iPS cell lines completely reprogrammed, HuMSC-iPS1 and HuMSC-iPS2. HuMSC-iPS1 expresses germ cell markers (DAZL, DPPA3, DDX4, SYCP3, PROTAMINE) at undifferentiated state. BMP4 (100ng/ml) can upregulate germ cell markers at different time points highly while the spontaneous differentiation just upregulate DPPA3, DAZL and VASA modestly at day 3. However, all of these genes were downregulated at day 14. VASA and SYCP3 immunofluorescence staining indicates there is a high VASA expression in BMP4 induced group in contrast to low expression in the spontaneous group at day 7. Meanwhile, there is a modest SYCP3 fluorescence in BMP4 induced group in contrast to no immunofluorescence in the spontaneous group.

Conclusions

OCT4, SOX2, Klf4, c-myc, Nanog, Lin28 can reprogram HuMSCs into iPS cells effectively. The MSC- iPS1 can differentiate into early germ cells spontaneously while the germ cells induced by BMP4 can enter meiosis.

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Germ Cell Tumours

OUTCOME OF EXTRACRANIAL GERM CELL TUMOURS IN CHILDREN AT NATIONAL HOSPITAL OF PEDIATRICS, HANOI, VIETNAM

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Objectives

Germ cell tumour (GCT) account for approximately 3% of childhood cancer. It can be benign or malignant. The aim of this study was to evaluate outcome of extracranial GCT in children at NHP. All patients were treated according to the Germ Cell III protocol.

Methods

A retrospective review of 168 children with extracranial GCT had been treated at NHP between 2008 and 2013. Result of treatment, recurrence, death, overall survival (OS) and event free survival (EFS) 5 years were analyzed.

Results

All patients with mature teratoma underwent surgery alone, but there was 1.4% recurrence, 2.9% death. Patients with immature teratoma had 5,9% recurrence, no died. The patients with yolk sac tumours underwent excision tumour or surgical biopsy, followed by chemotherapy (96.1%), 7.8% recurrence, 5.9% death. 9 patients died (5.4%) and 9 patients were recurrence (5.4%). Mortality and recurrence rate were high with sacrococcygeal, mediastinal tumours and mixed malignant GCT. Cause of death were respiratory failure, coma due to metastases.

Overall survival (OS) for the whole patient group was 88.9% and event-free survival (EFS) was 83.8% at 5 years. Patients with gonadal GCT had OS and EFS higher than those with extragonadal (OS:p=0.118, EFS:p=0.011). Patients with sacrococcygeal and mediastinal tumours had OS and EFS lower than those with gonadal and retroperitoneal GCT (OS:p=0.048, EFS:p=0). Patients with immature teratoma (OS:100%, EFS:92.6%) and yolk sac tumour (OS:94%, EFS:83.6%) had the highest probability of OS and EFS. Complication were infection and disorder of defecation and urination after operating tumour at sacrococcygeal.

Conclusions

The prognosis of GCT is quite good, especially with gonadal GCT.

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Germ Cell Tumours

CHARACTERISTICS OF EXTRACRANIAL GERM CELL TUMOURS IN CHILDREN AT NATIONAL HOSPITAL OF PEDIATRICS, HANOI, VIETNAM

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Objectives

The aim of this study was to evaluate characteristics of extracranial GCT in children at NHP.

Methods

A retrospective review of 168 children with extracranial GCT had been treated at NHP between 2008 and 2013. Pathology, age, sex, primary tumour, metastases and stage were analyzed.

Results

There was 78.6% of children under 5 years old in this study. Boy/girl = 1.2/1. Clinical signs could include big testis (41.7%), abdominal distension (30.6%), touching abdominal tumour (25%) or sacrococcygeal (11.1%), defecation and urination difficulty (8.3%).

Gonadal GCT hold 55,9%. Almost tumour at extragonadal were sacrococcygeal tumour (16.1%). Most of mature teratoma were found in ovary (50%), sacrococcygeal (55.6%) and mediastinum (61.5%). Tumour in testis almost were yolk sac tumour (56.5%). Children under 5 years old usually had tumour at testis (44.7%) or sacrococcygeal (18.9%). Children over 5 years old usually had tumour in ovary (55.6%) or mediastinum (19.4%).

All tumours had imaging of sound mix, heterogeneous. AFP were normal in all patients with mature teratoma. AFP increased in 1/3 of immature teratoma, almost of yolk sac tumour and mixed malignant GCT.

Teratoma were found most frequently (mature: 69, immature: 34), followed by Yolk sac tumour (n=51), Mixed malignant GCT (n=10), Dysgerminoma (n=2) and Embryonal carcinoma (n=2). The GCT were located in sites: testis (n=62), ovary (n=32), sacrococcygeal (n=27), mediastinum (n=13), retroperitoneum (n=14), abdominal cavity (n=13), neck (n=3), shin (n=1) and miscellaneous (n=10). Most patients (81) were Stage I, 64 patients were Stage II, 13 patients were Stage III, 6 patients were Stage IV and 4 patients operated in other hospitals could not classified.

Conclusions

Extracranial GCT in children had variable pathology and primary location. Most of patients admitted in early stage.

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Germ Cell Tumours

EXTRACRANIAL GERM CELL TUMORS: - THIRTEEN YEAR EXPERIENCE AT KANTI CHILDRENS HOSPITAL

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Objectives

To evaluate the treatment outcome of children with extra cranial Germ Cell Tumors (GCT) treated in our center.

Methods

This was a retrospective analysis of treatment outcome of children with extracranial germ cell tumors who were registered in our center from March 1999 to March 2012. All the cases had undergone surgical removal of the masses and biopsy. Alpha-feto-protein and beta-HCG were done pre-operatively, post operatively, during chemotherapy and on each follow up. If the tumor markers were raised post-operatively, they received JEB (Carboplatin, Etoposide, Bleomycin) Chemotherapy, 3 weekly until the tumor markers normalized, and 2 more cycles were added thereafter. Stage I tumors and mature GCT with normal tumor markers were kept in regular follow up.

Results

Out of 755 childhood cancers, 45 (5.96%) were GCT. The median age group was 1-3 years (Range: 1 day – 13 yrs), M: F=1:3. Based on histological findings the common tumor types were Yolk Sac tumor (49%), Immature Teratoma (22%), Mature Teratoma (11%), Mixed GCT (9%) and Embryonal Carcinoma (9%). The most common site was Sacrococcygeal (45%) followed by Gonads (35%) Mediastinal tumor (11%). Most common stage was II (40%).

Forty cases received chemotherapy and 5 were kept on a close follow up. All those who were started with chemotherapy completed their treatment. At the end of thirteen years, 22 (49%) are alive and on regular follow up, 11(24%) died and 12 (27%) lost to follow up.

Conclusions

: Extracranial Germcell Tumour, GCT was the most common GCT with 49% over all survival rate.

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Germ Cell Tumours

PRIMARY THYMIC GERMINOMA IN A BOY WITH LOWE SYNDROME

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Objectives

Mediastinal germ cell tumors are relatively rare, and among them thymic germinoma is an extremely rare tumor. We report a case of thymic germinoma associated with Lowe syndrome. To our knowledge, this is the first case report of thymic germinoma complicated with Lowe syndrome.

Methods

Case report.

Results

An 11-year-old boy who was diagnosed with Lowe syndrome has been followed at our outpatient clinic. Patients with Lowe syndrome have the following signs and symptoms: 1) renal tubular acidosis, 2) congenital cataract, and 3) intellectual disability. When he was 11 years and 9 months old, secondary sexual characteristics appeared rapidly in a few weeks. Serum HCG-b was high (278.2 pg/ml) and chest MRI showed a cystic tumor in the thymus. Although it was difficult to clarify whether the tumor was malignant or not, the tumor was functional and we decided to resect the tumor. The tumor was first biopsied and turned out to be a germinoma by prompt intraoperative diagnosis. We performed extended thymectomy with mediastinal lymph node dissection. After the operation, he was treated with four courses of JEB (carboplatin, etoposide, and bleomycin) chemotherapy; then, the dose was reduced by 40% considering his deteriorated renal function. He is now followed up at the outpatient clinic and has shown no recurrence.

Conclusions

We reported the first case of thymic germinoma complicated with Lowe syndrome.

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Germ Cell Tumours

IMAGING FEATURES OF MATURE AND IMMATURE EXTRA-GONDAL TERATOMA IN PEDIATRIC AGE GROUP

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Objective

Teratoma is the most frequent germ cell tumors. The most accepted theory for their origin suggests that most are due to abnormal differentiation of embryonic germ cells that arise from the fetal yolk sac. Normally, these cells migrate to gonads yet it can migrate abnormally to other locations so there are gonadal and extra gonadal teratomas. Teratomas range from benign, mature, to immature, poorly differentiated lesions with solid components and malignant transformation. The prognosis, clinical outcome and the risk of recurrence were reported to be related to the degree of tumor maturity. Our objectives are to demonstrate the radiological features of the extra-gonadal teratomas and to evaluate the potential accuracy of the imaging findings in differentiation between the mature and immature teratoma.

Methods

Seventy pediatric patients-30 male and 40 females- with pathologically proven teratoma who presented to our hospital in the past four years were included in this study. Their ages ranged from 20 days to 17 years. Retrospective review of their radiological studies was done and correlated with the pathological results.

Results

Gonadal teratoma found in 14 cases, ovarian (n=8), two of them were bilateral and testicular (n=6). Sacrococcygeal location is the commonest site of extragonadal teratomas (n=22) followed by retroperitoneal (n=13), intraperitoneal lesion (n=5), intraspinal (n=6), intracranial (n=4), neck (n=3), orbital (n=2) and penile (n=1). Pathological diagnosis shows 55 mature teratoma and 15 immature teratoma. Most of the mature teratoma (53 /55) show all fat, calcification, cystic and solid component whereas the immature lesion usually take one of these component mostly the fat component.

Conclusions

Extra-gonadal teratoma are more common than gonadal ones in pediatrics unlike the adults. Awareness of the imaging feature of these lesions especially the immature teratoma is of importance in proper management and improvement of the patient outcome.

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Histiocytosis

MALIGNANT HISTIOCYTOSIS: REPORT OF TWO CASES

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Background: Malignant Histiocytosis is a rare disorder characterized by a systemic proliferation of morphologically atypical histiocytes. The clinical presentations vary greatly, ranging from mild to life threatening.

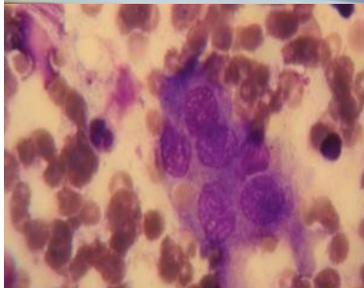
Objective: To draw attention of clinicians particularly in developing countries to this rare disorder that can easily be confused with acute leukemia.

Methods

Case Report.

Results

Case reports: Two boys aged 2 and 8 years respectively were admitted to Aminu Kano Teaching Hospital. They presented with recurrent fever for 2 months and bilateral neck swellings. During the same period, they had repeated blood transfusions. On examination, the two were underweight with significant cervical lymph-node enlargement, generalized petechiae haemorrhages and hepato-splenomegaly. They were initially suspected to have acute leukemia. However bone marrow aspiration biopsy revealed a diagnosis of malignant histiocytosis. They were treated with Cyclophosphamide Oncovin Doxorubicin and Prednisolone. The parents of the first child abandoned the course of chemotherapy 5 days into the first course and the patient died at home 6 days after leaving the hospital. The second patient completed six cycles of chemotherapy and the repeat bone marrow aspiration biopsy and the full blood count after the first course showed significant improvement and the patient is still on follow up.



Patient 1 Bone marrow infiltration by histiocytes, engulfing both mature and immature haemopoietic cells



Patient 2 Patient's chest radiograph at diagnosis



same patient after completing treatment Patient's chest radiograph after completing treatment

Conclusion: Histiocytosis is rare, but should be suspected as a differential diagnosis in a patient with significant lymph node enlargement, recurrent anaemia and repeated blood transfusion.

EP-189**Histiocytosis****HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR LANGERHANS CELL HISTIOCYTOSIS (EXPERIENCE OF EGE UNIVERSITY FROM TURKEY)***N. Çetingül¹, S. Aksoylar¹, S. Kansoy¹, M. Kantar¹, B. Demirag¹, B. Akinci¹**¹Pediatric Oncology, Ege University School of Medicine, Izmir, Turkey***Objectives**

Langerhans Cell Histiocytosis (LCH) is characterized by heterogenous lesions including Langerhans cells.. When the systems involved are "risk organs" and/or the patient is younger than 2 years at diagnosis, MS-LCH has been considered particularly devastating, and as carrying a potentially fatal prognosis.

Despite the treatment intensification, the mortality rate is approximately 40% in patients with MS-LCH .Refractory patients and those with multiple reactivations present a challenge. Cladribine , Cladribine –cytarabine arabinoside combination and clofarabine can be used as salvage therapy.

Methods

We report 3 refractory Langerhans Cell Histiocytosis patient who were treated successfully with hematopoietic stem cell transplantation using non myeloablative conditioning regimen

Results

Table 1. Patients characteristics

Patient no	Sex	Age at diagnosis	Type of LCH	Involved organs	6.th week response to frontline treatment	Therapy prior to HSCT
1	M	7,5 month	MS-HR	Liver, spleen, bone marrow, skin	Poor response	VBL+Prednisolone/MTX/CSA/ARA-C/ CSA+ Cladribine+ARA-C Clofarabine
2	M	8 month	MS-HR	Liver, spleen, bone marrow, skin	Poor response	VBL+Prednisolone/MTX/CSA/ARA-C/ CSA+ Cladribine+ARA-C Clofarabine
3	F	9 month	MS-LR	Skin, GIT	Good response	VBL+Prednisolon/ Cladribine/ clorafabine

M: male , F: female , VBL: vinblastine , MTX: methotrexate , CSA: cyclosporine A , ARA-C: cytarabine

Conclusions

Table 2. Details of hematopoietic stem cell transplantation and outcome

Patient no	1	2	3
Age at HSCT	20,5months	30months	27months
Duration from diagnosis	13months	22months	18months
Findings before HSCT	Liver 14cm, spleen 14cm Skin lesions pancytopenia	Liver 4-5cm, spleen 7cm thrombocytopenia	Liver 3cm, spleen 4cm
Conditioning	Melphalan/fludarabine/Alemtuzumab	Melphalan/fludarabine/ATG	Melphalan/fludarabine/Alemtuzumab

Sources	6/6 matched unrelated Cord blood	5/6 matched unrelated Cord blood	10/10 matched unrelated Perip stem cell
Infused NCC	6,5x107/kg	3,8x107/kg	6,4x108/kg
GVHD prophylaxis	CSA/MMF	CSA/MMF	CSA
Engraftment	+34'th day	+32'nd day	+17'th day
Post HSCT	+4 years	+12 months	+6 months
Outcome	Alive	Alive	Alive
Sequel	-	Liver, skin GVHD	-

MMFmicophenolate mophetile

HCST should be employed especially in high risk MS-LCH patients.

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Histiocytosis

ORBITAL EOSINOPHILIC GRANULOMA – CLINICAL PATHOLOGICAL STUDY

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Objectives

Orbital eosinophilic granuloma (aka: unifocal Langerhans cell histiocytosis) is a relatively rare entity among orbital tumors, with many unique clinical and pathological features and challenges. Currently the large scale clinicopathological study is missing.

Methods

We retrospectively collected 18 cases, nine cases in our institutional files from 1992 to 2013 and nine cases from medical literature. All cases have either electron microscopic confirmation with Birbeck granules or immunohistochemistry finding of CD1a and/or S100 positivity. The clinical information, selective radiology images and histopathology of cases from our institution were reviewed.

Results

The patients age ranges from 1 to 58 year old, with mean 9.3 years with male predominance (M/F=14:4). The lesion are equally distributed at right or left side (9 cases for each side). Almost all patients have superior lateral orbital lesions. Eye lid or forehead swelling, proptosis are the most common symptoms, with visions unimpaired or mildly affected.

Conclusions

1st and 2nd decade presentation, male predominance and the predilection of eosinophilic granuloma at superior lateral orbit with frequently remarkable adjacent bone destruction narrows down the differential diagnosis significantly. In contrast, rhabdomyosarcoma of orbit most commonly happens at superomedial quadrant if embryonal variant or at inferior if alveolar variant. Neuroblastoma, though the preferred metastatic location is the same, but the age are characteristically at the lower spectrum accompanied by higher frequency of bilaterality and hypertension caused by catecholamine secretion. From the pathologist's perspective, sparse Langerhans cell presentation and/or mixtures of other inflammatory infiltrates, inconspicuous eosinophils on frozen sections are major challenges.

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Histiocytosis

SECONDARY HEMOPHAGOCYtic LYMPHOHISTIOCYTOSIS IN CHILDREN WITH MALIGNANCY UNDERGOING INTENSIVE CHEMOTHERAPY

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Objectives

Hemophagocytic lymphohistiocytosis (HLH) is a condition of uncontrolled immune dysfunction induced by a hyperinflammatory response. Secondary hemophagocytic lymphohistiocytosis may be associated with a systemic viral, bacterial, fungal, or parasitic infection in individuals with an underlying immunological disorder such as malignancy. We aim to document the characteristics of secondary HLH in children with malignancy and to point out early diagnosis and treatment.

Methods

The characteristics, HLH inducing factors, treatment and outcome of 4 (2 girls, 2 boys) children with cancer and secondary HLH were evaluated.

Results

4 children (2 acute lymphoblastic leukemia with infection , 1 relapsed neuroblastoma with infection, 1 anaplastic large cell lymphoma at diagnosis) with fever, hepatosplenomegaly, anemia, thrombocytopenia, increased liver function tests, very high ferritin levels, high triglyceride levels and hemophagocytosis in bone marrow were diagnosed with secondary HLH. Infectious etiology was cytomegalovirus (CMV), CMV and probable invasive aspergillus, staphylococcus aureus infections, and malignancy itself. The treatment of hemophagocytic lymphohistiocytosis consisted of corticosteroids and/or intravenous immunoglobulins along with appropriate antimicrobial therapy and chemotherapy in these patients. One of the patients had a second reactivation of HLH during intensive chemotherapy due to concomitant CMV and fungal infections. All the symptoms and signs regressed gradually.

Conclusions

Secondary HLH can be diagnosed in up to 10% of patients with malignancy and may be life threatening. Patients with high fever and liver dysfunction should be further investigated and marrow aspiration samples carefully observed to detect hemophagocytosis. Earlier diagnosis and treatment may decrease the high mortality rate in these patients.

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Histiocytosis

IMPACT ON OUTCOME OF A MODIFIED LANGERHANS CELL HISTIOCYTOSIS (LCH) PROTOCOL WITH INTENSIFIED HIGH RISK INDUCTION AND AUGMENTED PROLONGED MAINTENANCE- A SINGLE INSTITUTION EXPERIENCE

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Objectives

Relapses in LCH, and mortality in Multisystem- High Risk (MS-HR) remain problematic. Disease progression on early reassessment necessitates expensive salvage options including transplant. Etoposide showed modest benefit in MS-HR and prolonged maintenance reduced recurrences in earlier studies. Methotrexate proved equivocal in shorter maintenance. These strategies were discontinued after LCH trials I-III. A regime with metronomic Etoposide for MS-HR and prolonged maintenance including Methotrexate was devised to reduce need for salvage. Patients accrued over 5 years were analyzed.

Methods

LCH records of 5 years from Jan 2009 were studied. Single System (SS) and Multisystem Low Risk (MS-LR) received 25 weekly Vinblastine doses, Prednisolone for 4 weeks, tapered over 2, then continued as 3-day weekly pulses till week 12, and 5-day 3-weekly pulses till week 25. 3-weekly pulses continued in maintenance for MS-LR and HR for 6 and 18 months respectively. Additionally, 3-weekly Vinblastine, daily 6- Mercaptopurine and weekly Methotrexate were given throughout maintenance. MS-HR also received daily Etoposide for 21 of every 28 day cycle for one year. Responses were evaluated at 3, 6 and 12 months or end of therapy.

Results

39 patients were evaluable. Median age was 36 months (4-189). 24 were SS, 4 MS-LR and 11 MS-HR. Five (3 MS-HR) were lost to follow up before first reevaluation. 30 had improvement (Active Disease- Better or No Active Disease) and 3 had intermediate response at first reassessment. 1 MS-LR progressed in a risk organ, and was managed as HR. 1 MS-HR relapsed within 5 months requiring salvage. On a median follow up of 25 months (5- 54), all 34 evaluable patients were alive, 3 with sequelae.

Conclusions

Induction and maintenance augmentation with metronomic Etoposide for MS-HR and prolonged maintenance with additional Methotrexate has shown promise in reducing mortality and relapses respectively, avoiding expensive salvage treatments.

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Histiocytosis

A CASE OF SECONDARY HEMOPHAGOCYTTIC LYMPHOHISTIOCYTOSIS (HLH) FOLLOWING INCOMPLETE KAWASAKI'S DISEASE (KD). IMPORTANCE OF DISTINGUISHING RECURRENT KD FROM HLH

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Objectives

Hemophagocytic lymphohistiocytosis (HLH) is potentially a life threatening disorder characterized by severe systemic inflammation caused by immune dysregulation. Secondary HLH is seen after various infections, rheumatologic disorders and malignancies.

Methods

We report a patient with secondary HLH developing after Kawasaki's disease (KD).

Results

A previously healthy one year old boy was initially admitted to the hospital with prolonged unremitting fever and diffuse maculopapular rash. He was diagnosed with incomplete KD after his echocardiogram showed dilated left coronary artery. He was treated with intravenous immunoglobulin (IVIG) and aspirin with initial response. Five days after his hospital discharge and a week after initial therapy he started having fevers, worsening of rash and developed hepatosplenomegaly. He had cytopenia with hemoglobin of 6,9 g/dl and platelets of 55K/uL. His ferritin and triglyceride levels were elevated (2215ng/ml and 486mg/dl respectively). Bone marrow aspirate and biopsy were performed which revealed hemophagocytosis. IL-2Rs level was elevated at 2764 U/ml. Perforin mutation was negative. He was diagnosed with secondary HLH and started on IVIG and dexamethasone as per HLH 2004 protocol. He had a rapid response to treatment with improved general status, resolution of fever and cytopenias, decrease in ferritin and triglyceride levels.

Conclusions

HLH may be secondary to KD. Differentiating recurrent KD from secondary HLH may be difficult. It's important to recognize the clinical and laboratory criteria of HLH quite early and initiate treatment accordingly to avoid mortality and morbidity due to HLH.

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Histiocytosis

CENTRAL NERVOUS SYSTEM IMAGING IN CHILDHOOD LCH

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Objectives

Langerhans cell histiocytosis (LCH) is a systemic disease with variable impact on the central nervous system (CNS). The aim of this study was to evaluate the cerebral abnormalities on MR imaging in children with LCH.

Methods

Two experienced neuroradiologists retrospectively reviewed the 31 MR examinations available from 94 children and adolescents with LCH. The typical cerebral pathologies of LCH were recorded and rated regarding their signal intensity on T2-w images and on contrast-enhanced T1-w images.

Results The most common locations of the visible structural changes were osseous, followed respectively by pineal enhancement, enlarged pituitary stalk/mass, white matter hyperintensity, dentate nucleus, parenchymal enhancement, hippocampus and meningeal enhancement. The inter-rater agreement was 69-100%. The lowest agreement was found for the pineal region and dentate nucleus.

Conclusions

The most common site of manifestation in LCH after the bone was the hypothalamic-pituitary system. But other parts of the CNS such as the cerebellum or the white matter may also be involved, indicating initial neurodegeneration in childhood.

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Histiocytosis

LATE PRESENTATION PREDICTS ENDOCRINE DYSFUNCTION IN PATIENTS WITH LANGERHANS CELL HISTIOCYTOSIS(LCH)- A RETROSPECTIVE ANALYSIS OF THE WEST OF SCOTLAND LCH SERVICE 1998-2012

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Objectives

Langerhans cell Histiocytosis (LCH) is a rare condition primarily affecting the paediatric population. It is characterised by clonal proliferation of Langerhans cells. Disease severity is dependent on the type and number of organs involved in addition to focality. Disease aetiology still remains unclear. We aimed to record the incidence and characteristics of West of Scotland LCH patients with a focus on predictive factors for endocrine dysfunction.

Methods

Consecutive diagnoses of LCH, at The Royal Hospital for Sick Children Glasgow, between January 1998 - December 2012 were selected. Patient notes were used to collect information on age, sex, postcode (Scottish index of deprivation-SIMD 1-most deprived, 6-least deprived), ethnicity, systems involved, signs and symptoms of presentation, disease progression, treatment and current status.

Results

23 patients were diagnosed with LCH. The median age of diagnosis was 2.7 years (Range: 1 month-15 years). 52%(n=12) were female. Over half of patients 57%(n=13) have SIMD scores of 1/2. 82% of the population were Caucasian, 13% South Asian and 4% of mixed origin. The head was the most common site of presentation. There was 1 mortality in the cohort. Common symptoms at presentation included skin rashes, lumps and musculoskeletal pain. All patients with high risk organ involvement (spleen, liver, hematopoietic system or lung) were girls. Endocrine dysfunction, with diabetes insipidus being most common, was seen in 35%(n=8). 62.5%(n=5) were diagnosed with diabetes insipidus alone. Patients with endocrine dysfunctions had a longer symptom interval compared to those without endocrine dysfunction; with 62.5%(n=5) diagnosed after 4 months compared to 13.3%(n=2) without endocrine dysfunction. (p=0.052)

Conclusions

Deprivation is associated with an increased incidence of LCH, with females more likely to develop high risk organ disease. A third of paediatric LCH patients develop endocrine dysfunction and these patients have a longer symptom interval. Further studies are required.

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Histiocytosis

SEVERE DISSEMINATED CNS JUVENILE XANTHOGRANULOMA PRESENTING WITH BRAINSTEM DYSFUNCTION AND COMA

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Objectives

to see the outcome of Juvenile xanthogranulomatosis(JXG) presenting with brainstem dysfunction and coma

Methods

3 years child presenting with coma, hemiparesis secondary to non langerhans cell histiocytosis has been treated with LCH 3 protocol .

Results

Three years boy, presented with nodular lesion on face since 9 months of age , gradually progressing to trunk, back and extremities. No abnormality at birth . There was history of polyuria& polydipsia from 18 months of age, frontal headache & vomitings for 4 months and weakness of left half of the body ,pooling of secretions for 1 month prior to presentation. On examination, had diffuse Xanthogranulomatous lesions over skin and eyes. Mouth was normal. There was no organomegaly. CNS examination revealed, GCS of 7/15, swallowing difficulty,restricted horizontal gaze , left hemiparesis with power of grade 3/5 with right facial palsy.

His CBP, CRP, electrolytes,bichemistry , Lipid profile were normal. CXR, USG abdomen, 2D Echo were normal. MRI brain showed diffuse circumscribed lesions in cerebrum, cerebellum, subcortex and ependymal region. Large lesion in right CP angle causing compression of IVth ventricle, mild hydrocephalus with distortion of brain stem.

The skin and brainbiopsy report revealed juvenile xanthogranuloma. Immunohistochemistry demonstrated histiocytic cells were positive for CD68, negative for CD1a & S-100. These combined results confirmed histiocytes are non-Langerhan's cells. In light of the clinical and histological findings, a diagnosis of JXG was made.

He was started on chemotherapy as per LCH III protocol.Treated diabetes insipidus with desmopressin. Bulbar dysfunction, hemiparesis, consciousness improved within 3 weeks. skin lesions gradually improved. MRI showed near total resolution of lesions. Maintenance was extended for 2 years as per neuroimaging findings. Currently he is off treatment for 6 months and well .

Conclusions

Severe disseminated CNS disease with JXG responds to chemotherapy with significant neurological improvement with near total MRI and skin lesions resolution .

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Histiocytosis

CYTOSINE-ARABINOSIDE, VINCRISTINE, AND PREDNISOLONE IN THE TREATMENT OF CHILDREN WITH MS LCH NOT RESPONDING TO FIRST LINE TREATMENT: EXPERIENCE OF A TERTIARY CARE HOSPITAL IN INDIA

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Objectives

The purpose of our study was to find the treatment outcome of patient of MS-LCH treated on VCR-Ara C steroid protocol after failure of first line treatment .

Methods

The medical records of 54 patients with a diagnosis of LCH, was examined to find the treatment response with first line protocol (steroid,VBL) and treatment of refractory LCH with subsequent course, survival, and late sequelae. They were followed up and outcomes assessed.

Results

Multisystem LCH was seen in 36 patient's. Duration of symptoms ranged from 2 months- 4.5 years (mean 10 months). Multisystem LCH was seen in 36 patients. 7 patients had refractory/recurrent LCH. One patient had low risk recurrent LCH which responded to steroids only. 3 patients were treated with AraC VCR protocol and other three received Cladribine based therapy. Both groups treated with cladribine and AraC VCR showed comparable response radiologically, clinically and in adverse reactions. Episodes of Febrile neutropenia were less with AraC VCR protocol. Risk organ most affected was liver. 25 % of patients with multisystem disease had some residual lesion or active disease.

Conclusions

AraC VCR based treatment for refractory LCH is a good alternative to cladribine based protocol. Cost benefit, less myelosuppression are advantages over cladribine. Low risk recurrent LCH can be treated with less cytotoxic regimes. Treatment of refractory LCH presents a challenge and treatment protocol needs to be decided based on risk organ involvement, organ dysfunction and response to less intensive protocols.

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TREATMENT OF RELAPSED LANGERHANS CELL HISTIOCYTOSIS ACCORDING TO LCH III PROTOCOL DID NOT PREVENT SUBSEQUENT RELAPSES; SINGLE CENTER EXPERIENCE

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Objectives

Langerhans cell histiocytosis (LCH) is a rare disease characterized by accumulation of malignant dendritic cells. In our study we analyzed the outcome of patients with LCH treated on LCH III protocol.

Methods

From 12/2002 to 1/2012 24 patients with LCH were treated at our institution. Event-free survival (EFS) and overall survival (OS) was analyzed using StatView statistical program.

Results

Patients with LCH were treated on LCH III protocol, 20 patients were treated at diagnosis, 4 patients underwent primary local therapy for osteolytic bone lesion first and then relapsed (in median 4.36 months); the protocol was used subsequently as the salvage therapy. Single-system (SS) LCH was diagnosed in 14 patients (bones, skin, lungs, pericardium), multi-system LCH had 10 patients (bones, skin, lymph nodes, thymus, lungs, liver, pituitary gland). 'Risk organs' were affected in 3 patients (2 lungs, 1 liver). Median age at diagnosis was 2.7 years (0.5-14.6), median follow up was 7 years (1.5-13.3). Three patients were stratified to therapeutic group 1: MS-'risk'-LCH, 10 patients to group 2: MS-'low risk'-LCH, 11 to group 3: SS multifocal bone or 'central nervous system special'-LCH. EFS of all patients is 75%, OS is 95.8%. EFS SS-LCH is 92.0%, MS-LCH 50.0%, P=0.02. Therapeutic group 1: 2 from 3 patients relapsed, group 2: 3 from 10 relapsed, group 3: 1 from 11 patients relapsed, P=0.04%. EFS of 4 patients that were treated for LCH progression is 25.0% in comparison to 85.0% in primary treated patients, P=0.004.

Conclusions

Patients with LCH treated on LCH III protocol have excellent prognosis at our institution. On the other hand LCH III protocol did not prevent subsequent progressions when used as a salvage treatment for relapsed LCH after primary local therapy. Large number of patients is needed to confirm our findings.

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Histiocytosis

STEM CELL TRANSPLANTATION IN PRIMARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS : EXPERIENCE FROM A TERTIARY CARE CENTRE IN INDIA

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Objectives

Hemophagocytic lymphohistiocytosis (HLH) can be primary or secondary. For primary HLH and refractory secondary HLH, hematopoietic stem cell transplant (HSCT) is the only curative treatment.

Methods

Retrospective review of our HSCT data was done. Out of 34 patients who underwent HSCT between 2010-2013, 3 were for HLH. All 3 patients were diagnosed as HLH based on the HLH 2004 criteria. Genetic workup was done whenever feasible.

Results

F, 11 month old girl, diagnosed as HLH, underwent Matched Sibling Donor (MSD) HSCT (Donor-elder brother;6/6 match) after conditioning with Fludarabine, Melphalan and Anti-Thymocyte Globulin with a peripheral blood stem cell dose of 6.9×10^6 / kg. Neutrophils engrafted on Day +22. Her GVHD (skin+gut) responded to immunosuppression. At present she is alive at 2yr post HSCT.

S, 15 months old boy, with abnormal NK cell activity and STX11 mutation underwent a double umbilical cord blood (UCB) HSCT post conditioning with Campath, Fludarabine, Melphalan. (Cord A: 5/6 match; nucleated cell (NC) dose 62.4×10^7 , Cord B: 4/6 match; (NC) dose 120.44×10^7). Post transplant, he had CMV reactivation. He died 1 month post transplant of acute renal failure.

N, 3 years old boy, with Munc 13.4 mutation underwent an unrelated UCB HSCT (5/6 match) after conditioning with Busalphan, Cyclophosphamide and Etoposide. Post transplant, he had complications of BK virus cystitis, skin & gut GVHD, hypertensive encephalopathy and vision impairment. He had neutrophil and platelet engraftment at day +24 and +40 respectively. He died of cardiogenic shock on day +198 post transplant.

Conclusions

HLH patients undergoing HSCT have many co-morbidities which need to be intricately managed. Success rates of transplants in these patients are improving with the evolving experience.

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Histiocytosis

MULTISYSTEM LANGERHANS CELL HISTIOCYTOSIS (LCH): CASE SERIES AND REVIEW OF LITERATURE FROM INDIA

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Objectives

The outcome of LCH in children varies from excellent response in single-system disease to poor response in multisystem disease. We analyzed patients diagnosed with multisystem LCH at our center and compared outcomes to published literature from India.

Methods

Retrospective analysis of patients diagnosed with LCH at our centre between 2006 to 2013 was done. All patients were stratified and managed as per LCH-III protocol.

Results

35 patients were diagnosed with LCH. M:F ratio was 2.5:1 and median age of presentation was 4.13 years. 20 patients(57%) had multisystem disease and 18 had risk-organ involvement. 5 patients(25%) had anemia (Hb<10gm%) and 10 (50%) had anemia with thrombocytopenia at presentation. Other features included fever(n=9), breathing difficulty(n=7), hepatomegaly(n=6), splenomegaly(n=1), skin rash(n=6), bone lesions(n=7), diarrhoea(n=6), rectal bleeding(n=2), bleeding from ears(n=1), neck swelling(n=2) and seizures(n=1). All patients received 2 courses of induction with prednisolone & vinblastine. Maintenance chemotherapy was given in 16 patients. 4 patients were switched to salvage protocol(2 relapses, 2 active disease). 5 patients(25%) completed treatment and are in remission, 3(15%) are on treatment, 6(30%) expired, 1(5%) abandoned treatment and 5 (25%) were lost to follow up.

We identified 2 case series from Indian literature which described outcome of children with LCH. Bansal D., reported 69 LCH patients over 19 years of whom 48(69.6%) had multisystem involvement. They were treated with prednisolone and vinblastine or etoposide over 6-8 weeks. 41.6 % had a fatal outcome. The 2nd case series by Singh T., reported 40 patients of LCH over 5 years, of whom 5 had multisystem disease. 3 received treatment; one is in remission, one relapsed and the other died.

Conclusions

Multisystem involvement is seen in >50% of pediatric patients presenting with LCH. The outcome of these patients from our series as well as that reported from the subcontinent continues to be poor.

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Histiocytosis

2-CHLORODEOXYADENOSINE AND CYTOSINE ARABINOSIDE COMBINED CHEMOTHERAPY FOR TREATMENT OF REFRACTORY OR RECURRENT LANGERHANS CELL HISTIOCYTOSIS

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Objectives

Children with Langerhans cell histiocytosis (LCH) may become refractory to standar therapy or present with repeated recurrences. Reports indicate that 2-chlorodeoxyadenosine (2-CDA) and cytosine arabinoside (Ara-C) combined chemotherapy is effective in this cases. The purpose of this review was to describe the experience in our Unit

Methods

Retrospective analysis on records from 5 patients admitted between January 2008 - December 2012. Patients had a confirmed diagnosis of LCH that had recurred several times or not responded to standard therapy. Patients were given a dose of 5 mg/m² daily 5 days plus concurrent Ara-C 100 mg/m²/day for 4 days with profilactic filgrastim A total of 6 courses were programmed , and courses were repeated every 3 weeks.

Results

28 patients with LCH were admitted during the refered period, 5 patients used the scheme with 2-CDA plus Ara-C (3 for multiples reactivation, 2 for progression of disease)

Median age of diagnosis was 54 months(range 3 months to 15 years)

3 patients had initial involvement of high-risk organs and 1 Central Nervous System(CNS) mass

3 patients completed 6 courses, 1 change per progression after two courses and one discontinued for severe (grade 3) liver toxicity in the first dose of the first course

All but one had myelosuppression as the main toxicity even the patient who does not complete the course (grade 2-3):

Three patients are free of active disease 6,14 and 36 months after completing 6 courses of chemotherapy (2 of the high risk organ involment patients and the one with CNS mass).

refractory patient and the patient with liver toxicity are alive conducting other lines of treatment

Conclusions

Patients with refractory LCH or with multiple subsequent reactivations to standard therapy have high chances of achieving remission with 2-CdA and Ara-C combined scheme as reports in the literature,with acceptable toxicity

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Histiocytosis

CLINICAL STUDY ON TREATMENT EFFICACY OF 15 CASES WITH MALIGNANT EOSINOPHILIC GRANULOMA OF ORBIT IN CHILDREN

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Objectives

To study clinical character and analysis efficacy of orbit malignant eosinophilic granuloma for first symptom with orbit mass in children.

Methods

A total of 15 patients with orbit malignant eosinophilic granuloma in children were diagnosed using pathology in our hospital from Apr. 2007 to Apr. 2013. 11 cases of male, 4 cases of female. The median age was 2.25 years old(1-12y). In 15 cases, 4 cases of chemotherapy using MVP project (methylamine [M]+ vincristine[V]+ prednisone[p]), and 11 cases of chemotherapy using DAL-HX 83/90 project (etoposide [VP-16], prednisone, and vinblastine). 13 cases were treated using surgery and chemotherapy , and 2 cases were treated using single chemotherapy. Statistics analysis clinical characters, efficacy and prognosis of 15 cases of malignant orbit eosinophilic granuloma in children.

Results

1) First symptom: 13 cases of orbit mass and extruded with eyeball,(86.7%), 3 cases of strabismus and diminution of vision and eyes pain(13.3%),and no fever of all patients (100%).

2) Eye of the disease come on: right orbit was 7 cases, account for 46.7%, and left orbit was 8 cases, account for 53.3%.

3). Follow up to October 2013, median time was 17 months (8-71months), 15 cases were followed. The niduses of 13 cases were complete absorbed, the niduses of 2 cases were most absorbed. In 15 cases, no patient was relapse. 5 patients with strabismus and diminution of vision and eyes pain were recover after chemotherapy and no function obstruction.

Conclusions

Malignant orbital eosinophilic granuloma in children insidious onset, and atypical clinical manifestations, should pay attention to the differential diagnosis. Orbital eosinophilic granuloma in children sensitive to chemotherapy. The focus absorption rate by comprehensive treatment and follow-up is higher.

EP-203

ICCCPO (Parent/Survivors)

LATE EFFECTS OF RADIATION THERAPY AND THE POWERS OF NEUROPLASTICITY

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Objectives

Description of the late effects that radiation therapy bears on adults who survived cancer as children and how it impacts their quality of life. Presentation will include current research, personal struggles faced as a childhood cancer survivor and information on different methods/programs that promote neuroplasticity.

Methods

Oral presentation

Results

NA

Conclusions

NA

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ICCCPO (Parent/Survivors)

REHABILITATION OF CHILDHOOD CANCER PATIENTS- COLLABORATIVE EFFORTS OF SRCC -CENTRE FOR CHILD DEVELOPMENT (CCD) WITH TATA MEMORIAL HOSPITAL(TM), & UGAM-CHILDHOOD CANCER SURVIVORS SUPPORT GROUP

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Objectives

To rehabilitate young cancer patients whose psychological and locomotor functions are affected due to treatment by providing therapy sessions in collaboration with SRCC- CCD rehabilitation centre

Methods

TMH collaborated with SRCC-CCD, multi specialty rehabilitation therapy centre in Mumbai to offer therapy for young cancer patients who have disturbance of their psychological and locomotor functions. Ugam-childhood cancer survivors support group under survivorship programme of Indian Cancer Society is responsible for implementation. An executive administrator of Ugam who is childhood cancer survivor is in charge of facilitating collaboration. The centre conducts physiotherapy, occupational therapy, speech therapy and educational therapy sessions to evaluate the patients. Patients are given ratings (Good, Fair, Poor) based on the aforesaid evaluation. A monthly report is sent to the hospital giving details of the assessment and the recommendation for follow up. The patient may or may not be advised follow up after giving due consideration to his/her sensory, Activities of Daily Living (ADL), psychological, and locomotor functions during the evaluation. These evaluations are done free of cost by SRCC-CDC.

Results

A total of 26 patients, median age 8 Years (Range 2-15) are beneficiaries. 22/26 (85%) are Brain tumor & 4/26 (15%) are non Brain tumor patients who received cranial irradiation; 12 reside in Mumbai & 14 are from outside Mumbai. Parental feedback regarding these sessions have been good in 80.8% and fair in 19.2%. Patients have shown overall improvement in their Activities of Daily Living after these therapy sessions.

Conclusions

SRCC-CCD has taken exceptional steps for rehabilitation of active cancer patients. These sessions have not only been a boon to the patients and their parents but also to the treating oncologists as they are able to deliver holistic care to the patients. It is expected that several eligible cancer patients will get benefited by this ongoing collaboration

EP-205

ICCCPO (Parent/Survivors)

LONG TERM TOLERANCE OF WHOLE ABDOMINO-PELVIC IRRADIATION IN CHILDREN WITH CANCER

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Objectives

To analyse the long-term sequelae in children who received whole abdomino-pelvic irradiation (WAPI) for cancer.

Methods

All patients with a follow-up longer than 5 years and treated during childhood for cancer with multimodal approach including WAPI at Gustave Roussy were reviewed. Data were collected from medical and technical files. Long-term toxicities were graded with the CTCAE v3.0.

Results

Twenty-six children were treated with WAPI between 1974 and 2006. Mean age at the time of irradiation was 5.9 years (1-17.5 years). Histologies were Wilm's tumor for 19 patients, Desmoplastic tumor (2), Clear cell sarcoma (1), Seminoma (1), Rhabdoid tumor (1), Rhabdomyosarcoma (1) and Mesoblastic Nephroma (1).

WAPI was delivered at the dose of 10 to 30 Gy by an anterior and a posterior field, with a boost in case of residual tumor. Contralateral kidney was protected at 12 Gy.

Median follow-up was 13 years (5-26,4 years). Long term renal failure concerned 3 patients (1 grade I, 2 grade III) of whom 1 grade III also received nephrotoxic chemotherapy.

Digestive disorders occurred in 5 patients: 1 grade I, 1 grade II and 3 grade III.

On the 11 girls, 6 needed treatment to induce puberty while the other 5 are still in prepubertal age. No endocrine disorder has been reported in boys. Short stature, defined by height < 2 DS for age and sex, occurred in 4 patients. Scoliosis was observed for 2 patients.

Secondary tumor occurred twice, one urothelial carcinoma and one chondrosarcoma of the ilium, both within the radiation fields.

Conclusions

Long-term sequelae of WAPI are limited except growth troubles (15,4%), secondary tumors (7,7%) and loss of ovarian function in all girls.

Thus, those patients need a close and prolonged follow-up and an ovarian tissue cryopreservation (at least for future in vitro oocyte maturation) for may be appropriate for girls who underwent WAPI.

EP-206

ICCCPO (Parent/Survivors)

RECEIVE, GIVE AND SUPPORT - A GERMAN CONCEPT THAT WORKS

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Objectives

The presentation will be about the concept “receive, give and support“ of the Deutsche Kinderkrebsstiftung (German Childhood Cancer Foundation). The main goal of the concept is to have a good mixture of giving support to the young adults and getting back their experiences and initiatives to support other concerned youths.

Methods

The young adults “receive“ special medical and social law support. The “give“ includes the “tour on the Rainbow“ and the mentoring-project. On the other handside, there is the “support“ with seminars, camps and different topic courses for teaching the young adults.

Results

To sicken with cancer as a young adult is a very difficult experience. The concept wants to gain a multidimensional view of the possibilities what can be achieved with this experience: the things we can learn during a cancer time and how to spread those impressions to other concerned.

Conclusions

The aim of the concept is, that the young adults with and after cancer get a platform of exchange (receive), invest their own time and experience to support other concerned youths (give) and are supported in their personality (support). I like to strengthen this idea and present it to you.

EP-207

ICCCPO (Parent/Survivors)

SURVEY PROJECT ON THE FATE OF MOROCCAN CHILDHOOD CANCER SURVIVORS

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Objectives

The present survey objectives are to establish a database of Moroccan childhood cancer survivors, to gather information about their current status, to meet their needs for treatment or prevention, and to lay-out a strategy of long-term monitoring in terms of prevention, early detection, treatment, and social-emotional support.

Methods

The survey will target Moroccan patients who have been treated completely or partially in Rabat from childhood cancer, which diagnosis has been put at least 10 years ago. The data to be collected will include civil status at diagnosis, cancer's characteristics, its treatment and evolution, and current medical and social status.

In order to reach the survivors, we will be using several means including phone, email, social networks, and postal mail. The questionnaire would be completed by the survivors themselves, their parents or their physician. We have hired as project coordinator a fellow epidemiologist who will write her thesis on this survey subject.

The project duration is expected to be about 12 months including: survey preparation, distribution and collection of the questionnaire, analysis of the results, writing and publishing the survey's findings

The project budget includes the coordinator's salary, training and meetings expenses and it would be financed by the Terry Fox Run which took place in Rabat, Morocco, on February the 16th 2014 as International Childhood Cancer Day's event.

Results

In 2010, when "the Path of Hope" association was founded, 300 Moroccan childhood cancer survivors attended the meeting or gave information by phone or mails. Many of them were doing well, but others were suffering from medical, educational or behavioral problems.

Conclusions

In conclusion, this survey will be crucial to establish a database on the Moroccan childhood cancer survivors in order to have a long-term monitoring system that will include key referential information, medical and social support at the national level.

EP-208

ICCCPO (Parent/Survivors)

THE L'AVENIR ASSOCIATION: 28 YEARS SUPPORTING CHILDREN WITH CANCER IN MOROCCO

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Objectives

In the developed countries, parents' groups are created to enhance research and well being of their children. In developing countries, associations of families are very rare and their first aim is to provide financial resources for treatments.

Methods

"L'Avenir" Association is one of the first parents of children with cancer associations in developing countries. It was established in 1986 by caregivers and parents of cancer patients. At that time, the State had many other problems to face such as infectious and nutritious diseases. Since its creation, the 'l'Avenir' has been getting stronger and more efficient; services provided are numerous: drugs, equipment, schooling, entertainment, housing, awareness, early diagnosis training and financial support. It has developed partnership with 'St Jude Research Children Hospital' to improve education, diagnosis and care in paediatric oncology. The 'l'Avenir' works with the hospital's caregivers, other cancer organizations and state departments. It has set up a local section in Fes and initiated a group of survivors 'the Path of Hope'.

In 1995, 'l'Avenir' has built a parents' house to provide accommodation for families who don't live in Rabat, to soften treatment conditions and to decrease treatment and follow up abandonments. 'La Maison de l'Avenir' is spacious: 22 bedrooms, a kitchen, dining room, living room, playroom, .. It provides meals to the families who have to pay only about 1 USD a day per adult. Since its opening, 3000 families have spent 10 days (1 to 60 days), 5 times a year (1 to 16 times). The house is run by the 'l'Avenir' which organizes fund raising events.

Results

La Maison de l'Avenir has significantly allowed to decrease treatment abandonment, and so, contributes strongly to cure children with cancer.

Conclusions

Parents or friends groups in developing countries can achieve remarkable results improving social and medical conditions of the patients.

EP-209

ICCCPO (Parent/Survivors)

HAYIM FOR CHILDREN WITH CANCER IN ISRAEL ASSOCIATION - IN THE SERVICE OF CHILDREN WITH CANCER IN ISRAEL

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Objectives

The Hayim Association was founded by parents of children with cancer in 1984. This voluntary organization is active in all Children's Oncology wards throughout Israel with the goal of assisting and reducing the suffering of children and their families, and to improve the quality of health care.

The association operates in all the medical centers nationwide, and is part of the oncology wards.

The association is a member of ICCCPO.

Methods

Main activities:

Supporting the Israel Medical Association for Pediatric Hematology and Oncology in gathering and coordinating medical information on child cancer.

Purchase of sophisticated equipment for improving diagnosis and treatment. (i.e. PFAX for early diagnosis of Leukemia, Vapor-Phase Refrigerators for storing stem cells etc.)

Funding studies and development of sophisticated methods for improving diagnoses and directing optimal care.

Improving the professional standards of medical, paramedical and psychosocial personnel, by funding participation in local and international conventions and seminars.

Fostering and improving the children's welfare and supporting surroundings:

Supporting families with financial problems due to their child's disease.

Funding transport for treatments.

Funding support groups for better coping with the disease.

Arranging trips and fun days for children and their families in Israel and abroad.

Monthly fun flights of children.

Assistance in classes and play corners in hospitals.

Individual tuition of children during and after treatment.

Grants and scholarships for children during their rehabilitation.

Results

The association's achievements include:

Assistance in establishing a night care ward for children with cancer, the first of its kind in Israel, in the Rabin Medical Center.

Assistance in setting up a bone marrow transplant ward for children in Schneider Hospital, the first in Israel.

Standardization of medical and psychosocial care among the various centers in Israel.

Improvement of child welfare and hospitalization conditions.

Conclusions

Much more must be done.

EP-210

ICCCPO (Parent/Survivors)

OVERVIEW OF PEDIATRIC AND ADOLESCENT MALIGNANCY AND ITS SCOPE AND CHALLENGES IN NEPAL

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Objectives

To find occurrence and type of pediatric malignancies, estimated cancer burden and facility required to treat.

Methods

We have collected data from hospital based national cancer registry of Nepal from 2003 to 2010 and division of pediatric oncology of B P Koirala memorial Cancer Hospital (BPKMCH) from 1999 to 2013. Data were analyzed for the occurrence and relative frequency of pediatric cancer in Nepal.

Results

2000 new pediatric cancer reported from 2003 to 2010 in HBCR, and 2000 new cases reported at BPKMCH (1999 to 2013), division of pediatric oncology. In BPKMCH there were leukemia (28%), Lymphoma (18%), Bone sarcoma 166 (12%), Brain tumor (6%), Retinoblastoma (6%), Germ cell tumor (4%), wilms tumor (4%), Skin and epithelia neoplasm (2%), Hepatoblastoma (1%), Neuroblastoma (2%), ENT and others (15%). In national wide HBCR, there was leukemia 502(34%), Lymphomas 172(12%), Bone sarcomas 166(11%), Brain tumors 96(7%), Retinoblastoma 94(6%) GCT 65(4%), Neuroblastoma 42(2%), epithelial neoplasms 28(2%), Hepatoblastoma 20(1%) and Others 116(9%). As there were 26 million of children 19 years of age in 2011 census, average incidence of childhood cancer are about 120/millions /year. There are 1459 new cases each year.

Conclusions

here are 4 pediatric oncologists and 50 beds available within Nepal, which is very much insufficient. Present bed capacity and oncologists can't cure more than 200 patients in a year. Large number of patients does not have treatment access due to inadequate human recourses and facilities. To give cancer treatment and care to 1450 new cases each, there should be 500 beds and 60 pediatric oncologists along with other supporting subspecialty experts and resources. We can cure more than 70% of pediatric cancer at low cost, this will save almost 1000 life each year.

EP-211

ICCCPO (Parent/Survivors)

PSYCHOSOCIAL NEEDS OF AND SERVICES FOR LONG-TERM SURVIVORS (AGE > 27 YRS.)

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Objectives

Today, the majority of children with cancer become long-term survivors. However, long-term survivorship often comes with different psychosocial problems beside medical side effects of the cancer treatment. Even adult survivors of childhood cancer are at risk for various social and psychological sequelae. Therefore there is a need for services especially for this steadily increasing group.

This presentation is about the psychosocial needs of long-term survivors (age > 27 yrs.) and shows the services of the Deutsche Kinderkrebsstiftung (German Childhood Cancer Foundation) for long-term survivors.

Methods

The Deutsche Kinderkrebsstiftung (German Childhood Cancer Foundation) owns the Waldpiratencamp, a camp for childhood cancer patients, survivors and their family. At this camp in Heidelberg there are also camps especially for adult survivors of childhood cancer. Since 2011 there is one seminar yearly for long-term cancer survivors > 27 years, arisen through urgent questions of survivors: How do I tell people (especially my boyfriend/ girlfriend) I am a cancer survivor? What are people going to think? Will anyone want to date me? Is it okay for me to have sex or be on birth control pills? Etc. Open and frank discussions of these sensitive topics may prevent unnecessary hurt and stress.

Results

Older childhood cancer survivors have other needs than younger ones. Seminars that are exclusively for adults > 27 years are always fully booked.

Conclusions

Services especially for long-term survivors age > 27 years are essential.

EP-212

ICCCPO (Parent/Survivors)

YOUTH AND THEIR FUTURE - GUIDANCE INTO WORKFORCE FOR CHILDHOOD CANCER SURVIVORS IN AUSTRIA

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Objectives

Former childhood cancer patients often face difficulties to enter workforce. Some have to deal with cognitive impairments, others have to cope with reduced long-bearing capacity. Further, many patients have problems communicating “gaps” in their CVs due to recent cancer treatments. In some cases patients also have to deal with prejudiced employers and co-workers, who “stigmatize” former childhood cancer patients and underestimate their abilities. So there is an urgent need for an initiative that supports former patients on their way entering workforce.

Methods

We had been looking for a suitable solution for former patients in Austria for a long time. Finally, an appropriate project was found in Munich, Germany, which has been running successfully since 2006. Therefore, we used the German model as a base for the Austrian intervention.

Results

In Austria the project ‘Youth and their Future’ started in the beginning of 2012 – in cooperation with local hospitals, the Austrian Childhood Cancer Organization (ACCO) and ‘die Berater’ (a leading consultancy focusing on coaching and training).

In the context of this collaboration the three institutions adopt different roles: While the hospitals recommend former patients to the ACCO (which funds the project), the consultancy provides, based on many years of experience, individual support for the clients. Amongst other things, their service includes personality development, clarification of physical and psychological abilities, career advice and application coaching.

Conclusions

The Austrian Childhood Cancer Organization feels obligated to support former childhood cancer patients also after their medical treatment. Especially former brain tumor patients need professional support to find “their” place in the world of workforce. For these patients a fixed trainee position or a regular working condition is of great importance by means of gaining economic independence, financial security and a stronger position within society.

EP-213

ICCCPO (Parent/Survivors)

WORKING TOGETHER TO WIN THE BATTLE AGAINST CANCER - LIVING A BETTER LIFE AND GIVING BACK TO THE COMMUNITY

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Objectives

To carry on our vision “Working Together to Win the Battle Against Cancer – Living A Better Life and Giving Back to the Community”

Methods

Ever since the establishment in 2002, the Little Life Warrior Society (LLWS) has grown from a relatively modest self-help and basically run by voluntary helpers to a unique model of providing mutual support services to cancer children and their parents in the community. The LLWS provides a much-needed platform where cancer children and their parents can get support from other families going through the same experience. In 2009, the LLWS, was registered as a charity society in Hong Kong. In 2010 Home of the Little Life Warriors was officially opened at the Cancer Centre to provide a comfortable area for the patients and their family members to rest and to play while waiting for outpatient treatment. Also, tutorial classes are arranged to help children catch up their schoolwork.

Results

With the generous help of many supporters over the decade, the Little Life Warrior Society has raised public awareness of childhood cancer and reached out to the Mainland China and the International stage. The numbers of our members was 1249 people in 2013. Nine Little Life Warrior Societies in the Mainland China were established and the impact of their work on the many childhood cancer patients and their families.

Conclusions

After all these years, the vision of Little Life Warrior Society has remained solid. The small warriors have grown up into big warriors and become volunteers of the Society to serve the childhood cancer patients in the hospital. Using the Home of Little Life Warrior as a reference to set up a Children Cancer Patients Resources Centre in Hong Kong Children Hospital which is can be put into service in 2018.

EP-214

ICCCPO (Parent/Survivors)

FIGHT YOUR SPIRIT TO CONQUER YOUR CANCER

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Objectives

As survivor I would like to motivate other cancer patients to have the same spirit as when I was a patient. After the diagnosed, I have so many new goals that I want to complete in my life. I want to help all of my friends who suffered from cancer by giving them support. I think that supporting is one thing they needed most to keep their spirit, so they don't give up in the middle of their treatment.

Methods

Its obvious that during the medical treatments there were times when I felt so sad and even depressed. My sister asked me to write something like a journal to help me to feel better. And to be honest I didn't think that writing would really do, until I finally began to write after a couple of days. Since I love singing I was thinking why don't I make my writing into something that everyone can enjoy? So I started writing a couple of songs based on my experience and the diary that I have been writing. After gathering all the songs that I wrote I made an album.

Results

With the help of my family I was able to produce an album that I made. My thought was when I sell my album I will donate 40% of the income for the cancer patients through the Indonesian Childhood Cancer Foundation (YOAI). In fact I would love to be able to donate for other children with cancer throughout the world through their foundation.

Conclusions

Up to present I am still Writing songs in English and Indonesian. And for the time being I have been distributing my album to several friends. I was able to give several album to the foundations at ICCCPO Conference in Hongkong. I wish my idea will inspire other cancer patients.

EP-215

Late Effects

RISK FACTORS ASSOCIATED WITH ANTHRACYCLINE INDUCED CARDIAC DYSFUNCTION IN PEDIATRIC PATIENTS

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Objectives

Anthracyclines have significant impact on outcome in many pediatric chemotherapy protocols and therefore remain the mainstay of treatment. The aim of this study was to identify the risk factors for anthracycline induced cardiac dysfunction in pediatric oncology patients.

Methods

We performed a prospective cohort study during July 2010- Jun 2012 at Aga Khan University Hospital, Pakistan. All pediatric oncology patients aged 0 to 16 years, who received anthracycline as a chemotherapy and remain in regular follow up for at least 1 year post chemotherapy, were included for final analysis.

Results

Out of 110 patient, 75 (66%) were males and mean age was 74±44 months. ALL (n=70, 64%) was the most common primary diagnosis followed by lymphoma (n=19; 17%) and AML (n=12, 11%). Doxorubicin alone or in combination was used in (n=94, 85%) of patients and cumulative doses 300mg/m² (p < 0.001, OR: 7) and mode of delivery (p 0.048, OR 9.7) were also found statistically significant.

Conclusions

Anthracycline induced cardiac dysfunction is mostly related to cumulative dose > 300mg/m², radiation therapy and sepsis. Regular long term follow up with cardiologist is the key point for early diagnosis and therapy for a long term survival.

EP-216

Late Effects

ANTHRACYCLINE INDUCED ACUTE AND EARLY ONSET MYOCARDIAL DYSFUNCTION IN CHILDHOOD MALIGNANCIES

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Objectives

Anthracyclines (i.e., doxorubicin, daunorubicin) are the backbone of chemotherapy for most childhood malignancies but are well known for their cardiotoxicity, which includes cardiomyopathy with systolic and/or diastolic dysfunction, arrhythmias and pericardial effusion. The objective of this study was to identify anthracycline induced acute and early onset chronic progressive cardiotoxicity in various childhood malignancies.

Methods

All children who received anthracycline as chemotherapy and three echocardiographic evaluations (baseline, one month and 1 year) at Aga Khan University, Karachi between July 2010 and June 2012, were prospectively analyzed for cardiac dysfunction. Statistical analysis across systolic and diastolic dysfunction at baseline, 1 month and 1 year were made by repeated measures analysis of variance (ANOVA).

Results

Among 110 study participants, 75 (68.2%) were males. Mean age was 74±44 months, majority 70 (64%) of them were Acute lymphoblastic leukemia (ALL). Doxorubicin alone was used in 59 (54%) and combination therapy was used in 35(32%). Fifteen (14%) children developed cardiac dysfunction at 1 month while 28(25 %) children within a year. Of these 10/15 (66.6%) & 16/28 (47.2%) had isolated diastolic dysfunction respectively while 5/15 (33.3%) and 12/28 (42.8%) had combined systolic and diastolic dysfunction at 1 month and 1 year echocardiography respectively. Seven (6.4%) patients expired due to severe cardiac dysfunction.

Eight (14%) children receiving doxorubicin showed dysfunction mostly related to higher cumulative dose (p<0.001).

Conclusions

Our study reports a high incidence of anthracycline induced cardiotoxicity. Presence of ALL, high cumulative dose, doxorubicin alone or in combination with daunorubicin and patients with trisomy 21, AML, Ewing sarcoma were identified as high risk.

EP-217

Late Effects

EVALUATION OF IRON OVERLOAD IN ACUTE LYMPHOBLASTIC LEUKEMIA AFTER THE END OF TREATMENT

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Objectives

Leukemia is the most common malignancy in children. Treatment of the disease causes bone marrow suppression that necessitates excessive blood transfusion. The aim of this study was to evaluate iron overload by assessing serum ferritin level in Acute Lymphoblastic Leukemia (ALL) and its correlation with number of blood transfusion in children under 15 years of age.

Methods

During this study patients who were referred to oncology department of Ali-Asghar children hospital and had known ALL were enrolled. Serum level of ferritin, serum iron, TIBC and transferrin saturation at the end of treatment, 6 months and 12 months after treatment were evaluated. Patients with signs of infection or any inflammation were excluded. At the end all data were analyzed by SPSS version 18 software.

Results

50 patients were evaluated (30 boys and 20 girls). Mean serum iron was 94.8 ± 14.3 . Mean TIBC was 316.1 ± 15.5 . Transferrin saturation was 30%. Mean value of ferritin were 637.1 ± 179.2 , 380.4 ± 146.4 and 201 ± 73.3 at the end of treatment, 6 months and 12 months after treatment. Mean number of transfusion was 7.9 ± 1.02 (2-16). There was significant correlation between serum level of ferritin and number of transfusion.

Conclusions

Present study showed that after treatment of ALL serum level of ferritin is high comparing normal values. Number of blood transfusion was proved to be the only determining factor for iron overload.

EP-218

Late Effects

A FEASIBILITY PILOT STUDY OF SETTING UP A FERTILITY CLINIC FOR SURVIVORS OF CHILDHOOD CANCER TREATMENT IN INDIA

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Objectives

Cancer in children and its treatment has implications for their future fertility. Hitherto, there have been no studies on fertility preservation or infertility management for these patients from India. This study was a pilot initiative to address this gap.

Methods

Childhood cancer survivors who either work or whose parents work for Cankids...Kidscan were invited to attend a late-effects clinic focussed on fertility from Dec 2013 to Mar 2014. The survivor was seen by a paediatric oncologist and a reproductive medicine specialist.

Results

20 survivors (70% males) with median age 18.5 years (range 13-30 years) who were off treatment for median 7 years (range <1-16 years) were seen. Original diagnosis was ALL 12 (including 2 relapses), AML 2, NHL 3, Retinoblastoma 1, Wilms 1, Bone sarcoma 2, Gonadal GCT 1. Any alkylating agent exposure was seen in 14 (70% survivors), most commonly cyclophosphamide median dose 3000mg/m² (range 900-6600mg/m²). Any radiotherapy exposure was seen in 12 (60%), 18Gy cranial radiotherapy for ALL in all and testicular radiation in one. One survivor had gonadal surgery for ovarian dysgerminoma. No one had a HSCT.

Based on clinical and treatment variables 14 (70%) survivors were classified as low risk for infertility, 4 (20%) as medium risk and 2(10%) as high risk. All except one (13 year old) had achieved puberty. Hormonal and semen analysis was requested where appropriate. None was planning to start a family. None had received counselling on fertility preservation at the time of diagnosis.

Conclusions

A late-effects fertility clinic for survivors of childhood cancer treatment in India is feasible and can be part of an overall survivors clinic. When resources are limited, appropriate risk grouping can identify which children can benefit from fertility preservation and which need early intervention once cancer treatment is complete.

EP-219

Late Effects

AN INSIGHT INTO THE BIOMARKERS OF OBESITY IN SURVIVORS OF ACUTE LEUKEMIA

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Objectives

Acute lymphoblastic lymphoma (ALL) survivors are predisposed to obesity, and consequently increased risk of death due to cardiovascular diseases. The exact mechanism of obesity is not known, although it has been attributed to steroids, cranial irradiation and consequent hypothalamic disturbances.

The study was done to assess the prevalence and potential biomarkers of obesity in the survivors of acute leukaemia patients.

Methods

This is a cross-sectional study conducted at All India Institute of Medical Sciences in the survivors of acute myeloid leukaemia (AML) and ALL who had completed the treatment atleast one year before enrolment in this study. The prevalence of obesity was studied by determining the body mass index (BMI). A BMI of more than 85th percentile is classified as overweight and more than 95th as obese. Potential biomarkers were studied by assessing serum leptin, resistin and adiponectin levels by ELISA and were compared between the obese and non-obese leukaemia survivors.

Results

159 acute leukaemia (126 ALL and 33 AML) patients were enrolled in the study with a median follow up of 36.8 months post treatment. The median age was 10 (range: 3-18) years. 123 (77.3%) patients were males. The prevalence of overweight/obesity in acute leukaemia survivors was 27%, compared to 10% in 40 normal healthy controls. The mean serum leptin and resistin levels were similar in obese and non-obese leukemia survivors (3.7 vs 2.85 pg/mL, p= 0.064; 8.01 vs 9.33 ng/mL, p=0.36). However, the mean serum adiponectin levels were significantly lower in the obese leukaemia survivors as compared to non-obese leukaemia survivors (7.97 vs 11.5 µg/mL, p=0.023).

Conclusions

The prevalence of obesity is higher in acute leukaemia survivors. The lower levels of adiponectin in obese leukemic survivors may be one of the mechanisms for predisposition in the survivors of acute leukaemia.

EP-220

Late Effects

HEALTH-RELATED QUALITY OF LIFE AND FUNCTIONAL OUTCOMES OF CHILDREN/ADOLESCENT SURVIVORS OF MALIGNANT BONE TUMORS

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Objectives

Health-related quality of life (HRQL) is an important outcome measure due to increasing survival rates. Although HRQL in long term-survivors of pediatric cancer is mostly comparable with that of the general population, bone tumors HRQL is relatively poor compared with other cancer survivors. We aim to assess HRQL and functional performance in these survivors in order to establish individualized programs to promote early detection of chronic health problems.

Methods

Prospective cross-sectional study of a cohort of malignant bone tumor survivors, < 21 years old at diagnosis and > one year off therapy with no evidence of disease at inclusion in study. All patients were interviewed by a pediatric oncologist and an orthopedic surgeon. The Health Utilities Index (HUI3) was used to measure HRQL and the Musculoskeletal Tumor Society Score (MSTS) to assess physical disability. Bone tumor HRQL was compared to age- and sex- matched leukemia/lymphoma survivors. Data was analyzed using SPSS 20.0.

Results

Fifteen osteosarcoma and eleven Ewing sarcoma patients were included, median age at diagnosis of 10.8 y (2.4-20.8), at evaluation of 22.6 y (range: 11.1-45.5) and follow-up of 10.0 years (range: 2.1-27.6). Fourteen were male and twelve females. Seven patients had undergone amputation. 81% of bone tumor survivors rated their health state as good/very good/perfect compared to 100% of leukemia/lymphoma group ($p=0.019$). HUI3 multi-attribute score in bone tumor group was significantly lower (0.74 vs 0.89, $p=0.038$) as well as ambulation and pain single-attribute scores (0.95 vs 1.00 $p=0.026$; 0.93 vs 0.98, $p=0.044$, respectively). Median MSTS score was 83% (range: 13-100%).

Conclusions

Malignant bone tumor survivors have poorer overall HRQL compared to age- and sex-matched leukemia/lymphoma survivors, however most consider their health state as good/very good/perfect. Long-term follow-up focused in adequate pain control and impairment-driven rehabilitation in this group of patients is needed.

EP-221

Late Effects

UTILISING A REQUIREMENTS MANAGEMENT APPROACH TO INTEGRATE USER AND PROFESSIONAL VIEWS INTO THE DESIGN OF A TEENAGERS AND YOUNG ADULTS (TYA) CANCER SURVIVORSHIP SERVICE

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Objectives

Interventions applied early after cancer diagnosis may be the most effective way to help TYA patients re-establish life-trajectory during and after treatment. These should be informed by patient/professional experience but integrating such views into delivery of patient care demands a structured approach to the collection and prioritisation of data. Requirements Management(RM), a systems engineering process, was used to evaluate and develop a regional TYA clinical service.

Methods

Data was sought by postal questionnaire/interview/focus group (patients n=108; family/friends n=32); online questionnaire/interview (professionals, n=219). Each data item was extracted and summarised as a 'Finding' then assessed for underlying 'Requirements' for change to care/delivery of the service. For example, a patient 'Finding' about exercise: 'Going to a public gym wouldn't be comfortable. Fears about being exposed/judged' generated two different, possible 'Requirements': (1)'Patients need access to sports/health facilities which afford a sense of privacy/protection from the public' and (2)'Patients should be offered psychological support to help them deal with feelings of being different and/or perceptions of being judged negatively'. All Requirements derived in this way were evaluated against factors reflecting health policy and practical applicability, including: Benefits achievable in terms of Quality/Innovation/Productivity/Prevention/Personalised care (QIPPP); Difficulty(Very Difficult-Very Easy); Priority(Must/Should/Could/Would do); Benefit to Service(None-High); Benefit to Patient(None-High).

Results

1,764 individual Findings generated 3,332 Requirements, reduced to 184 Unique Requirements after review/de-duplication. These were then prioritised (selecting those considered easiest to achieve with high direct benefit to patients) and used to design interventions to modify/enhance patient care in areas such as physical and psychological wellbeing, work mentoring and staff training.

Conclusions

RM is a useful tool to support service development based on user/professional views using large volumes of data and when applied alongside methodologies such as co-creation/co-design accurately responds to user needs. An audit trail links each 'Finding' to a final step in service change.

EP-222

Late Effects

USING THE FATIGUE THERMOMETER TO SCREEN ADOLESCENT AND YOUNG ADULT BRAIN TUMOR SURVIVORS

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Objectives

Cancer related fatigue (CRF) is one of the most common and distressing symptom experienced by adolescent and young adult (AYA) cancer survivors and may disproportionately affect brain tumor survivors. While national guidelines recommend screening for CRF during routine follow-up, data supporting specific screening measures is limited. The objective of this study is to assess the validity of a one-item Fatigue Thermometer (FT) measure for assessing fatigue in AYA brain tumor survivors.

Methods

142 survivors (age 12-32) with a median time since diagnosis of 10.5 years (range 2.4 – 28 years) completed the 1-item Fatigue Thermometer (FT) and the 18-item Multidimensional Fatigue Scale (MFS) at a single clinic visit.

Results

57 survivors (40%) were identified as clinically fatigued on the MFS. ROC analysis indicated good concordance between the FT ratings and the MFS criterion (AUC = 0.812), but no FT cut-off score to reliably identify survivors with elevated MFS scores was identified. A low FT cut-off score of 1 had good sensitivity (93%), but poor specificity (59%), and higher FT cutoff scores of 3 had good specificity (78%), but missed too many cases of fatigue identified by the MFS (sensitivity = 65%). No FT cutoff score met study criteria for screening accuracy (sensitivity \geq .85 & specificity \geq .70).

Conclusions

Results from this study indicate the FT, a single-item screening measure for fatigue, is not able identify clinically significant fatigue in AYA brain tumor survivors. Results are discussed in the context of research on other “ultra-brief screening measures as well as clinical and research implications of the findings.

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Late Effects

ANTICANCER CHEMOTHERAPY AND DEVELOPMENTAL ANOMALIES OF TEETH IN CHILDREN

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Objectives

Anticancer treatment during childhood carries a risk of dental anomalies and denticles. Aim: correlation of developmental anomalies of teeth with type of anticancer drugs administered and chemotherapy related early complications

Methods

Sixty patients who completed anticancer treatment (median 4.9±3.4 yrs from treatment completion) and 60 healthy children aged 6-18 years were assessed. Clinical and radiological evaluation was performed and included assessment of enamel anomalies (DDE-Index), anomalies in the number, size and tooth structure. Medical records were reviewed and data collected on; tumor type, age at diagnosis and treatment, chemotherapy duration, type/doses of anticancer agents, emesis and mucositis during treatment and its severity (according to CTCAE v 4.0 criteria). Statistical analysis was performed using U Mann – Whitney and Spearman test.

Results

Children treated with chemotherapy had statistically higher incidence of enamel anomalies, teeth agenesis, microdontia, root shortening, taurodontism and denticles as compared to health controls. Administration of vincristine and its total dose correlated with every type of tooth anomaly, cyclophosphamide, ifosfamide, doxorubicin, with hypodontia, microdontia, root shortening and enamel anomalies, etoposide and cisplatin with microdontia, root shortening, enamel anomalies, methotrexate, teniposide with root shortening and carboplatin with denticles and enamel anomalies. Mucositis and emesis potentiated root shortening, microdontia and enamel anomalies.

Conclusions

Chemotherapy and its early complications (emesis and mucositis) result in development of dental anomalies. Vincristine, cyclophosphamide/ ifosfamide and doxorubicin are anticancer agents which most likely have the greatest impact on the incidence of these complications. Mucositis and emesis add to the severity of the anomalies.

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Late Effects

HEALTH OUTCOMES OF CHILDHOOD MEDULLOBLASTOMA/PNET. ONE CENTER RESULTS

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Objectives

Assessment of health outcomes in survivors of childhood medulloblastoma /PNET (MB/PNET).

Methods

113 MB/PNET patients (70 boys 43 girls) at least 2 yrs (median 5.5 yrs) from treatment completion were examined. Median patient's age at MB/PNET diagnosis was 8 yrs 2 m, at assessment 14.5 yrs. All patients were treated with surgery, cranio-spinal irradiation, chemotherapy and followed-up in our clinic. Health problems were assessed and graded according to CTC AE v 3.0 criteria.

Results

The following health problems were recorded: decreased physical activity -38% of patients, neurological disorders- 32%, fatigue - 60%, IQ below average -40% , short stature <3percentile – 46.6%, hypothyroidism- 17%, renal dysfunction-15%, hearing impairment- 87%, requiring hearing aids-56%, dental caries 100%, other dental 68 %, musculoskeletal 23%, skin -60%, BMI <18 - 28%, >25-16%, second malignancy 4pts . Among 112 patients there were 678 adverse health events. Ninety % of patients demonstrated at least 1 health problem, 75 % more than 5 (median 6 health problems to one patient) of which 15% were severe and life-threatening (CTC AE- grade3 and 4). Four patients developed second malignancy –AML-2 pts, 2 pts MDS.

Conclusions

Survivors of childhood MB/PNET are at high risk of developing various, multiple, chronic and acute health conditions. Due to complexity of the observed adverse health problems lifelong, careful follow-up of children cured from MB/PNET is essential.

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Late Effects

HEALTH PROBLEMS IN SURVIVORS OF CHILDHOOD SOLID TUMORS

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Objectives

Evaluation of health status of 151 consecutively presenting children followed-up after treatment of solid tumor (excluding CNS tumors).

Methods

151 patients (79 boys, 72 girls), median age at examination of 15yrs (8 yrs 2m at tumor diagnosis) were examined. At least 2 years elapsed since treatment completion. There were survivors of NHL -30pts (B-22, T-7, DLBCL-1), Hodgkin Lymphoma- 20, Soft Tissue Sarcoma (STS)- 27, Bone sarcoma -17 (Ewing/PNET-8, osteosarcoma-9), Wilms tumor-13, Hepatoma -7 (HBL-6, HCC-1), Retinoblastoma-16, Mixed Germ Cell Tumors-13 (ovary-10, testes-3) and other-8. Their treatment followed tumor specific protocols. Patients were examined by physician and their health status was assessed and graded according to CTC AE v3.

Results

Among the 151 survivors there were 5 children with genetic syndromes (NBS-1 pt, NF1-4). Nutritional status was normal in 65%, obesity-23.8%, undernourished-11.2%. Short stature was observed in 15.8%. All but 4 patients (2.6%) presented with at least one of the following health issues: endocrinopathy (33%), nephropathy (15.9%), skin abnormalities (21.2%), bone and skeletal deformations (34.4%), osteoporosis (9.3%), immunological and *hematological* (5.3%), neurological (13.2%), gastrological (16.5%), cardiological (27.1%) disorders, hearing and sight impairment (9.8%), dental caries (10%), psychosocial (7.2%) and psychiatric (5.3%) problems. Two patients had a history of second malignant neoplasm (Ewing sarcoma/PNET-1, AML-1). Over 97 % of patients presented with at least one disease and therapy related health problem requiring treatment and close follow-up.

Conclusions

Disease and treatment related complications are common in survivors of childhood malignancy. Due to a wide spectrum of observed health problems children cured from solid tumor should be followed up lifetime and when transitioning to adults care specific recommendation should be given for further medical and psychosocial assistance.

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Late Effects

SECOND MALIGNANT NEOPLASMS (SMN). REPORT FROM ONE CENTER

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Objectives

Second malignant neoplasms (SMN) are the most serious complications of anticancer treatment. Since childhood malignancies have a cure rate of 75% and since there is a growing number of patients with SMN assessing the risk of such conditions is mandatory. The aim of our study was to review patients with SMN treated in our department.

Methods

Clinical features of patients with SMN; gender, age, primary diagnosis, treatment of first disease, time from primary tumor to SMN, SMN type, treatment and outcome were analyzed. Pathology of primary and SMN were reviewed.

Results

Among 3,316 patients treated between 1997-2013 44 children (21 girls, 23 boys), aged 2 yrs 8 months- 27 yrs (median 12.5 yrs) were diagnosed with SMN. 19 patients had a primary diagnosis of CNS tumor, 6-lymphoma, 4-soft tissue sarcoma (STS), 3-neuroblastoma, 3-Wilms tumor (WT). There were 2 cases of osteosarcoma, hepatoblastoma, germ cell tumor, ALL and 1-retinoblastoma. 22 patients (50%) had radiotherapy for primary tumor, 2 had CNS prophylaxis, 40 (91%) received chemotherapy. Time from diagnosis of primary disease to SMN ranged from 6 months to 15.5 years (median- 5.5 years). The following SMNs were diagnosed: hematologic malignancies 20 pts (45.4%) (AML- 13, ALL-3, MDS-2, NHL-T-2 pts), malignant brain tumors-12 (27.3%), osteosarcoma – 4 (9%), STS-2 (4.5%), thyroid cancer -2 (4.5%), WT, clear cell sarcoma and renal cell carcinoma -3 (7%), ovarian cancer – 1 (2.3%). In 9 patients SMN occurred in irradiated field (7 pts CNS, 2 pts thyroid). Seven (37%) of 19 pts with primary CNS tumors developed AML or MDS. Out of 44 SMN patients 22 are alive from 2 years 5 months to 21 years, median 8 years.

Conclusions

Our observations confirm the risk of SMN in children cured of cancer. Long latency period for some SMNs warrants lifelong surveillance for these conditions.

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Late Effects

PULMONARY COMPLICATIONS IN LONG- TERM SURVIVORS OF CHILDHOOD AND ADOLESCENT CANCER

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Objectives

Pulmonary complications are among the most common and serious sequelae seen in childhood cancer survivors (CCSs). Cancer types, age at diagnosis, thoracic involvement, pulmonary metastasis at diagnosis and type of treatment modality (chemotherapy, pulmonary/ thoracic radiotherapy and surgery) are affective in pulmonary complications.

Methods

In this study, we examined the pulmonary complications of 50 cancer patients over 7 years old whose treatment had been completed and were in remission for at least 3 years. Their physical examination, chest X-ray and pulmonary function tests (PFT) (spirometric testes and DLCO) evaluated in Ege University, Department of Pediatric Oncology. Also 40 healthy and within the same age range children and young adult were evaluated as control group.

Results

Our patients were 16 acute leukemias , 15 lymphomas , 10 bone and soft tissue sarcomas, 4 CNS tumors and 5 other solid tumors. In the surviving patients the disorders of PFT were found to be 52%, (24% small airway disease, 14 % diffusion disorders and 14 % combined disorder ; restrictive disorder + other disorders) and in the control group disorders of PFT were 22,5 % (p:0,007). Being diagnosed with cancer at under 2 years of age increased the risk of restrictive disorders and small airway disease (p=0.027). In bone and soft tissue sarcomas increased the risk of small airway disease (SAD), in other solid tumors observed especially diffusion disorder (p=0.01) . Receiving high doses of alkilating agents increased the risk of restrictive disorders. Also pulmonary/thoracic RT increased the risk of impaired PFT. We saw that follow up time can cause variable impaired PFT.

Conclusions

Pulmonary disfunctions in CCSs are prevelant . Diagnostic age , pulmonary RT/surgery and high doses of alkilating agents are important risk factors. CCSs have to be followed up late pulmonary function impairment and complications.

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Late Effects

SECOND NEOPLASMS: A SINGLE CENTER EXPERIENCE

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Objectives

Despite to improvement of childhood cancer patient survival at the same time second cancers are being another problem. Radiotherapy, epipodophyllotoxins and alkylated agents are most responsible factors. In the United States, secondary malignancies percentage is about 6% to%10. This percentage is increasing to 30% when the diagnosis is Hodgkin lymphoma. Aim of this study to evaluate second neoplasm and affecting factors in our center.

Methods

The files of patients with diagnosed second neoplasm were evaluated retrospectively between 1985-2004. Mostly diagnosis of patients is performed during regular follow up. Only diagnosis of two patients are performed in adult oncology center. First diagnosis of patient are including seven acute leukemia(six acute lymphoblastic leukemia; one mixt type leukemia), two Wilms tumor, two non-Hodgkin lymphoma, one Hodgkin lymphoma, one ganglioneuroblastoma, one Langerhans cell histiocytosis respectively.

Results

In this period totally 2356 childhood cancer patients diagnosed in our center between 1985-2014. Fourteen second neoplasm were diagnosed during this period. Eight out of fourteen patients were male. Median period between the cessationof therapy of the initial disease and the diagnosis of the secondary neoplasm were was 74,8 month(range,0 to 314 month) Two patient developed second malignancies during treatment of first diagnosis. In all, Six had AML , three soft tissue sarcoma , one osteoblastoma, one paraganglioma, one Hodgkin lymphoma, one squamous cell carcinoma of tongue, one papillary type carcinoma of thyroid respectively. Four out of the 14 patients who diagnosed acute myeloid leukemia (AML) were died. Three out of the 14 patients are under the treatment

Conclusions

In our series, epipodophyllotoxins, alkylated agents and radiotherapy seems risk factors of second neoplasm. Results of second AML are dismal. Our number of second cancer likely under the estimation because of insufficient number of follow up. All childhood cancer patients are need to regular follow up during lifetime.

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Late Effects

TRIPTORELIN TO PRESERVE FERTILITY IN ADOLESCENTS TREATED WITH CHEMOTHERAPY FOR CANCER

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Objectives

Triptorelin, a GnRH agonist analogue, may be administered to post-pubertal girls with cancer who receive chemotherapy in order to obtain menstrual suppression and decrease the hemorrhage risk due to thrombocytopenia. Our objective is to evaluate if triptorelin administration has also a protective role against gonadotoxicity of chemotherapeutic drugs.

Methods

This retrospective observational analysis includes all girls who received chemotherapy for cancer in our Unit from 2000 to 2013, aged between 10-17, who already had the menarche. After informed consent, they received monthly depot intramuscular triptorelin at the dose of 3.75 mg. This report includes patients who concluded their treatment since at least one year and who are still alive. We evaluated the long-term ovarian function looking for clinical signs and symptoms of ovarian damage as amenorrhea or menstrual changes. We also searched for possible pregnancies and abortions. We made a laboratory follow-up, dosing serum FSH, LH, PRL, E2 and progesterone, and an ovarian ultrasound.

Results

Patients evaluable according to eligibility criteria are 29 (15 lymphomas, 11 leukemias, 1 PNET, 1 Ewing sarcoma, 1 rhabdomyosarcoma). Four of them received high-dose chemotherapy (HDCT). Over the 25 patients who did not receive HDCT, only one developed amenorrhea. The others maintained a normal ovarian function at clinical, laboratory and ultrasound evaluation. Three of them achieved spontaneous, physiologic pregnancy and gave birth to healthy babies. Three of the 4 patients who made HDCT developed premature ovarian failure (POF).

Conclusions

During HDCT, it seems that triptorelin is not able to preserve the ovarian function. In this case it could be recommended triptorelin followed by cryopreservation of ovarian tissue or oocytes. Our study suggests that GnRH-a during chemotherapy may prevent POF in patients treated without HDCT, indicating both the appropriateness and the need of a prospective randomized trial with a larger population.

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Late Effects

LONG TERM FOLLOW- UP OF CHILDHOOD CANCER SURVIVORS IN LEBANON

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Objectives

Despite high survival rates of pediatric cancers, evaluation of the long-term medical and psychosocial effects on survivors in Lebanon is scarce.

Methods

Children treated for various types of cancer, cured and over 5 years from diagnosis at three major hospitals in Lebanon were identified. Data collection was based on chart review and extensive questionnaire administered to the parents or the patient. Excel sheets were filled and data was analyzed.

Results

93 eligible cancer survivors were identified with an average follow-up period of 8 years (range 5 to 15 yrs). 42 patients were included in the initial survey. Mean age was 17 (range 7 to 30 yrs). There were 17 females and 25 males. 36.5% had leukemia, 12.9% lymphoma, 19.5% sarcoma and the rest had various malignancies. Most common physical symptoms reported were weight problems (48.8%) and chronic fatigue (24.2%). Emotional manifestations included anxiety in 38.1% (16), while 54.8% felt adventurous and confident. 80.5% of the patients complained that the treatment affected their education: 58.5% (24) repeated their academic year, 16.6% (7) had trouble continuing education and dropped out, while 29.2% (12) of the patients attended college. Only one was a smoker and none were drug abusers. Out of 42 survivors only 27 (64%) knew the truth about their previous cancer. All had a positive insight about their medical treatment and follow-up, the hospital team and the family support during and after therapy.

Conclusions

This study is the first in Lebanon looking at long-term outcome of childhood cancer survivors. Although many are successful and leading a normal life, there is a significant number whose health, overall well-being and education were affected. Medical and psychological follow-up is critical for reintegration into the society. Long-term follow-up programs are lacking in our country and need to be developed further.

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Late Effects

PULMONARY FUNCTION AFTER TREATMENT FOR EMBRYONAL BRAIN TUMORS ON SJMB03 THAT INCLUDED CRANIOSPINAL IRRADIATION

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Objectives

Treatment of children with embryonal brain tumors (EBT) includes craniospinal irradiation. There are limited data regarding the effect of radiation therapy (RT) on pulmonary function.

Methods

Protocol SJMB03 enrolled patients 3 to 21 years of age with EBT. Pulmonary function tests (PFTs) [forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) by spirometry, total lung capacity (TLC) by plethysmography and diffusing capacity of the lung for carbon monoxide corrected for hemoglobin (DLCO_{corr})] were obtained. Differences between PFTs obtained following the completion of RT and 24 or 60 months ACT were compared using exact Wilcoxon signed rank tests.

Results

303 eligible patients (spine dose: ≤ 2345 cGy – 201; > 2345 cGy – 102; proton beam, N = 20) were enrolled between June 24, 2003 and March 1, 2010, 260 of whom had at least one PFT. Median age at diagnosis - 8.9 years (range, 3.1 to 20.4 years). Median spinal RT dose - 23.4 Gy (range, 23.4 to 50.4 Gy). Median cyclophosphamide dose was 16.0 g (range, 0 to 17.9 g/m²). 24 and 60 months after completion of treatment, DLCO was < 75% predicted in 23% (27/118 evaluated) and 25% (21/84 evaluated), FEV1 was < 80% predicted in 21% (32/154 evaluated) and 29% (32/109 evaluated), FVC was < 80% predicted in 27% (46/172 evaluated) and 28% (30/108 evaluated) and TLC was < 75% predicted in 9% (13/138 evaluated) and 11% (10/92 evaluated) of patients. DLCO was significantly decreased 24 (median difference (MD) in % predicted, - 3.00%; p = 0.028) and 60 months ACT (MD in % predicted, - 6.00%; p = 0.033) compared to the end of RT.

Conclusions

DLCO was significantly decreased 24 and 60 months after completion of spinal RT compared to immediately post-RT. TLC was marginally decreased 60 months ACT (p = 0.072). Continued monitoring of this cohort is planned.

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Late Effects

PREVALANCE OF HYPERTENSION AMONG CHILDHOOD CANCER SURVIVORS

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Objectives

There are limited number of studies regarding prevalence of hypertension among childhood cancer survivors. The aim of this study is to determine prevalence of hypertension and its relationship with obesity.

Methods

The patients treated and followed at least two years without relapse or second malignancy were included in the study. In all patients ambulatory blood pressure monitoring was performed over 24 h using the Microlife WatchBP03 oscillometric device. Hypertension was defined as a systolic blood pressure and/or diastolic blood pressure of > 95 the percentile. The weight was measured by bioelectrical impedance analysis (BIA) and BIA was determined by Tanita TBF 300 body composition device. Obesity was defined as indicated in International Obesity task force's international standards and in diagnostic criteria of International Diabet Foundation, respectively.

Results

The average age of 52 patients (female/male, 25/27) were 12.84±3.88 years. Time off therapy ranged 24-125 month (median: 54.50). The diagnosis of patients were hematologic malignancies (33), Wilms tumor(9) and other solid tumors (10). Thirty six (69.2%) of patients were normotensive while 16 (30.8%) patients had hypertension. Hypertension prevalence was 44.4%, 28.5%, 27.7% in patients with Wilms tumor, other solid tumors and hematologic malignancy, respectively. Forty three (82.7%) patients were at standard weight whereas 15.4% (8) was overweight and 1.9% (1) was obese. Fourteen (30.4%) patients had abdominal obesity being particularly high in hematologic malignancies. No relationship between hypertension and obesity or waist circumference was found (p>0.05).

Conclusions

Childhood cancer survivors are at increased risk for the development of obesity, abdominal obesity and hypertension. Hypertension prevalence in patients with Wilms tumor is higher than the patients with other malignancies. These results might point out the importance of follow up and early diagnosis of hypertension especially in Wilms tumor survivors.

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Late Effects

PATTERNS AND PREDICTORS OF WHO ACCOMPANIES ADULT SURVIVORS OF CHILDHOOD CANCER TO ROUTINE LONG-TERM FOLLOW-UP CLINIC VISITS

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Objectives

Many adult survivors of childhood cancer have difficulty transitioning to health care independence. As an indication of patient dependency, we determined 1) patterns of attending long-term follow-up clinic with others, and 2) associated predictors, among survivors.

Methods

In this cross-sectional study of survivors of childhood cancer, age ≥ 18 years at follow-up, attending their first routine Yale HEROS Survivor Clinic visit, the presence of family and non-family member companions was routinely ascertained from 8/1/2003 through 3/31/2014 as part of the standard evaluation for 152 (98%) of 155 eligible patients. Frequencies of who attended clinic with others were calculated overall, and stratified by patient and disease characteristics. Potential predictors of attending clinic with others were analyzed in logistic regression.

Results

The participants were a mean age of 11.2 ± 5.4 years at diagnosis, 62% female, with a history of leukemia/lymphoma (61%), CNS tumor (11%), sarcoma (19%) or other solid tumors (9%). Age at follow-up was 25.7 ± 6.7 years (range 18.1-49.2). Overall, 52% of patients ≥ 18 years attended clinic with other(s): parent (81%), spouse/significant other (15%), other relative (10%), friend (3%) [categories not mutually exclusive]. Patients aged 18-25 were more likely than those ≥ 25 years to attend with another (68% vs. 28%, $p < 0.0001$), but parents and spouses/significant others comprised $>75\%$ and $>10\%$ of companions, respectively, for both age groups. History of a CNS tumor was significantly associated with attending survivor clinic accompanied ($p = 0.04$). Age at diagnosis, gender, and insurance type were not significantly associated with attending clinic with others.

Conclusions

We found a high percentage of adult childhood cancer survivors, particularly with CNS tumors, accompanied by others at routine survivor care visits. Research is needed to evaluate the role of family and other companions in childhood cancer survivors' health care and how to assist young adult patients' transition to independent management of their own health.

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Late Effects

THE SURVIVORSHIP PASSPORT FOR LONG-TERM CARE OF CHILDHOOD CANCER SURVIVORS. AN INITIATIVE OF THE EUROPEAN NETWORK FOR RESEARCH ON CANCER IN CHILDREN AND ADOLESCENTS (ENCCA)

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Objectives

As 80% of young people with cancer are now surviving and at least half have reached or are entering adulthood, it is essential that health systems are able to inform survivors and all relevant stakeholders about possible risks or late effects of the cancer treatment received.

Methods

A partnership among professionals, survivors, parents and IT experts has been established through the ENCCA network to create the "Survivorship Passport". It is a paper and electronic-based document, and designed to be given to each patient after the planned end of treatment containing simple cancer history and therapy information. The passport includes recommendations for individualised follow-up based on up-to-date clinical guidelines developed within the PanCareSurFup project and the International Guideline Harmonization Group (IGHG) to facilitate the prevention, early detection and treatment of potential late effects.

Results

An international ballot involving expert clinicians was held to define the passport template. The passport is generated through a secured web-based platform which is patient-oriented, accessible in multiple languages by all type of users and can be integrated with national/hospital, and clinical trials databases. Linkage with guidelines for screening of some relevant possible late complications (secondary breast cancer, cardiomyopathy, premature ovarian insufficiency) has been established, and new guidelines will be implemented as soon as they will become public.

Conclusions

The Survivorship Passport aims to harmonize follow-up of former cancer patients across Europe by promoting homogeneous criteria and evidence-based guidelines from clinical practice for prevention, early detection and treatment of physical and psychosocial late adverse effects. In the age of personalized medicine, this simple and accessible tool can enhance age-appropriate healthcare and address individual patient issues specific for pediatric cancer survivors, possibly leading to important breakthroughs in the monitoring and cure of childhood cancer survivors in the long-term, which will contribute to an optimal health-related quality of life for survivors.

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Late Effects

CENTRALISED LONG TERM FOLLOW-UP CLINICS FOR CHILDHOOD CANCER SURVIVORS: WHY DO SO MANY SURVIVORS NOT ATTEND?

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Objectives

Childhood cancer survivors remain at elevated risk of developing life-threatening chronic disease after the completion of cancer treatment. As such, long term follow up (LTFU) care is recommended for early detection/intervention. However, many childhood cancer survivors (CCSs) do not remain engaged with LTFU services in the decades post-treatment completion. This national study assessed CCSs perceived benefits and barriers to attending specialised LTFU care.

Methods

Childhood cancer survivors (>5 years from diagnosis), including adult CCSs and parents of CCSs <16 years of age, from four paediatric oncology hospitals completed a mailed questionnaire. Data was analysed using SPSS20.

Results

N=209; 47% male; 64% adult survivors (mean age 32-years, SD=9.5, mean time since diagnosis 24-years, SD=10.9), 36% parents (mean age of child 13-years, SD=4.8, mean time since diagnosis 10-years, SD=3.4). Many CCSs (42%) do not currently attend LTFU clinic, despite dissatisfaction with the alternate care they currently receive (65% dissatisfied, versus 11% of LTFU clinic attendees). Non-attendees recognised LTFU clinic attendance as 'important'/'very important' to learn about late-effects (96%), to learn about screening/diagnostic tests (91%), and to check they had not developed a second cancer (91%). CCSs also reported unmet information needs in the area of late effects (80%) and second cancers (65%) and the follow-up care they should receive (57%). However, lack of awareness regarding the availability of a LTFU clinic (57%) and prompts/reminders to attend once disengaged (51%) were reported as key barriers to attending LTFU.

Conclusions

The current model of centralised LTFU care does not meet the needs of over 40% of CCSs. Future research designed to engage and empower survivors to seek and receive care through alternate LTFU care pathways, including multidisciplinary, nurse-led, or primary care clinics or community health services, to overcome their barriers to receiving care, while meeting their needs, is critical.

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Late Effects

THE PREVALENCE OF ABNORMAL GONADAL HORMONES IN YOUNG MALE CANCER SURVIVORS

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Objectives

The gonadal function can be affected by chemotherapy, radiation to the pelvic or head area and total body irradiation, leading to temporary or permanent oligospermia and deleterious changes in sperm quality in males. Anticancer protocols include some cytostatics that exert various effects on the gonads. The most frequent pediatric cancers was divided into three groups according to their gonadotoxic treatment: high(HR), middle (MR) and low(LR) risk. In our study gonadal and pituitary hormones were analyzed in young cancer survivors.

Methods

We evaluated gonadal function in 231 young (mean age 16.0 ± 8.6 years, > 2 years after the end of treatment) cancer survivors and 57 controls by measuring the levels of gonadotropins (FSH, LH), testosterone and inhibin B.

Results

The entire cohort of cancer survivors, independently of risk group, had (as compared to the control group) lower mean inhibin B (86.56 ± 67.42 ng/L vs. 127.8 ± 72.6 ng/L; $p=0.0001$), higher FSH (7.67 ± 11.72 IU/L vs. 2.7 ± 2.46 IU/L; $p=0.0001$) and LH (3.78 ± 3.49 IU/L vs. 2.25 ± 2.35 IU/L; $p=0.001$). Testosterone levels were comparable to the control. Abnormal levels of inhibin B were found in 40.8% of the survivors: 35% in LR group, 32% in MR and 80.6% in HR group. Elevated FSH levels were observed in 46.3% of the survivors (26.7% in LR, 47.8% in MR, 85.2% in HR group). The inhibin B:FSH ratio was lowered in all risk groups, most profoundly in HR group. Taking consideration the age of treatment as well as the time that passed since treatment termination, survivors in comparable risk groups presented similar hormonal abnormalities.

Conclusions

after anticancer treatment the risk of gonadal damage is increased (particularly in high risk group). The patients and parents have to be informed about the possibility of lowered reproductive function and pretreatment semen cryopreservation could be recommended.

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Late Effects

ADOLESCENT & YOUNG ADULT (AYA) SURVIVORS OF CHILDHOOD CANCERS- A CHALLENGE IN AFTER COMPLETION OF THERAPY (ACT) CLINIC

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Objectives

To assess the evolution of late effects in childhood cancer survivors who have transitioned to AYA age group on longitudinal follow up in ACT clinic at Tata Memorial Hospital, Mumbai.

Methods

ACT clinic database was analyzed for childhood cancer survivors who have attained 15-30 yrs age at last follow up for demographics, grade of late effects & impact on QOL

Results

Of 1614 childhood cancer Survivors (> 2 yrs off therapy & disease free) registered in ACT clinic from Feb1991-Feb2014, 776(48%) survivors are in AYA group, M.F=563/213 (2.7:1), Hematolymphoid:Solid tumours = 428/348 (1.2:1), Mumbai: Non Mumbai based=249:527(1:2). Median age at diagnosis 7yrs, current median age 20yrs, median duration of follow up since ACT clinic registration 12 yrs (range 2-27 yrs). At registration 343 (44%) had no late effects. 205 (26%) had grade I, 58 (7.5%) grade II 161(21%) had grade III. Only 9(1.2%) had grade IV late effects which increased to 46 (6%) at last follow up mainly due to recurrence 20/46 (43.5%) second neoplasia 21/46 (46%) death due to late effect 1/46 (2%) & 4 (8.7%) due to other medical reasons & accident. Only 25(3%) were at low risk of developing potential late effects. 319 (41%) were in intermediate risk & 56% (432) fell in high risk category requiring at least annual follow up. Nearly 60% of survivors registered in first decade had stopped follow up as compared to 16% registered in subsequent decade (p<0.01)

Conclusions

AYA survivors of childhood cancers form major (48%) group in Long Term Follow up clinic. The increasing incidence of life threatening late effects on longitudinal follow up combined with statistically significant increasing trend of stopping follow up over period of time since ACT registration is alarming & calls for innovative approaches for maintaining good follow up through survivor-centric approaches such as use of IT based communication & formation of support groups like Ugam.

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Late Effects

PREVALENCE AND MONITORING OF COMPONENTS OF THE METABOLIC SYNDROME IN ADOLESCENT SURVIVORS OF CHILDHOOD CANCER

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Objectives

The components of metabolic syndrome (MS) have been tended to increase and associated with cardiovascular risks in long-term survivors of childhood cancer. We investigated the prevalence of components of MS in adolescent survivors of childhood cancer and tried to monitor them periodically.

Methods

We investigated 44 adolescent survivors of childhood cancer, median age 14.9 years (range 10–19.8 years) and median follow-up time elapsed after off-therapy 7.4 years (range 5–16.5 years). We measured body mass index (BMI), systolic and diastolic blood pressure, triglycerides (TG), high-density lipoprotein (HDL)–cholesterol, and fasting glucose. Fatty liver was evaluated by ultrasound examinations during follow-up period.

Results

No survivors demonstrated MS with 3 components, however, 18% of survivors (8/44) have 2 abnormal components and 43% (19/44) have 1 abnormal components, respectively. The frequency of each component was: increased BMI, 11%; elevated blood pressure, 0%; elevated TG level, 41%, low HDL cholesterol, 27%; and elevated fasting glucose, 9.3%. Among these components, the increased TG levels were highly prevalent in survivors than in general population ($p=0.000$). Fatty liver was identified in 8 survivors (18.2%). Sixteen of 44 survivors (36.4%) received at least 3 repeated examinations annually. Twelve out of 16 survivors have 1 or 2 abnormal components at initial examination. Their number of metabolic components have been shown to decrease in 4, persisted in 3, and increased in 5 survivors. Three of 4 survivors who have no components of MS at initial examination showed at least 1 abnormal component during follow-up.

Conclusions

We observed the high incidence of increased TG level in adolescent survivors of childhood cancer, and detected abnormal components of MS during periodic follow-up. Lifestyle interventions and periodic long-term follow-up monitoring would be needed to reduce the metabolic risks in childhood cancer survivors.

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Late Effects

RISK-TAKING BEHAVIOURS AMONG CHILDHOOD CANCER SURVIVORS: A META-ANALYSIS

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Objectives

Survivors of pediatric cancer are at risk for late effects of their therapy, some of which may be exacerbated smoking, alcohol or drug use. We undertook a meta-analysis of the literature to determine whether survivors of childhood cancer engage in these risk-taking behaviours at rates different from their peers.

Methods

MEDLINE (1946-), EMBASE (1947-), PsychINFO (1806-) and CCTR were examined for studies comparing engagement in risk-taking behaviours between cancer survivors and sibling or matched peer controls. Two reviewers assessed studies for inclusion, and extracted data independently. Studies were combined with Forrest plots in Review Manager 5.2, using inverse variance weighting, and a random effects model to determine the odds ratio (OR) and incidence rates of risk-taking behaviors in survivors compared to controls. Risk of bias was assessed with the Health Evidence Bulletins – Wales: Critical Appraisal of Observational Studies tool.

Results

Of 1562 studies identified, 14 met criteria for inclusion. Twelve studies assessed smoking rates, 6 binge drinking and 7 drug use. Compared to their siblings, childhood cancer survivors were less likely to smoke (OR 0.72 [95% confidence interval 0.52, 0.98]) or binge drink (OR 0.77 [0.68, 0.88]), but similarly likely to use drugs (OR 0.33 [0.03, 3.28]).

Compared to matched peers, survivors were less likely to smoke (OR 0.54 [0.42, 0.70]) or use drugs (OR 0.57 [0.40, 0.82]), but equally likely to binge drink (OR 0.97 [0.38, 2.49]).

Among survivors, 21% [0.17, 0.25] smoked, 20% [0.08, 0.51] binge drank and 15% [0.10, 0.23] used drugs. Studies included had a generally low risk of bias.

Conclusions

Survivors of childhood cancer generally engage in similar or lower rates of risk-taking than their siblings and peers. Future studies should examine which youth are engaged in risk-taking behaviours and use this information to focus intervention strategies to minimize these activities among survivors.

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Late Effects

SUBSEQUENT NEOPLASMS AFTER CHILDHOOD CANCER: A 20-YEAR EXPERIENCE AT HOSPITAL INFANTIL DE MEXICO FEDERICO GOMEZ

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Objectives

To assess patient characteristics and outcome of subsequent neoplasms (SN) in survivors of pediatric cancer at our institution.

Methods

We reviewed the records of all patients who developed a SN after treatment for childhood cancer. Clinical characteristics, leukemia subtype or histology, latency, treatment and outcome were recorded.

Results

From a total of 5,121 malignant neoplasms diagnosed between January 1993 and December 2012, 27 patients developed 28 SN (cumulative incidence = 0.54%), 25 of them occurred from 2003-2012. Mean age at diagnosis of the primary neoplasm was 6.2 years. The most common primary was Retinoblastoma (7) followed by Acute Lymphoblastic Leukemia (6), Langerhans Cell Histiocytosis (3), Brain Tumors (3), non-Hodgkin's Lymphoma (2), Germ Cell Tumors (2), Soft Tissue Sarcomas (STS) (2) and Osteosarcoma (2). Genetic susceptibility could be identified in 7 cases. The average interval between diagnosis of the first and second malignancy was 5.1 years for all patients and 4.3 for those with genetic predisposition. The second malignancies included AML (11) STS (4), Brain Tumors (4), Osteosarcoma (2), Thyroid Carcinoma (1), Ewing Sarcoma (1) Hepatocellular Carcinoma (1) Gastric Carcinoma (1), nonmelanomatous Skin Cancer (1) and Lymphoma (1). A Retinoblastoma patient developed AML as a third malignancy. Eight secondary AML cases had received high doses of etoposide, cyclophosphamide or platinum compounds for the treatment of their first neoplasm and 8 out of 16 secondary solid tumors received radiotherapy. Nine patients are alive and disease free and 18 died due to their second malignancy. The risk of dying was higher among the patients who developed AML (91%).

Conclusions

We found a low cumulative incidence of SN and differences in the types of primary and secondary neoplasms with respect to other series. Ten years ago we had 30% of abandonment and higher mortality rates, consequently, patients died before the development of SN.

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Late Effects

THE ASSOCIATIONS BETWEEN COGSTATE COMPUTERIZED TESTS OF COGNITION AND STATE STANDARDIZED ACHIEVEMENT TEST SCORES IN SURVIVORS OF CHILDHOOD CANCERS

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Objectives

Childhood cancer survivors are at risk for impaired neurocognitive functioning that can impact educational performance, but screening by neuropsychologists is time-intensive and costly. We sought to determine if the Cogstate battery, a computerized measure of neurocognitive functioning, is associated with academic achievement.

Methods

Patients with a history of chemotherapy, cranial radiation, or neurosurgery for a CNS tumor at ≤ 21 years who were at least 2 years after diagnosis were administered the 25-minute Cogstate computer battery (5 tasks measuring neurocognitive functioning; see table) in the Yale Pediatric Oncology Clinic. Connecticut state standardized assessments for math and reading achievement were obtained; performance was categorized as *at/above* vs. *under* the state-defined goal.

Results

The 39 participants (74.0% male) were a median of 15.9 (range 8.5-26.3) years old and 7.0 years after diagnosis. Overall, state-defined goals in math and reading were achieved in 60.5% and 61.5% of participants, respectively. T-tests revealed significant associations between achievement scores and Cogstate tests of cognition (see table). Students under goal for math performed significantly worse on the problem solving/reasoning test. Those under goal for reading performed significantly worse on the processing speed, attention, and working memory tests. The effect sizes for these associations were moderate to large.

Cogstate Test	Math		Reading	
	<i>p</i>	Effect-Size [~]	<i>p</i>	Effect-Size [~]
Problem Solving/ Reasoning (errors)	.03*	0.78	.07	0.64
Visual Associative Memory (errors)	.07	0.64	.11	0.54
Processing Speed (seconds)	.43	0.27	<.01*	1.15
Attention/Vigilance (seconds)	.88	0.06	<.01*	1.07
Working Memory (seconds)	.62	0.17	.04*	0.69

[~] Cohen's *d*: 0.2= small, 0.5=medium, 0.8= large

Conclusions

Our results suggest that the 25-minute Cogstate computer battery is a significant predictor of academic achievement. Large effect-sizes suggest worse performance on at least 4 Cogstate tests may be helpful in identifying children vulnerable to academic difficulties.

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Late Effects

BONE TOXICITY EVALUATION IN BRAZILIAN PATIENTS TREATED ON TWO CONSECUTIVE STUDIES: GBTLI 93 AND GBTLI 99

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Objectives

To evaluate the impact of therapy on bone mineral density (BMD) in acute lymphoblastic leukemia (ALL) survivors treated according to the Brazilian Cooperative Childhood Protocols – GBTLI LLA-93 and 99.

Methods

BMD by dual energy X-ray absorptiometry was performed in 101 treated patients in a cross-sectional study and its values were evaluated according to clinical and treatment characteristics and body composition. Correlations between BMD values and all variables were tested using χ^2 test, Fisher's exact test, likelihood ratio and t-Student test with significance level of 5%.

Results

Sixty patients were female and 78% were white, current mean age was 17 ± 4.7 years. Forty-four patients were treated according to GBTLI LLA-93 and 57 according to GBTLI LLA-99. Twenty patients (19.8%) received cranial radiotherapy. The nutritional diagnosis was 22.8% overweight and 15.8% obesity. It was observed 2% of fractures and 2% of osteonecrosis in assessment of bone toxicity. In group younger than 20 years of age, three patients (3.8%) had low BMD and 16 (20.2%) had risk values for low BMD (Z-score between -1.1 and -1.9). This group had lower lumbar spine ($p=0.01$) and total body ($p=0.005$) BMD compared to the group with normal values. Moreover that group had lower lean body mass ($p=0.03$). In group older than 20 years of age, ten patients (45.4%) had osteopenia and they were older than the group with BMD normal values ($p=0.001$).

Conclusions

It was characterized a risk group for low BMD comprising 15.8% that presented significant low values of BMD. The study suggests that this group needs a better attention in monitoring bone loss and they may benefit through preventive actions to avoid bone loss and to promote good habits of life. Furthermore it encourages the development of protocols for longitudinal monitoring of these patients.

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Late Effects

HEPATIC FOCAL NODULAR HYPERPLASIA IN PATIENTS PREVIOUSLY TREATED FOR PEDIATRIC SOLID TUMORS

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Objectives

Focal nodular hyperplasia (FNH) is a benign condition of the liver which may occur in patients previously treated for malignancies. The aetiopathogenic mechanism underlying FNH is poorly understood.

Methods

In our Institution, FNH was diagnosed in 14 patients (6 male, 8 female) previously treated for a pediatric cancer: 3 patients were treated for neuroblastoma, 3 for Ewing sarcoma, 3 for medulloblastoma, 2 for Wilm tumor, 1 for osteosarcoma, 1 for hepatoblastoma, and 1 for malignant mesothelioma. Median age at the time of the original cancer diagnosis was 7 years (range 3 months to 15 years). All patients received multi-agent chemotherapy, 8 underwent myelo-ablative regimens (with busulphan, melphalan or thiotepa) and 9 also received radiotherapy.

Results

The median age of FNH diagnosis was 14 years (range 4-23) and the median interval between the diagnosis of cancer and FNH was 5 years (range 3-18).

In 2 cases, radiological findings, including MRI scanning, were inconclusive and liver biopsies were performed. Four patients had a single liver lesion, while in 10 patients FNH was multifocal.

The median of the maximum nodule diameter (of the largest lesion in the case of multifocality) at time of diagnosis was 20 mm (range 8-40). After a median of 45 months follow-up (range 3-100) the median diameter was 30 mm (range 10-70), driven by 9 cases that increased size. This increase was not linear over time, with a median increase of 3.5 mm/year (range 1.8 to 9.6). Interestingly, in 3 out 4 cases with single lesion FNH became multifocal. No patients received surgical treatment and all patients remain on active follow-up.

> Conclusions

Our experience is consistent with the concept of focal nodular hyperplasia as a benign condition. Biopsies improve diagnostic accuracy in cases where radiological findings are not conclusive. With regard to treatment, we recommend a conservative, "wait and see" approach.

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Late Effects

NUTRITIONAL STATUS, DIETARY INTAKE AND PHYSICAL ACTIVITY IN CHILDHOOD CANCER SURVIVORS

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Objectives

Nutrition related late effects are an important consideration in childhood cancer survivors (CCS). The aim of this study was to examine the nutritional status, dietary intake and physical activity levels of CCS.

Methods

This cross-sectional study involved 43 CCS (n=14 solid tumors). Measurements included body mass index (BMI), body cell mass index (BCMI) via measures of total body potassium, percent fat (%fat) via the Bodpod® and energy intake and Physical Activity Level (PAL) by three day diet and physical activity diaries.

Results

The population had a mean (+/- SD) age of 14.6±3.7 years and a mean (+/- SD) time since active treatment of 9.7±3.0 years. The mean height, weight and BMI Z score fell within the range of 0.00±1.00. Based upon BMI, no patients were obese and two were classified as thin. However, when %fat was measured, 49% were considered obese (>20%males; >30% females) and when BCM was measured, 54% were considered to be malnourished (BCMI Z score <-2). Sixty-six percent of CCS consumed between 75-110% of estimated energy requirements. The mean (+/- SD) PAL of the group was 1.46±0.13 and 88% of the subjects were classified as having a sedentary/lightly active lifestyle (PAL<1.70). There was a positive relationship between BCMI Z score and PAL (r=0.34; p=0.03) and a negative relationship between %fat and PAL (r=-0.32; p=0.03).

Conclusions

Malnutrition, both under and over nutrition, is a problem for CCS, which is under recognized by assessment of BMI. Childhood cancer survivors appear to have dietary intakes similar to the general population but have a sedentary lifestyle, with decreased BCMI and increased %fat related to decreased activity levels. It is recommended that physical activity interventions in combination with dietary guidance should be a focus both during and after cancer treatment to minimize the level of malnutrition seen in CCS.

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Late Effects

RELATIVE DIFFERENCES IN RISK FOR NEUROPSYCHOLOGICAL OUTCOMES POST PROTON RADIATION FOR INFRATENTORIAL VERSUS SUPRATENTORIAL PEDIATRIC BRAIN TUMORS

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Objectives

Describe neuropsychological (NP) outcomes after proton radiation (PRT) for infratentorial and supratentorial pediatric brain tumor patients.

Methods

Fifty-four patients completed NP evaluations pre-PRT; 22 patients completed evaluations 1-3 years post-PRT (infratentorial n=13, 9 males, median age 7.0 years [range, 3.2-29.4]; supratentorial n=9, 6 males, median age 16.4 years [range, 12.7-20.4]). Cumulative tumor bed dose ranged from 5400-5940cGy. Neuropsychological measures included: Adaptive Behavior Assessment System-2, Behavior Assessment System for Children-2, Beery-Buktenica Developmental Test of Visual-Motor Integration, Behavior Rating Inventory of Executive Function, California Verbal Learning Test-C/II, Purdue Pegboard Test, Rey Complex Figure Test, and Wechsler IQ measures.

Results

At baseline, IQ ranged from impaired to superior (infratentorial: n=30, range 70-128, mean = 103.8, SD=14.6; supratentorial: n=24, range 67-127, mean = 96.1, SD = 14.1). Both groups struggled with visual-motor integration and fine motor functioning. The infratentorial group's performance on measures of attention, inhibition, visual and verbal memory, problem solving, organization, social-emotional and executive functioning was average to superior. The supratentorial group consistently demonstrated average abilities with some variability (impairment) on a task of visual organization.

At follow-up, the infratentorial group demonstrated low average to superior intelligence (range 86 to 121, mean = 103.1, SD = 11.4); the supratentorial group demonstrated average to high average intelligence (range 94-118, mean = 106.1, SD = 7.8). Both groups evidenced below age expectation fine motor dexterity, list learning and visual organization/memory, and average reported executive and social-emotional functioning. Infratentorial group's inhibition and visual and verbal memory abilities declined to the average range, with low average adaptive functioning. Supratentorial group's performance remained average, with continued visual-motor integration weakness.

Conclusions

Post-PRT supratentorial mean group performance was stable. Despite strong pre-PRT performance, the younger, infratentorial group declined, with greater variability between group members. A subset of the infratentorial population was uniquely vulnerable to early PRT cognitive late-effects.

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Late Effects

SYMPTOMATIC OSTEONECROSIS IN CHILDREN UNDERGOING CHEMOTHERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Objectives

Osteonecrosis (ON) has been increasingly documented in pediatric acute lymphoblastic leukemia (ALL) as it can result in joint dysfunction and subsequent impairments in activities of daily living among long-term survivors. Risk factors for ON include age above 10 years, female sex, and use of dexamethasone. We report the incidence of symptomatic osteonecrosis in children treated for with acute lymphoblastic leukemia in our department.

Methods

We retrospectively assessed the incidence of symptomatic ON in a total of 115 patients with acute lymphoblastic leukemia treated with protocols BFM 95 and ALLIC 2009. Symptomatic ON was diagnosed in 5 patients with ALL. They were 2 boys and 3 girls with median age 12 years (range, 7.5 to 14). The ON patients were identified based on clinical symptoms such as persistent bone pain, limping and limited motion of joints. Osteonecrosis was further confirmed with diagnostic imaging studies (x-ray and magnetic resonance imaging [MRI]).

Results

The cumulative incidence of ON was 4.3%. ON was diagnosed at median treatment weeks 66.5 (range, 24 to 108). The most commonly affected joints and bones were the hip joint (60%) and the knee joint (40%). Two patients (40%) exhibited multiple lesions. All patients underwent weight bearing restrictions and pain management. One patient (20%) needed surgical intervention. With the median follow-up times of 29 months (range 6 to 65), the clinical outcomes of ON were as follows: n1 with amelioration of ON, n4 with stable disease and n1 with deterioration of ON.

Conclusions

A significant number of patients develop ON during or after treatment for childhood ALL. Weight-bearing joints are most commonly affected. Clinical screening of ALL patients especially within 3 years from diagnosis is necessary for early recognition of ON.

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Late Effects

SCARS IN CHILDHOOD CANCER SURVIVORS

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Objectives

Childhood cancer survivors have to cope with scars, with at least one chest scar from a central venous catheter (CVC). Scars cause esthetic discomfort and are a visual reminder of disease. The impact of scars on cancer survivors' quality-of-life (QOL) has rarely been investigated. We evaluated coping with scars and their effect on body self image and health-related QOL in survivors of pediatric cancer.

Methods

Thirty-four survivors of childhood cancer, aged 15-30 years, 56% (19) girls and 44% (15) boys, on long-term follow-up (LTFU) completed a questionnaire concerning demographic details, disease and treatment, and scars: number, length (in cm), localization, psychological impact of scars on esthetic aspect, self body-image, affective and social life and health-related QOL. Statistical analysis of variants was performed by the SPSS method.

Results

Patients showed 1-9 scars, but 44% (15) had only one chest scar from the CVC. Forty-seven percent (16) had at least two scars, one from the solid tumor resection and one from the chest CVC. Average scar length was 4.42cm (range, 1-50cm). Most survivors ignored or hid the scars, even if they were not found to influence the self body-image, activities or social life. For 52% of survivors, the scars were at the origin of health concern. Coping with scars and hiding scars were found to be related with a statistical significance to self body image (p

Conclusions

Forty-seven percent of childhood cancer patients had at least two scars. Survivors cope with scars ambivalently: by hiding the scars, they decrease their negative impact esthetically, and ameliorate the self body image, affective and social QOL, but they remain a health concern.

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Late Effects

**LONG-TERM FOLLOW-UP OF PEDIATRIC HEMATOPOIETIC CELL TRANSPLANTATION
CANCER SURVIVORS**

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Objectives

Increasing numbers of hematopoietic cell transplantation (HCT), autologous as well as allogeneic, are being performed with a greater number of long-term survivors. The purpose of this study was to review late effects secondary to treatment exposure before HCT and to the HCT conditioning therapy.

Methods

Subjects included 38 childhood cancer survivors on long-term follow-up (LTFU) who had HCT; 28 patients had autologous and 20 had allogeneic HCT

Results

Median age at diagnosis was 9 years (y) (range, 0-21y). Median age at LTFU was 27y (range, 8-37y). Median years of LTFU was 16 (range, 5-27). Male to female ratio was 1.1. We found 40 late effects in 23 survivors, 27 late effects in 13/19 cancer patients post-chemotherapy, radiotherapy and HCT; 13 late effects in 10/19 cancer patients post-chemotherapy and HCT without radiotherapy. Of 40 late effects, 26 were found in patients post-autologous and 14 in patients post-allogeneic HCT. Late effects were: 2 cataracts, 1 hemianopsia, 1 hemiparesis, 1 convulsive disorder post Acute Disseminated Encephalomyelitis, 1 attention deficit disorder, 2 dental problems, 2 avascular necrosis, 1 leg length discrepancy, 6 hypothyroidism, 1 cardiac valve insufficiency, 4 chronic hepatitis, 5 oligo-azoospermia, 4 primary ovary failure, 3 second cancer, 4 osteoporosis (female), 1 failure to thrive, 1 obesity. Survivors who received radiotherapy had more late effects, mainly musculo-skeletal disorders, hypothyroidism, cataract and second cancer. Osteoporosis was reported in females. Infertility rate was almost equal in both genders. No case of metabolic syndrome, hyperlipidemia or diabetes mellitus was reported.

Conclusions

Conclusion: This study reported 60% late effects in childhood cancer survivors post-HCT, the most in those treated by radiotherapy pre-HCT. The few cardiovascular late effects reported may be explained by median LTFU of 16y. High risk of late effects in HCT survivors warrants lifelong structured LTFU.

EP-249

Late Effects

**MUSCULOSKELETAL SEQUELAE OF SOLID TUMOURS AND CANCER
REHABILITATION OF CHILDREN TREATED WITH INTENSIVE CHEMOTHERAPY,
SURGERY AND RADIATION THERAPY**

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Objectives

Recommendations for screening, prevention, and management of survivors.

Methods

95 children and adolescents at the mean age of 13,7 years with solid tumours were treated between 1987 and 2013 years, followup of 6 to 324 months. 36 patients had metastases, 19 patients had solitary metastases, 17 –multiple. Treatment consisted of chemotherapy, radiotherapy, oncologic surgery, included limb-sparing procedures. The most common late effects we had observed were: scoliosis - in 75 cases, muscular hypoplasia – 66, osteopenia – 47, limb-length discrepancy in spite of usage of growing endoprosthesis - 46, deformation of chest wall and limbs – 32, pathological fractures - 6, poor joint movement – 61, neurological disturbance - 22, lymphedema - 5, deforming osteoarthritis - in 3 cases. 20 patients had more, than 6 late effects. 43 patients underwent individual combined rehabilitation program. Patients underwent a course of postoperative inpatient physical therapy. This study evaluated the short and long-term changes in physical fitness of a child with a childhood malignancy, using an individual rehabilitation program, consist with combined physical exercise, kinesiotherapy, aquatic rehabilitation implemented shortly after treatment. Training is performed individually, under the supervision of an experienced paediatric physical therapist.

Results

We suggest that the usage an individual rehabilitation program can decrease pain, improve muscle strength and range of motion in joints, an increased supply of blood to the muscles, higher muscle metabolism, and more circulation in the limbs, improves tissue nutrition and helps the healing process.

Conclusions

Long-term survival is possible, even for patients with metastatic disease. All long-term survivors of childhood cancer should attend a specialized therapy in rehabilitation clinic.

EP-250

Late Effects

THYROID CARCINOMA AFTER TREATMENT FOR CHILDHOOD AND ADOLESCENT MALIGNANCIES: THE EXPERIENCE OF FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI OF MILAN

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Objectives

To describe natural history, therapeutic approach and histopathology of secondary thyroid cancers in individuals who had a malignant disease in childhood and adolescence.

Methods

We conducted a retrospective analysis of patients treated at our Institute who developed a thyroid neoplasm between 1980 and 2012 after being treated for malignancy in pediatric age.

Results

Thirty-six patients with secondary cancer of the thyroid were identified. Most of the primary cancers had been Hodgkin's lymphomas. All patients had received radiotherapy for their first malignancy. Total thyroidectomy was performed in 27 cases (6 with lymphadenectomy), hemithyroidectomy in 9 (1 with lymphadenectomy); 12 patients received radiometabolic therapy, and all but 2 had TSH-suppressive therapy. The histological diagnoses were 31 papillary and 5 follicular carcinomas. OS was 100% and 95%, and PFS 96% and 83%, at 5 and 10 years, respectively. None of the patients died of their thyroid disease. Nodal involvement at onset was the only factor correlating with recurrence. Surgical sequelae only occurred in patients who underwent total thyroidectomy.

Conclusions

Survival did not depend on the aggressiveness of surgery. Our data confirm a good prognosis for secondary thyroid cancer, prompting us to encourage a 'minimalist' approach to the treatment of these particular patients, wherever possible.

EP-251

Late Effects

VALUES OF HIGH SENSITIVE TROPONIN T IN LONG-TERM SURVIVORS OF CHILDHOOD CANCER TREATED WITH ANTHRACYCLINES

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Objectives

Cardiac biomarkers can play an important role in the early detection of subclinical heart failure. In this study we aim to 1) obtain values of high sensitive cardiac Troponin T (hs-cTnT) in long-term survivors of childhood cancer 2) investigate the potential role of this biomarker in the detection of subclinical late-onset cardiotoxicity.

Methods

Hs-cTnT and N-terminal-pro-brain natriuretic peptide (NT-pro-BNP) were measured in 75 survivors of childhood cancer. Electrocardiography and echocardiography were performed to evaluate cardiac function.

Results

Mean follow-up period was 9.4 years (range 4.5 - 34.1 years). All survivors were clinically asymptomatic and had no history of heart failure during or immediately after treatment with anthracyclines. Electrocardiography was available in 59 of 75 survivors and showed no signs of myocardial injury related to ischemia or abnormal QTc. Echocardiography was performed in 64 of 75 survivors. Mean left ventricular shortening fraction (SF) was 34% (range 28 - 43%); mean ejection fraction (EF) was 61% (range 48 - 74%). Seven survivors had a mildly decreased EF between 48% and 55%. Normal hs-cTnT levels were detectable in all 75 survivors (range 3 - 13 ng/L). The hs-cTnT concentration did not differ among the different anthracycline dosage groups: ≤ 120 , 120-300 and ≥ 300 mg/m². Yet, 7 of 75 survivors (9.3%) had elevated NT-pro-BNP levels (range 7 - 25 pg/ml). Of these 7 survivors one had a mildly abnormal EF of 51%. The other EF's, all SF and all ECG findings were normal in these 7 survivors.

Conclusions

Hs-cTnT concentrations are normal in long-term survivors of childhood cancer, even in the subpopulations with elevated NT-pro-BNP and/or a mildly decreased EF, indicating that it is not a sensitive marker for late onset subclinical anthracycline induced cardiotoxicity.

EP-252

Late Effects

**LATE EFFECTS IN LONGTERM SURVIVORS OF CHILDHOOD HODGKIN LYMPHOMA:
A SINGLE CENTRE EXPERIENCE**

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Objectives

To assess the spectrum of late effects in long-term survivors of Childhood Hodgkin Lymphoma(HL), treated with combination chemotherapy+/- radiation therapy(RT).

Methods

Retrospective analysis of all survivors of HL registered in After Completion Therapy(ACT)Clinic of a Paediatric Oncology Department between February1991 and February2014. Records were analysed for demographics as well as late effects and their possible causative factors.

Results

Of a total 1,614 survivors registered during this period,385(23.8%)had a diagnosis of HL.The median age at diagnosis was 8years(range2-19y)and age at last followup was 19years(7-53y).The median followup was 10years(range2-40y).A disproportionate male enrolment (M:F ratio 8:1)was noted. Patients had been treated between 1972 and 2010;all had received chemotherapy(doxorubicin in 240/385;alkylating agent in 98/385)and 217(56.4%)had received RT.Although only 38(10%)of patients had severe/life-threatening complications (grade3/4)at ACT registration,66(17.1%)had grade3/4 complications at last followup.30 patients had multiple significant issues.The common problems in this cohort included impaired growth in 42(10.9%)and chronic HepatitisB and complications in 24(6.2%).Hypothyroidism was detected in 106/209 tested(50%)and was significantly associated with RT to neck(p

Conclusions

Childhood HL has a high cure rate,and therefore more longterm survivors with potential for late effects.The high incidence of late effects,especially with older modalities of treatment,is an impetus for risk-adapted,response-based therapy with less intensive and toxic treatment protocols.

EP-253

Late Effects

LONG-TERM RENAL TUMOURS FOLLOW-UP: A SINGLE INSTITUTION STUDY

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Objectives

Late morbidity and mortality in renal tumors (RT) treated following five consecutive SIOP protocols.

Methods

A single-institutional retrospective cohort study, assessed RT survivors diagnosed from 1978 for mortality, subsequent malignant neoplasms, cardiac function, musculoskeletal effects, fertility and pregnancy and renal function. Out of 82 pts with RCC (6), CCS (1), WT (73), synchronous BWT (2), 12 died of disease, 1 of renal failure (WAGR) and 2 of accident. At mean FU of 19 yrs the OS is 81.7%. Sixty-seven survivors were previously treated with: unilateral nephrectomy (53), nephrectomy in one side and partial nephrectomy in the other one (1), nephron sparing surgery (13); local RT (9), lung RT (2), whole abdomen RT (1). Twenty pts received anthracyclines (14 with cardioxane association).

Results

Out of 67 survivors, 8 did not participate and 4 with short FU were excluded, 55 (M24/ F31) mean age 22 yrs were evaluated.

Second neoplasm: 2 cases (3.6%) presented an osteosarcoma and a colon carcinoma, respectively, in irradiated site.

Cardiac function: FE ranged from 56% to 77% in 18 cases it was borderline in 2 (50% and 52%). FS ranged from 30% to 48% in 18 cases, it was borderline in 2 (25% and 27%).

Fertility and pregnancy: 3 females had successful pregnancy, 1 male an abortion for Dandy-Walker malformation. Infertility in a whole abdomen irradiated case.

Musculoskeletal Effects: 5 irradiated cases had scoliosis and flank hypotrophy.

Renal function: out of 40 uncomplicated uninefrectomized cases, 23 (53.7%) presented eGFR<90 ml/min/1.73m², but only 5 (12.5%) had stage 2-3 chronic kidney disease (CKD). One BWT case had stage 2 CKD. One NSS case had eGFR<90 ml/min/1.73m².

Conclusions

In our series of pts with a long FU, second tumor is the main problem in RT survivors. In contrast with other similar reports we found a good cardiac function.

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Late Effects

**ADVERSE EVENTS OF LOCAL TREATMENT IN HEAD AND NECK
RHABDOMYOSARCOMA SURVIVORS AFTER EXTERNAL BEAM RADIOTHERAPY OR
AMORE TREATMENT**

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Objectives

The majority of head and neck rhabdomyosarcoma (HNRMS) patients need radiotherapy to achieve local control. Radiotherapy is a well-known cause of adverse events (AEs). To reduce AEs, an innovative local treatment was developed in the Emma Children's Hospital Amsterdam (EKZ-AMC): Ablative surgery, Mould brachytherapy and surgical Reconstruction (AMORE).

Aims: to determine the prevalence of AEs in HNRMS survivors and to compare AEs between survivors treated with the international standard: external beam radiotherapy (EBRT-based:

London) and survivors treated with AMORE if feasible, otherwise EBRT (AMORE-based: Amsterdam).

Methods

All HNRMS survivors, treated in London or Amsterdam between January 1990 and December 2010 (N=153), and alive ≥ 2 years post-treatment were eligible (N=113). A predefined list of AEs was assessed in a multidisciplinary clinic and graded according to the Common Terminology Criteria for Adverse Events v4.0.

Results

Eighty HNRMS survivors attended the clinic (median follow-up 10.5 years); 63% experienced ≥ 1 grade 3/4 event, and 76% had ≥ 5 AEs (any grade). Survivors with EBRT-based treatment experienced significantly more frequent and more severe AEs than survivors with AMORE-based treatment ($p=0.019$ and $p=0.028$ respectively). Five year overall survival (source population) after EBRT-based treatment was 75.0% and after AMORE-based treatment 76.9%, $p=0.56$.

Conclusions

This study is a baseline for new methods of local control and can be used in the future to assess AEs caused by novel local treatment modalities. AMORE-based local treatment resulted in similar overall survival and a reduction of AEs secondary to local treatment.

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Late Effects

RADIATION-INDUCED HEARING LOSS IN SURVIVORS OF CHILDHOOD HEAD AND NECK RHABDOMYOSARCOMA

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Objectives

The majority of children with head and neck rhabdomyosarcoma (HNRMS) need radiotherapy to achieve and maintain local control. However, radiotherapy to this region can cause significant adverse events, especially in young patients. The prevalence of hearing loss as an adverse event in this population of survivors is unknown. Therefore we assessed the hearing status of HNRMS survivors in a long-term follow-up clinic. Furthermore, we compared hearing loss between survivors with external beam radiotherapy (EBRT)-based local treatment with survivors with AMORE-based local treatment. AMORE is an innovative multi-disciplinary local treatment and consists of: Ablative surgery, MOld technique afterloading brachytherapy and surgical REconstruction (AMORE).

Methods

A prospective analysis was conducted of hearing thresholds at low and high frequencies obtained by long-term pure tone audiometry. The difference between hearing thresholds between treatment groups was assessed using repeated measurement linear regression analyses. Clinically relevant hearing loss was defined as a deterioration of ≥ 20 dB at PTA 0.5-1-2 kHz or at 4 kHz.

Results

Seventy-three out of 80 survivors were included (median follow-up 11 years). We found clinically relevant hearing loss in 19% (14/73) of the survivors at Pure Tone Average 0.5-1-2 kHz; 13/14 (93%) had a conductive or mixed type of hearing loss. Fewer survivors experienced clinically relevant hearing loss after AMORE-based treatment compared with EBRT-based treatment: 15% versus 26% ($p=0.26$). Multivariable regression analysis showed that survivors treated with EBRT-based treatment and those with parameningeal tumors had significantly more hearing impairment post-treatment when compared to survivors with AMORE-based treatment and non-parameningeal tumors

Conclusions

We found clinically relevant hearing loss in 19% of all HNRMS survivors. Furthermore, this study shows a trend towards less radiation-induced hearing loss after AMORE-based treatment compared to local treatment with EBRT in HNRMS survivors.

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Late Effects

IMPAIRMENT OF BONE HEALTH IN CHILDREN AFTER TREATMENT WITH POLYCHEMOTHERAPY FOR RETINOBLASTOMA IN EARLY CHILDHOOD IS SUBTLE

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Objectives

Impairment of bone health in survivors of childhood cancer occurs frequently.

Retinoblastoma (RB) is a malignant eye tumor in very young children. Enucleation is usually curative. However chemoreduction, as an eye sparing treatment attempt is being applied increasingly. Chemotherapy is commonly combined with local treatment modalities.

We conducted a cross sectional study to analyze the impact of chemotherapy for retinoblastoma on bone health.

Methods

The study (DRKS00003636) was approved by the local ethics committee.

33 Patients (12 female, age at diagnosis 0.75 ± 0.67) were recruited at regular visits to the Essen University-Hospital. Of these, 14 patients had unilateral, 19 bilateral RB.

Patients underwent polychemotherapy (33) and either enucleation (21), intra-arterial melphalan (2), thermo-chemotherapy (12), brachytherapy (10), percutaneous radiation (10) or a combination of therapies.

Polychemotherapy consisted of cyclophosphamide (4800 mg/m²), etoposide (1800 mg/m²), vincristine (9mg/m²) and carboplatin (1200mg/m²).

Clinical and biochemical parameters of growth, pubertal development and bone health were obtained. The history of fractures and bone pain were assessed. Age dependent parameters were calculated as SDS (height, weight, BMI, pubertal stage, IGF-1) or assessed using age appropriate norms (Bone specific alkaline Phosphatase (BAP), osteocalcin (OC)).

Results

Mean chronological age: 4.4 ± 3.8 (0.69-15.8) y, height SDS -0.5 ± 0.92 (-2.92 - 1.21), BMI SDS 0.46 ± 0.81 (-1.41 - 2.28). SDS for testicular volume/breast development: -0.02 (-1.3 - 1.41). 25 OH-vitamin D deficiency (VD: 23.2 ± 13.6 (8-73.8) ng/ml) was observed in 52% . Hyperparathyroidism (PTH 37.4 ± 22 (14.5-100) pg/ml) in 15% of patients. BAP was elevated in 16%. 7% reported bone pain. 9% experienced fractures.

Conclusions

Impairment of bone health after treatment with chemotherapy for RB was only subtle.

However, some children presented with bone pain and altered parameters of bone health.

Since identification of children at risk is difficult, we recommend long term monitoring and supplementation of vitamin D.

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Late Effects

LATE MORBIDITY AMONG SURVIVORS OF CHILDHOOD CANCERS : EXPERIENCE AT TERTIARY CARE CANCER HOSPITAL

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Objectives

1. To study the cohort characteristics and late effects of various treatment modalities in childhood cancer survivors at our center.
2. To organize exposure-based health screening guidelines among childhood cancer survivors.

Methods

All children under the age of 18 years with diagnosis of cancer during Jan 1995 to Dec 2008 at SKMCH, who fulfilled the following inclusion criteria were enrolled in the study:

1. Treatment at our center with chemotherapy and/ or radiation and/ or surgery
 2. Five years or more post primary diagnosis and followed in long term follow up clinic (LTF)
- Data were analyzed retrospectively to determine each candidate's clinical, demographic characteristics and details of treatment. Toxicity evaluations were tailored according to specific therapeutic exposures. Frequency of toxicities attributed to chemoradiation agents was calculated.

Results

Three hundred patients were studied. Male to female ratio was 2.7:1. At the time of diagnosis 20% were under 4 years, 44% between 5-9 years, 26% between 10-14 years and 10% were above 15 years of age. Current median age was 18 years (range 10 -32 years) . Hodgkin lymphoma was the most common diagnosis (49.6%) followed by acute leukemia (17%), NHL (13.4%), GCT (9.7%), retinoblastoma (5%) respectively. Duration of survival was more than 10 years in 69% and less than 10 years in 31% of patients. Regarding treatment modalities, 57% received chemotherapy, 23%-chemo and XRT, 15% chemo and surgery, 3% chemo, surgery and radiation and 2% surgery only.

On toxicity evaluation, azospermia was the most common late effect (49%) followed by oligospermia (15%). 13.5 % of our patients had hypothyroidism, 6.5% develop ototoxicity, 4.6% had impaired DLCO ,4% low bone density and 2.4% had cardiomyopathy.

Conclusions

Our study confirms high prevalence of persisting end-organ toxicities from chemoradiation exposure among survivors of childhood cancers. There is need to implement risk based and exposure related guidelines for life long follow up of cancer survivors.

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Late Effects

LONG TERM RISK OF CARDIAC MORBIDITY AFTER CRANIO-SPINAL IRRADIATION

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Objectives

To evaluate long term risk of cardiac morbidity in patients treated with cranio-spinal radiotherapy (CSI). Approx Odds ratio of development of cardiac morbidity for non radiated medulloblastomas is 2.3.

Methods

The study included six medulloblastoma patients that were simulated in supine position after immobilization using thermoplastic cast. Target delineation included CTV_brain that encompassed whole of the brain tissue CTV_spine included entire spinal canal that extended caudally till the lower end of thecal sac, CTV_Boost encompassed posterior fossa. Additional 7 mm margin generated respective PTV. CSI dose was 23.4 Gy/13#/2.5 wks for low risk disease and 35Gy/21#/4.1wks for high risk disease, posterior fossa boosted to a dose of 54-55Gy. Organs at risk delineated included heart, lungs, thyroid, esophagus, eyes, cochlea, hypothalamic-pituitary axis kidney and liver. Patients were planned either by 3DCRT, IMRT, VMAT either in Xio V4.80.00.7 or Moanco V 3.03.01. All patients were planned in SAD technique. 3DCRT was planned using a systematic junction shift where IMRT/VMAT using a junction dose gradient technique. For evaluation of late cardiac morbidity D_{max} , D_{mean} and volume of heart was recorded in all patients. Odds ratio for development of late long term cardiac morbidity was calculated by the formula $OR = 1 + \alpha_1.D + \alpha_2.D^2$ where D is mean dose received by heart and value of $\alpha_1=0.19$ and $\alpha_2=0.002$ were used in the equation.

Results

Median age of presentation was 12.5 years (range 2-26 yrs). Four patients were standard risk medulloblastoma whereas two were in high risk category. Median volume of heart was 367cc (range 213-577cc). D_{max} for heart was 32.03 Gy (range 21.06-33.47Gy) whereas D_{mean} received by the heart was 12.77Gy (range 8.36-14.67Gy). Odds ratio for development of late long term cardiac morbidity after CSI was 3.75 (range 2.59-4.21).

Conclusions

Risk of late long term cardiac morbidity after CSI is higher than non-radiated medulloblastoma patients

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Late Effects

TISSUE DOPPLER EVALUATION OF LEFT VENTRICULAR FUNCTIONS AND PLASMA CONCENTRATIONS OF NT- PRO BNP IN SURVIVORS OF CHILDHOOD HODGKIN LYMPHOMA

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Objectives

To evaluate long-term cardiovascular status of childhood Hodgkin lymphoma (HL) using plasma NT pro BNP and the non invasive tissue Doppler imaging (TDI)

Methods

A total of 45 HL survivors children who completed therapy with a mean cumulative anthracycline dose of (255 ± 141) mg/m² and recieved mediastinal radiotherapy and a control group of 40 healthy children were evaluated by conventional echocardiography, Tissue Doppler imaging (TDI) velocities, Tissue Doppler derived myocardial performance index (TD MPI) and NT- Pro BNP.

Results

Plasma NT-pro-BNP levels in HL patients were significantly elevated in comparison with healthy controls (p<0.001). Conventional echocardiographic measurements for LV systolic functions -ejection fraction (EF) and fraction of shortening (FS) - showed no difference statistically from the control group. TDI velocities revealed decreased S' velocity, reflecting systolic dysfunction in HL survivors, at medial and lateral mitral annuli (P<?0.01). Moreover, TDI showed decreased peak E' velocity (tissue Doppler peak velocity of the early atrial filling) at medial and lateral mitral annuli (P<?0.01) and the ratio of early peak velocity of rapid filling on pulse Doppler to tissue Doppler (E/E') values were statistically higher in patient group than control group (p < 0.001) reflecting diastolic dysfunction in HL survivors. The MPI index increased significantly in patients versus controls (p < 0.001). BNP values significantly correlated with E/E' ratio values (r = 0.81; p < 0.001) and TD-MPI (r = 0.72; p < 0.001)

Conclusions

Plasma NT-pro BNP helps to diagnose early cardiac dysfunction in survivors of HL. Tissue Doppler imaging is a non-invasive and reliable tool for detecting subclinical systolic and diastolic dysfunction post therapy in childhood HL. TDI parameters especially TD- MPI and E/E' can be useful in periodic screening of cardiac dysfunction in HL survivors follow-up.

EP-260

Late Effects

FOLLOW-UP CARE AND CANCER RELATED COMMUNICATION WITH PROVIDERS AMONG YOUNG ADULT SURVIVORS OF CHILDHOOD CANCER AFTER TRANSFER TO ADULT CARE

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Objectives

Approximately 30% of childhood cancer survivors receive cancer-focused follow-up care as recommended. However, no study has assessed engagement in and perceived quality of adult survivorship care following formal transfer from pediatric to adult care. This study describes: (1) rates of and satisfaction with follow-up care of transferred young adult survivors (YAS) and (2) patient-reported cancer-related communication from adult primary care providers (PCPs).

Methods

YAS transferred from a Survivorship Program to adult providers within 1 - 5 years completed online measures. Data collection is ongoing; final N ~ 90 by conference.

Results

Participants (N=66) were 23-36 yo (M=27.5), 48% male and 93% Caucasian. 95% of patients reported seeing a healthcare provider in the past year. 23% (n=15) reported attending an adult survivorship clinic and 30% (n=20) reported seeing a PCP for survivorship care in the past year. Quality of cancer care was perceived as good to excellent for 80% of patients attending survivorship clinic and 65% of patients attending primary care. YAS who saw PCPs for survivorship care reported discussions regarding (% who endorsed): prior diagnosis (45%), treatment (35%), risk for late effects (25%), and screening for late effects (35%). Of patients who reported they had not received survivorship care, 38% (n=26) saw PCPs for non-cancer-related reasons. In those cases, the following % of survivors reported discussions about: prior diagnosis (38%), treatment (23%), risk for late effects (16%), and screening for late effects (21%).

Conclusions

Almost half of transferred YAS did not seek cancer-related follow-up care in the past year. YAS receiving "survivorship care" from a PCP reported only marginally better rates of survivorship-focused communication than those seeking care from a PCP for other reasons. Results highlight the need to better understand barriers of seeking adult survivorship care and improve the competence of PCPs to provide optimal survivorship care.

EP-261

Late Effects

RELATIONSHIP BETWEEN CISPLATIN ADMINISTRATION AND THE DEVELOPMENT OF OTOTOXICITY

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Objectives

Cisplatin-induced ototoxicity is an important dose-limiting side effect. Our purpose is to determine the audiologic toxicity associated with cisplatin in pediatric oncology patients.

Methods

We performed an audiometric analysis of 58 pediatric oncology patients who received cisplatin therapy between January 1998 and January 2014, who were treated with cisplatin with the diagnosis of neuroblastoma, medulloblastoma, osteosarcoma, germ cell tumour, and hepatoblastoma.

Results

The median age at the time of diagnosis was 9.7 (range 3.4–16.9) years. There were 26 males and 32 females. The underlying diseases were neuroblastoma (18 cases) , medulloblastoma (18 cases), osteosarcoma (11 cases) , germ cell tumors (9 cases), and hepatoblastoma (2 case). The median individual dose was 100 mg/m²/cycle (56-200). The median cumulative dose was 480 mg/m² (200-1,200). Sixteen patients received cranial radiotherapy. Of the 58 patients, 24 developed hearing loss, leading to an overall incidence of 42%. Logistic regression analyses showed that the age at treatment (P=0.02) and cumulative dose of cisplatin (P=0.005) were the significant risk factors in predicting hearing loss in children treated with cisplatin. There was neither improvement nor aggravation during the follow-up in all of the patients who had hearing loss (3–68 months).

Conclusions:

The cumulative dose of cisplatin (>500 mg/m²) and the younger age at treatment (<12 years) were 2 mainly important risk factors for ototoxicity in patients treated with cisplatin. Serial audiometric evaluations are needed in the patients with risk factors during and after cisplatin treatment.

EP-262

Late Effects

THYROID DYSFUNCTION FOLLOWING TREATMENT FOR HODGKIN'S DISEASE

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Objectives

Thyroid dysfunction is an important morbidity of therapy for Hodgkin's disease, which should be well recognized by the doctors of these patients. Our aim is to investigate the thyroid dysfunction incidence among our Hodgkin lymphoma patients after treatment

Methods

Forty eight pediatric patients (less than 18 years old at diagnosis), who were treated with chemotherapy and radiotherapy with the diagnosis of Hodgkin's disease between 1995 and 2013, were periodically evaluated thereafter. 29 of the patients were irradiated to the neck and the others were irradiated to the other regions according to the involvement of the disease at the first diagnosis.

Results

The median age at diagnosis was 11 years, and the median duration of follow up was 10 years. 18 patients, out of 38 who were irradiated to the neck region, developed biochemical hypothyroidism. The median time to the development of hypothyroidism was 5 years.

Transient hyperthyroidism developed in two patients, 6 and 11 months after treatment for Hodgkin's disease. Among the 10 patients who were irradiated to the regions other than neck, none developed thyroid dysfunction. Four patients, although with normal thyroid functions, had hypoechoic nodule diagnosed at thyroid ultrasonography. The nodules showed histological multinodular goiter (3), and single colloid nodule (1).

Conclusions

There is a high risk of thyroid disease development following neck radiation therapy for Hodgkin's disease, reinforcing the importance and need for continued clinical and biochemical evaluation of those patients during follow up.

EP-263

Late Effects

ELECTROEJACULATION AS A METHOD OF FERTILITY PRESERVATION IN BOYS DIAGNOSED WITH CANCER: A SINGLE-CENTRE EXPERIENCE AND REVIEW OF THE LITERATURE

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Objectives

To evaluate the feasibility of electroejaculation to perform semen cryopreservation in pubertal boys before gonadotoxic therapy, and to review literature on this topic.

Methods

We performed a retrospective cohort study and review of the literature. The retrospective single-centre study was performed in an academic children's hospital and included boys diagnosed with cancer to whom sperm cryopreservation was offered before start of gonadotoxic therapy. We studied the outcome of electroejaculation, including patients' characteristics, hormone levels, and pre-treatment semen parameters.

Results

Pre-treatment semen samples were obtained by masturbation in 106/114 boys with cancer, of which 78/106 were adequate for preservation. In 11 boys electroejaculation was offered, of which 3/11 appeared adequate for preservation. Reviewing all reported electroejaculation cases in children with cancer in the literature, 13/29 (45%) cases were successful. Testosterone levels were higher in patients with successful sperm yield obtained by electroejaculation (testosterone: median 8.3 nmol/l (5.2-42.4) in successful versus median 1.7 nmol/l (0.01-17.9) in unsuccessful harvests).

Conclusions

Semen cryopreservation should be offered to all pubertal boys. If masturbation fails, electroejaculation can be considered as a useful option for semen cryopreservation, and leads to adequate material for cryopreservation in about half of the cases.

EP-264

Late Effects

SLIPPED CAPITAL FEMORAL EPIPHYSIS AFTER TOTAL BODY IRRADIATION

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Objectives

A significantly increased risk of slipped capital femoral epiphysis (SCFE) has recently been identified in survivors of childhood cancer treated with recombinant growth hormone (rhGH) after receiving total body irradiation (TBI) conditioning for hematopoietic stem cell transplantation (HSCT)¹.

Methods

We identified 4 cases (1 female) of SCFE in our cohort of 104 children who received TBI conditioning prior to HSCT over the past 30 years, of which 3 were rhGH *naïve* at the time of presentation.

Results

The children presented 4.8-10.3 years after 12Gy TBI conditioning for autologous HSCT. Presentation was atypical compared to idiopathic SCFE²: younger age (6.9-12.2 years), all prepubertal and only one overweight (BMI z-score -2.4 to 1.7). Two were bilateral at presentation, and three of the four patients presented with the uncommon valgus variant of SCFE. Overall time from symptom onset to radiological diagnosis was 5-27 months. The only child presenting with SCFE (unilateral) whilst on rhGH was a 12.2 year old girl with unreplaced hypogonadism. She was diagnosed 11 months after commencing rhGH though had experienced x-ray 'negative' transient hip pain 7 months prior. Upon review of her original radiographs, by Yngve's criteria³, there was subtle evidence of valgus slip.

Conclusions

We conclude that TBI alone is a significant risk factor for SCFE, with delays in diagnosis due to the atypical clinical and radiological presentation being common⁴. Valgus slips are frequently subacute in presentation with standard radiology inadequate. Yngve's criteria are a more sensitive method of screening initial radiographs in children with hip symptoms. However, if standard radiological techniques are negative or equivocal, other modalities such as ultrasound and/or MRI must be considered and early orthopaedic referral mandatory. Furthermore, rhGH therapy is frequently considered in this population. The risk of developing SCFE must be carefully considered by clinicians and clearly discussed with families before embarking on rhGH therapy.

EP-265

Late Effects

LATE-EFFECTS IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH NON-CNS GERM CELL TUMORS TREATED WITH PEB CHEMOTHERAPY REGIMEN

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Objectives

The incidence and severity of the cisplatin-etoposide-bleomycin (PEB) regimen have not been reported in children treated for non-CNS germ cell tumors (GCT). The purpose of this study was to evaluate the incidence and severity of audiologic, reproductive, renal, and pulmonary toxicity in pediatric and young adult patients with non-CNS GCT patients treated with PEB.

Methods

We performed a retrospective chart review of the audiologic, renal, pulmonary, and reproductive toxicity in patients ≤ 20 years of age with non-CNS GCT diagnosed and treated at Ann & Robert H. Lurie Children's Hospital of Chicago from January 1991 to December 2007. Patients who received radiation or other chemotherapy agents were excluded.

Results

26 patients who received 3-4 cycles of PEB had a median follow-up of 82.3 months. 50% had no measureable hearing loss, 23% had CTCAE grades 1-2 hearing loss and 8% required hearing aids following treatment. The 2 patients who required hearing aids received 800 mg/m² of cisplatin, while all others with hearing loss received standard dose. Of 23 patients with data available to assess kidney function, 70% had normal kidney function, and 30% had stage 2 chronic kidney disease (CKD) with a GFR 60-90 mL/min/1.73m². None required electrolyte supplementation. 11 patients had pulmonary function tests performed after treatment. All were normal, excluding 1 patient who had obstructive disease prior to and after treatment. 4 out of 5 patients tested had normal FSH, LH, estradiol or testosterone values. One became pregnant during follow-up.

Conclusions

Our series suggests that a significant proportion of pediatric patients who receive PEB for non-CNS GCT do not have audiologic, renal, pulmonary, or reproductive toxicity. Hearing loss, usually not requiring hearing aids, and reduced GFR, qualifying as stage 2 CKD, were the most frequent late-effects.

EP-266

Late Effects

ESTABLISHING PAEDIATRIC LONG TERM FOLLOW-UP TRANSITION CLINICS IN THE TERTIARY ADULT HEALTH CARE SECTOR

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Objectives

The number of new patients referred to the Paediatric Long Term Follow-up (LTF) Program, in addition to existing LTF patients requiring ongoing review, exceeds current clinic capacity.

Methods

The Long Term Follow-up Program (LTFP) has collaboratively established transition clinics with two tertiary adult health care providers to support the process of transition and to enhance transfer of adolescent/young adults (AYA) to the tertiary adult health care sector.

Results

In the three years (36 months) prior to June 2012, 14 patients were transitioned to tertiary adult health care providers (an average of 4.6 patients per year). Transition clinics were implemented in July 2012. In the period July 2012 to December 2013 (18 months) a total of 28 patients have been transitioned to tertiary adult health care providers (an average of 18.7 patients per year). An additional 15 patients are planned for transition by June 2014 (an average of 21.5 patients per year).

Conclusions

Following the implementation of formalised transition clinics, transition of AYA's to tertiary adult health services has increased to 7% of all patients referred to the LTFP. Transition has increased from 5 patients per year to 22 patients per year, creating capacity within the LTFP for new referrals and reducing waiting list times. The implementation of formalised transition clinics supports AYA patients receiving a personalised and supported transition, reduces the numbers of AYA patients 'bouncing back' to the paediatric sector, and provides the opportunity for the adult health care sector to receive an in-depth 'face to face' hand over of these complex patients.

EP-267

Late Effects

OPTIMISING FOLLOW UP FOR CHILDREN WITH BRAIN TUMOURS

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Objectives

The aim of this project was to optimise the follow up for children with brain tumours recognising that this group of children often have multiple sequelae of their disease or treatment, including growth, endocrine, neurological and neuropsychological sequelae, with ongoing rehabilitation needs. Attending multiple appointments interferes with their schooling and their parents' work commitments, and comprehensive management plans are often difficult to achieve.

Methods

We identified the patients who have been attending both oncology-endocrine and neurosurgical-oncology clinics, many of whom had additional ongoing rehabilitation needs. We produced a clinic proforma summarising the diagnosis, treatment given and complications, and included prompts to address all medical issues, schooling, neuropsychological needs and potential transition plans. In September 2013 the Oncological-Neurosurgical-Endocrine (ONE) clinic was established to bring all the multiprofessional teams together to provide a holistic review of these children. A pre-clinic multi-disciplinary team meeting was established to fully discuss each patient, including their rehabilitation issues. Families move through rooms with the same key worker, one of the Clinical Nurse Specialist team, to ensure all aspects are addressed but not repeated unnecessarily. After each clinic, a comprehensive clinic letter is produced, summarising the medical needs, rehabilitation review, schooling and future management plan for the patients and carers, their local shared care hospital, allied health professionals and their general practitioner.

Results

Three clinics have been run so far. Patient and staff feedback has been very positive particularly in relation to fewer appointments and the more holistic approach to the review.

Conclusions

Children with brain tumours who have multiple sequelae of their disease or treatment benefit from dedicated specialist clinics which address all their medical and holistic needs in a one stop clinic. This also provides an opportunity for patient/parent education around medical, neurological and neuropsychological issues using a variety of different tools.

EP-268

Late Effects

THE FUNCTIONAL IMPACT OF PERIPHERAL NEUROPATHY IN CHILDREN AND YOUTH TREATED FOR ACUTE LYMPHOBLASTIC LEUKEMIA: MULTIDIMENSIONAL ASSESSMENT

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Objectives

To describe a multi-dimensional functional assessment of chemotherapy induced peripheral neuropathy (CIPN) and related impairments, activity limitations, and participation restrictions in children/youth treated for acute lymphoblastic leukemia (ALL).

Methods

Participants were a purposeful sample of children/youth on or off treatment for ALL with varying degrees of CIPN. Multidimensional assessment as outlined in the results and 3-D instrumented gait analysis were conducted. Analyses were descriptive. Normative values provide context.

Results

Fourteen participants were assessed (median age 7 years, range 5-21), 6 males, 6 receiving maintenance therapy and 8 off treatment (mean time off 28 months, range 1-80). Data is presented as mean(standard deviation)[range]{normative}. Pediatric modified Total Neuropathy Scale:4.9(2.7)[2-12]{0-4}; 6 minute walk test (metres):400.3(113.7)[180.0-586.7]{400-600}; Bruininks-Oseretsky Test of Motor Proficiency Running Speed and Agility subtest (Standard Score): 1.1(0.5)[1-3]{10-20}; Oxford Foot and Ankle Questionnaire (%) Physical: 46.1(27.2)[0-75]{100}; School Play: 64.7(31.6)[6.3-100]{100}; Emotional: 80.2(24.8)[25.0-100]{100}; Shoe Wear 69.5(36.7)[0-100]{100}; Gross Motor Function Measure-ALL (%) Standing 88.4(11.8)[66-100]{100}; Walk,Run,Jump 81.6(14.2)[50-100]{100}; Pediatric Outcomes Data Collection Instrument Transfers and Basic Mobility: 36.7(27.2)[-49-53]{50}, Sport and Physical Functioning 24.1(19.0)[-27.0-42]{50}, Pain and Comfort 33.4(19.7)[-6-57]{50}; Edinburgh Gait Scale: 6.2(4.6)[0-14]{0}. Common kinematic gait characteristics included knee hyperextension, decreased dorsiflexion, delayed heelrise, and decreased ankle plantarflexion pre swing in stance; and decreased ankle dorsiflexion with compensatory hip and knee motion in swing. Temporal spatial data showed reduced step length with a corresponding reduction in velocity. Kinetics demonstrated decreased ankle moments/power generation at push off. Tibialis anterior and gastrocnemius electromyography showed timing and amplitude abnormalities.

Conclusions

Multi-dimensional functional assessment in children/youth participants treated for ALL demonstrated variability in impairments, activity limitations, and participations restrictions related to CIPN. These measures have the potential to inform clinical decision making regarding vincristine dosing, exercise, and orthotics; facilitate evaluation over time; and provide tools for further research of the impact of CIPN during and following treatment for ALL.

EP-269

Late Effects

RECALL OF FERTILITY DISCUSSION IN ADOLESCENT FEMALE CANCER PATIENTS

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Objectives

Current clinical guidelines emphasize that oncologists should discuss the risk of treatment-related infertility and preservation options before starting therapy. The purpose of this study was to determine whether female adolescent cancer patients at Ann & Robert H. Lurie Children's Hospital of Chicago remembered a discussion about fertility and preservation options at initial treatment planning and whether they were satisfied with information received.

Methods

We surveyed females who were 13 – 18 years old at cancer diagnosis and were 6 months - 3 years from diagnosis at enrollment regarding initial treatment planning, current feelings including mental health status, and demographics.

Results

Of the 16 subjects surveyed, 10 (A) recalled a discussion of decreased fertility as a potential side effect of therapy while 6 did not (B). 8/10 in A recalled a discussion of preservation options. 100% of subjects in A (9/9, 1 non-respondent) were satisfied with information received at diagnosis, contrasted with 50% satisfaction in B ($p < 0.04$). Presently, 80% of subjects in A (8/10) remain satisfied compared to 50% in B. Half the subjects in A reported making joint medical decisions with their parents compared to only 1/6 in B. More subjects who had looked forward to future pregnancy before cancer diagnosis recalled a discussion of fertility (5/7 = 71%). Overall, more subjects in A now anticipate difficulty in becoming pregnant because of treatment and one woman believes she will not be able to become pregnant.

Conclusions

A majority of subjects recalled a discussion of treatment-related infertility and preservation options. These young women were more satisfied with the information they received than were those who did not recall a discussion about fertility. Shared decision-making may be an important factor in recall of these discussions.

EP-270

Liver Tumours

NON HEPATOBLASTOMA LIVER TUMORS IN CHILDREN - A SINGLE CENTRE EXPERIENCE

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Objectives

The aim of this study was to review the clinical features, management and the outcome of children diagnosed with non hepatoblastoma liver tumors (NHLT).

Methods

All pediatric patients with NHLT managed in our institute from 2006 to 2013 were included in the study. Biopsy was performed if serum tumor markers were normal, radiological features were not suggestive of hepatoblastoma or age was less <6 months or > 3 years. All lesions were staged retrospectively as per the pretext staging system. The clinical findings, imaging, surgical details, intraoperative and postoperative complications, relapse and survival details were analyzed. Chemotherapy or radiotherapy was utilized when indicated.

Results

Of the total 14 liver lesions, 9 were benign: hemangioendothelioma (3), mesenchymal hamartoma (3), hemangioma (1), adenoma (1) and focal nodular (FNH) (1). Primary liver tumors were hepatocellular carcinoma (HCC) (1) and synovial sarcoma (1) and three had metastatic lesions. The primaries in metastatic patients were ovarian germ cell tumor (GCT), pancreaticoblastoma and Wilms tumor. The PRETEXT distribution was: I (5), II (6), III (2), and IV (1). Right hepatectomy was performed in four, left lateral sectorectomy (LLS) in three and non anatomic resections (NAR) in seven. The median blood loss was 250 ml (range 10 to 2100ml) and median intraoperative time was 3.30 hours (range- 2 -8 hours). All patients had negative margins except one with FNH. There were no intraoperative or postoperative complications. At mean follow-up of 30 months there were no local recurrences and all patients are alive and disease free.

Conclusions

NHLT are often low PRETEXT stages. Safe surgery is feasible without morbidity and is associated with good outcome.

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Liver Tumours

TREATMENT OUTCOME OF CHILDREN WITH HEPATOBLASTOMA

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Objectives

To evaluate treatment results of patients with hepatoblastoma (HB).

Methods

Medical records of patients with HB who diagnosed and treated between 1996-2013 were reviewed retrospectively.

Results

There were 18 patients with diagnosis of HB, and 16 of them were eligible. Two patients refused the treatment. Median age of diagnosis was 13 months (3months-10.5yrs), 81%of patients were <2years of age; M/F ratio was 1.0. Stage distribution: PRETEXT-I 12.5% (n:2), PRETEXT-II 12.5% (n:2), PRETEXT-III 62.5% (n:10), PRETEXT-IV 12.5% (n:2). Two patients had pulmonary metastasis. The median AFP level was 8112 ng/mL (53–148.206). Histopathologic examination revealed epithelial HB in 69%, and HB-NOS in 31%. Primary total resection was performed in four cases who had PRETEXT-I and PRETEXT-II disease. A 10 years-old boy had PRETEXT-I-HB and AFP<100ng/mL; CR was achieved by primary total tumor resection and COG-high risk chemotherapy protocol. Twelve patients received chemotherapy according to the SIOPEL protocol (SIOPEL-2 in four, SIOPEL-4 in 9 patients), then delayed surgery was performed. Dextrazoxan was provided only for three patients who received SIOPEL-4 protocol. Delayed surgery was resulted in microscopic residue in two patients with PRETEXT-III disease. One of these two patients relapsed with pulmonary metastases at the 26th month and the other relapsed at primary tumor site at the 7th month. Liver transplantation was performed in patient who had primary relapse. The median follow-up time was 76months (11months-12years). Survival analysis was done 14 patients who treated according to the SIOPEL protocol. The 2-years EFS rate was 93%, 5 and 10-years EFS rates were 83%; the 5 and 10-years OS rates were 100%. There was no early or late chemotheapy toxicity.

Conclusions

Performing surgery in experienced centers is important for hepatoblastoma treatment. There was no death related to chemotherapy toxicity or surgery. Survival rates were acceptable. SIOPEL protocol was found applicable and successful in our conditions.

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Liver Tumours

**LIVER MASSES, CLINICAL AND RADIOLOGICAL DIFFERENTIAL DIAGNOSIS –
REPORT OF 4 CASES ADMITTED IN A SINGLE MONTH**

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Objectives

In this paper, we report four cases of liver mass in children admitted to our hospital in August of 2013.

Methods

With ages ranging from 3 months to 4 years, all male, with abdominal distension and palpable liver mass as the chief complaint, associated with other signs and symptoms (weight loss, respiratory distress, cough, dyspnea, jaundice, acholic stools and dark urine). Two of them had elevated alpha-fetoprotein (AFP), two had abnormal liver enzymes and one had hyperbilirubinemia. They underwent examination of biopsy: three were malignant (two hepatoblastomas and rhabdomyosarcoma of the biliary tract) and one was mesenchymal hamartoma.

Results

Hepatoblastoma is the most common liver tumor in childhood, most often before the age of three, male to female ratio is 2:1 and is not associated with cirrhosis; the mass is usually large single and most often increases AFP.

Biliary rhabdomyosarcoma is a rare tumor (0.8 %), which is the most common cause of malignant obstructive jaundice in this age group, occurs around the age of 3, can have jaundice, acholic stools, dark urine, and hepatomegaly. With increased bilirubin and liver enzymes.

Mesenchymal hamartomas are more frequent in children under 2 years, they are congenital and benign lesions, presenting as palpable abdominal mass with abdominal distension, painless and without altering liver function or AFP.

The most common radiological findings are: hepatoblastoma is well circumscribed and may appear lobulated with septa; rhabdomyosarcoma biliary can be present and solid-cystic dilatation of bile and mesenchymal hamartoma pathways appear as cystic liver injury, multilocular with thin internal septa.

Conclusions

The ultrasound is an excellent screening test for suspected liver mass because is no ionizing radiation and no need for sedation. If confirmed hepatic mass, CT scan and MRI should be performed, to guide biopsy or surgery subsequently.

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Liver Tumours

HEPATOBLASTOMA: CLINICAL CHARACTERISTICS AND OUTCOME OF 13 PATIENTS

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Objectives

To evaluate the clinical features and treatment results of the patients with hepatoblastoma (HB) in our department.

Methods

Medical records of children who diagnosed, and treated with HB were analyzed retrospectively.

Results

There was 13 children with HB. Median diagnosis age was 20months (1.5mos-16.5yrs), M/F ratio was 0.44. Stage distribution: PRETEXT IV in 46%, PRETEXT II in 31%, PRETEXT III in 15% and PRETEXT I in 8% of patients. The median AFP level was 83000ng/mL (320-1129000). Histopathologic examination revealed epithelial HB in 69% (fetal in 46%, mixed fetal+embryonal in 23%), epithelial+mesenchymal HB in 23%, HB not-otherwise specified in 8% of patients.

PRETEXT I-II HB (n:5) Primary (n:3), and delayed (n:2) surgery were performed without residue. Chemotherapy was given accordingly to SIOPEL1 in one, SIOPEL3 in four patients. For a 16.5 year-old girl who had PRETEXTII-HB relapsed at primary site at the 20th month, and died with progression at the 58th month. Other cases has been followed-up without disease. Median follow-up time was 3yrs (13mos-12.5yrs).

PRETEXT III-IV HB (n:8): Patients received SIOPEL3 (n:4) and SIOPEL4 (n:4) chemotherapy schema. Delayed surgery was performed in all patients of which liver transplantation was done in six. Surgical margin was tumor positive in one, and residual tumor thrombus remained in one, both patients relapsed and died with progression. First one had out of primary relapse at the 13th month and died at the 15th month. Second one relapsed at primary site at the 11th month and died at the 14th month. Median follow-up time was 16.5months (9mos-4yrs). Two- and 4-years EFS were 71% and OS were 69%.

Conclusions

The oldest patient had poor outcome despite having PRETEXTII-HB. Residual tumor after liver transplantation had resulted an early relapse and death in two cases.

Multidisciplinary treatment and performing surgery in experienced centers are essential in management of HB.

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Liver Tumours

MANAGEMENT OF PEDIATRIC HEPATOCELLULAR CARCINOMA: A MULTIMODAL APPROACH

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Objectives

Pediatric hepatocellular carcinoma (HCC) is exceedingly rare and accounts for 0.5-1.5% of childhood tumors. Survival rates for primary unresectable HCC have been dismal. Cisplatin and doxorubicin (PLADO) regimen has demonstrated a 5-year event free and overall survival of 17%, and 28%, respectively. Adjunctive sorafenib has shown favorable results in adults with very little, but promising, data in children. Furthermore, hepatic arterial chemoembolization (HACE) has been proven as an effective treatment strategy to achieve resectability with minimal systemic toxicities. Liver transplant may be considered with unresectable HCC. Our objective is to describe a multimodal approach for management of unresectable HCC.

Methods

Case report and literature review.

Results

A 12 year-old girl presented with abdominal pain, firm hepatomegaly and elevated alpha-fetoprotein (62,645 ng/mL; range <6). MRI abdomen revealed a large liver mass involving all sections and the left portal vein. Liver biopsy showed poorly differentiated HCC with angiolymphatic invasion and fibrosis. Metastatic work-up was negative. She underwent 5 cycles of PLADO and sorafenib followed by HACE with doxorubicin and mitomycin to further decrease tumor burden. Alpha-fetoprotein levels declined dramatically with reduction in liver size allowing complete tumor resection and orthotopic liver transplant. Explanted liver demonstrated 20-30% tumor viability. Sorafenib was restarted but discontinued after 4 months due to significant hand-foot syndrome. A trial of sirolimus (mTOR inhibitor) for post-transplant immunosuppression was initiated for added benefit of recurrence risk reduction; however development of mild acute rejection resulted in restitution of tacrolimus. She is currently 21 months post-transplant and in remission with a 100% performance score.

Conclusions

Limited pediatric literature exists on HCC management, especially in unresectable cases. Multimodality treatment involving chemotherapy with PLADO and sorafenib, HACE, timely liver transplantation, and mTOR inhibitors in the post-transplant period may help improve outcomes and prolong survival in pediatric patients with unresectable HCC.

EP-275

Liver Tumours

STUDY ON THE CLINICAL CHARACTERISTICS AND PROGNOSTIC FACTORS IN 15 CASES OF HEPATOBLASTOMA

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Objectives

To investigate the clinical characteristics and survival analysis of childhood hepatoblastoma for prognostic factors.

Methods

Between February 2009 to September 2012, 15 cases of hepatoblastoma diagnosed in Shanghai children's hospital were included in this study, with 9 boys and 6 girls, median age was 19 months (range, 3-51 months). Follow up to December 30, 2013, the median follow-up time was 34 months (9-58 months). All patients' staging referred to Pretext staging before operation. Surgery and chemotherapy were used according to different stage. Evaluation of correlation between the survival rate, stage and treatment strategies.

Results

According to Pretext staging, the number of cases in stage II, III and IV was 3(20%), 10(66.7%) and 2(13.3%). The 5-year overall survival (OS) of stage II, III and IV were 100%, 90.0%±9.0% and 50.0%±35.4%(P=0.304); and the EFS were 100%, 67.59%±20.7% and 0%(P=0.012). 2 cases received tumor complete excision at first diagnosis both cured. 13 cases received chemotherapy after tumor biopsy, second tumor resection were given when tumor shrinkage. 2 cases of 13 relapsed, 11 cases cured.

Conclusions

Onset age of pediatric hepatoblastoma were younger, Surgical resection combined with preoperative and postoperative chemotherapy was the main way to improve the survival rate. Stage and complete resection may be the risk factors with children hepatoblastoma.

EP-276

Liver Tumours

PEDIATRIC HEPATOBLASTOMA IN THAILAND: AN 18-YEARS EXPERIENCE IN SINGLE INSTITUTE

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Objectives

To assess the treatment outcome and disease-free survival (DFS) of children with hepatoblastoma who were treated at our institute.

Methods

We retrospectively reviewed the medical record of hepatoblastoma patients under 15 years old who were diagnosed and treated at Siriraj hospital, Thailand during June 1994 to December 2011. The demographic data, investigation results, treatment approach and treatment outcome were collected and analyzed.

Results

Forty-one patients were diagnosed with hepatoblastoma during the study period, with the median age at diagnosis 1.17 years old (range 0-11.05 years old). Patients had the following Children Oncology Group (COG) stages: I (22%), II (2.4%), III (56.1%), and IV (19.5%). Seven patients (17.1%) had initial lung metastasis. Thirteen patients with resectable tumor underwent upfront surgery followed with adjuvant chemotherapy. The remaining 28 patients received neoadjuvant chemotherapy; 23 of these patients achieved total tumor removal later. The most common chemotherapy regimens were continuous doxorubicin plus either carboplatin or cisplatin. Eighteen patients (43.9%) had hematologic toxicity; cardiotoxicity was not reported. Thirty-one patients achieved complete remission; 4 patients subsequently had local relapsed at the median duration of 1 year (range 0.25-1.7 years). Eleven patients (26.8%) died of disease. Median follow-up time was 5.1 years (range 0.2-18.4 years). Five-year DFS for COG stage I, II, III, and IV were 77.8%, 100%, 73.9% and 25%, respectively. DFS was significantly better in those who achieved total tumor removal ($p=0.013$), and significantly worse in those with metastatic disease ($p=0.002$).

Conclusions

Treatment outcome of hepatoblastoma in developing country is comparable to that of developed country. Total tumor removal is the key of the treatment success. Neoadjuvant chemotherapy, rather than attempt surgery, is suggested if complete resection is unlikely at the beginning. Total tumor removal can eventually be achieved in most cases, leading to a more favorable outcome. However, more intensive treatment is needed in metastatic disease.

EP-277

Liver Tumours

PAPILLARY THYROID CARCINOMA AFTER CHEMOTHERAPY AND LIVING-DONOR LIVER TRANSPLANTATION FOR HEPATOBLASTOMA

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Objectives

Hepatoblastoma is a rare childhood malignancy and may present as a familial cancer such as familial adenomatous polyposis (FAP). However, association of papillary thyroid carcinoma and hepatoblastoma has been rarely reported.

Methods

We describe here a girl who had papillary thyroid carcinoma after treatment for hepatoblastoma.

Results

The patient was diagnosed as having non-metastatic PRETEXT III hepatoblastoma at six-month old age, and underwent preoperative chemotherapy (cisplatin/pirarubicin, Ifosfamide/pirarubicin/etoposide/carboplatin) followed by living donor liver transplantation from her mother. She received postoperative three courses of irinotecan. During follow up, chest-abdominal CT scan accidentally revealed thyroid mass, and fine needle aspiration biopsy led to the diagnosis of papillary carcinoma. At nine years old, total thyroidectomy and cervical lymph node dissection was performed and the disease was diagnosed and staged as papillary carcinoma pT3 N1b pEx with lymph node metastasis. Because of extrathyroid extension and lymph node metastasis, radioiodine ablation was performed to prevent recurrence.

Conclusions

Papillary thyroid carcinoma is rare in childhood, and has been reported to be associated with radiation exposure.

Association of hepatoblastoma with papillary thyroid carcinoma might be related to FAP. However, the patient has no history of radiation exposure, no family history suggesting FAP, and pathology of the thyroid cancer was not cribriform pattern that is typical to FAP. FAP mutation analysis was currently underway.

EP-278

Lymphomas

PRIMARY IMMUNODEFICIENCY DISEASES (PID) PRESENTING AS LYMPHOMA AND TREATED WITH HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT): DESCRIPTIONS OF 6 PATIENTS

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Objectives

PIDs are one of the risk factors for lymphoma in children. Management strategies for lymphoma due to PIDs are still evolving. HSCT is the treatment of choice for many PIDs. We present 6 patients who underwent HSCT who presented with lymphoma due to PID

Methods

We retrospectively reviewed clinical details and outcome of six patients with PID who presented with lymphoma.

Results

Patient1

4 years old boy diagnosed as EBV driven lymphoproliferative Disease (LPD) resembling Hodgkin Disease and confirmed as Interleukin 2 inducible T cell Kinase (ITK) deficiency.

Patient2

Brother had ITK deficiency. Therefore he was confirmed to have ITK deficiency at birth. While waiting for transplant, he developed EBV driven LPD similar to Diffuse Large B cell Lymphoma (DLBL).

Patient3

12 year old boy diagnosed as MALT lymphoma and found to have Combined Immune Deficiency (CID).

Patient4

11 year old boy diagnosed as EBV negative DLBL and confirmed as CID.

Patient 5

One year old boy diagnosed as CID due to T cell activation disorder and developed multiple lymphadenopathies, confirmed as EBV positive LPD.

Patient6

5 year old girl with family history of family history of undiagnosed PID and developed Nodular Sclerosing Classical Hodgkin Disease and subsequently confirmed as CID.

All patients had successful HSCT. Lymphoma resolved in all patients. All patients are surviving at different post transplant follow up periods. They are 28, 2, 13, 9, 18, and 45 in months respectively in patients 1 to 6.

Conclusions

PID should be ruled out in all atypical, chemotherapy resistant, or relapsed cases of lymphoma. As chemotherapy is unlikely to be effective in lymphoma due to PID and HSCT is the treatment of choice for several PIDs, HSCT can be curative for lymphoma due to PIDs.

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Lymphomas

INTRACARDIAC LYMPHOMA; TREATMENT CHALLENGES AND OUTCOME IN A RESOURCE LIMITED SETTING

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Objectives

To highlight the need for early recognition, diagnosis and the challenges involved in the treatment of intracardiac lymphoma.

Methods

Malignant lymphoma presenting as intracardiac mass is rare. Morbidity and mortality may be high if associated with pericardial effusion and cardiac tamponade without timely interventions.

A 9-year old girl who presented to our Children Emergency Ward with clinical features of pericardial effusion with cardiac tamponade is reported. Echocardiography confirmed massive pericardial effusion with a huge mass attached to the anterior tricuspid valve that impeded diastolic flow into the right ventricle, a dilated right atrium with interatrial shift to the left almost collapsing the left atrial wall. She had emergency pericardiostomy and pericardial biopsy done. Cytology and histology reports of pericardial fluid and biopsy confirmed B-cell Non-Hodgkin lymphoma positive for CD 45 and CD 20, negative for CD 3, CD30 and CD 34 on immunohistochemistry. Peripheral blood and bone marrow were free of blasts. She had pre-phase cylophosphamide, oncovin and prednisolone (COP pre-phase) for one week followed by cylophosphamide, oncovin cytosine arabinoside and prednisolone (COAP) regimen. She received only two of six cycles of COAP for financial reasons. Serial follow up echocardiography at the end of the COP pre-phase and at the end of each cycle of COAP confirmed significant reduction in intracardiac mass. She was alive and well for one year and later became symptomatic and died.

Results

Nil

Conclusions

Intracardiac lymphoma is rare but life-threatening if associated with pericardial effusion and cardiac tamponade. Cost of treatment is enormous and challenging in resource limited setting.

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Lymphomas

NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMAS. EXPERIENCE IN A SINGLE INSTITUTION IN ARGENTINA

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Objectives

Nodular lymphocyte predominant Hodgkin Lymphoma (NLPHL) represents 5% of Hodgkin Lymphoma (HL) and has distinct clinical-pathological features with an overall good prognosis. Treatment strategies have been based on protocols for HL. Selected patients can be treated with surgery alone.

Our aim was to describe the clinical characteristics, management and outcome of patients with NLPH.

Methods

Between October-1997 and January 2014, 13 patients (11 M/2 F), median age: 9.8 (range 4.9-14.5) years, were consecutively diagnosed in our institution. Initial chemotherapy schedules were ABVD (Doxorubicin, Bleomycin, Vinblastine and Dacarbazine), COPP/ABVD or AV-PC (Adriamycin/Vincristine/Prednisone/Cyclophosphamide). When response was partial or null, additional chemotherapy was administered, IF-RT, Anti CD20 and/or HDC/ASCT. A watch-and-wait strategy after lymph node complete surgery was used in two cases when this strategy became trustworthy.

Results

Eleven patients (84.6%) showed nodal compromise, cervical localization was the most frequent. Ten patients (77%) presented localized disease (stage IA: 8, stage IIA:2) and 3 (23%) advanced disease (stage IIIA:1, stage IVA:1, IVB:1). One patient had B symptoms. Two IA stage cases (15.3%) had complete node resection. Five patients (38.4%) received 4 cycles of ABVD. One patient (7.7%) received COPP/ABVD. Three patients (23%) received 3 cycles of AV-PC. One patient (8.3%) received 6 cycles of AV-PC plus 4 doses of Rituximab. One patient (8.3%) presented progressive disease after 3 cycles of ABVD, additional chemotherapy was administered and HDC/ASCT. Three (23%) received IF-RT plus chemotherapy. One patient is still on treatment. Response to treatment was: CR 8 pts (66.6%), Partial-response: 2 pts (16.6%), NR: 2 pts (16.6%). Median follow up: 50.5 (range 1-132) months. All patients remain in CR.

Conclusions

Although the management of NLPHL was not uniform in our retrospective analysis, the results were excellent. Tailored therapy according to staging and disease response, seemed to be a good strategy in our setting.

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Lymphomas

3 DIFFERENT TYPES OF MALIGNANCY IN A CHILD DURING DIFFERENT TIME PERIOD OF LIFE

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Objectives

Cancer survivors have a higher risk of new primary cancer, in the same or in another organ, than the general population. We describe a case of 13 yrs. old male who presented with multiple malignancies at 6 , 12 and 13 years of age..

Methods

Pediatric case report

Results

A 5 year old male born to G4 P3 2nd in birth order , non-consanguineous marriage with strong family history of malignancy. His 3 paternal uncles had died of unknown reasons and his elder brother had died of Neuroblastoma Stage IV at 4.5 years of age. His 4th sibling had died of Glioblastoma Multiforme at 1.5 years of age and he had one healthy 7 years old female sibling. He was diagnosed as Stage II ileocecal Burkitt's lymphoma which was surgically resected followed by 2 cycle of COPAD chemotherapy. He was asymptomatic till 12 years of age when he had features suggestive of superior vena cava syndrome. CECT chest showed anterior mediastinal mass. CECT abdomen, bone marrow and CSF were normal. Trucut biopsy was suggestive of Unclassifiable lymphoma. He was treated with 2 cycles of CHOP chemotherapy. Repeat CECT after 2 cycles showed marginal shrinkage so he further received 2 cycles of ICE chemotherapy and after that he went in to CR 2. He underwent autologous stem cell transplant following BEAM conditioning regimen. He was asymptomatic till 100 days post-transplant when he had abdominal lump. CECT abdomen revealed diffuse mesenteric lymphadenopathy with conglomerated necrotic mass encasing SMA. Biopsy and flowcytometry of the mass revealed features of T- cell malignant lymphoma. Genetic studies could not be performed due to monetary problems. Unfortunately due to economic constraints parents opted for palliative care.

Conclusions

Three malignancy during childhood is a rare event. Each family member should be scrutinized in details including genetic studies.

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Lymphomas

AVASCULAR NECROSIS IN PEDIATRIC PATIENTS WITH HODGKIN'S DISEASE IN KING HUSSEIN CANCER CENTER

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Objectives

There is limited data on the incidence of avascular necrosis (AVN) of bone in adolescents and children with HL. We reviewed our institutional experience were higher incidence of AVN is reported.

Methods

We conducted a retrospective analysis of children (<18 years) with Hodgkin's lymphoma who developed AVN during treatment , presented from December 2008 until June 2013. Patients' characteristics, treatment regimen, steroids cumulative dose and treatment modalities of AVN were analyzed.

Results

We identified 9 patients (7 females) who developed AVN during treatment of HL . the median age at diagnosis was 15 years (range 14 to 17). Eight were treated as high risk with BEACOPP regimen and one as intermediate risk with 4 cycles of ABVD and 2 cycles of COPP. An MRI of the lower limbs was requested during therapy due to symptoms . The cumulative dose of steroids (range 1.2 gm/m² to 4.8 gm/m²), one patient received radiotherapy with field involving the femoral head . Two patients underwent joint decompression , the rest of the patients (N=7) were treated with conservative management .

Conclusions

We observed higher than expected number of patients with HL who developed AVN. This may reflect genuinely increased risk in our population or under-diagnosis of this condition by others. Careful clinical follow up is warranted to detect the early signs of AVN in adolescents with HL.

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Lymphomas

**AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN
RELAPSED/REFRACTORY LYMPHOMAS IN CHILDHOOD: SINGLE CENTER
EXPERIENCE**

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Objectives

We evaluated treatment outcome of patients with relapsed/refractory lymphoma receiving autologous stem cell transplantation (ASCT) in childhood.

Methods

We retrospectively analyzed the outcome of 12 patients who were done ASCT, between January 2012 - December 2013.

Results

The median age was 13,5 years (range, 11-16 years), 8 males, 4 females. There were 5 non-Hodgkin lymphomas (NHL), and 7 Hodgkin lymphoma (HL) patients. Seven patients received BEAM (BCNU, etoposide, ara-C, melphalan), and 5 patients received BuMel (busulfan, melphalan) supported with ASCT.

At the time of study, 10 patients were alive, 2 patients died due to progressive disease. There was no transplant-related mortality. Overall survival (OS) and disease free survival (DFS) were 83,3% and 75% with a median follow-up of 17 months (range, 2 – 26 months) for all patients, respectively. There was no differences in efficacy between the conditioning regimens were found.

Conclusions

ASCT is an effective treatment for patients with relapsed/refractory lymphoma. No significant differences in outcomes were observed between BEAM and BuMel conditioning regimens.

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Lymphomas

COMPARISON OF TWO TREATMENT REGIMENS IN NON HODGKIN LYMPHOMA PATIENTS; SINGLE INSTITUTION EXPERIENCE AT CHILDREN HOSPITAL, LAHORE

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Objectives

The Children Hospital, Lahore is a tertiary care Pediatric Hospital in Pakistan with a 60 bedded Hematology/oncology unit. We report our experience in treating Non Hodgkin Lymphoma (NHL) using 2 regimens, CCLG-NHL guidelines and MCP842 protocol in 50 patients

Methods

Fifty consecutive biopsy proven patients of NHL (Burkitts, Burkitt-like and Diffuse Large B cell Lymphoma) were included in the study. The first 25 patients were treated according to CCLG guidelines(containing High dose Methotrexate,3-6 gm/m²) and the next 25 according to the less intensive MCP842 consisting of cyclophosphamide, adriamycin, vincristine, ara-C, etoposide, ifosfamide & low dose methotrexate(15 mg/m²).

Results

There were total of 50 patients. Thirty seven (74%) patients were male. Majority 29(58%) of patients were 5-9 years of age. Majority presented with abdominal symptoms 48(96%). Abdominal mass 33(66%), intussusception 9(18%), and intestinal obstruction was presenting complaint in 6(12%) patients. One patient each had nasopharyngeal mass and symptoms of obstructive uropathy. Majority 40(80%) presented in stage III, 10(20%) in stage IV. None presented in stage I or II. The group that received treatment according to CCLG guidelines, overall survival was 7(14%)with abandonment and 37% without abandonment, 12(24%) expired, 6(12%) left against medical advice (LAMA). Cause of mortality was high dose methotrexate(MTX) toxicity in 06(12%),sepsis in 03(08%), not documented in chart 3(6%) Overall survival had been 17(68%) with abandonment and 85% without abandonment for patients treated with MCP842 protocol, 2(8%) relapsed, 01 (04%) expired due to sepsis, 05(20%) LAMA.

Conclusions

High dose MTX toxicity has been a major cause of mortality in patients receiving treatment according to CCLG guidelines. MCP 842 involving low dose MTX was better tolerated in our patients. Therapy was offered mostly on outdoor basis and had better outcome. In developing countries need is to adopt protocols that demand limited supportive care facilities and are more tolerable

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Lymphomas

STUDY OF 4 CASES OF PRIMARY BONES OF LYMPHOMA

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Objectives

Hodgkin and non-Hodgkin lymphomas represent approximately 10-15% of tumors in children under 15 years. Bone presentation is very rare in children; diffuse large B-cell lymphoma of the most frequent.

Methods

We report 4 cases of lymphoma of bone as a primary site; admitted between December 2010 and February 2014.

Results

There were 2 females and 2 males, aged between 10 and 15 years. All patients had bone pain as the main symptom. Some associated with claudication and paresthesia. The time of onset of symptoms was five months to a year. The diagnoses were confirmed by biopsy. According to histology and clinical aspects they were: 1-lymphoblastic lymphoma B left acetabulum - stage IV; 1-Lymphoblastic Lymphoma T right tibia - stage III; 1-diffuse large B-cell lymphoma in the left humerus - stage III and 1-diffuse large B-cell lymphoma in right iliac bone with involvement of the pubis and ischium body - stage III.

Immunohistochemical exam with Ki-67 (90 %) in all cases, TdT, CD45, CD20, CD99, CD 79a, CD 43 positive, confirmed the diagnosis.

Conclusions

The clinic, the radiology (bone destruction, lytic areas, sclerotic variables and involvement of the entire bone with extension into the soft tissues) and the histology (diffuse infiltration of small, round cells) are not specific to bone lymphomas. Because of that is mandatory to extend the immunohistochemical panel including CD99, TdT, CD 43 and CD 79a (done for these cases), avoiding possible errors in diagnosis.

We conclude that bone lymphomas should be included in the differential diagnosis of bone tumors.

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Lymphomas

CLINICAL CHARACTERISTICS AND TREATMENT OUTCOME OF PEDIATRIC HODGKIN LYMPHOMA AT CHILDREN HOSPITAL BENGHAZI - LIBYA

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Objectives

Lymphoma is the third most common childhood malignancy. However, little data is available on lymphoma in our developing country. The present work was performed to identify clinical characteristics and treatment outcome of pediatric Hodgkin lymphoma (HL) at our center.

Methods

A retrospective study on 51 patients diagnosed with HL between 1995 and 2012. Used chemotherapeutic regimens were ABVD, COPP. For stage IV BEACOPP (Bleomycin, Etoposid, Adriamycin, Cyclophosphamide, Vincristin, Procarbazine, Prednisolone) and VVAC (Vinblastin, Vp16, AraC, Cisplatin) were added. 30 patients received radiotherapy. Ann Arbor HL staging criteria was applied for staging. Rye system was used for histopathologic examination. Treatment outcome was evaluated using Kaplan-Meier methods. Differences between outcome were tested using Logrank test.

Results

There were 34 males and 17 females. Male to female ratio was 2:1. Median age was 9 years (4-14 years). Bulky disease and B symptoms found in 7 and 27 patients respectively. Stage distributions were 11, 9, 19, and 12 patients in stage I, II, III, and IV respectively, 60.8% patients presented at stage III and IV. Histopathologic subtypes were nodular sclerosis, mixed cellularity, lymphocytic predominance, lymphocytic depletion in 22, 19, 9, and 1 respectively, 80% of death and 60.5% of relapse in mixed cellularity. 84.3% patients had complete remission, 5.9% relapsed then cured, 9.8% relapsed and died. Overall survival (OS) and event-free survival (EFS) rates were 90.2% and 84.3% respectively with median follow up of 5 years. OS rate was 75% with bulky disease and 95.3% without, ($P>0.05$). OS rate was 88.9% with B symptoms and 97.7% without, ($P>0.05$). Histopathology, stage, and relapse had effect on OS rate, ($P<0.05$, $P<0.01$, $P<0.05$) respectively.

Conclusions

Stage, histopathology, and relapse are statistically significant predictive factors for OS rate. Our patients are commonly presented with advanced stages; further studies are required to evaluate causes.

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Lymphomas

PAEDIATRIC PLASMABLASTIC LYMPHOMA: A SINGLE UNIT EXPERIENCE IN KWA-ZULU NATAL, SOUTH AFRICA

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Objectives

To describe patient characteristics, treatment response and survival of patients with Plasmablastic Lymphoma, at a single centre from 2003 – 2013

Methods

A retrospective chart review of patients with Plasmablastic Lymphoma diagnosed between January 2003 and December 2013

Results

Sex	Age at Diagnosis	Site	Stage	Treatment	Survival
M	12Y	Jaw, Zygomatic arch, abdominal mass, bone marrow	4	COP x 2 ACOP-BVM x 4	Died after 16m Palliated
M	6Y	maxillary antrum	2	COP x 2 ACOP-BVM x 10	Alive after 5yrs
M	5Y	maxillary antrum	2	COP x 1 COPADM x 3	Died after 12m, Palliated
M	10.5Y	maxillary antrum	2	COP x 1 COPADM x 3 DXT to oral cavity	Alive after 21m
F	11Y	multiple bone lesions	4	COP x 2 COPADM x 3 ongoing	Alive after 4m, on treatment

5 patients were diagnosed with Plasmablastic Lymphoma. There was a male predominance. All 5 patients were Black. Three patients had stage 2 disease, and two patients had stage 4 disease. 4/5 patients presented with maxillary/nasal masses, 1 had abdominal and maxillary disease, and the female patient presented with multiple bony lesions. None of the patients had CNS involvement. All patients were HIV positive and were HAART (highly active anti-retroviral disease) naive at diagnosis. CD4 counts were available in 4 patients. 2 patients had CD4 counts < 100, and the count was 390 and 629 in the other 2 patients. 2 patients were treated with cytoreductive therapy (cyclophosphamide, vincristine, prednisone - COP), followed by a hybrid of vincristine, doxorubicin, cyclophosphamide and prednisone alternating with bleomycin, methotrexate and vincristine. 3 patients were treated using a BFM based COPADM protocol.

Conclusions

Plasmablastic Lymphoma is a rare HIV associated malignancy with a predilection for the nasal and maxillary areas. Low CD4 counts are not predictive of survival. Treatment protocols are poorly defined.

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Lymphomas

ROLE OF FDG-PET SCAN IN THE MANAGEMENT OF MATURE B CELL PEDIATRIC NON-HODGKIN'S LYMPHOMA. CCHE EXPERIENCE

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Objectives

To evaluate the sensitivity, specificity and predictive values of PET scan during management of pediatric Non-Hodgkin's lymphoma(NHL).

Methods

A retrospective study enrolled on pediatric patients with NHL at Children Cancer Hospital of Egypt (CCHE) during the period from July 2007 till end of June 2013 was done. Inclusion criteria included the diagnosis of mature B cell NHL, for whom PET - in addition to conventional CT scan- was done at any stage of the treatment. Blind revision of all PET and CT scans was specifically done for this study.

Results

For 115 pediatric NHL patients, 152 PET and 152 CT scan were done. Median age was 5.7 years (range 1-18 years). They were 85 males (74%) and 30 females (26%). One hundred twenty six scans (82.9%) were done for 100 Burkitt lymphoma patients, while 26 scan (17.1%) done for 15 DLBC. Nineteen examination (12.5%) were done before starting chemotherapy, 107 (70.3%) at time of evaluation while 26 (17.1%) during Follow up. For all patients, sensitivity was 91.6% for PET, while was 70.0% for conventional CT (p=0.02). Specificity was 84.1% for PET and 58.9% for CT (p< 0.001

In burkitt lymphoma; sensitivity of PET was 91.6%, while was 66.6% for CT (p=0.08).

Specificity was 82.4% and 57.8% for PET and CT respectively (p=

Conclusions

PET scan is significantly more sensitive than conventional CT in the management of aggressive mature B cell pediatric NHL.

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Lymphomas

CLINICAL REVIEW OF 18 POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD) CASES ARISING IN YOUNG LIVER TRANSPLANT RECIPIENTS

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Objectives

To make the clinicians have a better understanding of PTLD in young children, reduce the delayed diagnosis in early stage, and to explore feasible means for the prophylaxis and treatment.

Methods

Retrospective analysis of clinicopathologic features, and treatment outcome in 18 consecutive cases with PTLD after liver transplant from January 2001 to December 2012. The initial symptoms, delayed diagnosis time, both of the EBV and CMV status, completely blood count, LFTs, pathology results, imaging results, treatment outcome were reviewed respectively.

Results

6 cases were diagnosed clinically, majority of them had the IM-like symptoms, snoring, and deranged LFTs, the median time from initial symptoms onset to PTLD diagnosis was 2 months. 12 cases had the histopathology diagnoses, and the initial symptoms were various among the different pathological subtypes, and T-cell mononorphic LPD cases were more systemic and aggressive. For these 12 cases, the interval between initial symptoms onset and the final diagnosis were also various, **12** out of 18 had a delayed diagnosis due to the extra-nodal/graft organ involvement or the especial clinical manifestations. PTLD treatment consisted of reducing or stopping the immunosuppressant, followed by rituximab and chemotherapy if required. 16 cases were in remission (CR=15, PR=1) and two died of PTLD related multiple organ failure. The episode of liver rejection post-PTLD was in 2 cases. Two-year OS and EFS were 75% and 88.9%, respectively.

Conclusions

The delayed diagnosis of PTLD in young children was common due to the various clinical manifestations among different pathological subtypes. The timely diagnosis and treatment were very essential to the prognosis. Rituximab was an efficacious drug for PTLD. Since the high incidence of PTLD after liver transplant, the rejection episodes post-PTLD was few, and relapse of disease was possible, it was always essential to keep low dose immunosuppressant if possible. Monitor the patients during and after treatment of PTLD are necessary.

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Lymphomas

CLINICAL REVIEW OF MEDIASTINAL T-LYMPHOBLASTIC LYMPHOMA (T-LBL) IN PEDIATRIC PATIENTS - A SINGLE CENTER EXPERIENCE FROM CHINA

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Objectives

The clinical features and the treatment outcome of mediastinal T-LBL in Beijing Children's Hospital were studied.

Methods

We retrospectively examined the clinical features and treatment outcome of 54 patients with mediastinal T-LBL, within the period of Jan. 2003 to December 2009 (18 cases did not have the bone marrow involvement, 6 cases were <25% bone marrow involvement, the rest 30 cases had >25% bone marrow involvement). We used the modified BFM 90 LBL protocol.

Results

1) In 72 newly diagnosed T-LBL cases, with a median age of 7.9 years, 18 patients (25%) had "B" symptoms, 54 (75%) had bulky mediastinal mass (diameter >10cm), and 15 cases (27.7%) had superior vena cava syndrome (SVCS), 9 cases (16.7%) had the upper airway obstruction symptom, 5 cases had the acute tumor lysis syndrome (ATLS). 2) Among the 54 cases, the median time from initial symptoms onset to the final diagnosis was 34d. 3) In our study group (n=54), stage I n=24, stage II n=30. 11 cases had elevated uric acid (UA), and 44 cases had elevated lactate dehydrogenase (LDH), among the 44 cases, 15 cases were >1000U/L, 29 cases were >500U/L. 4) 7 cases died during or after chemotherapy (6 was dead as the disease progress or relapse, 1 was dead because of the severe infection). Estimated the 5-year overall survival (OS) and event free survival (EFS) were 84.4% and 80.5% respectively.

Conclusions

Bulky mass was common in T-LBL, which mostly cause SVCS, upper airway obstruction or ATLS, and the advanced disease (stage II & III) was common. It was a dependent poor prognostic factor.

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Lymphomas

CLINICAL REVIEW OF 4 B-CELL LYMPHOBLASTIC LYMPHOMA (B-LBL) WITH CUTANEOUS INVOLVEMENT CASES IN CHINESE CHILDREN

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Objectives

B-cell Lymphoblastic lymphoma (B-LBL) with cutaneous involvement is special, and we sought to describe the clinical-pathological features and the treatment outcome of these patients in Beijing Children's hospital.

Methods

We retrospectively examined the clinical-pathological features and treatment outcome of 4 patients with cutaneous involvement out of 40 new diagnosed B-LBL.

Results

- 1) 4 patients all had one skin lesion involvement (head/neck/lower limb), no patients developed multiple skin lesions.
- 2) The median time from initial symptom onset to the final diagnosis was 120d (range from 30d to 240d), 4 cases all had a misdiagnosis at first.
- 3) In our study group, 4 cases all had a systemic disease, stag? n=4.
- 4) Complete remission (CR) was achieved in 4 patients, no patients dead, no patients relapsed during the study period, the 5-year overall survival (OS) and event free survival (EFS) were both 100%.

Conclusions

Cutaneous involvement was a special characteristic of B-LBL, and it was not a dependent risk factor, which was easily misdiagnosed initially, the advanced disease was more common than literatures reported, the prognosis was better.

EP-292

Lymphomas

A SINGLE CENTER CLINICAL ANALYSIS FOR CHILDHOOD NON HODGKIN'S LYMPHOMA

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Objectives

To retrospectively analyze the clinical efficacy for childhood non Hodgkin's lymphoma (NHL) according to 2008 World Health Organization classification of tumors.

Methods

From January 2000 to December 2012, 58 patients newly diagnosed with NHL verified by clinic, imaging, cell morphology and immune phenotype, histopathological classification. There were 56 patients in total received treatment, 45 males and 13 females. The average age was 6.8 years (ranged from 2 years to 14 years). According to St. Jude staging classification, 6 of 56 cases (10.7%) were divided into stage II, 25 cases (44.6%) into stage III and 25 cases (44.6%) into stage IV. The chemotherapy regimens were based on phenotype, pathologically sub-classified and clinical stages. Precursor / lymphoblastic lymphoma received the treatment as acute lymphoblastic leukemia.

Results

1. Among 56 cases, 25 (44.6%) were Burkitt's/Burkitt's like lymphoma, 13 (23.2%) were anaplastic large cell lymphoma (ALCL), 5 (8.9%) were diffuse large B-cell lymphoma (DLBCL) and 13 (23.2%) were precursor / lymphoblastic lymphoma (11 cases were T cell and 2 cases were B cell).
2. The Kaplan-Meier estimates of 5-year event-free survival (EFS) was 83.7% for all patients (figure 1) while 96% for Burkitt's/Burkitt's like lymphoma, 58.3% for ALCL, 80% for DLBCL and 84.6% for precursor / lymphoblastic lymphoma (figure 2). The difference of 5-year EFS between Burkitt's/Burkitt's like lymphoma and ALCL was significant ($P=0.004$), while the difference of ALK positive or not in ALCL was not ($P>0.05$).
3. 5-year EFS was 100% for stage II, 79.6% for stage III, 83.8% for stage IV ($P=0.245$).

Conclusions

Correct cell phenotype and pathologically diagnosis of NHL are the key step for the prognosis for NHL. Burkitt's/Burkitt's like lymphoma have good prognosis in child though it is aggressive. Current treatments are effective and safe for childhood NHL.

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Lymphomas

PATTERNS OF FAILURE AND OUTCOME OF PEDIATRIC PATIENTS WITH RELAPSED OR PROGRESSIVE HODGKIN LYMPHOMA

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Objectives

In this study, we present clinical characteristics, failure patterns and outcomes of pediatric patients with Hodgkin lymphoma (HL) treated with chemotherapy and low- dose involved field radiotherapy (LD-IFRT) in a single institution.

Methods

This retrospective analysis comprise 123 patients with HL treated at our institution from 1990 to 2013 who received four or six cycle of ABVD/COPP alternating chemotherapy based on their stages followed by LD- IFRT (20-25 Gy).

Results

Out of 123 patients nine had recurrence or progression at 1- 58 months after the diagnosis. Median follow-up was 68.6 months (8-152 months) after the progression or recurrence. The mean age at diagnosis was 12.8 ± 3.4 years. Five patients had localized (Stage IIA, IIB) and four patients had advanced disease (stage IIIB,IV) at diagnosis. Two patients had progressive disease during first line chemotherapy: One of them did not respond to high dose chemotherapy (HDCT) and autologous hematopoietic stem cell transplantation (HSCT), and died of disease. The other patient was lost to follow-up with disease. Two patients had early relapse while five patients had late relapse. One patient with early relapse died with disease in 2 months during salvage therapy. The other patient with early relapse received HDCT allogeneic HSCT and is alive at 104 months without disease. Five patients with late relapse achieved complete remission (3 with autologous HSCT, two with second line chemotherapy) and are alive without disease at 14-125 months from recurrence. Three patients had local, two patients had distant, and two patients had both local and distant relapses. The lung parenchyma was the most common extralymphatic site of involvement (44%) in patients with relapsed or progressive disease.

Conclusions

We have seen both local and distant relapses in almost equal number of patients. The outcome of the patients with early relapse or progressive disease was poor.

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Lymphomas

PEDIATRIC T-CELL-RICH LARGE B-CELL LYMPHOMA: CLINICAL FEATURES, TREATMENT, AND OUTCOME

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Objectives

T-cell-rich large B-cell lymphoma (TCRLBCL) is a subtype of diffuse large B-cell lymphoma (DLBCL) characterized by small numbers of scattered large B-cells with numerous reactive T-cells. Pediatric TCRLBCL is uncommon and not well understood. The goal of this preliminary study is to characterize the clinical features of pediatric TCRLBCL at primary diagnosis, treatment, and outcome.

Methods

Three pediatric patients with TCRLBCL were evaluated for clinical features, treatment, response to therapy, and outcome.

Results

Clinical features included: age 14-16 years; male: female 2:1; Murphy stage – I (axilla), II (cervical, tonsil, nasopharynx), III (abdomen, pelvis, spleen, spine/epidural); elevated lactate dehydrogenase 1. Treatment was according to the CCG-5961 protocol with the two patients with stages I and II following arm B1, and the patient with advanced disease (stage III) following arm C1. All patients achieved a complete response (CR), and had no subsequent relapse and remain in remission for more than ten years from diagnosis.

Conclusions

Pediatric TCRLBCL occurs in adolescents, and may present in lymph nodes or extranodal sites as localized or advanced disease. Treatment with a current pediatric B-cell lymphoma regimen in these patients achieved CR with durable remission.

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Lymphomas

LATENT EPSTEIN-BARR INFECTION AND IMMUNOLOGICAL STATUS OF THE HOST IN PEDIATRIC HODGKIN LYMPHOMA. A SINGLE CENTER STUDY

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Objectives

Association between latent Epstein-Barr virus (EBV) infection association and Hodgkin Lymphoma (HL) is well documented. However scanty data on host immunological status in aspect of EBV latent infection of Hodgkin and Reed-Sternberg cells are available for pediatric patients.

Methods

To assess the impact of latent EBV infection on immunological status of the patient an analysis of 61 HL cases (age 2.6-18.0; median: 14,2 years) was performed. HIV infection and inherited immune deficiency syndromes were excluded. EBV status of neoplastic cells was determined by EBER-specific in situ hybridization and by immunohistochemical LMP-1 protein detection (respectively 27 and 14 cases were positive) as well. Serum IgA, IgM and IgG concentration data were collected for 59 cases. Lymphocyte subpopulation studies were available in 47 cases and lymphocyte transformation tests were performed in 16 cases only. Immunological tests results were compared both for LMP-1 expression status and EBER status as well.

Results

No differences between both groups of patients were found for IgA and IgG serum concentration. IgM serum concentration was significantly lower ($p=0.03$) in LMP-1 positive than in LMP-1 negative group (median: 1.06 and 1.57 g/L respectively). No differences between groups were also found for serum immunoglobulin concentration below and above the reference values. Also a trend towards slightly lower IgM concentration in EBER-positive than in EBER-negative cases ($p=0.06$) was observed. No difference in CD3, CD4, CD8 and CD19 lymphocyte subpopulations in respect to LMP-1 or EBER status was found. Only a trend towards higher mitogen response index to PWM was observed ($p=0.07$) in an EBER-positive group. No other differences in lymphocyte transformation tests were found respective to EBER or LMP-1 status.

Conclusions

No relation to EBV status was found except for IgM concentration. Larger group is to be analyzed to identify differences between host immunological status and EBV latency in HL.

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Lymphomas

LIFE-THREATENING CONDITIONS AT THE MOMENT OF DIAGNOSIS OF NON-HODGKIN LYMPHOMAS IN CHILDREN.

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Objectives

Non-Hodgkin lymphoma (NHL) is the third most common malignancy in children. Although prognosis is good (5 year survival rates of up to 95%), delayed diagnosis may lead to life-threatening conditions without giving the patient chance to react to the treatment. The aim of the study was to show patients with newly diagnosed NHL who presented life-threatening conditions.

Methods

Among 34 patients diagnosed with non-Hodgkin lymphoma in the Department of Pediatrics, Hematology and Oncology Medical University of Gdansk in years 2008-2014, there were 12 patients who presented life-threatening conditions at the moment of the diagnosis (35%).

Results

Among all the patients there were 20 children with B-cell, 3 with pre-B, 8 with T-cell, and 3 with anaplastic NHL. We observed no life-threatening conditions in children with anaplastic NHL. Children with B-cell NHL presented vena cava inferior syndrome (2 patients), cholestasis with pancreatitis (2), ileus (5), and pleural effusion (3). Patients with T-cell malignancy showed vena cava superior syndrome (4 patients), and cardiac tamponade (1). Almost all the patients with T-, pre-B, and B-cell NHL presented acute tumor lysis syndrome (ATLS). 50% of the patients with life-threatening symptoms were successfully treated with chemotherapy before histopathological diagnosis was made due to emergency.

Conclusions

NHL is a very aggressive malignancy because of its high mitotic index. It may lead to life-threatening conditions in a very short time. Life-saving chemotherapy even without histopathological diagnosis may be needed in order to increase the chances of survival.

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Lymphomas

CLINICAL CHARACTERISTIC AND PROGNOSIS OF POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER: A SINGLE INSTITUTE EXPERIENCE IN JAPAN

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Objectives

Post-transplant lymphoproliferative disorder (PTLD) caused by Epstein-Barr virus (EBV) recently has been recognized as a serious complication of the various organ transplantation. We investigated clinical features of PTLD retrospectively in a single institute in Japan.

Methods

The evaluation period was from July 2004 to February 2014. Seven patients with PTLD (4 male, 3 female) were diagnosed PTLD by the blood examination, lymph node histology and EBV viral load.

Results

PTLD was associated with various organ transplantation (5 heart, 1 lung, 1 liver). In our institute, we have the follow-up of twenty-eight patients post heart transplantation, six post lung transplantation and fifty patients post liver transplantation. Median age at onset was 3.8 years old (range 2-16). Six patients were alive in remission, and one patient died of toxicity. Median time to onset of PTLD from transplantation was 23 months (range, 7-54). Six patients were EBV-seronegative recipient for EBV-seropositive donor. Abdominal lymph node involvements were detected in all cases, and they had severe abdominal symptoms including intestinal perforation. Bone marrow and CNS invasion was not detected. After the reduction of immunosuppressive agents, the chemotherapy combined with rituximab was performed in 6 patients and resulted in remission. A patient had disappeared the lesion by the discontinuation of the immunosuppressive agents.

Conclusions

Although reduction of immunosuppressive agents may be an effective treatment for PTLD, it is difficult to reduce the dose because of the risk of rejection in many cases. All patients but one were EBV-seronegative status, so it could be one of the factor to develop PTLD. Gastrointestinal lesion was detected in all cases, so it was important to select the treatment carefully. We should establish the appropriate treatment strategy according to the prognostic factor because of the distinctive character of PTLD by accumulating more cases.

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Lymphomas

PEDIATRIC HODGKIN LYMPHOMA: EXPERIENCE AT THE CHILDREN'S CANCER CENTER OF LEBANON OVER TEN YEARS

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Objectives

We describe our experience with hybrid chemotherapeutic regimen consisting of COPP with ABV in children with Hodgkin lymphoma (HL).

Methods

65 patients were treated through 2002-2012. Patients were classified into Group 1 (disease stages I and IIA), Group 3 (stage IV), and Group 2 patients not belonging to either.

Results

Median age was 13 years (range, 1-20); M:F was 2:1. 1(1.5%) patient had non classical HL. 24(36.9%) patients had bulky disease (BD), 33(50.7%) had B symptoms, 23(35.3%) had active disease after 2 cycles and 24(36.9%) patients had stage IV disease at presentation. 22(33.8%) patients had Group 1 disease, and were treated with 4 cycles of COPP/ABV, 13 received radiotherapy (RT), and none of them relapsed. 19(29.2%) had Group 2 disease and received 6 cycles of ABV/COPP, 14 had B symptoms, 10 had BD, 2 had ICR after 2 cycles of chemotherapy, and 15 received RT. 24(36.9%) patients had stage IV and were treated with 2 courses of intensive chemotherapy, 18 had B symptoms, 10 had BD, 13 had ICR after 2 cycles, and 18 received RT; 7(29.1%) recurred. Patients who received involved-field RT were 46(70.7%); 5(10.8%) relapsed. At 34-month follow-up, 8 patients recurred, 7 had stage IV disease among whom 6 had B symptoms, 5 had ICR after 2 cycles, 3 had bone marrow involvement, and 1 had BD. 1 patient had stage II BD, with B symptoms, achieved CR after 2 cycles and received RT, however recurred outside RT field. OS and EFS were 98.5% and 86%. All 17 pubertal males developed azoospermia after therapy.

Conclusions

Majority of Lebanese children with HL had advanced-stage disease. Despite excellent OS and EFS, this protocol was associated with azoospermia. Patients who did not have stage IV disease, B symptoms, nor bulky disease and who achieved CR after 2 cycles did not recur regardless of RT.

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Lymphomas

BURKITT LYMPHOMA CHALLENGES IN RESOURCE LIMITED RURAL COMMUNITIES

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Objectives

Burkitt lymphoma (BL); the most prevalent children cancers in Cameroon, is lethal if not treated; but 50% curable with lone cyclophosphamide (CPD) therapy or combination with methotrexate. Huge palliative care responsibilities, challenges and support needs especially for paediatric oncology health professionals exists, compelling a June 2010 - June 2012 cross-sectional community study to ascertain paediatric palliative care, support needs, challenges and also alternative approach to meeting these needs.

Methods

Survey using questionnaires based on aspects of palliative care in relation to the cultural views and traditional beliefs of the community with special attention on paediatric oncology needs where this care and support is provided to ascertain palliative care needs and possible practical interventions.

Results

Much difference exist between the western palliative care and support approach, to this community because of their unique super attachment to their cultural views and beliefs; some of which are not compatible with a typical modern approach. Death rates, as much as 50% result from the late diagnosis, lack of health units, inaccessibility of treatment products and more.

Conclusions

Poverty and primitive cultures noted as the main hurdle not only to accessing BL care and treatment; but also to palliative care and support hence our study outcome will guide our new guidelines drafting and implementation. It is difficult to 'copy and paste' a modern approach to palliative care and support though startling study results portray that, reviewing paediatric palliative care and support guidelines with consideration and probably with the improvisation of the guidelines for resource limited communities may be more beneficial and successful in enhancing quality of life for families with cancer requiring palliative care and support.

EP-300

Lymphomas

EVALUATION OF FDG-PET/CT AND CONVENTIONAL IMAGING TECHNIQUES IN PEDIATRIC HODGKIN LYMPHOMA PATIENTS IN A SINGLE CENTER

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Objectives

We aimed to evaluate the role of FDG-PET/CT in diagnosis, staging and response to therapy during follow-up in children and adolescents with Hodgkin Lymphoma and to compare them with conventional imaging techniques.

Methods

We retrospectively evaluated the FDG-PET/CT and conventional imaging findings of 46 patients with Hodgkin Lymphoma diagnosed between January 2006-December 2013 at Gazi University, Department of Pediatric Oncology.

Results

The mean age of the patients with Hodgkin Lymphoma at the time of diagnosis was $12,1 \pm 3,5$ years (range 5-17) with a F/M ratio of 0,53(16/30). Primary involvement area was head and neck region in 16 patients, mediastinum in 3, head & neck + mediastinum in 24, axillary region in 1 and bone in 2 patients. All of the patients received alternate COPP/ABVD frontline chemotherapy plus involved field low-dose radiotherapy. Median follow-up time was 46 ± 28 months (range 5-94) for the patients. FDG-PET/CT was performed for 40 patients at the time of diagnosis, interim for 16 patients and at the end of therapy for 38 patients. When FDG-PET/CT and conventional imaging techniques at diagnosis were compared, there was no statistically significant difference in determining the stage ($p=0,754$).

The sensitivity and specificity of FDG-PET/CT for evaluation of advanced stage Hodgkin lymphoma were 75% and 100%, respectively whereas positive predictive value (PPV) and negative predictive value (NPV) were 100% and 80%, respectively. The sensitivity and specificity of conventional imaging techniques were 81%, 96% and PPV and NPV were 94%, 86%.

There were 9 patients who had partial regression at interim PET/CT. One of them had a relapse after 2 months, while the other patient was accepted as refractory. There were 7 patients who had normal interim FDG-PET/CT; only one of them had a relapse after 15 months.

Conclusions

We could find no statistically significant difference between FDG-PET/CT and conventional imaging techniques in our patient group but a larger number of patients is needed for evaluation.

EP-301

Lymphomas

CD10 – BCL6 – BCL2 – MUM1 – TCL1 EXPRESSIONS IN CHILDHOOD MATURE B-CELL NON-HODGKIN LYMPHOMA

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Objectives

To differentiate germinal center B-cell like (GCB) and non-GCB B-cell non-Hodgkin's lymphomas (NHL) types with immune phenotype analysis, evaluation of amount of TCL1 expression, and their effects on prognosis are the main objectives of this study.

Methods

The paraffin tissue blocks of 27 patients (age = 3-16 years) with mature B-cell NHL were examined. CD10, BCL6, BCL2, MUM1 and TCL1 expressions were evaluated with the immunohistochemistry staining methods. C-MYC and BCL-2 translocations were evaluated by FISH.

Results

The expressions of CD10, BCL6, BCL2 and MUM1 in Burkitt Lymphomas (BL, n=14) were 78.6%, 100%, 21.4% and 7.1% respectively. GCB phenotype was present in all cases of BL. In cases of diffuse large B-cell lymphoma (DLBCL, n=11) the expressions of these markers were 27.2%, 45.4%, 36.3%, 72.7% respectively. Three cases of DLBCL (27.3%) were GCB phenotype and other 8 cases (72.7%) were non-GCB phenotype. Although there was no statistically significance ($P > 0.05$) between immune phenotype groups and prognosis of DLBCL, we found that overall (OS) and event free survival (EFS) were higher in GCB patients (GCB phenotype = 100% / 100% ; non-GCB phenotype = 71.4% / 71.4%).

The expression of TCL1 in BL and DLBCL were 64.3% and 54.5% respectively. While C-MYC translocation was positive in all BL cases, no C-MYC translocation was found in DLBCL. According to these results there was no statistically significant correlation (Pearson's $R = 0.106$, $P > 0.05$) between C-MYC translocation and TCL-1 expression in mature B-cell NHLs.

Conclusions

In this study, no correlation was found between C-MYC translocation and TCL-1 expression in mature B-cell NHLs. There is a need for future studies with a larger number of patients for immune phenotypic classification in order to show the impact on the prognosis.

EP-302

Lymphomas

POSTTRANSPLANT LYMPHOPROLIFERATIVE DISORDERS: EXPERIENCE OF THREE PATIENTS

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Objectives

To present our treatment experience in posttransplant lymphoproliferative disorders (PTLD).

Methods

Medical records of the patients with diagnosis of PTLD were reviewed. Oncologic treatment details and treatment responses were summarized.

Results

There were three patients with PTLD after liver transplantation (LT). The cause of LT was biliary atresia in two, and chronic liver disease in one of them.

Case1: 27months-old, boy. He applied with fever, abdominal pain and distension at 21st month of LT. Multiple abdominal enlarged lymph nodes, hepatic nodules, bilateral renal infiltrations were detected by CT. Bone marrow examination revealed L3 lymphoblasts, EBER was positive. Burkitt-like lymphoma, EBV-related PTLD was diagnosed. Gancyclovir, 5 courses chemotherapy (prednisolon, VCR, CYC, VP-16, DOXO, it MTX) were given. He has been followed without disease for 13 years.

Case2: 48 months-old, boy. He applied with fever, abdominal mass at 39th month of LT. Multiple enlarged abdominal lymph nodes and thickening of the intestinal walls were detected by CT. Gastrointestinal (GIS) endoscopic biopsy revealed B cell PTLD (CD 20+). At admission EBV DNA and CMV DNA were positive. Acyclovir, gancyclovir and 4 courses of chemotherapy (prednisolon, CYC/rituximab) were given. He has been followed without disease for one month.

Case3: 28 months-old, girl. She applied with diarrhea at 22nd months of transplantaion. Endoscopic GIS biopsy revealed. PTLD(CD 20+) and H.pylori like microorganisms in stomach. Sirolimus and 3 courses of chemotherapy (prednisolon, CYC/rituximab) were given. She has been followed without disease for 6 months.

Conclusions

PTLD may be related with EBV, CMV, H. Pylori. Endoscopic biopsies may be helpfull in diagnosis and follow-up. Complete remission can be achieved by antiviral treatment and reduced intensity chemotherapy. Rituximab is an effective agent in CD 20+ PTLD. In follow-up of patients undergoing solid organ transplantation, symptoms should be carefully evaluated in terms of PTLD.

EP-303

Lymphomas

COMPLEX VIZUALIZATION DIAGNOSIS OF RENAL INVOLVEMENT OF PEDIATRIC NON-HODGKIN LYMPHOMAS

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Objectives

Renal involvement in children with non-Hodgkin lymphomas (NHL) should be specified. We analyzed and assessed a role of ultrasound (US), computed tomography (CT) and magnetic resonance tomography (MRI) data in children with NHL renal involvement.

Methods

It was analyzed results of complex examination (US, CT, MRI) of 21 pediatric patients (age from 2 to 16 years old) with NHL with renal involvement. Statistics was performed with program SPSS19.

Results

We found the following types of renal lesions, based on ultrasound, computed and magnetic resonance tomography data : infiltrative, small focal, medium focal, and nodular. The most common types were infiltrative and focal -76.2% ($p < 0.05$); medium focal type was associated with Burkitt lymphoma (BL) 62.2% ($p < 0.05$). In patients with T-lymphoblastic lymphoma (T-LL) it was found small focal type of lesions in 80% ($p < 0.05$). Nodular type was found in patients with B-lymphoblastic lymphoma and primary mediastinal B-cell lymphoma, but not in BL and T-LL ($p < 0.05$).

Conclusions

It was found a correlation between renal lesion type (based on complex visualization diagnosis) and morphologic and immunologic NHL variant.

EP-304

Lymphomas

ABVE-PC AND MODIFIED BEACOPP REGIMENS FOR HODGKIN LYMPHOMA IN INDIAN CHILDREN: TOXICITY AND OUTCOME

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Objectives

To study the usefulness of ABVE-PC (Adriamycin, bleomycin, vincristine, etoposide, prednisone and cyclophosphamide) and modified BEACOPP (m-BEACOPP) regimens in the treatment of intermediate risk and high-risk Hodgkin's lymphoma (HL) patients regarding their toxicity and outcome.

Methods

High risk patients received 4 cycles of modified BEACOP (m-BEACOPP): bleomycin, etoposide (100 mg/m²/day x3), doxorubicin, cyclophosphamide, vincristine, procarbazine and prednisone (for 7 days) plus 4 cycles of ABVD. Intermediate risk patients received 4 cycles of ABVE-PC (doxorubicin, bleomycin, vincristine, etoposide, prednisone and cyclophosphamide) plus 2 cycles of ABVD.

Results

Over a 4-year period, 14 patients received 55 cycles of m-BEACOPP and 8 received 37 cycles of ABVE-PC. In the m-BEACOPP and ABVE-PC courses respectively, thrombocytopenia (<50,000) occurred in 5.4 % vs 0%; significant anemia (Hb. <8 gm/dl) in 27.2% vs 8.5%; neutropenia (ANC<500) in 50.9% vs 27%; and febrile neutropenia in 34.5% vs. 16.2%. The mean duration of hospitalizations was 4.6 vs 2.9 days respectively. There was one episode of localized infection (hepatic abscess) in the ABVE-PC courses; and none in m-BEACOPP. There were no episodes of bacteremia or sepsis in either regimens. Two of 14 high-risk patients required additional chemotherapy and involved field radiation therapy to achieve complete remission (CR). All 22 patients are in CR and doing well with a median follow-up of 27 months (range 3-35); and there have been no relapses. Thus the relapse free and event free survival are 100%.

Conclusions

m-BEACOPP is more likely to cause cytopenias than ABVE-PC. But both regimens are well tolerated with acceptable toxicity profile in Indian children and thus can be used in most institutions with adequate facilities for optimum supportive care. These two regimens offer a high-rate of remission and relapse free survival in intermediate and high-risk Hodgkin lymphoma patients

EP-305

Lymphomas

CLINICAL PROFILE AND CHEMOTHERAPY RESPONSE IN CHILDREN WITH HODGKIN LYMPHOMA AT A TERTIARY CARE CENTRE

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Objectives

Optimal treatment strategy in children with Hodgkin Lymphoma(HL) still remains controversial, especially in advanced disease.

To review the clinical profile of pediatric HL at a tertiary care centre, and to evaluate the efficacy of chemotherapy (CT) alone as a treatment modality in childhood HL.

Methods

Retrospective evaluation of case records of children treated for HL for five years at a tertiary center in India was done.

Results

Thirty-five children (31 boys, 4 girls) with a median age of 8 years (range 3.5 – 13years) were studied. Twenty-four (68.6%) were <10 years old, and 23 (65.7%) had late stage disease (stage III to IV). B-symptoms were present in 21(60%), bulky mediastinal disease in 9(25.7%), and spleen involvement in 21(60%) cases. None had bone marrow involvement. The histological types were: nodular sclerosis in 10(28.6%), mixed cellularity in 9(25.7%), lymphocyte predominant in 9(25.7%), and unclassified in 7(20%) patients. Most patients received ABVD/COPP or ABVD regimen. Two patients needed BEACOPP due to progressive disease, and 4 patients needed low-dose involved field radiotherapy (RT). At a mean (SD) extended event-free follow-up of 42.7(±17.1) months, 4 patients relapsed. Of these one was lost to follow-up, while 3 were treated with chemotherapy. No child died due to the disease. Two patients had asymptomatic mild restrictive pulmonary function test pattern, while 1 patient developed hypothyroidism after radiotherapy. There was no association of adverse prognostic factors with survival.

Conclusions

Systemic CT alone is an effective therapy in childhood Hodgkin lymphoma. This avoids potential long-term organ dysfunction or secondary malignancy associated with radiotherapy, which may be used as salvage therapy

EP-306

Lymphomas

CLINICOPATHOLOGICAL STUDY OF PEDIATRIC HODGKINS LYMPHOMA WITH IT TREATMENT OUTCOME - A 5 YEARS EXPERIENCE (2008-2012) AT RESOURCE LIMITED SETTING (BPKMCH), BHARATPUR, CHITWAN, NEPAL

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Objectives

To know clinicopathological profile of childhood Hodgkin's lymphoma, chemotherapy effectiveness, outcome and follow up in resource limited setting.

Methods

We analyzed all the patient's records from 2008 to 2012 coming to division of pediatric oncology with the suspicious of lymphoma. We recorded the major clinical details and histopathological reports. Pretreatment assessments were done for staging with hematological, biochemical, radiological and Bone marrow examination. All diagnosed patients were treated with standard chemotherapy Protocol with Doxorubicin, Bleomycin, Vinblastine and Dacarbazine. Radiotherapy was recommended for residual disease and patients were advised for follow up.

Results

There were total 46 Patients diagnosed as Hodgkins Lymphoma during this period. 36 numbers of children started recommended chemotherapy. There were 3 children below 5 years, 24 children between 6 to 12 years of age and 9 children between 13-19 years. 30 out of 36 numbers of patients were male. 89% (32) of children had primary disease in cervical area. Other sites were inguinal, abdominal, waldeyer's ring, axillaries. 42% patients presented within 2 to 6 month of illness, 25% presented before 2 months and 33% presented beyond 6 months. Histological types were Mixed cellularity (44.40%), lymphocyte predominant 36.10% and 19.40% nodular sclerosis. Children present in stage III were 55.60%, stage II 27.8% , 13.90% in stage I and 2.80 % at stage IV. 75% patients completed and cured their primary disease . 25% patients were dropped out due to financial constrain. Only 28% (10/36) childrens were in regular follow up. Organ involvements included Spleen (9/36), Liver (6/36), lungs (1/36) without bone marrow involvement.

Conclusions

Hodgkin's Lymphoma was common in male between 6-12 years. Cervical lymphadenopathy was the commonest presentation. 2/3rd presented after 2 months of illness. Mixed cellularity was commonest type. 55.6% presented in stage III. 75% Hodgkin's lymphomas were cured. 28% patient presented for follow up without any significant side effects.

EP-307

Lymphomas

NON-HODGKIN LYMPHOMA IN CHILDHOOD: CLINICOPATHOLOGICAL FEATURES AND THERAPY OUTCOME AT TWO EGYPTIAN CENTERS

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Objectives

To describe the epidemiological and clinicopathological characteristics and treatment outcome Non-Hodgkin lymphoma (NHL) treated at two Egyptian centers.

Methods

This was a cross-sectional study. Data were collected by a retrospective review of 142 medical records of children with NHL admitted to the 2 oncology units during the period of February 2004 to February 2012.

Results

Abdominal involvement was the most common presentation 70.3%. Burkitt's lymphoma was the most common NHL subtype (69%). The majority of patients had been diagnosed with advanced disease (Murphy stage III / IV disease) 88.7 %. The 5 years OS and EFS for all patients was 88.7% and 85.4% respectively. None of the clinical, epidemiological or pathological characteristics had a significant association with the probability of survival.

Conclusions

NHL occurs in younger age, with a higher incidence of Burkitt's lymphoma and advanced disease. The outcome of NHL in our two centers were satisfactory approaches the international percentage

EP-308

Lymphomas

OUTCOME OF TREATMENT OF KI-1+ ANAPLASTIC LARGE CELL LYMPHOMA (ALCL) BY BFM-NHL 90 PROTOCOL FOR KI-1+ALCL PATIENTS

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Objectives

To present the outcome of treatment of CD30+ve (Ki-1+) ALCL by BFM-NHL 90 protocol of chemotherapy.

Methods

This was a series of 4 cases. Cases were included purposively in the series. They were diagnosed clinically as NHL. Histopathology of biopsied tumor mass was suggestive of Anaplastic Large Cell variety of NHL. Immunohistochemistry confirmed the diagnosis of ALCL by having positive stain for CD 3 & 30 along with negative stain for CD 20.

Results

In our short series, all the four cases were diagnosed as ALCL. All of them were found CD30+ve by immunohistochemistry. Two of them presented with systemic manifestations only, two of them had both systemic and cutaneous manifestations. All the cases were treated by BFM-NHL 90 protocol for CD30+ (ki-1+) ALCL. All of them completed their scheduled chemotherapy regime. All of them have already been past their 5 years of event free survival.

Conclusions

BFM-NHL 90 protocol specifically for Ki-1+ cases of ALCL was found very effective in the treatment of Ki-1+ ALCL.

EP-309

Lymphomas

ABVD WITHOUT CONSOLIDATION RADIOTHERAPY (RT) AFTER COMPLETE REMISSION (CR) IN PEDIATRIC HODGKIN LYMPHOMA (HL): PRELIMINARY RESULTS OF A PILOT STUDY

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Objectives

Children with HL have a good survival but treatments bring on appreciable morbidity. To minimize sequelae, we designed a study with ABVD, for stages 1-3, including B symptoms, without RT in CR patients and reduced RT volumes and doses for PR patients.

Methods

From 1998 onwards 69 consecutive children with HL (median-age 13 yrs; stage I/12; II/40, III/17; B symptoms 30%) were treated. Chemotherapy consisted of 4-6 courses of ABVD followed by RT for patients in PR (25 Gy on PR sites). CR was defined on the basis of clinical and imaging. After 2008, to assess early response, we regularly performed PET2 after 2nd ABVD.

Results

Fortyfive/69 pts achieved CR after CT (12 stage I, 24 stage II, 9 stage III). 18 children were irradiated, only one after introduction of PET2. The number of irradiated patients did not differ between stages I-II and III (p= ns) and presence of B symptoms. 56/69 patients are in CCR at a median follow up of 7 years. Seven patients relapsed (median time 12 months): 2 after CT only (1 in previously uninvolved and 1 in involved nodes), 5 after CT+RT (3 within RT field, 2 outside). Three primary refractory were intensified. Six out of 10 relapsing-refractory patients are in CR (5 in 2nd, 1 in 3rd); three pts died, 1 is alive with disease. We observed two second malignancies: one osteosarcoma outside RT-field and one lung synovial-sarcoma adjacent to the radiation field, at 81 and 89 months after diagnosis. With a median follow-up of 7 years PFS, EFS and OS were 83.4%, 81.5% and 96.2%, respectively.

Conclusions

A significant number of pts (69%) could be cured without RT in any stage. Those poor responders may deserve an intensified treatment. The systematic use of PET has improved response evaluation and reduced the number of irradiated patients.

EP-310

Lymphomas

TREATING HODGKIN DISEASE IN A RESOURCE POOR SETTING: PROBLEMS AND OUTCOME

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Objectives

To assess the problems encountered in managing children with Hodgkin disease (HD) in a resource poor Indian setting and to describe the clinical profile and outcome of these children.

Methods

Case records of 184 previously untreated children (age 0-18yr) diagnosed to have HD at our center between 1994 and 2012 were reviewed. 148 children consented to take treatment at our center (16 refused treatment; 20 abandoned treatment). The clinical characteristics, treatments offered and outcomes of these children were analyzed.

Results

There were 130 boys and 18 girls with a median age of 8yrs. 62% children came from rural areas. 60% children were malnourished, 66% had anemia and 69% had hypoalbuminemia. Median duration of symptoms prior to treatment was 12 months (range 1-96 months). 82% children had advanced disease (stage IIb-IV) at presentation. Mixed cellularity was the most common histological subtype (46%). 91 children (61%) experienced complications during treatment (deranged liver function in 49, fever in 33, anemia in 20). 41 children acquired hepatitis B and 7 hepatitis C during treatment. 22 children died during treatment (12 deaths due to chemotherapy related toxicity, 9 due to advanced disease, and 1 unrelated death due to CNS Tuberculosis). 126 children completed treatment, out of which 20 relapsed. 36 children experienced delays in chemotherapy due to various reasons (deranged liver function-25, fever-5, neutropenia-2, social-4). 118 children (80%) were surviving free of disease with a median follow up of 3.3yrs (range 0.3-19.3yrs).

Conclusions

Children with HD coming to our center tend to have a delayed presentation with advanced disease. Abandonment rates are high. Over one-third of these children get infected with hepatitis B or C during the course of treatment. Complications are common during treatment, leading to therapy delays. These factors are responsible for a poor outcome as compared to developed countries.

EP-311

Lymphomas

RITUXIMAB IN CHILDHOOD MATURE B-CELL LYMPHOMA: REPORT FROM A SINGLE CENTER OF CHINA

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Objectives

To evaluate the efficacy and safety of Rituximab in childhood mature B-cell lymphoma.

Methods

We treated 22 children with progressive B-cell lymphoma with in combination with Rituximab. Data on patients' were analyzed.

Results

Fourteen were stage III; 8 were stage IV. Sixteen patients were diagnosed with Burkitt's lymphoma, 3 were DLBL and the rest were B cell lymphoma. Seventeen patients were initially treated with Rituximab and the rest were treated in replaced. Among patients with Rituximab as initial therapy 15 had LDH>1000U/L, 1 had LDH>500 U/L, 1 < 500U/L. Three patients experienced relapse and died. The mean follow up duration were 18.5 month with EFS 82.4%. All five Patients with relapsed lymphoma died. Deaths in our studied cohort were not related to Rituximab treatment.

Conclusions

No serious adverse effects were observed. Initial therapy with Rituximab might improve the prognosis of B-cell lymphoma in children with heavy tumor load.

EP-312

**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
SIMULTANEOUS PRESENTATION OF ACUTE MYELOID LEUKEMIA AND BURKITT
LYMPHOMA. CASE REPORT AND REVIEW OF THE LITERATURE**

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Objectives

To perform a case report and review of the literatura of a simultaneous presentation of two hematologic malignancies: Burkitt lymphoma and acute myeloid leukemia in a child in the Pediatric Oncology-Hematology Service of Centro Medico Nacional 20 de Noviembre ISSSTE in Mexico city.

Methods

All the pathological, flow citometric, cytogenetic and assays were performed in certified clinical laboratorios using standard techniques. Inmunohistochemistry was performed with antibodies to CD18,CD54,LFA-1,Ki-67,CD45,BCL-6,CD10,CD20,CD22,CD79a,sIgM,TdT.

Results

This paper reports a 6 year old child with Burkitt lymphoma Stage III. No cytogenetic abnormalities were found and VEB infection was discarded. He received COPADM scheme and after four months of treatment, he presented leukocytosis, cephalea and bilateral proptosis. The bone marrow aspiration showed 86% of myoblasts, with CNS infiltration with involvement of the optic neve and meninges. He received treatment according to the Acute Myeloid Leukemia high risk protocol, achieving complete remission. We didn't find donos for the bone marrow transplantation. After 3 months, he relapsed of Burkitt's lymphoma. He finally died.

Conclusions

This is the first review of the literatura of simultaneous presentation of acute myeloid leukemia and Burkitt lymphoma. This patient had a short response to treatment with early relapse and poor prognosis.

EP-313

**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
PEDIATRIC MYELODYSPLASTIC SYNDROME: EXPERIENCE FROM A SINGLE
CENTER**

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Objectives

Pediatric myelodysplastic syndrome (MDS) is a group of heterogeneous clonal disorder with lesser frequency compared to adults. Additionally, there is much rare data in pediatric age group in relation to presentational findings and treatment.

Methods

The clinical and laboratory data, in addition to therapeutic interventions and outcomes of 47 patients in a single who were diagnosed between 2001-2014 were summarized.

Results

Median age of the study group was 2.8 years (0.1-16.8). The most common complaints at presentation included fever (27%), fatigue (17%), bleeding (15%), abdominal distention (13%), in addition to other rare presentational complaints including pallor, rash, vomiting, irritability, jaundice, stridor, abdominal pain and easy bruising. The underlying disorder was established as: neurofibromatosis in 5, Down syndrome in 3, secondary to prior chemotherapy in 2 (ALL and PNET), Fanconi anemia in 1, Jacobsen syndrome in 1, Klinefelter in 1. Final diagnosis was MDS in 22, JMML in 19, hypoplastic MDS in 4 and chemotherapy related MDS in 2. Median Hb, WBC, thrombocyte counts at presentation were 8.7 g/dl (4.1-12.7), $10.3 \times 10^9/L$ (1.3-117) and $55 \times 10^9/L$ (4-1515), respectively. Of the mutations studied related to MDS in 22 of the patients, k-ras positivity was the most common (23%). The most common cytogenetic abnormality was chromosome 7 related abnormalities (25%). Of the patients, 21 (45%) are alive and of these alive patients 62% are alive subsequent to hematopoietic stem cell transplantation (HSCT).

Conclusions

The patients with pediatric MDS may present with various complaints and they may have underlying genetic diseases causing propensity for MDS. The survival is better among patients who underwent HSCT.

EP-314

**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
SUCCESSFUL MANAGEMENT OF CASE OF GRANULOCYTIC SARCOMA WITH
CONCURRENT HEMOPHAGOCYTIC LYMPHO HISTIOCYTOSIS**

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Objectives

Granulocytic sarcoma (GS) is rare extra medullary tumor usually associated with Acute Myelogenous leukaemia (AML M2). Hemophagocytic Lympho Histiocytosis (HLH) has rarely been reported in a child presenting with GS. We describe a successful management of GS concurrent with HLH in a 6-year-old.

Methods

Medical records from our institute were reviewed

Results

A 6 years old admitted to us with complaints of pain in her right frontal region with swelling of the right eye .She received oral antibiotics for a week from an ophthalmologist, thought to be peri-orbital cellulitis and in view of no improvement, was evaluated further and found to have a mass visible through the right nasal cavity. MRI brain with paranasal sinuses was done which revealed a mass in the posterior aspect of the nasal cavity extending into the nasal choana. Biopsy of the mass was suggestive of GS. Subsequent BMA and flow cytometry was consistent with diagnosis of AML-M2 with 34% blast and AML-ETO (translocation 8:21) positivity .She was treated as per modified UK AMLXII protocol. She had a seizure after first lumbar puncture for which no cause was found. After first induction she developed persistent fever and was diagnosed with HLH. No other cause for HLH could be identified. We meticulously treated her with chemotherapy for AML and dexamethaone for HLH.

Conclusions

High suspicion is necessary to diagnose GS in children. Early diagnosis and immediate initiation of treatment are mandatory to overcome this condition. Further clinical data describing the clinical course and the management of children with MAHS are warranted.

EP-315

**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
CYTOGENETICS OF PEDIATRIC ACUTE MYELOID LEUKEMIA: A SINGLE CENTRE
EXPERIENCE**

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Objectives

Acute myeloid leukemia (AML) is a clinically and genetically heterogeneous disease and accounts for 15-20% of all childhood leukemias. The current WHO classification for hematology malignancies has defined distinct entities of myeloid disorders based on the presence of recurrent cytogenetic abnormalities. The cytogenetic abnormalities are divided into following three prognostic groups used in risk stratification for treatment: favorable risk: t(8;21)(q22;q22), t(15;17)(q22;q21), and inv(16)(p13q22); adverse risk: monosomy 5/deletions of the long arm of chromosome 5 [del(5q)], monosomy 7, abnormalities of 3q, and complex karyotypes; and intermediate risk: other changes. Because AML is rare in children, the true prognostic significance of individual chromosomal abnormalities in this age group remains unclear. The present study was undertaken to determine the cytogenetic abnormalities in pediatric AML and their prognostic significance.

Methods

Bone marrow samples collected from 52 pediatric AML patients, cultured for 24 hours without any stimulating agent. The samples were treated with colcemid followed by hypotonic treatment and fixation. The karyotypes were analyzed using the GTG banding technique, described according to International System for Human Cytogenetic Nomenclature 2009.

Results

Out of 52 AML patients, 33(63.4%) were male and 19 (36.5%) were female. The median age of patients was 14.5 years. Cytogenetics abnormalities were detected in 31 (59.6%) patient while 21 (40.3%) had a normal karyotype. In the favorable prognostic category, there were 20 (64.5%) cases with t (8;21)(q22;q22) and 3 (9.6%) cases with t(15;17)(q22;q21). Out of 20 t(8;21) cases, 12 had only t(8;21) with no accompanying structural abnormality, where as 8 had either loss of sex chromosome or other structural abnormality. In the unfavourable prognostic category, Trisomy 8 was found in 1 (3.2%) case, hyperdiploidy in 1 (3.2%) and complex karyotype in 6(19.3%).

Conclusions

Larger studies of this kind may provide more information about prognostic significance of cytogenetic abnormality in pediatric AML.

EP-316

**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
MAINTAINENCE THERAPY IN ACUTE MYELOID LEUKEMIA : EXPERIENCE FROM A
DEVELOPING COUNTRY**

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Objectives

The objective of this study is to determine if the addition of maintainence therapy(MT) would improve the survival of children with acute myeloid leukemia(AML) when compared with those treated without MT.

Methods

Retrospective analysis of cases with AML,0-15 years,diagnosed from 2000-2013,with patient demographics and therapy details.2001-2007,a regimen of induction with 7+3 and 5+2 followed by Denver protocol was used.2008 onwards to current,patients are treated with 7+3,5+2 followed by 3cycles of high dose cytarabine with additional MT.

Results

Of total 88 patients with AML,50 patients were diagnosed between 2000-07 and 38 from 2008-13.28/88-recieved complete therapy,3/88-currently on medication,5/88-relapsed on therapy,6/88-refractory,16/88-expired during treatment(secondary to infection),17/88-lost to follow up and 13/88-refused treatment.14/38 patients received MT in 2008-13.10/14 patients are surviving and 4/14 have relapsed.Remission period in the survivors is 1month to 2.9years(median:2years),3children had WBC >1lac/cumm,3 had unfavourable cytogenetics(1-complex,1-5q deletion),1 patient did not achieve complete remission (CR) after 1st induction. Of the 4 which relapsed,1 had WBC>1lac/cumm,2 had unfavourable(complex) cytogenetics.2patients did not achieve CR after 1st induction, of which 1 had dysplastic changes in the bone marrow.They probably needed bone marrow transplant. 14/50 children were treated without MT from 2000-2007.12/14 relapsed and 2/14 surviving until their last follow up.Median remission period in the relapsed patients is 5months.Of them,1-complex cytogenetics;1-WBC>1lac/cumm,1-did not achieve CR after 1st induction.For the 2 survivors,followup is 1-3.5years and 2nd-6years.1 had WBC>1lac/cumm, both had achieved CR.Cytogenetic analysis was not done in both.

Conclusions

While there has been impressive progress in the treatment of AML,majority of patients still die from this disease.As compared to before,the disease free remission period for AML has improved at our centre with the use of MT. However the initial chemotherapy(induction and consolidation) , supportive care and financial help are also better now, which may have been an added factor for the improvement.

EP-317

**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
USE OF MODIFIED MRC-10 PROTOCOL FOR ACUTE MYELOBLASTIC LEUKEMIA IN
INDIAN CHILDREN**

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Objectives

To analyze the results of treatment of AML with modified MRC-10 protocol; and to assess the toxicity of this regimen

Methods

This study is a retrospective analysis of 39 consecutive AML patients treated over a period of 4 years (2010-2014). Male: female ratio, 19:20. Median follow-up for living patients is 29 months (3-46). Thirty-four patients had denovo AML and 5 patients had a pre-leukemi MDS phase. (MDS-AML). Two patients had acute promyelocytic leukemia. Six had t(8;21) and one had inversion 16. Eight patients had chloromas- two of them with no evidence of AML in bone marrow. The modifications of MRC -10 protocol included reduced number (14 instead of 20) of cytarabine doses and etoposide doses (3 instead of 5) during induction; and only 3 doses of mitoxantrone instead of 4 during intensification. All patients received 3 cycles of oral maintenance therapy with 6-TG 40 mg/m² and etoposide 50 mg/m² daily x 3 weeks—given every 28 days. All patients received above treatment without risk stratification.

Results

Six of 39 (15.3%) patients died of infectious complications during induction. Five patients (12.8%) failed induction; 28 patients (71.8%) achieved complete remission. Four of 5 patients who failed induction therapy had MDS-AML. Seven patients died in remission—due to sepsis in 5 and other infections in 2. Six of 28 patients (21.4%) relapsed in 3 to 13 months. Two of the 6 relapsed patients are alive, 4-5 months from relapse. Three patients developed significant cardiac dysfunction; all three died of infectious complications in remission. The 3-yr estimated overall survival is 47.5%; and the 3-yr event-free survival 40%.

Conclusions

The modified MRC-10 regimen is poorly tolerated by Indian children, The unacceptably high mortality during induction and in remission requires reduction of treatment intensity during induction and consolidation, especially for good-risk patients.

EP-318

**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
CYTOGENETIC PROFILE OF ACUTE MYELOBLASTIC LEUKEMIA IN CHILDREN AND
ADOLESCENTS: ABOUT 119 CASES**

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Objectives

Determine the cytogenetic profile of children and adolescents with AML and evaluate the prognostic impact of cytogenetic abnormalities.

Methods

We conducted a retrospective study between March 2004 and March 2009, including patients with de novo AML, aged 0 to 20 years. The diagnosis is confirmed by cytology by FAB classification +/- immunophenotyping. All children treated with Moroccan protocol AML-MA03 (2 induction+2consolidation).

The karyotype was performed at diagnosis on samples from bone marrow. The cytogenetic study was made RHG band after 24 hours of culture. The cytogenetic abnormalities found were classified into 3 prognostic groups: favorable, intermediate and unfavorable.

Results

125 cases of AML were diagnosed, the karyotype was performed in 119 patients (95%) including 2 culture failures (1.6%).

These 58 boys and 61 girls (sex ratio M/F=0.95). The median age is 15 years (7months - 20 years). The cytological type was the most common type M2 (45%).

Of the 119 karyotypes performed, 87 patients (74.5%) had acquired clonal abnormalities. We noted 2 cases of culture failure (1.6%).

103 patients (84%) were treated by the national protocol AML-MA 03, the continuous complete remission (MCR) for groups favorable, intermediate and unfavorable was respectively 41%, 25% and 10% with a decline of 24 months.

The distribution of prognostic groups is as follows:

- Favorable group: 34 (29%) patients with 31 (26.5%) cases of t (8;21), 2 cases of inversion of chromosome 16 and one case of t (15; 17).
- Intermediate Group: 64 (54.5%) patients. 30 (25.5%) had a normal karyotype and 3 cases had a deletion of band 11q23.
- Unfavorable group: 19 (16.5%) patients had 3 or more abnormalities in karyotype, monosomy 7 in one patient (1%).

Conclusions

These results enabled us to identify the cytogenetic profile of our patients and to guide our therapeutic strategy including better management.

EP-319

**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
A PEDIATRIC CASE OF DNMT3A GENE MUTATION-POSITIVE ACUTE MYELOID
LEUKEMIA**

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Objectives

Recent reports have revealed that epigenetic changes (such as DNA methylation) are important causes of leukemia. Although mutation in *DNMT3A* is very rare in pediatric AML patients, it remains an important diagnostic and prognostic factor for which patients are commonly screened. Here, we report a pediatric case of AML that was positive for the *DNMT3A* gene mutation at onset of diagnosis.

Methods

A two-year-old boy first presented with a scalp lump that, upon examination, suggested myeloid sarcoma. The lump disappeared after anti-infection treatment, and there was no other evidence to suggest the presence of leukemia, except *DNMT3A* gene mutation-positive. Five months later, the boy presented with testicular swelling, which resulted in a diagnosis of AML.

Results

Eventually, the boy was diagnosed with acute monocytic leukemia, testicular leukemia, and central nervous system leukemia. Chemotherapy successfully eliminated *DNMT3A* mutant-positive bone marrow cells. Although the child also received hematopoietic stem cell transplantation, he had a relapse of testicular leukemia for which he received radiotherapy.

Conclusions

The *DNMT3A* gene mutation is important for both prognosis and early diagnosis of pediatric AML.

EP-320

Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
A PRELIMINARY REPORT OF A DIAGNOSTIC STUDY WITH (18)F-FDG-PET (PET) FOR
DETECTION OF EXTRAMEDULLARY DISEASE (EMD) IN PEDIATRIC ACUTE MYELOID
LEUKEMIA (AML)

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Objectives

The primary purpose of the study is to assess the diagnostic usefulness of PET for detection of EMD in pediatric AML at diagnosis. The secondary purposes include assessing usefulness to evaluate remission status after induction therapy and to analyze relationship between the findings of PET and clinical outcome. During the study, we consecutively experienced 2 children with AML with PET-detectable EMD. Considering significant importance of the findings, we decided to present as a selective case report of the 2 cases.

Methods

Patients enrolled in this study undergo PET scan immediately after the diagnosis, prior to starting induction therapy. The prevalence of EMD detected by PET scans and by conventional assessments are compared. The second scan is performed prior to consolidation therapy to evaluate the response to chemotherapy judged by FDG uptake change in EMD area and bone marrow (BM). Correlation between PET findings and clinical outcome will be analysed after accumulation of the data of all cases.

Results

The first case is an 8-month-old boy diagnosed AML (FAB M4) with inv(16) and CBFβ-MYH11 fusion gene. The second case is a 9-year-old boy diagnosed AML (FAB M4) with t(8;21) and AML1-ETO fusion gene. The first PET demonstrated 2 EMD lesions in the case 1 and 4 in the case 2, while standard diagnostic examination detected only 1 lesion in each case. Both of them achieved complete remission (CR) after the induction therapy by conventional criteria. The second scan could confirm CR by reduced uptake of FDP in EMD and BM in both of the patients.

Conclusions

We present two cases of childhood AML with EMD who were performed PET scan. These cases demonstrate the usefulness of PET for diagnoses of EMD and assessing treatment responses of EMD and BM.

EP-321

Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes CYTOGENETIC AND MOLECULAR GENETIC ABNORMALITIES EVALUATION IN PEDIATRIC ACUTE MYELOBLASTIC LEUKEMIA

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Objectives

Genetic aberrations underlying Acute Myeloblastic Leukemia (AML), is the importance landmark for better managing the pathogenesis of disease. Two main referral centers for childhood malignancies in Tehran (capital city of Iran) are MAHAK Pediatric Cancer Treatment and Research Center (MPCTRC) and Children Center Hospital. Children less than 15 years old with all kind of childhood malignancies will admitted in these two centers for diagnosis and therapy. Patients from all parts of Iran can refer there.

The main goal of this study was to evaluate genetical abnormalities in patients with AML for better managing this disease in future.

Methods

Enrolled Patients have been referred from all parts of Iran to two referral childhood malignancy centers in Tehran, Iran (MPCTRC, Children Center Hospital) during April 2007 to April 2013. There was a unique check list for all patients than implied basic data about sex, age, date of dead,,,. Bone marrow aspirates of 104 pediatric AML cases were analyzed by G-banding technique, karyotyping and Real Time-PCR for translocations. Finally data analysed by SPSS version 19.

Results

There were 57 boys (54.81%) out of 104 enrolled patients. The mean age of patients were 6.9 ± 0.43 years. Immunophenotyping results showed the M4 (n=20, 19.2%) and non-M3 (n=19, 18.3%) groups as the majority phenotypes respectively. Twenty out of 104 patients (19.2%) had genetic abnormalities; t(15;17) (n=6, 30%), inversion (n=5, 25%), mosaicism with deletion (n=2, 10%), t(8;21), t(6;11), hyperdiploidy, mosaicism with translocation, mosaicism with monosomy, trisomy 8 and gene deletion (n=1, 5%). Fourty-four patients died (42.3%) during this study. The three-years survival rate was 88%.

Conclusions

Analysis and literature reviews revealed that t(15;17) was the most prevalence abnormalities. Authors suggestion is comprehensive studies with larger patients series to confirm these evaluation. Focusing on cytogenetic abnormalities will consider prognostic significances of patients with AML that can affect treatment planning.

EP-322

**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
IMATINIB MESYLATE INDUCED BONE MARROW APLASIA : NEED EXTRA VIGILANCE
FOR A RARE COMPLICATION**

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Objectives

Imatinib mesylate, a signal transduction inhibitor molecule, has revolutionized the management of chronic phase of chronic myelogenous leukemia (CML). The drug is generally well tolerated. Severe bone marrow (BM) aplasia has rarely been reported.

Methods

A 6-year-old male child presented in November 2013 with a history of low-grade fever for 15 days and fatigue. On examination he had good general condition with mild pallor without organomegaly. The rest of the systemic examination was within normal limits. Haemoglobin (Hb) was 7.9 g/dl, white blood cell count (WBC) $126 \times 10^9/l$ and platelets $1979 \times 10^9/l$. Differential counts and bone marrow studies confirmed the diagnosis of chronic phase CML. Cytogenetic studies revealed 100% Ph-positive metaphases.

Results

He was started on 400 mg/day on 21 November 2013, with weekly monitoring of counts. He tolerated the drug well and did not require any dose modification. On 20 December 2014, during a follow-up visit, he was found to have pancytopenia. Hb was 8.5 g/dl, WBC $435 \times 10^9/l$, and platelet count $95 \times 10^9/l$. BCR-ABL by quantitative method was 13.37. Repeat CBC on 24 January 2014 showed Hb was 8.3 g/dl, WBC $351 \times 10^9/l$, and platelet count $79 \times 10^9/l$. His Imatinib was discontinued. The Bone marrow aspiration was hemodiluted, biopsy showed severely hypoplastic marrow (10-15% cellularity) with no increase in blasts with a mild increase in fibrosis on reticulin stain. CBC on 13 Feb and 26 Feb 2014 showed Hb 8.9/8.8, WBC $599/617 \times 10^9/l$, and platelet count $150/230 \times 10^9/l$ respectively. His BCR-ABL by quantitative method was zero. He was restarted on low dose imatinib (200mg/day).

Conclusions

Imatinib induced severe bone marrow aplasia is a rare complication. CML patients on imatinib therapy need close monitoring.

EP-323

Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes ACUTE ERYTHROLEUKEMIA IN A CHILD-IMMUNOPHENOTYPIC AND CYTOGENETIC FEATURES

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Objectives

Erythroleukemia is a rare disorder characterized by uncontrolled proliferation of erythroblasts and myeloblasts comprising 2-7% of all acute myeloid leukemias. The French American British (FAB) classification of these leukemias is AML M6. They are generally seen in old age. Very few cases of pediatric erythroleukemia have been reported in literature, comprising less than 1% of pediatric leukemias.

Methods

One rare de novo case is presented of pediatric erythroleukemia, AML-M6 in a 2-year-old patient who presented to our department. The clinical, morphologic, immunophenotypic and cytogenetic features of the patient are reviewed. The purpose of this study is to correlate the bone marrow morphology with the immunophenotype and the karyotypes of the neoplastic cells.

Results

The patient was presented with thrombopenia. The peripheral blood examination showed anemia (Hb 8g/L), thrombocytopenia (26 x 10⁹/L) and 7% blasts. Multiple cervical lymph nodes were present, measuring 1-2 cm, which were free and mobile. There were multiple purpuric spots present all over the body. Bone marrow (BM) aspirates showed predominantly erythroid population with scant to moderate amount of pale blue cytoplasm, round or oval nuclei and many coalescent vacuoles. Erythroblasts showed positivity for periodic acid Schiff (PAS). Myeloperoxidase (MPO) was negative. Flow cytometry demonstrated blast population 28% expressing myeloid markers (CD33, CD13, CD117). The blasts do not express monocytic markers (CD34, HLADR, CD64, CD14, CD15, CD11b, CD56, CD4) or megakaryocytic markers (CD61, CD41). Immunophenotypes of the pretreatment bone marrow showed CD36, CD71, CD235 (glycophorin-A) positivity. Chromosomal analysis revealed an abnormal karyotype, 46,??, t(5;16)(q13;p11.2)[11]/48,+19,+21. Our patient is in first complete remission after 2 cycles of AML-BFM protocol under search for compatible donor for bone marrow transplantation (BMT).

Conclusions

The prognosis of erythroleukemia is very poor. Our patient was good responder to AML induction regimen and long-term survival could be achieved with BMT in first complete remission.

EP-324**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
RELATION OF HLA-A, -B, -DRB1 ALLELES AND HAPLOTYPES IN PATIENTS WITH
ACUTE MYELOBLASTIC LEUKEMIA**

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Objectives

Previous studies have demonstrated some significant differences in HLA allele frequencies in leukemic patients and normal subjects. The purpose of this study is to evaluate the frequencies of HLA class I (A, B) and class II (DRB1) alleles in acute myeloblastic leukemia and compare with unrelated healthy controls.

Methods

We investigated the relation of the HLA alleles in 32 acute myeloblastic leukemia (AML) patients and 126 unrelated normal subjects by PCR-SSOP method using Luminex technology.

Results

Allele frequencies of HLA-A*03 and HLA-A*11 were higher in patients with AML compared with the controls ($p=0.007$ and $p=0.041$). On the contrary, HLA-B*13 allele frequency lower than controls ($p=0.017$).

Conclusions

These results suggest that HLA-A*03 and HLA-A*11 alleles may play a presumptive predisposing factor in AML. In addition, HLA-B*13 allele has been found to be negatively associated with AML.

EP-325

Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes INTENSIVE CONSOLIDATION COMPARED WITH LOW-INTENSITY CONSOLIDATION AND MAINTENANCE THERAPY FOR ADOLESCENTS AND YOUNG ADULTS WITH ACUTE MYELOID LEUKEMIA

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Objectives

To examine the efficacy of intensive consolidation without maintenance versus low-intensity consolidation plus maintenance therapy for adolescents and young adults with acute myeloid leukemia (AML).

Methods

A total of 108 patients with median age 29.9 years (range, 15-45) with de novo AML were enrolled in this non randomly trial. Of these, 50 patients were assigned to receive 2 cycles of induction '3+7' (daunorubicin 45 mg/m² on days 1-3; cytarabine 100 mg/m² every 12 hours [q12h] on days 1-7) and consolidation of 3 cycles '1+5' following by maintenance chemotherapy also cycles for 2 years. Other 58 patients were treated 2 cycles of induction '3+7' or '3+7' plus HAM (cytarabine 3 g/m² per q12h on days 1-3; mitoxantrone 10 mg/m² on days 3-5) if the complete response (CR) was not documented after the first cycle. Then there were 4 cycles of consolidation HiDAC (3 g/m² per q12h on days 1-3) without following by maintenance.

Results

CR was documented for 74.0% (intensive consolidation) and 62.1% (low-intensity consolidation followed by maintenance therapy) patients. Median of overall survival (OS) was 2.03 years versus 0.87 years (HR 0.61; 95% CI 0.37-1.02; P=0.056). The median of follow-up for surviving patients was 9.4 and 3.1 years respectively. Two-years OS was 52.0 ± 7.1% vs. 33.8 ± 6.3% (P=0.052 by log-rank test). However, the 5-years OS rate was the same (31.1 ± 6.7% vs. 26.5 ± 7.1%; P=0.184) due to the high frequency of late relapses for longer tracked by time group (26.0% vs. 8.6%; P=0.035). Intensive consolidation compared with low-intensity consolidation accompanied by a higher frequency of adverse events III/IV degrees, including neutropenia (100.0% vs. 68.9%; P

Conclusions

Both the concept of post-remission therapy for adolescents and young adults with AML was demonstrated an equivalent clinical efficacy.

EP-326

**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
ACUTE MYELOID LEUKEMIA IN CHILDREN : EXPERIENCE FROM A TERTIARY CARE
FACILITY IN INDIA**

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Objectives

To document the demographic profile and outcome of children with acute Myeloid Leukemia (AML) treated at a tertiary center in India.

Methods

Retrospective review of case records of children diagnosed and treated for AML was done.

51 patients were diagnosed in two years.

Results

The average age at presentation was 7.74 ± 2.75 years. 64.6% were males. The most common presenting features were fever and pallor followed by bleeding. Hyperleukocytosis was seen in 4 patients. CNS disease was present in 1 patient. The cytogenetics profile will be presented. 10 patients declined treatment at diagnosis / soon after initiation of treatment. Of the 41 patients 21 patients are undergoing treatment/completed treatment. Average duration of follow up ranges between 7-12 months. The reasons for expiry include febrile neutropenia and myocardial dysfunction. Fungal sepsis emerged as an important cause of febrile neutropenia.

Conclusions

Outcome of pediatric AML is inferior to that seen in some western countries. However patients are more receptive to initiation of treatment of AML now. Mortality is high. There is a need for sensitization towards importance of supportive care and infection control in management of childhood AML.

EP-327

Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes IMPROVING SURVIVAL RATES OF ACUTE MYELOID LEUKEMIA IN DEVELOPING COUNTRIES USING AML_15 PROTOCOL

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Objectives

To look at the outcome of children with Acute Myeloid Leukemia (AML) using AML 15 protocol

Methods

A 2.1 years prospective and 1.9yrs retrospective observational study done in tertiary care center, in 6 months to 15years children from January 2009 to December 2012.

Results

Total 32 children identified. Most of them below 5 years (14 /32). 19/32 are girls . Common presenting symptom is fever and organomegaly 22 and 21 respectively. 2 had subcutaneous deposits & one had Leukemia cutis. Severe anemia <7 gm % noticed in 15 cases. Six out of 32 had Hyperleucocytosis. 24 cases had platelets less than 50,000cells/mm³. Most of them(29/32) had blasts in peripheral blood. Most common type of AML is AML M5(13/32). Acute promyelocytic leukemia(APML) was noticed in 6 . M1and M4 are 2 each. M2 and M7 were 6 and 3 respectively. Cytogenetics performed in all. All APML's, t(15,17) positive; 3 were t(8,21)(one M1, one M2, one M5); 2 were Inv 16(one M5 and one M4), 2 had t(9,22)(one M5, one M7) and 1 case is MLL(M7) positive. Karyotype t(x,3) was noted in one case. 3 were CNS positive(1 Facial nerve palsy, 1 CSF positive and 1 Cerebral deposits).

All received chemotherapy as per UK AML 15 protocol,30/ 32 went into remission after induction except 2 AML- M7 cases.Post treatment 5 had relapse, all within 6 months off treatment and all died with progressive disease. Out of 5 relapses one was M5 with t(9,22), one M5 with normal genetics, one was M1 with CNS positive disease, One M7 with t(X,3) & one M2 with normal genetics. Two expired with febrile neutropenia. Overall 23 /32(71.87%) are alive&well . Out of 23, 13 are 2.5 to 3 .6 years off treatment & 10 are 1 to 2 years.

Conclusions

With good supportive care overall survival rates of AML can improve even in developing countries.

EP-328

**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
ORBITAL MYELOID SARCOMA IN ACUTE MYELOID LEUKEMIA: EXPERIENCE OF A
TERTIARY CARE CENTRE IN INDIA**

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Objectives

Orbital myeloid sarcoma is a rare pediatric malignancy. We would like to review the clinico epidemiological profile of children presenting with orbital myeloid sarcoma at diagnosis or antedating a leukemia.

Methods

The clinico epidemiological data of children with a diagnosis of orbital myeloid sarcoma registered in our centre from jan 2012 to dec 2012 was collected retrospectively.

Results

There were 8 children with orbital myeloid sarcoma amongst the 50 new cases of acute myeloid leukemia. Leukocytosis (>50,000) was noted in 6(75%). Acute myeloid leukemia (AML) occurred concurrently in 6(75%) and antedated in 2(25%). AML M2 in 4(50%), AML M1 and AML M4 in one each and AML undifferentiated in 2(25%) were noted. Complete remission was achieved in 6(75%) while progression was noted in 2(25%). Relapse of the leukemia was noted in 2 children within 6m. At the end of 1y 4(50%) children are alive.

Conclusions

AML M2 is commonly associated with orbital myeloid sarcoma in children.

EP-329

Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes OUTCOME OF CHILDHOOD ACUTE MYELOID LEUKEMIA IN MALAYSIA

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Objectives

The aim of this study was to review the treatment outcome of children diagnosed with Acute Myeloid Leukemia (AML) treated with a modified UK MRC AML 12 protocol in a middle income country.

Methods

A retrospective review of all patients diagnosed with AML between 2000 till 2011 treated in Hospital Kuala Lumpur was made. Patients less than 1 year old were excluded. Patients with Down Syndrome, chronic myeloid leukemia in acute myeloid blast crisis, transient myelodysplasia of Down Syndrome and juvenile myelomonocytic leukemia were excluded.

Results

154 patients were identified. One patient refused treatment. Four patients died of severe bleeding before treatment. One patient abandoned treatment and defaulted follow up after the first course. Of the 149 patients who received treatment, 117 (79%) achieved remission. Ten patients (7%) died within 30 days of diagnosis - six due to severe sepsis and four due to uncontrolled bleeding. Fifteen patients (13%) died of sepsis in remission. There were 36 relapses (31%). The estimated 10 year event free survival (EFS) & overall survival (OS) was 31.7 +/- 5% and 50.3 +/- 5% respectively. Segregation of patients into 3 different time periods (2000 – 2004 [period A], 2004 – 2008 [period B], 2009 – 2011 [period C]) showed an improvement in EFS with the introduction of Amsacrine in period C. The estimated 2 year EFS were 35 +/- 6.3% [period A], 30.7 +/- 6.1% [period B] and 67.9 +/- 11.2% [period C] respectively. These differences were only partially explained by the differences in septic death (21% [period A], 10% [period B], 4% [period C]). Autologous / allogeneic haematopoietic stem cell transplantation (HSCT) performed on 34 patients enhances their survival.

Conclusions

Survival of children with AML had improved following adoption of regimes used in developed countries and improvement in supportive care.

EP-330

Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes UNUSUAL CYTOGENETIC FINDINGS IN CONGENITAL LEUKEMIA - A CASE REPORT

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Objectives

This study aimed to report a rare case of congenital acute myeloid leukemia with unusual cytogenetic alterations

Methods

A sixteen days-old female was referred to our neonatal intensive care unit due to a respiratory distress and with a firm, nontender, erythematous node in the superior left palpebra. The perinatal history was uneventful. Blood count showed: leucocytes of $58,7 \times 10^9/L$ (76% blasts), hemoglobin of 13.9 g/dL, platelets of $199 \times 10^9/L$. Bone marrow with 31% of undifferentiated blasts. Flow cytometry showed expression of MPO, CD13, CD33, CD117, CD7. Cerebrospinal fluid revealed 525 cells with 70% blasts. Directed conventional cytogenetic study of bone marrow was performed by G-banding and the FISH techniques. She was treated with the AML protocol used in our Pediatric Oncologic Unit and is now in bone marrow transplantation process

Results

In 20 metaphases analyzed deletion of long arm of chromosome 7 (confirmed by FISH) and probable translocation involving the short arm of chromosome 12 was displayed. FISH using LSI *ETV6/RUNX1* probe confirmed translocation of the short arm of chromosome 12 surrounding the *ETV6* gene with the deleted region of the long arm of chromosome 7. Furthermore, interphase nucleus containing 4 signs of *ETV6* gene were detected in 16.5% of them. FISH for *MLL* rearrangement search was done with the probe LSI *MLL* break apart that was negative for the presence of rearrangements and deletions involving this gene. After these studies, final karyotype was: 46,XX,del(7)(q11.2),t(12;?)(p13;?) .
ish der(7)t(7;12)(q11.2;p13)del(7)(q11.2)

Conclusions

Deletion of chromosome 7 and absence of involvement of the *MLL* gene, as well as the involvement of *ETV6* gene are rare events related in neonatal leukemias. The del(7q) and no rearrangements and deletion of *MLL* gene that were seen in the FISH study using probe LSI *MLL* have an unfavorable prognosis

EP-331

Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes RESULTS OF AIDA-BASED TREATMENT FOR CHILDREN WITH NEWLY DIAGNOSED ACUTE PROMYELOCYTIC LEUKEMIA - A SINGLE BRAZILIAN-CENTER EXPERIENCE

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Objectives

To describe the results of AIDA-based treatment for children with newly diagnosed Acute Promyelocytic leukemia.

Methods

Twenty newly diagnosed children with Acute Promyelocytic Leukemia (APL) were treated at *Centro de Tratamento Infanto Juvenil Fabiana Macedo de Moraes* (CTFM-GACC) from December/2001 to January/2013 (13M:7F, median age 111.5 months). 20/20 were analyzed by PCR or cytogenetics regarding the presence of *PML-RARA/t(15;17)*, 18/20 (82%) being positive, and two negative but with isochromosome 17. All of them, were initially treated with all-trans-retinoic acid (ATRA) 45mg/m²/day from the first day maintained throughout the initial 90 days+ Idarrubicin (IDA) 5 mg/m² (4 doses), being added when fibrinogen level became stable without any hemorrhagic manifestation Intensification with IDA and Mitoxantrone plus an additional year of maintenance with 6 mercaptopurine/Methotrexate backbone and ATRA, every 3 months.

Results

Median leukocyte count at diagnosis was 3,550/mm³ (1,400 - 43,500/mm³) and median platelets count 18,500/mm³ (6,000-70,000/mm³), 5/20 were high risk patients (leukocyte >10,000/mm³ and platelets < 40,000/mm³). 6/20 died, 2 with early hemorrhagic events, one with thromboembolic complications at diagnosis, 2 due to refractory leukemia and one after an early relapse; 3/6 of deaths were in the high risk group. The two patients with isochromosome 17 treated initially with ATRA, did not respond to it. Only one PM/RARA positive patient had no response to ATRA+ IDA and was resistant even with the use of Arsenic Trioxide (ATO), dying of sepsis and pulmonary bleeding.

Conclusions

Hemorrhagic disturbances remain a particular adverse event during the initial treatment of APL. Patients with a high leucocyte count and a low platelet level had the worse prognosis; prompt introduction of ATRA at any APL suspicion is crucial for a better outcome and, finally, we want to point out that the two patients who had isochromosome 17q and PML/RARA negative gene fusion did not respond to ATRA.

EP-332

**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
INDUCTION TREATMENT RESULTS WITH THE NATIONAL PROTOCOL IN ACUTE
MYELOID LEUKEMIA AT NATIONAL INSTITUTE OF PEDIATRICS IN MEXICO**

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Objectives

Results of treatment of children with acute myeloid leukemia (AML) is a challenge. In low income countries toxicity of these regimens is the main cause of death. We present promising results of a cohort of patients under 18 treated in a single institution.

Methods

A longitudinal clinical study was performed from January 2005 to September 2013. Nineteen cases of patients with AML were included. All patients received ADE as induction therapy (cytarabine 100mg/m² q12h for 20 doses, daunorubicin 50mg/m² days 1,3,5 and etoposide 100mg/m² over days 1 to 5 and Medical Research Council (MRC) maintenance with four cycles. M3 AML were treated with ATRA and MRC protocol.

Results

Median age was 124 months (21-210). 10.5% were M0, 15.5% M2, 21.1% M3, 26.3% M4, 10.5% M5, 15.8% M7. Two patients had inv16, two t(15;17), two t(8;21) and one 11q23. 42.1% had extramedullar infiltration at diagnosis. Three patients needed one cycle for remission, ten needed two cycles and 5 three. The remission rate was 100%. Patients had between one and 9 infectious events, none fatal. One patient abandoned two die of hemorrhage and one of septic shock. Four patients had bone marrow relapse and were rescued with progenitor cell transplantation. Analyzing non-M3 patients overall survival was 77.4% at 100 months.

Conclusions

As an oncology department we have a selection bias with almost half of patients with extramedullar infiltration. However, ADE induction therapy showed improved results in overall survival compared with other standard regimens. This regimen can be useful in other developing countries.

EP-333

**Myeloid Leukemias, Myelodysplastic Syndromes, Myeloproliferative Syndromes
DIFFERENCES OF SOMATIC MUTATIONS AND GENE EXPRESSION IN BLASTS OF
TRANSIENT LEUKEMIA AND ACUTE MYELOID LEUKEMIA OF DOWN SYNDROME**

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Objective: Transient leukemia (TL) occurs in 30% of newborns with Down syndrome (DS) and typically resolves spontaneously. Approximately 20% of infants with TL go on to develop acute myeloid leukemia of DS (DS-AML) within the first four years of life. The blasts of both TL and DS-AML harbour somatic mutations of *GATA1*. The objective of this study was to identify genetic events associated with the progression of TL to DS-AML.

Methods: Leukemic blasts of TL and DS-AML and normal T lymphocytes were sorted from blood and bone marrow samples of five patients who successively developed both disorders. In addition, blasts of one patient with subsequent relapse of DS-AML were analyzed. Gene expression and mutational spectrum were determined by RNASeq and exome sequencing.

Results: TL blasts harbored fewer mutations than those of DS-AML. Mutations of cohesin and RAS pathway genes were identified in a subset of DS-AML but not TL. In the patient with relapse, different cohesin gene mutations were detected at initial diagnosis of AML and relapse; a minor clone present at initial diagnosis of AML emerged as the predominant clone at relapse. Differential gene expression was predominantly higher in TL blasts compared to DS-AML. It included genes encoding chemokines and related to IL1 and TGF β signaling. The latter result is consistent with the occurrence of frequently fatal organ fibrosis in TL.

Conclusions: The pathogenic sequence culminating in DS-AML is initiated by a unique event in children with DS (somatic mutation of *GATA1*). In contrast, events associated with the transformation of TL to DS-AML resemble progression factors also found in non-DS AML.

EP-334

Neuroblastoma

ACETYL L CARNITINE INTERFERES WITH ANTITUMOR EFFECT OF CISPLATIN

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Objectives

Acetyl-L-carnitine (ALCAR) is a well known antioxidant. In our previous studies, we showed protective effects of ALCAR against cisplatin induced neuro, oto and nephrotoxicities in vitro and in vivo experimental models. The aim of this study is to investigate whether ALCAR interferes with antitumor effect of cisplatin against neuroblastoma.

Methods

Atymic male nude mice, 20 gram 6 week of age (7 animals per group), were subcutaneously injected with 10 million C1300 neuroblastoma cells. The study consisted of four groups: Control, ALCAR, Cisplatin, ALCAR+Cisplatin group). Tumor size reached 1-2 cm in 10 days. Intraperitoneal injection of isotonic solution in control group, 16mg/kg Cisplatin, 100 mg/kg ALCAR and combination at the same time were applied. Animals were sacrificed at day 10. Antitumor activity was evaluated by gross measurement of tumor, microscobic evaluation of tumor necrobiosis and apoptosis evaluation.

Results

In control and ALCAR tumor group with no agent given, tumor cells were alive with minimal necrosis and apoptosis. There was prominent mitosis. In cisplatin group, tumor showed prominent necrosis and necrobiosis with prominent apoptosis. In ALCAR+cisplatin group, tumor showed lesser necrosis compared with cisplatin group.

Conclusions

In this animal model in vivo study, we showed that ALCAR given at the same time with cisplatin interferes with its antitumor activity against neuroblastoma. Using ALCAR as a protective agent against cisplatin induced toxicities should be very well questioned.

Acknowledgement: This study was supported by Turkish Society of Pediatric Oncology.

EP-335

Neuroblastoma

MOLECULAR PROFILE OF NEUROBLASTOMA IN TURKEY ON BEHALF OF THE TURKISH SOCIETY OF PEDIATRIC ONCOLOGY

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Objectives

Neuroblastoma is the most common pediatric neuroendocrine tumor arising from the neural crest of sympathetic nervous system. Neuroblastic tumors exhibit extreme heterogeneity, which affects the outcome of the therapy differently. Neuroblastoma is mainly categorized into three risk levels as low, intermediate and high. The molecular evaluation has come into prominence for the determination of the risk categories of patients. In this study, the results of the molecular analysis performed within the scope of the TPOG (Turkish Society of Pediatric Oncology) protocol were evaluated.

Methods

We compiled molecular analysis of 189 patients diagnosed/pre-diagnosed with Neuroblastoma from oncology centers of Turkey's various government, university and private hospitals. We have analysed Nmyc amplification, 1p LOH, 11q del and 17q gain status for these patients with real-time PCR analysis and DNA ploidy index with flow cytometer.

Results

Molecular analysis of the 189 patients were evaluated. The age interval of these patients were between 1- 168 months. The average age was 36.34 ± 34.75 . The percentage of Nmyc positivity was 14.9%, while for 1p LOH, 11q del and 17q gain the percentage of positivity were 36%, 16.9% and 39.2%, respectively. DNA ploidy index was DPI >1 for 21.4% of the analysed samples. Positive correlation between Nmyc amplification and 1p LOH were found ($p=0.001$), while no correlation was found among 11q deletion, 17q gain and Nmyc amplification. 67 samples out of 189 were negative for all of the four genetic parameters.

Conclusions

Our results show that, there exists a positive correlation between Nmyc amplification and 1p LOH, which is consistent with several previous studies. Almost 40% of 189 samples were shown to be positive for 17q25 gain, which is the mostly seen aberration among the samples evaluated.

EP-336

Neuroblastoma

SURGICAL COMPLICATIONS AND LONG-TERM OUTCOME OF PERI-VASCULAR ABDOMINAL NEUROBLASTOMAS: A SINGLE INSTITUTION STUDY

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Objectives

Because of their anatomic relations, surgical excision of peri-vascular abdominal neuroblastomas (PVAN) is a challenging procedure. The aim of our study is to evaluate complications and long-term outcome of patients operated on for such tumours in a single institution.

Methods

From 1997 to 2012, 45 patients were operated on for neuroblastoma encasing abdominal aorta, main abdominal arteries and renal pedicle. Preoperative chemotherapy was given to all patients according to current ongoing protocols. According to the International Neuroblastoma Risk Group (INRG) classification, 21 patients were L2(46%), 21 were metastatic M(46%) and 3 were Ms(7%). We assessed perioperative and long-term outcome.

Results

Median age at surgery was 4 years (5.5months-15years). Two patients underwent staged procedures. Excision was complete for 25 (56%) patients. We performed 13 planned nephrectomies. Operative complications consisted in 8 vascular adverse events in 8 patients, including: 1 accidental injury of superior (SMA) and 1 of inferior mesenteric artery, 3 spasms and 1 injury of renal artery, 1 spasm of hepatic artery, and 1 injury of renal vein. Post-operative complications occurred in 3 patients: 1 died of mesenteric ischemia (after accidental injury of the SMA), 1 patient had kidney atrophy and 1 patient with thrombosis of the celiac trunk and renal vein, responsible for hemodynamic instability, acute liver ischemic necrosis and renal insufficiency finally recovered without any sequelae. Five patients developed a temporary ascitis and 2 had bowel obstruction. At a median follow-up of 27 months [5months-12years] 31 patients (69%) were alive, 9 patients died of local recurrence (in 5, initial resection was macroscopically incomplete) and 4 died of metastatic recurrence.

Conclusions

Surgery for perivascular abdominal neuroblastoma is challenging and bears potential life threatening complications, mainly vascular. Most of them could be prevented and/or reversed by an appropriate peri and post-operative management of hemodynamic changes.

EP-337

Neuroblastoma

HINGE LAMINOPLASTY IS A USEFUL TECHNIQUE FOR URGENT DECOMPRESSION OF NEUROBLASTOMA CAUSING SPINAL CORD COMPRESSION IN APPROPRIATELY SELECTED CASES

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Objectives

To highlight the utility and safety of hinge laminoplasty as a technique for urgent decompression of Neuroblastoma causing spinal cord compression (SCC), in appropriately selected cases.

Methods

In a 12 month period, 3 children presented to the paediatric oncology service of Royal Aberdeen Children's Hospital with a diagnosis of Neuroblastoma with SCC. The first, aged 16 months, with a 4 month history of grade 4 weakness of the lower limbs, had urgent hinge laminoplasty, with high dose Dexamethasone and then emergency Carboplatin and Etoposide. The second, aged 8 months, with a 10 day history of grade 4 weakness of the lower limbs and constipation, had emergency Carboplatin and Etoposide with Dexamethasone, followed by urgent hinge laminoplasty the following day. The third, aged 8 weeks, presented with an abdominal mass, and MRI revealed SCC. There was constipation but no weakness and treatment was with emergency Carboplatin and Etoposide with Dexamethasone.

Results

The first patient, 14 months after diagnosis, is in remission and walks with a frame, with power 4/5 in the lower limbs. The second, 8 months after diagnosis, is in remission with no neurological deficit. The third, 2 months from diagnosis, remains on treatment, with no neurological deficit.

Conclusions

Neuroblastoma with SCC is associated with a relatively good prognosis oncologically, but neurological prognosis varies with severity of motor deficit at presentation¹. Concerns about symptomatic deterioration, scoliosis, and compromised ability to deliver chemotherapy have caused early decompression to fall out of favour. We show that, in appropriately selected cases, hinge laminoplasty can be an effective approach to urgent decompression, and need not compromise, nor be compromised by, chemotherapy delivery. It also carries a smaller risk of scoliosis².

References

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EP-338

Neuroblastoma

A ROLE FOR INTERLEUKIN-7 IN HUMAN NEUROBLASTOMA TUMOURIGENESIS

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Objectives

Interleukin-7 (IL7) is a cytokine that has neurotrophic effects during development of embryonic nerve cells leading to neuronal differentiation (Michaelson et al *Developmental Biology*, 179, 251-263, 1996). IL7R α sequence variations are pathogenic for the neurological disorder, multiple sclerosis (MS). Neuroblastoma (NB), the most common extracranial childhood solid tumour, shows remarkable heterogeneity with respect to neuronal differentiation. Microarray studies indicate IL7 has significantly increased expression in good prognosis NB tumours with treatment outcomes. We present several other lines of evidence that implicate altered IL7 signalling in NB development.

Methods

The expression of IL7, IL7 receptor (IL7R α) and its downstream signalling proteins JAK1, JAK3, STAT5 were analysed using immunohistochemistry in 100 stroma poor NB tumours and 24 with stroma rich ganglioneuroma (GN). Their expression was correlated to the level of S100 (stromal marker), NB84 (neuroblast marker) and CD99 (negative marker).

Results

IL7 protein expression was positive exclusively in Schwannian stroma in favourable and unfavourable histology tumours. Specialised digital image analysis determined the expression of IL7, IL7R α , JAK1, STAT5 and pSTAT5 were all increased in GNs compared to NBs. Expression of pStat5 was found to be significantly reduced (t-test, p=0.00013) in stroma poor NB compared to GN. Like the undifferentiated tumours, a NB cell line panel demonstrated uniform expression of IL7R α , very low expression of Stat5 and the absence of pStat5. The IL7R α partner, IL2R γ was depleted in two cells lines. Ion Torrent next generation sequencing of the coding regions of 10 key IL7 signalling pathway genes in 13 NB cell lines identified non-synonymous sequence variations in IL7R α that are known to be associated with MS (eg T244I) (Zhang *et al* *Molecular Biology Report*, 38:5079-5084, 2011).

Conclusions

Our findings implicate IL7 within the Schwannian stroma of the tumour architecture as having a paracrine signalling effect on neighbouring neuroblasts, which in turn have varying capacity to differentiate in response.

EP-339

Neuroblastoma

IN VIVO EFFECT OF SANGUINARINE ON NEUROBLASTOMA

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Objectives

Neuroblastoma is among the most common extracranial solid cancer in children and originated from primordial crest. Approximately half all patients with neuroblastoma are diagnosed with high-risk poor prognosis disease, and novel therapies are needed.

Sanguinarine is a benzophenanthridine alkaloid and has anti-microbial, anti-oxidant and anti-inflammatory properties. We had previously showed antitumor effect of sanguinarine against neuroblastoma in cell culture studies. The aim of this study is to determine *in vivo* effect of sanguinarine against neuroblastoma.

Methods

Atymic male nude mice, with a mean weight of 20±3 g and 6 weeks of age (7 animals per group), were subcutaneously injected with 10 million C1300 neuroblastoma cells. The study consisted of three groups: Control, sanguinarine and cisplatin). Tumor size reached 1-2 cm in 10 days. Intraperitoneal injection of isotonic solution in control group, 16mg/kg cisplatin, 15 mg/kg sanguinarine were applied. Animals were sacrificed at day 10. Antitumor activity was evaluated by gross measurement of tumor, microscobic evaluation of tumor necrobiosis and apoptosis evaluation.

Results

In control tumor group with no agent given, tumor cells were alive with minimal necrosis and apoptosis. There was prominent mitosis. In cisplatin group, tumor showed prominent necrosis and necrobiosis with prominent apoptosis. In sanguinarine group, tumor revealed necrosis and apoptosis as much as prominent compared with cisplatin group.

Conclusions

In this animal model *in vivo* study, we demonstrated that sanguinarine compared with with cisplatin has antitumor activity against neuroblastoma. Further studies are needed to determine the inhibitory effects of sanguinarine on tumor growth in experimental tumor models. Our study suggest that sanguinarine is a likely candidate for further evaluation in neuroblastoma treatment.

EP-340

Neuroblastoma

THE ROLE OF NAMPT-NAD-SIRTIIN PATHWAY IN NEUROBLASTOMA CHEMORESISTANCE

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Objectives

Chemoresistance is a major obstacle in the successful treatment of high-risk neuroblastoma (NB). Sirtuins (SIRT) are NAD⁺ dependent deacetylases which are activated during periods of stress leading to cellular protection. In cancer, the activity of SIRTs is largely dependent on the NAD⁺ salvage pathway, of which Nampt is a key enzyme. Inhibiting NAD⁺ metabolism or downstream targets may represent a novel way to enhance cancer chemotherapeutics.

Our objective is to determine the therapeutic potential of SIRT and NAMPT inhibition as a novel method to increase NB chemosensitivity to AKT pathway inhibition.

Methods

Cell viability was determined by MTS and LDH assay and cell signaling pathways were evaluated by western blot analysis. NB cells were treated with perifosine and everolimus to inhibit the PI3K/AKT/MTOR pathway.

Results

Both sirtinol (SIRT1 and 2 inhibitor) and APO866 (Nampt inhibitor) induced dose dependent NB cell death. Combined SIRT and AKT pathway inhibition induced PARP cleavage and NB1691 cell death (viability; vehicle=100±1.9%, sirtinol=70±1.9%, perifosine=76±1.9%, sirtinol+perifosine=28±0.9%, everolimus=87±3.2%, sirtinol+everolimus=23±2.2%). Inhibiting SIRTs by targeting NAD production with APO866 (10nM) also significantly increased NB cell death in response to AKT pathway inhibitors.

Conclusions

Our data indicates that SIRTs regulate cell survival following chemotherapeutic insult. Most SIRT inhibitors are in pre-clinical trials, however Nampt inhibitors are in clinical trials and could potentially be used to inhibit SIRTs thereby enhancing the therapeutic effect of AKT pathway inhibitors as well as other chemotherapeutic agents. Here we provide novel insights in role of SIRTs in NB and suggest a new therapeutic regimen for a cancer with minimal survival.

EP-341

Neuroblastoma

PERSISTENT IODINE-123 (¹²³I) METAIODOBENZYLGUANIDINE (MIBG) SPOT IN LONG TERM FOLLOW-UP METASTATIC NEUROBLASTOMA OVER YEAR OF AGE

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Objectives

The iodine-123 (¹²³I) metaiodobenzylguanidine (MIBG) scintigraphy is a useful tool for diagnosis, staging and evaluation of response to treatment in neuroblastoma (NB). Aim of this study is to report on features and implications of a residual ¹²³I-MIBG uptake in metastatic NB long-term survivors.

Methods

We retrospectively reviewed a series of metastatic NB over 1 year of age enrolled in two consecutive local protocols with at least 3 years follow-up. Medical records were reviewed to check patients with persistent MIBG spots. All MIBG scans were reviewed.

Results

58 metastatic NB patients treated between July 1996 and August 2009 were enrolled in this study. All but one had ¹²³I-MIBG positive disease at diagnosis. Out of 17 survivors, 3 patients presented a persistent and stable ¹²³I-MIBG uptake at 195, 130 and 129 months since diagnosis, respectively. All three patients were younger than 24 months at diagnosis, none had MYCN amplification and all achieved a partial response/very good partial response at the end of the induction phase and before high dose chemotherapy.

Conclusions

A residual and persistent MIBG uptake is reported in few metastatic NB patients younger than 24 months and without MYCN amplification with no impact on survival. These spots may reflect a residual differentiating disease. Further analyses on large series are needed to clarify the implication of residual uptake in a sub-group of metastatic NB, both to modulate treatment and MIBG timing.

EP-342

Neuroblastoma

TREATMENT OF NEUROBLASTOMA WITH AN TOPOTECAN REGIMEN

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Objectives

To summarize our experience on the treatment of neuroblastoma with an topotecan regimen.

Methods

Sixty-eight newly diagnosed patients with neuroblastoma were included in this study from January 2007 to December 2012. The age of the patients was from 4 days to 108 months. The diagnosis was made by imageology, bone marrow biopsy and postoperative pathological diagnosis. The staging of patients was determined by INSS system as follows: 7 cases in stage ?(10.3%), 14 in ?(20.6%),11 in ?(16.2%), 23 in ?(33.8%) and 13 in ?s (19.1%). The treatment scheme was according to a protocol of topotecan regimen.

Results

The remission rate after the new assistant chemotherapy was 60.7%(17/28). Gross total resection rate of this group was 71.7%. The overall survival rates of 2 and 5 years in this group were 75.6% and 62.1% respectively. The overall survival rates of 2 and 5 years in patients with gross total resection were 83.3% and 70.2% respectively. 2 years event-free survival rate is 67.3%, 5 years event-free survival rate is 57.4%. Age of EFS (Event-Free Survival) ROC (receiver operating characteristic) curve analysis showed the best discrimination threshold was 867 day. The sensitivity and specificity were 75.00% and 66.67% respectively. Area under the curve was 0.713.

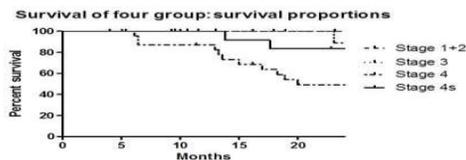


FIGURE 1 Two-year overall survival rate of the patients according to the tumor stages.

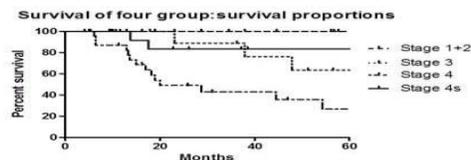


FIGURE 2 Five-year overall survival rate of the patients according to the tumor stages.

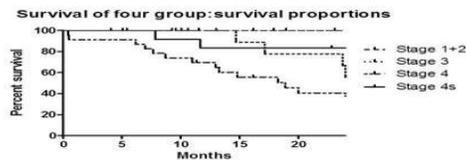


FIGURE 3 Two-year event-free survival rate of the patients according to the tumor stages.

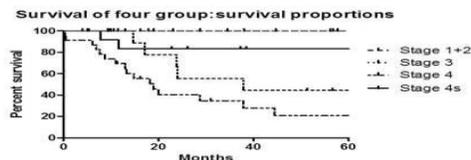


FIGURE 4 Five-year event-free survival rate of the patients according to the tumor stages.

Conclusions

This study showed the treatment of neuroblastoma according to the America COG protocol is better than that of the Japanese Study Group Protocol. Patients in the low risk group with no MYCN amplification can undergo surgery alone, and achieve a favorable prognosis. Through the 68 cases of patients with age of EFS ROC curve analysis, we obtain the best discrimination threshold, 867 day, is much longer than the data we used before.

EP-343

Neuroblastoma

STAGE IV NEUROBLASTOMA: EXPERIENCE FROM A TERTIARY CARE CENTER IN INDIA

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Objectives

Stage IV neuroblastoma is a systemic disease that requires multimodal intensive treatment. Our objective was to study the clinical profile and outcome of Stage IV neuroblastoma diagnosed at our institution.

Methods

Retrospective analysis of data of patients diagnosed with Stage IV neuroblastoma over a period of 10 years (2003-2013). All patients were treated on uniform induction protocol consisting of 8 cycles OPEC/OJEC chemotherapy. After 4 cycles, if there was no evidence of metastatic disease and the primary was surgically amenable, resection/debulking of the was attempted. At the end of induction therapy, myeloablative chemotherapy with autologous stem cell rescue followed by local therapy was given. Cis-retinoic acid was given to few patients at completion of treatment.

Results

Total of 27 patients had stage IV neuroblastoma out of 40 patients diagnosed. Majority were males (n=18, 66.6%) and mean age at diagnosis was 3.5 years (range 0.17 to 7.2). Fever and abdominal distension were the most common (21/27) presenting symptoms. 16 of the patients had primary tumour in suprarenal region, 4 in retroperitoneal region, 2 in posterior mediastinum. Skin involvement seen in 2 patients. Bone marrow was the most common metastatic site (15/27) followed by liver (11/27) and Bone (9/27). Urinary VMA was elevated in 20 patients (74%). N myc done in 4 patients, MIBG scan done in 5, PET CT done in 10. 5 children underwent ABMT of which one expired during therapy, 2 had CNS relapse and expired. Total of 14 children expired, 8 lost to follow up and 4 children abandoned treatment, 3 children are receiving treatment at present.

Conclusions

The survival of patients with stage IV neuroblastoma is dismal. Stem cell rescue has improved survival in recent times which is yet to be supported by strong evidence in Indian scenario. Indian data on Neuroblastoma stage IV outcome is lacking and needs further study.

EP-344

Neuroblastoma

NEURONAL LEUCINE RICH REPEAT PROTEIN1 (NLRR1) SUPPRESSES NGF/TRKA SIGNAL IN NEUROBLASTOMA

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Objectives

NLRR1, a type 1 transmembrane protein, is highly expressed in unfavorable neuroblastoma (NB). Previously we reported that NLRR1 accelerated EGF and IGF signals and enhanced cell proliferation in NB. However, the functional role in other receptor tyrosine kinases including TrkA was elusive. TrkA is associated with favorable outcomes of NB and enhances cell survival and differentiation upon nerve growth factor (NGF) treatment in NB cells. In the present study, we investigated the functional interactions between NLRR1 and TrkA.

Methods

The mRNA expression of NLRR1 and TrkA was evaluated by quantitative real-time PCR (qPCR) in primary NB samples. NGF/TrkA signal was investigated by western blot analysis in NLRR1-expressing NB cells.

Results

In NB clinical samples, we found that the mRNA expression of *TrkA* was inversely correlated with the expression of *NLRR1* (chi-square test, $p=0.04$). In TrkA-stably expressing SH-SY5Y cells, the cell growth in NGF-containing medium was reduced compared to control cells. Upon NGF treatments, levels of phosphorylated TrkA and ERK, one of the downstream molecules of TrkA, decreased in NLRR1 expressing cells.

Conclusions

Our data suggests that NLRR1 and TrkA show the mutually exclusive expression pattern in NB clinical samples and that NLRR1 contribute to aggressiveness of NB in part by suppressing TrkA signals.

EP-345

Neuroblastoma

DECREASE TREATMENT OF NEUROBLASTOMA AND MULTIDISCIPLINARY CARE

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Objectives

The treatment of low and intermediate risk (L/IR) neuroblastoma needs judicious use of different modalities. This group of patients is typically over treated when their care is scattered. We report our experience with emphasis on the role of multidisciplinary care. We also propose an algorithm for management in countries with limited resources.

Methods

We conducted a retrospective analysis of children with L/IR NB who presented from Jan2003 until Dec2009. Patients' characteristics, treatment modalities and outcome were analyzed. All cases were discussed in multidisciplinary clinic that included at least a pediatric oncologist, a radiologist, a pediatric surgeon and a radiation oncologist

Results

We identified 40 patients (21 males) who presented with L/IR NB to our center (25 LR). The median age at diagnosis was 9 months (range, 2 to 48). Stage distribution was as follows: stage I, 8; stage II, 14; stage III, 7 and stage IVs, 10 patients. MYCN was amplified in 3 patients with stage I. Gross macroscopic resection was achieved in 21 patients (out of 26 who had surgery). Chemotherapy was given to 20 patients (50%) with most of them (15 patients) receiving ≤ 4 cycles. The 5-year EFS was $92 \pm 4.4\%$ and the 5-year OS was $98 \pm 2.5\%$. Three patients died; two relapsed 15 and 39 months after diagnosis and died of disease; the third patient died of hemorrhage and renal shut down after surgery. Another patient developed progression of the residual mass 47 months after diagnosis and was lost for follow up.

Conclusions

For children with non-high risk neuroblastoma in developing countries there is a possibility for treatment reduction with good outcome. Treatment can be modified through multidisciplinary team discussion. We propose that in countries with limited resources, minimal treatment is provided to all patients with neuroblastoma unless more advanced therapies are available, including stem cell transplantation and immunotherapy.

EP-346

Neuroblastoma

SYNERGISTIC ANTITUMOR INTERACTIONS BETWEEN MK-1775 AND PANOBINOSTAT IN HIGH-RISK NEUROBLASTOMA CELLS

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Objectives

Despite recent advances in treatment regimens, patients with high-risk neuroblastoma have long-term survival rates of <40%. Resistance to the current anti-neoplastic agents continues to be one of the main reasons for treatment failure and progressive disease among this group of patients. Therefore, new agents are urgently needed to improve treatment outcomes for patients with high-risk neuroblastoma. In this study, we utilize the Wee1 inhibitor MK-1775 in combination with panobinostat to determine the antitumor interactions and the underlying molecular mechanisms.

Methods

In vitro cytotoxicities of panobinostat and MK-1775 at clinically achievable concentrations, either alone or in combination, were evaluated in SK-N-AS, SK-N-DZ, and SK-N-BE(2) high-risk neuroblastoma cell lines using MTT assays. The mechanism of antitumor activity was investigated using propidium iodide (PI) staining and flow cytometry analysis to determine apoptosis, as well as Western blotting to assess expression of phosphorylated CDK1/2, CHK1, and H2AX.

Results

Treatment of neuroblastoma cell lines with 500 nM MK-1775 caused growth arrest and apoptosis in SK-N-DZ and SK-N-AS, while it had minimal effect on the SK-N-BE(2) cell line. The combination of panobinostat and MK-1775 resulted in synergistic antitumor interactions in all three of the cell lines tested. MK-1775 treatment in SK-N-BE(2) cells induced increased levels of p-CHK1^{S345}, which could be decreased by the addition of panobinostat. This was accompanied by increased DNA damage and apoptosis. CHK1 selective inhibitor, LY2603618 potently and synergistically enhanced MK-1775-induced proliferation inhibition in the SK-N-BE(2) cells, supporting that CHK1 plays an important role in mediating the synergistic antitumor interactions between MK-1775 and panobinostat.

Conclusions

The combination of panobinostat and MK-1775 has synergistic antitumor activity against high-risk neuroblastoma cell lines and holds promise as a potential effective treatment strategy for the management of high-risk neuroblastoma patients.

EP-347

Neuroblastoma

ADHERENCE TO UK CHILDREN'S CANCER & LEUKAEMIA GROUP GUIDELINES FOR THE MANAGEMENT OF LOW AND INTERMEDIATE RISK NEUROBLASTOMA, 2011-2013

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Objectives

To evaluate how UK children with low (LR) and intermediate risk (IR) Neuroblastoma are managed compared with national CCLG guidelines (v1 August 2011) based on SIOPEN low and intermediate risk Neuroblastoma (LINES) trial.

Methods

CCLG centres were asked if they followed guidelines for LR and IR Neuroblastoma between August 2011-2013. Patient numbers, genetic testing including MYCN and segmental chromosomal abnormalities (SCA), and outcome data for specific subgroups were collected.

Results

All 21 CCLG centres replied describing 80 cases (53 LR, 27 IR). Principally all centres adhered to the guidelines. 74/80 cases were tested for MYCN amplification and SCA either locally or via the central reference facility in Newcastle.

LR: 6 LR patients were not biopsied due to co-morbidity, need for emergency chemotherapy, primary surgery or antenatally diagnosed adrenal masses. 38% LR tumours had SCA, 17q gain was the commonest (13/20). 8 patients had 4s disease without life threatening symptoms, 4 with SCA but 6 received 4-6 cycles of chemotherapy. 12 patients were < 18 months of age with localised, unresectable (L2) tumours and no SCAs, 10 had chemotherapy followed by surgery in 4 cases, and one surgery alone. 11 patients are alive, and one died from disease progression.

IR: 67% IR tumours had SCA, the commonest was 17q gain (11/17). 12 patients were > 18 months old with L2, undifferentiated tumours, 9 with SCA. All 12 received chemotherapy, but 7/12 surgery, 9/12 radiotherapy and 7/12 retinoic acid. One child is still on treatment, one progressed and died and the remainder are in first remission.

Conclusions

This study shows that all CCLG centres are broadly following the guidelines, but in depth analysis of specific subgroups shows variable adherence. It is important to capture this data as currently the LINES trial is not open in the UK.

EP-348

Neuroblastoma

TUMOR HISTOLOGY FOLLOWING INDUCTION CHEMOTHERAPY AND / OR HIGH-DOSE CHEMOTHERAPY AND ITS IMPACT ON THE OUTCOME OF PATIENTS WITH HIGH-RISK NEUROBLASTOMA

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Objectives

In the recent years in Japan, an increasing number of patients with neuroblastoma (NB) are being treated by the "delayed local treatment (DL)" policy, undergoing surgery after the completion of high-dose chemotherapy with hematopoietic stem cell rescue (HDC). We reviewed the histopathological findings of second-look operations, including those of patients treated with DL.

Methods

From 1998 to 2013, 26 patients with high-risk NB underwent second look operation following chemotherapy. Surgery was performed after induction chemotherapy in 17 cases (STD), whereas 9 cases completed induction chemotherapy and HDC before undergoing tumor resection (DL). Treatment effect was measured by the amount of necrosis. The degree of differentiation was assessed according to the international neuroblastoma pathology classification INPC.

Results

Eighty-eight percent of the tumors showed necrosis in more than 1/3 of the specimen. Two DL cases showed complete disappearance of viable tumor cells. Contrarily, seven contained viable neuroblasts at various proportions. However, the amount of necrosis did not affect the prognosis of the patient within the entire cohort. On the other hand, the degree of differentiation within the viable tumor component, evaluated with INPC, had impact on the survival of the patient. Tumors with immature phenotypes (*i.e.* undifferentiated and poorly differentiated NB) at second-look operation had an extremely poor outcome.

Conclusions

Our results support the previous reports advocating that tumors that sustained unfavorable histology after chemotherapy behave aggressively thereafter. To our knowledge, this is the first report focusing on the histological characteristic of tumors resected after the completion of high-dose chemotherapy with hematopoietic stem cell transplantation.

EP-349

Neuroblastoma

THE RESULTS OF APPLYING THE STRATEGY «SEE AND WAIT» IN CHILDREN WITH SUSPECTED NEUROGENIC TUMOR.

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Objectives

To determine the role of dynamic monitoring of children with suspected neurogenic tumor

Methods

From 2011 to 2012 8 patients aged 0 to 9 months were monitored with «see and wait» strategy at the Research Institute of Pediatric Oncology and Hematology. In 6 of 8 children neoplasm was localized in the adrenal gland, in the 1 child in the posterior mediastinum, and 1 child in the pelvis. 7 of 8 patients had MIBG-positive tumor. 1 child had MIBG-negative neoplasm, neoplasm was found in the prenatal period, now this child is alive without evidence of disease progression. In 7 children progression of the disease noted by the increase of tumor size between 2 to 6 months from the start of observation.

Results

7 of 8 children underwent surgical treatment due to disease progression, they are all alive at the moment without evidence of disease progression, the observation period is from 14 to 17 months. 5 adrenalectomies, 1 tumor removal of the posterior mediastinum and 1 tumor removal pelvis were performed. All the children who received surgical treatment, morphologically and molecular genetically proven low-risk neuroblastoma.

Conclusions

For all children with suspected neurogenic tumors at any location, we recommend to perform surgery to determine the diagnosis and strategy for further treatment.

EP-350

Neuroblastoma

GENETIC PREDISPOSITION SYNDROMES IN CHILDREN WITH NEUROBLASTOMA

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Objectives

The etiology of neuroblastoma (NB) is not fully understood. The aim of the study was to analyze the incidence and nature of cancer predisposition syndromes in a cohort of patients with neuroblastoma

Methods

During the period from 01.2012 to 01.2014 (25 months) 177 children with NB were treated. Diagnosis of NB were made according to the international criteria. Patients were stratified into risk groups and treated according to NB2004 protocol. Cytogenetic analyses tumor tissue was done by FISH for *MYCN*, 1p and 11q status. Karyotyping was performed for all infants < 1 year. Patient's and familial history were collected. All patients were clinically examined for search of clinical abnormalities. Patients with clinical abnormalities were consulted by medical genetic, chromosomal microarray analysis was done if necessary.

Results

Cancer predisposition syndromes was diagnosed in 3 (1.7%) patients. Case 1: 7-month-old girl with left adrenal neuroblastoma, stage 4S had Turner syndrome. The diagnosis was confirmed by karyotyping (45XO). Case 2: 2-month old boy with right adrenal neuroblastoma, stage 1 was diagnosed with 1q21.1 microdeletion syndrome. Malformations include heart abnormalities and deafness. Case 3: 38-month-old boy was diagnosed with left adrenal neuroblastoma, stage 1 and Sotos syndrome. At the age of 7 days the child was operated because of congenital sacroccocygeal teratoma. Multiple malformations were observed including heart abnormalities, hydrocephalus and myotonic syndrome. In case 2 and 3 the cancer predisposition syndromes were confirmed by chromosomal microarray analyses. FISH analyses showed no unfavorable abnormalities. All patients had phenotypic features typical for the each syndrome. In all cases the presence of genetic syndrome was suspected after the diagnosis of cancer had been done.

Conclusions

Genetic predisposition to neuroblastoma is rare. Genetic consultation including karyotyping and chromosomal microarray analysis is indicated to all patients with malformations.

EP-351

Neuroblastoma

BILATERAL ADRENAL NEUROBLASTOMA: SINGLE CENTER EXPERIENCE

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Objectives

Bilateral adrenal involvement in neuroblastoma (NB) is a rare event. Extent of the surgical procedure is a matter of debate. The purpose of the study was to analyse clinical features and outcomes of the cohort of patients treated in single center in Russia.

Methods

During the period 01.2012-01.2014 (25 months) 177 children with NB were treated. The diagnosis was confirmed according to the international criteria. Stage was assigned according to INSS. Patients were stratified into risk groups and treated according to NB2004 protocol. Cytogenetic analyses of tumor tissue was done by FISH for *MYCN*, 1p and 11q status. Morphologic verification was recommended in patients aged 3 months or older.

Results

Bilateral adrenal involvement was diagnosed in 7 (4%) patients. Median age was 1.6 months (range 0.5 -8.8). Male to female ratio was 2.5:1. Initial diagnosis was based on clinical data in 5 (71%) and histology in 2 (29%) patients. Stage distribution: stage 4S – 5 (71%), stage 2 – 1 (14%), stage 1 – 1 (14%). Site of distant metastasis included liver in 4 patients (57%) and liver and bone marrow – 1 (14%). 2 (29%) patients were operated at the age of 3 months. Cytogenetic analysis showed lack of unfavorable abnormalities in all 4 studied cases. 5/6 (83%) patients had MIBG-positive primary tumor, 2/4 had MIBG-positive liver metastasis. Extent of the surgical procedure was gross total resection (1/4), subtotal resection (1/4) and biopsy (2/4). No patients had bilateral adrenalectomy. 3/7 patients received chemotherapy, 1 patient abdominal irradiation. 2/7 patients were observed and showed tumor regression. Median follow-up was 5.8 months (range 1.5-21.9). Outcomes: 6 patients alive (3 archived complete response), 1 patients with stage 4S died due to massive hepatomegaly.

Conclusions

Our data confirmed favorable features of neuroblastoma in patients with bilateral involvement and association with stage 4S. Aggressive surgery is not warranted in such cases.

EP-352

Neuroblastoma

CONCURRENT EXTRARENAL NEPHROBLASTOMA AND NEUROBLASTOMA IN AN INFANT

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Objectives

Nephroblastoma is the most common malignant renal tumor in children. Extrarenal nephroblastoma is rare. Concurrent extrarenal nephroblastoma and neuroblastoma is extremely rare. We report a 9 month old girl with extrarenal nephroblastoma presenting with inguinal mass who was a surrenal mass during investigations for nephroblastoma.

Methods

Case report

Results

A previously healthy 9 month old infant, born after in vitro fertilization was referred to us after being diagnosed with extrarenal nephroblastoma. She was in good health until 7 months of age when parents noticed a left sided inguinal mass. The ultrasound showed a 39X24X26 mm solid mass. Her AFP, B-HCG, ferritin, LDH levels and CBC were within normal limits. She was seen by a pediatric surgeon at another medical center and underwent a total resection. The pathology was consistent with nephroblastoma, with no anaplasia. The computed tomography of the chest and abdomen showed no lung metastasis, no lesion arising from kidneys but a left suprarenal mass. The NSE was slightly elevated. She then underwent a total excisional of the suprarenal mass with lymph node sampling at our institution. The pathology revealed neuroblastoma with no lymphatic involvement. The bone scan and the bone marrow biopsy showed no metastatic disease. She was diagnosed with totally excised stage 1 neuroblastoma and stage 1, favorable histology extrarenal nephroblastoma. She was started on chemotherapy as per NWTS-5 EE-4A protocol 3 days after the second surgery.

Conclusions

The co-existence of extrarenal nephroblastoma and neuroblastoma is extremely rare. During the diagnostic and metastatic workup for a rare tumor, in case of co-existence of another mass, detailed investigations should be done in order to stage properly before deciding on further therapy. The correlation, if there is one, of in vitro fertilization and co-existence of the two tumors should also be studied in a larger population of infants.

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Neuroblastoma

PROGNOSTIC SIGNIFICANCE OF 1P36, 17P DELETIONS, MDM2 GENE EXPRESSION IN NEUROBLASTOMA WITH NEGATIVE MYCN GENE STATUS

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Objectives

The high clinical heterogeneity of neuroblastoma reflects the complexity of genomic abnormalities characterized these tumors. The role of *MYCN* gene amplification in neuroblastoma pathogenesis was first established in the early 1980s due to its association with high risk tumors and low patients survival. Currently prognostic significance of several other genetic abnormalities in neuroblastoma are under consideration. The purpose of our study is to determine the prognostic significance of 1p36, 17p deletions, *MDM2* gene expression in neuroblastoma with negative *MYCN* gene status.

Methods

Seventy two children diagnosed with II-IV stage neuroblastoma, aged 6 months to 12 years were enrolled in our study. Patients were assigned to treatment on the basis of age, tumor *MYCN* status, and tumor cell ploidy. The investigations of 1p36 and 17p deletions and *MYCN* gene amplification in tumor cells were performed by FISH method. The *MDM2* gene expression study was performed by the real-time RT-PCR, tumor cell ploidy study - using flow cytometry.

Results

It has been shown that the negative status of the *MYCN* found in 66% of neuroblastoma cases with unfavorable disease course. No chromosome 17p loss has been found in these tumors. Assumed that in these tumor cases transcriptional function of *TP53* are under control of *MDM2* protein. High *MDM2* gene expression level in tumors is associated with poor response to chemotherapy, regardless of the gene *MYCN* status. We have revealed that deletion of chromosome 1p36 in tumor cells occurs in 22% of all investigated neuroblastoma tumors and in 50% of cases associated with *MYCN* gene amplification. In 30% of patients with negative status of *MYCN* gene, deletion of chromosome 1p36 associated with disease progression.

Conclusions

Deletions of 1p36 and 17p and elevated levels of *MDM2* gene expression are important for prognosis in neuroblastoma and could be recommended for the replenishment of the genetic component of the risk grouping stratification complex.

EP-354

Neuroblastoma

TREATMENT OF STANDARD AND HIGH RISK PATIENTS GROUP WITH NEUROBLASTOMA. ONE CENTRE EXPERIENCE

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Objectives

Historically, high-risk neuroblastoma patients have had long-term survival probabilities of less than 15%. With the advent of comprehensive treatment approaches that include intensive induction chemotherapy, myeloablative consolidation therapy with stem cell rescue and targeted therapy, OS rates have improved. However, the current survival rates remain unacceptable and have come at the expense of substantial immediate and long-term morbidity

Methods

In 2007-2013, 182 patients with neuroblastoma: 87 standard-risk (SR) patients and 95 high-risk (HR) patients received treatment in the Science Research Department of Pediatric Oncology at the National Cancer Institute. All enrolled patients received treatment according to NB-2004 and HR-NBL-1/ESIOP protocols. 54 HR patients were cured high-dose chemotherapy (HDCT) with autologous stem cell support, of these, 13 patients were cured with tandem HDCT

Results

The 5-year overall survival (OS) was 67 % for SR patients and 30.4 % for HR patients. The following unfavorable prognostic factors for neuroblastoma were used in our study: the child's age at the time of making a diagnosis, stage, N-myc amplification. Depending on the child's age: the OS was 58.8 % for patients under 1 year of age, while the OS was 19.2 % for patients aged 1 year or over. We also analyzed the survival rate of HR patients based on whether the patient has N-myc amplification. The OS was 49.8 % for N-myc negative subjects and 24.3% for N-myc positive subjects. Currently, the OS is 69.2 % for patients who were treated with tandem HDCT with autologous stem cell support

Conclusions

Depending on the therapeutic program used, the OS were 22.7 % (NB-2004) and 38.9 % (HR-NBL-1/ESIOP) for HR patients. The results of treatment of HR patients with receive tandem HDCT with autologous steam cell support are encouraging

EP-355

Neuroblastoma

TANDEM PERIPHERAL BLOOD STEM CELL TRANSPLANTATION IN CHILDREN WITH NEUROBLASTOMA

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Objectives

Based on the results recent of investigations, application of autologous stem cell tandem transplantation (TT) could improve the treatment results of patients with some malignant solid tumors. Nowadays TT is investigated for medulloblastoma, germ cell tumor and high-risk neuroblastoma. Nevertheless effectiveness convincing results haven't been obtained.

Methods

During the 2012 year the Department of Pediatric Oncology at the National Cancer Institute have been carried out 13 tandem transplantations in children with high-risk of neuroblastoma. Patient's age was 1 - 14 years. 10 pts. with primary neuroblastoma got TT after chemotherapy on HR-NBL-1/ESIOP protocol, 3 pts. as a consolidation of relapse second-line therapy. The first part of tandem chemotherapy was BuMel in all patients. Ten patients had topotecan-based regimens as the second part of tandem transplantation and three patients had CEM regimen. A time interval between parts of tandem was 1 - 3 months. For autologous transplantation have been used only peripheral stem cells. All patients received 13-cis retinoic acid after of conventional treatment.

Results

All patients successfully completed first high-dose chemotherapy. WBC count recovered more then 500/ μ L on +10-15 day, PLT count recovered on +13-28 day after PBSC. In one patient was observed neurotoxicity like short clonic and tonic seizures after second high-dose chemotherapy. Chemotherapy was cancelled immediately (patient received 2/ 3 doses of cyclophosphamide and topotecan full dose). There were neutropenia and thrombocytopenia 4th rate, oral mucositis with different degrees of severity in all patients. WBC count recovered more then 500/ μ L on +9-14 day, PLT count recovered on +12-22 day. Currently, 5 of 13 patients are in CR, 4 patients had early relapse and continue treatment, 4 died of PD. The follow-up period after accomplishment of TT is 2 - 14 months.

Conclusions

Application of TT in children with high-risk neuroblastoma resulted to two-year disease-free survival rate of about 38 % and the overall three-year survival rate to 47 %

EP-356

Neuroblastoma

SURGICAL APPROACH TO THORACIC INLET TUMORS ARISING FROM THE SYMPATHETIC CHAIN IN CHILDREN - A SINGLE INSTITUTION'S EXPERIENCE

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Objectives

Neuroblastoma (NB) is the commonest extra-cranial pediatric solid tumor in Singapore. NBs arising at the thoracic inlet may carry a better prognosis despite the challenging surgical access to this area. We examine our center's experience with these tumors.

Methods

With IRB approval, clinical charts of patient with thoracic inlet tumors fulfilling ICD-O-3 (International Classification of Diseases for Oncology) 95003 (neuroblastoma); 94903 (ganglioneuroblastoma); and 94900 (ganglioneuroma), managed in our center between 2007 and 2013, were reviewed.

Results

There were 4 girls and 1 boy with median age of 32 months old (10 months – 60 months) of age. Three patients had neuroblastoma, one had ganglioneuroblastoma and one had a ganglioneuroma. Amongst those with neuroblastomas, 1 had stage 4 disease with bony metastases, the other 2 had stage 3 and 2b disease; with an enlarging neck mass in one and a neck abscess in the other. Following chemotherapy, anterior trap-door thoracotomies were performed for the first 2 patients while thoracoscopic assisted resection was performed in one. Upfront thoracoscopic-assisted resection was performed for the ganglioneuroblastoma and resection using the Da Vinci robot was performed for the ganglioneuroma. All patients had post-operative Horner's syndrome which improved over time. One patient had phrenic nerve-praxia that resolved. Aside for the child with stage 4 NB, all patients are well with no residual disease at a mean follow-up of 24.8 months (4 months – 75 months). One child succumbed to refractory bone marrow disease.

Conclusions

While the thoracic inlet poses challenges for resection of NBs at this site, mature elements in these tumors may lend themselves to a favourable prognosis. Minimally invasive approaches allowed superior visualization of the anatomy while anterior trap-door thoracotomies facilitate dissection around critical structures.

EP-357

Neuroblastoma

THREE CASES REPORT OF PEDIATRIC ATYPICAL NEUROBLASTOMA

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Objectives

To show the clinical characteristics of atypical neuroblastoma in three Chinese pediatric patients.

Methods

Retrospective analysis was made of three cases of atypical neuroblastoma.

Results

Atypical neuroblastoma refers to the primary onset of neuroblastoma without a detectable mass in common sites, but in bone marrow or/and other metastasis parts, is an infrequent occurrence. We present three unusual cases of Chinese atypical neuroblastoma that the extramedullary substantial mass not be found. Moreover, the three cases both presented with typical neuroblastoma cells that forming Homer-Wright rosettes in bone marrow smear. The diagnosis of neuroblastoma was further established by markedly elevated of vanillylmandelic acid (VMA) in urine, serum neuron-specific enolase (NSE) and neuroblastoma MRD level in peripheral blood, amplifications of bone marrow N-myc were all absent. Noteworthy, the first case showed no other parts of the tumor infiltration in addition to bone marrow, while in the second case and third case the involvement of neuroblastoma both in bone marrow and bone. The three patients were treated with nine courses of induction chemotherapy as high-risk neuroblastoma protocol, which includes CAV (Cyclophosphamide+Pirarubicin+Vincristine), PVP (Cisplatinum+ Etoposide) and CT (Cyclophosphamide+Topotecan). Although the first patient achieved complete remission, the child is not free of recurrence at a follow-up of half a year due to lack of consolidation chemotherapy. In the second case, by contrast, complete remission was not obtained, and then he abandoned further treatment for economic reason. The third case achieved partial remission after the entire induction chemotherapy, and he experiences consolidation chemotherapy at present.

Conclusions

In case of atypical neuroblastoma, chemotherapy might be the only effective firstline treatment for the absence of visible solid mass. In our limited experience, it seems that the patients of atypical neuroblastoma have unfavorable prognosis after conventional intensive chemotherapy, especially in the presence of bone involvement.

EP-358

Neuroblastoma

EFFECTS OF ARSENIC TRIOXIDE AND CONVENTIONAL CHEMOTHERAPEUTIC DRUGS ON EXPRESSION OF P-GLYCOPROTEIN IN HUMAN NEUROBLASTOMA CELL LINE SK-N-SH

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Objectives

The aim of this study was to investigate the effects of arsenic trioxide (As₂O₃) and conventional chemotherapeutic drugs on the apoptosis and P-glycoprotein (P-gp) expression of neuroblastoma SK-N-SH cells.

Methods

The change of expression level of P-gp was measured by Western blotting after SK-N-SH cells were incubated with various anti-cancer drugs including As₂O₃, cisplatin(DDP) and etoposide(Vp16). Flow cytometry with Annexin V-PI staining was used to monitor the ability of As₂O₃ to induce SK-N-SH cells apoptosis.

Results

In our previous studies, we found that As₂O₃ may be a potent anti-cancer agent in human neuroblastoma cell lines. Our results further determined findings reported previously and shown that As₂O₃ had a dose- and time-dependent toxic effect on SK-N-SH cells via induction of apoptosis. The IC₅₀ of As₂O₃ for 72h treatment was found to be 3uM. The Western analysis showed that the expression of P-glycoprotein began to decrease with in the micromolar range As₂O₃ exposure for 48h and further decrease after 72h and 96h. With 3uM As₂O₃ exposure for 72h, the expression of P-glycoprotein reduced mostly rapidly. However, the expression of P-glycoprotein of SK-N-SH cells was increased when treating with DDP and VP16 as the drugs concentration and effective time increase.

Conclusions

We show that As₂O₃ exerted its anti-tumor effect in SK-N-SH cells via induction of apoptosis. These findings of western analysis provide experimental evidence that low dose As₂O₃ reduces the P-gp expression in human neuroblastoma cell line. To the contrary, conventional chemotherapeutic drugs increase the P-gp expression. Taken together, we propose that As₂O₃ was probably not the substrate to be extruded by P-glycoprotein in SK-N-SH cells because it reduces cellular P-glycoprotein expression.

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Neuroblastoma

MULTIDISCIPLINARY TREATMENT FOR HIGH RISK NEUROBLASTOMA IN BEIJING CHILDREN'S HOSPITAL FOR 3-YEAR RESULTS

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Objectives

Beijing Children's Hospital (BCH) has established a multidisciplinary program for neuroblastomas (NB) since early 2007. We summarized high-risk NB (HR-NB) in BCH for 3-year results.

Methods

Retrospectively reviewed medical records of children presenting with clinically and/or histologically confirmed NB between Apr 1, 2007 to March 31,2011. HR-NB must have over 1 year of age. All stage III unresectable, IV and patients with tumour genomic N-myc copy number more than 10 (irrespective of stage or age) were eligible. Multimodality treatment for HR-NB protocol included intensive chemotherapy, surgery and radiation therapy for local control ,followed by autologous haematopoietic stem cell transplantation (auto-PBSCT) for consolidation therapy and also isotretinoin for maintenance treatment. Total courses were 1.5years. All children followed up to Dec 31,2013.

Results

Total 67 HR-NB children, 43 boys,24 girls, median age 49 months(12~147) , 66 of INSS-IV and 1 of ?, 16 of primary postmediastinal tumor, 51 of retroperitoneal and pelvic tumor. Of 52 patients with fully known biologic features, 31 cases of NB or NB chemotherapy change, 19 cases of ganglioneuroblastoma, only one for ganglioneuroma. 4 had N-myc gene amplification by FISH. 51 of HR-NB children were treated and followed-up regularly, median time 36 (6 ~76) months for follow up, 26 occurred event, 7 were relapsed after stopped treatment for median 28 (8~50) months, 17 for tumor progression, 2 patients were died by severe infections. Using *Kaplan-Meier* analysis showed the expected 3-year overall survival rate was 49%.

Conclusions

HR-NB prognosis is far lower than the common childhood leukemia and lymphoma. The most important role was multidisciplinary treatment in order to improve HR-NB children survival rates . Moreover, it's still the possibility for recurrence and relapse after stopping treatment 1~5 years, the long-term follow up for HR-NB was necessary.

EP-360

Neuroblastoma

COMPARATIVE STUDY BETWEEN PET AND MIBG IN DIAGNOSIS AND MANAGEMENT OF NEUROBLASTOMA

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Objectives

¹²³I-metadiodbenzylguanidine is the conventional radiopharmaceutical imaging (¹²³I-MIBG) in neuroblastoma diagnosis, with a sensitivity of about 90% and specificity of nearly 100%. Although neuroblastoma cells can concentrate ¹⁸F-FDG, several conflicting results about PET scan in the evaluation of Neuroblastoma, were reported. The purpose of the study was to prospectively evaluate the diagnostic significance of PET/CT imaging and to compare its diagnostic and prognostic value to ¹²³I-MIBG scintigraphy in patients with neuroblastoma at different phases of disease.

Methods

A Total of 30 patients (14 males and 16 females), less than 18 years, all diagnosed and treated at the Children's Cancer Hospital-Egypt according to COG A3973 for high risk patients and COG A3961 for intermediate risk patients. They all did ¹²³I-MIBG and ¹⁸F-FDG PET scans (within 1 month) at diagnosis and at different points during their management.

Results

Scans (MIBG and PET) were examined for 30 patients at different management stages with comparison to CT scans for primary tumor site, with bone scan for bone involvement, and with bone marrow biopsy result for bone marrow infiltration. PET scan was positive in 60% of scans for primary site, in 23.3% for bone involvement, and in 13.3% for bone marrow infiltration, whereas MIBG scan was positive in 36.7 % for primary site, in 10% for bone, and in 10% for bone marrow infiltration. PET scan was more sensitive than MIBG in detecting primary tumor (0.8 for PET versus 0.5 for MIBG), in detecting bone metastases (0.6 for PET versus 0.3 for MIBG), and for bone marrow involvement (0.28 for PET versus 0.21 for MIBG). Incorporating all modalities lead to better treatment decisions.

Conclusions

The authors recommend the use of PET/CT in evaluating primary tumor either at diagnosis or at different stages of therapy although further extended double blinded studies are needed.

EP-361

Neuroblastoma

NEUROBLASTOMA IN PATIENTS UNDER 18 MONTHS: A SINGLE INSTITUTION EXPERIENCE IN ARGENTINA

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Objectives

To evaluate the outcome of patients under 18 months diagnosed with neuroblastoma.

Methods

Between April 2006 and October 2012, 38 consecutive patients were retrospectively reviewed.

Results

Mean age of 8.9 months (0.7-18 months). Frequently sites: adrenal gland (n=15) paravertebral (n=8), 2 or more sites involved (n=7), cervical (n=4), and mediastinal (n=4). Histopathological diagnosis: poorly differentiated neuroblastoma (n=24), in differentiation (n=3), metastatic neuroblastoma (n=2), intermixed ganglioneuroblastoma (n=1), neuroblastoma uncharacterized (n=7), not biopsied (n=1). N-myc amplification was detected in 4 patients (7 not studied), deletion of 1p (del1p) in 3 patients (12 without evaluating), and 11q aberration in one patient (only 8 patients studied).

According to INRG pretreatment classification schema, 19 patients belonged to the L1 category, receiving chemotherapy (n=1), surgery (n=15), chemotherapy+surgery (n=3) and observation only (n=1). Nine patients were L2 category, 3 received chemotherapy, 4 surgical treatment and 2 surgery+chemotherapy (1 N-myc amplified and 1 del1p). Seven patients were stage M, (1 amplification of N-myc, one del1p, one aberration of 11q, 2 amplification of N-myc with del1p) receiving treatment for intermediate-risk (n=2) and high-risk groups (n=5). Three patients were classified as stage Ms, one received treatment for intermediate and 2 for low-risk groups.

With a median follow-up of 25 months (3-80 months), at 24 months the EFS of all patients was 85% (SE 6%) and OS of 91% (SE 5%). Significant difference was found in OS and EFS between patients with stages L1, L2 and Ms vs stage M. EFS for each stage: L1 89% (SE 7%), L2 100%, MS 100%, vs M 57% (SE 18%), p=0,01. OS: L1 94% (SE 6%), L2 100%, MS 100%, vs M 71% (SE 19%), p=0,03.

Conclusions

Although OS and EFS results are similar to those reported in international studies, improvements in obtaining results of biological prognostic factors will warrant an accurate staging and consequently an appropriate treatment.

EP-362

Neuroblastoma

RETROSPECTIVE EVALUATION OF CLINICAL CHARACTERISTICS AND OUTCOME OF PATIENTS WITH HIGH-RISK NEUROBLASTOMA TREATED AT THE CHILDREN'S CANCER INSTITUTE IN LEBANON

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Objectives

To evaluate clinical characteristics and outcome of patients with high-risk neuroblastoma treated at the Children's Cancer Institute in Lebanon.

Methods

After IRB-approval, clinical data for 35 patients diagnosed between April 2002 and December 2013 at a single multidisciplinary center were retrospectively analyzed. Risk stratification was based on Children's Oncology Group (COG 9641/3961 studies).

Results

21 patients had high-risk disease. Median age at diagnosis was 3.6 years (range 0.5–13.9 years) with a male-to-female ratio of 1.3:1, and a median follow-up of 22.6 months (range 5–116 months). Based on International Neuroblastoma Staging System, all patients had stage IV disease. MYCN-gene was amplified in 6 /15 tested tumors (40%). All patients were treated as per COG-A3973 protocol, and 81% (n=17) achieved complete response (CR), while 19% (n=4) had progressive disease on therapy (PD). Sixteen patients (76%) underwent autologous stem-cell transplantation (ASCT) as consolidation therapy; the rest did not qualify due to poor response (n=4) or relapse before consolidation (n=1). Thirteen patients (62%) received radiotherapy as part of local control; reasons for not receiving radiotherapy included PD (n=5) and death of toxicity (n=3). Currently, 48% (n=10 patients) are alive at a median follow-up time of 2.7 years: Eight patients are in CR1 and two are in CR2. Eleven patients died, eight (38%) due to tumor progression, and 3 (14%) due to toxicity during consolidation (CNS toxoplasmosis, failure of engraftment, and sinusoidal obstruction syndrome, respectively).

Conclusions

Overall survival for high-risk neuroblastoma in Lebanon seems to be comparable to that in developed countries when multimodality therapy is given in a multidisciplinary setting. Further improvements will likely depend on the availability of novel therapies that are not yet easily accessible in developing countries.

EP-363

Neuroblastoma

HOW THE EUROPEAN CLINICAL TRIAL DIRECTIVE IMPACTS TRIAL IMPLEMENTATION: LINES, ON BEHALF OF SIOPEN COOPERATIVE GROUP

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Objectives

European Low and Intermediate Risk Neuroblastoma (LINES, EudraCT: 2010-021396-81, ClinicalTrials.gov Identifier: NCT01728155) is an international SIOPEN clinical trial, in the framework WP10 (ENCCA PROJECT: European Network for Cancer research in Children and Adolescents). LINES stratifies patient's treatment according to biological and clinical markers in order to: i) minimize the treatment burden in those low-risk patients who in previous studies were shown to have an excellent long-term outcome, ii) intensify treatment in those patients with biologically unfavourable but not MYCN amplified neuroblastoma to improve outcome.

Methods

LINES includes ten separate therapeutic groups, one of them randomised. All the cases are registered at *Siopen-r-net* database with check-points to monitor the quality of prospectively entered staging data, including real time central review for biology and histology. Neonatal adrenal masses (NAM) in infants below 3 months are also registered and observed, without initial surgery.

Results

LINES trial-sponsored by IIsLaFE was first launched in Spain (28 sites) in July 2011 and it was opened in Italy (21 sites), Austria (5 sites) and Denmark (3 sites) in 2012. Then, France (29 sites), Norway (4 sites), Israel (1 site) and Belgium (2 sites) were authorized in 2013. Switzerland, Ireland, Slovenia and New Zealand are expected to be authorized in the coming months. In summary, only 8 of 21 expected participating countries have been opened for recruitment and 142 patients have been enrolled and grouped (73 low risk, 32 intermediate risk and 37 NAM) in the last 2.5 years.

Conclusions

Since European Clinical Trial Directive 2001/20/EC implementation, it has been very difficult to launch academic pediatric cancer trials due to high cost, additional national requirements and bureaucracy, delaying clinical trial initiation. We hope the new Clinical Trial Regulation will bring a process of harmonisation and shorten timelines across Europe.

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EP-364

Neuroblastoma

GANGLIONEUROMA: SINGLE CENTER EXPERIENCE IN RUSSIA

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Objectives

Ganglioneuroma is a rare benign tumor of the sympathetic nervous system. The standards of care including indications for surgery and radiation therapy for this rare condition have to be determined. The aim of the study was to analyze the clinical features and outcomes in the cohort of patients in single center in Russia.

Methods

193 patients with sympathetic nervous tumors were treated during the period 01.2012-03.2014. Initial work-up included CT/MRI of the primary site, tumor markers, MIBG scintigraphy and bone marrow evaluation. Pathological diagnosis was done according to the International Neuroblastoma Pathology Classification. Patients were stratified and treated according to the NB2004 protocol. Surgery was the treatment of choice in patients without image-defined risk factors.

Results

Ganglioneuroma was confirmed by histology in 6 (3.1%) cases. Primary GN was diagnosed in 5 patients, secondary in 1 patients (second-look operation after 5 cycles of chemotherapy). Male-to-female ratio was 2:1. All patients were older than 1 year. Median age was 60.3 months (range 51.0-82.1). All 5 patients with primary GN were symptomatic at the time of the diagnosis, mild pain was the most common symptom. Distribution of patients by the primary site: 3/6 – retroperitoneum, 2/6 – posterior mediastinum, 1/6 – presacral. 3/6 had elevated neuron-specific enolase level (< than 2 upper limits). 3/4 patients had MIBG-positive tumor. The extent of surgery was gross total resection (3/6, 50%), macroscopic residual tumor (1/6, 17%), biopsy (2/6, 33%). Surgery was limited to biopsy because major vessels involvement in 2 patients (presacral and retroperitoneum localization). Median follow-up was 8.4 months (range 0.4-22.4). All patients alive without evidence of disease progression. Two patients after biopsy showed no progression of both the tumor and symptoms.

Conclusions

Surgical treatment depends on the presence of image-defined risk factors. In cases with image-defined risk factors the benefits of the surgery should be balanced with the risk of severe morbidity.

EP-365

Neuroblastoma

ANALYSIS OF SHORT TERM EFFICACY FOR 59 CASES OF CHILDREN WITH NEUROBLASTOMA

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Objectives

A retrospective analysis of 59 cases of children with neuroblastoma (NB) correlation short term efficacy and prognostical factors.

Methods

Total 59 newly diagnosed NB patients from July 1, 2008 to June 30,2013 were divided into low risk(LR), medium risk(MR) and high risk(HR) groups depends on age and clinical stage. Chemotherapy and 13-cis-retinoid acid and/or second tumor resection were used at the end of treatment referring to different risk groups.

Results

1. According to INSS, the number of cases in stage I, II, III, IV and IVs was 4 (6.8%), 7 (11.9%), 18 (30.5%), 22 (37.3%) and 8 (13.5%), respectively. Follow up to Dec 31, 2013, 43 cases (43/59, 72.9%) achieved complete remission (CR) or partial remission (PR). The 3-year overall survival (OS) of stage I, II, III, IV and IVs were 100%, 100%, 65.6%,34.8% and 85.7%;and the EFS were 100%, 66.7%, 65.6%,30.4% and 34.3%(P=0.013, 0.004). The 3-year OS and EFS of LR, MR, HR were 100%,92.7%,28.3% and 100%,53%,25%(P=0.001,0.001).

2. In 59 cases, 45 of diagnosed with pathologic diagnosis whose different histopathological subtype, stroma and mitosis karyorrhexis index (MKI) were not statistically significant with survival. The 3 year OS and EFS were obviously higher from the patients with favorable histology(FH) than the one with unfavorable histology(UH) (P=0.046,0.030).

3. Univariate statistical analysis showed that the factors significantly correlated with prognosis were age, stage and risk group(P=0.004,0.013,0.001). Age, bone marrow metastasis at diagnosis and risk group were important for event of NB patients(P=0.005,0.009,0.002).

Conclusions

1. Stage,risk group and age are important prognostic factors for NB. In the absence of N-MYC data, 18 months is the dividing line for prognosis of patients.

2. Histologic category combined with age, MKI and pathology is in favor of prediction the prognosis of NB patients.

EP-366

Neuroblastoma

DIAGNOSTIC IMPLICATIONS OF N-MYC ONCOGENE AMPLIFICATION IN UNILATERAL PEDIATRIC RENAL TUMOR: A CASE REPORT

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Objectives

Renal tumors of childhood occasionally exhibit histopathologic and clinical features that prevent accurate diagnosis. Molecular and cell culture techniques may be helpful in better characterizing these cases

Methods

In this case report, n-myc FISH was used to examine unusual renal tumors from a 11 month old female to establish the accurate assessment of the tumor and to stratify the risk group. FISH testing was performed on formalin fixed paraffin embedded tissue of suprarenal area using commercially available probe.

Results

Histopathological evaluation of right kidney showed features of Wilm's tumor with predominant epithelial component. The resected margin of the ureter and capsule were free of tumor. She also had mass in right suprarenal area which on histopathology showed features suggestive of undifferentiated neuroblastoma. Three lymph nodes isolated from the hilar area showed deposit of Wilm's tumor. FISH analyses of the supra renal mass revealed amplification of n-myc gene thus favouring neuroblastoma.

Conclusions

Although histopathologic features could not clearly distinguish between Wilms' tumor and neuroblastoma, but n-myc gene amplification strongly suggested that this neoplasm would behave as an aggressive neuroblastoma. FISH analyses therefore contributed to a revised diagnosis of neuroblastoma and is an effective approach in case such dilemmas occur.

EP-367

Neuroblastoma

TREATMENT OUTCOME OF LOW-RISK AND MEDIUM-RISK NEUROBLASTOMA TREATED ACCORDING TO GERMAN NB 2004 PROTOCOL

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Objectives

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Retrospective evaluation of the treatment outcome in patients from observation (OG) and medium-risk (MRG) groups of NB2004 Protocol.

Methods

Among 90 children with primary neuroblastoma treated according to NB2004 in our hospital from December 2005 till October 2013 58 (64%) patients were stratified to OG and 12 (13%) ones referred to MRG. Median age of these OG/MRG patients was 8 months (range 10 days-15 years). Patients' distribution by stage was as follow: stage I had 35 (50%) children; stages II, III, IV and IVS were diagnosed in 5 (7.1%), 17 (20.7%), 6 (8.6%) and 7 (10%) patients respectively. Median of follow up period is 43 months.

Results

In 13(22,4%) patients from OG (10 with stage III, 3 with stage IVS) chemotherapy started immediately after diagnosis because of the huge size of primary tumor or life-threatening symptoms. All the patients from MRG were treated according to medium-risk arm. At present time 66 (94.3%) patients are alive; 63 (90%) are alive without progression. Unfavorable events were registered in 7(10%) cases. Among them there were 2(2.9%) relapses, 4(5.7%) cases of progressive disease, 1(1.4%) therapy-related death. Other 3(4.2%) patients died from tumor progression. 7-years EFS in the whole group was 86%±4% and OS was 90%±4%. EFS and OS in patients from OG and MRG did not differ significantly: 85%±5% vs. 90%±9% (p=0.69) and 88%±5% vs. 100% (p=0.30), respectively. The worst prognosis had patients with stage IVS in comparison with other children: EFS is 35%±19% vs. 91%±4% (p<0,0001) and OS is 57%±24% vs. 94%±4% (p=0.003), correspondingly.

The worst outcome had patients with stage IVS in comparison with other children. EFS 35%±19% vs. 91%±4% (p<0,0001) and OS 57%±24% vs. 94%±4% (p=0.003), correspondingly.

Conclusions

The prognosis of children with low-risk and medium-risk neuroblastoma is excellent. Existing NB2004 Protocol criteria of patients' stratification demonstrated their effectiveness and in the majority of cases allow reducing the treatment intensity.

EP-368

Neuroblastoma

LOCALIZED ABDOMINAL NEUROBLASTOMA , PRESENTING WITH CHYLOTHORAX- A RARE ASSOCIATION

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Objectives

to describe the rare association between localized abdominal neuroblastoma and chylothorax

Methods

3.7 years old male presented with respiratory distress secondary chylothorax and found to have abdominal neuroblastoma

Results

A 3.7 years boy presented with one month fever , abdominal pain & distention. He developed breathing difficulty 20 days prior to presentation and greenish discoloration of left upper chest a day before. He was tachycardic , tachypneic and had retraction along with reduced air entry on left side of chest. Abdomen distended in left upper quadrant with palpable mass. His initial hemogram showed Hb 7.4 gm%, other parameters being normal. X-ray chest showed left pleural effusion . USG abdomen showed large well defined lobulated solid mass 9x8x6 cms lesion with areas of necrosis in left suprarenal region compressing renal vessels but not encasing. Pleural fluid tapped and analyzed. It was milky white fluid with specific gravity of 1.012, leukocyte count 5000/ μ L with 90% lymphocyte, while the triglyceride and cholesterol content 220 and 50 mg/dl respectively. Lipoprotein electrophoresis of fluid showed chylomicron band, conclusive of chylothorax. USG guided biopsy of abdominal mass HPE and immunohistochemistry suggestive of neuroblastoma with NSE and chromogranin being positive. After initial stabilization patient was started on chemotherapy Rapid COJEC. he was started on octreotide and continued 2 weeks to control Chylothorax as it was symptomatic and was reaccumulating rapidly post tapping.

Post rapid cojec mass was resected followed by autologous stem cell therapy as it was N myc amplified.

Conclusions

Thoracic Neuroblastoma produces chylothorax due to either extrinsic compression or infiltration of the thoracic duct, which causes increase in intraductal pressure. In our case interestingly the abdominal neuroblastoma has presented with chylothorax which is not described earlier. It resolved in 3 weeks with chemotherapy and octreotide.

EP-369

Neuroblastoma

IMPROVING TREND IN SURVIVAL OUTCOME OF HIGH RISK NEUROBLASTOMA IN SINGAPORE

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Objectives

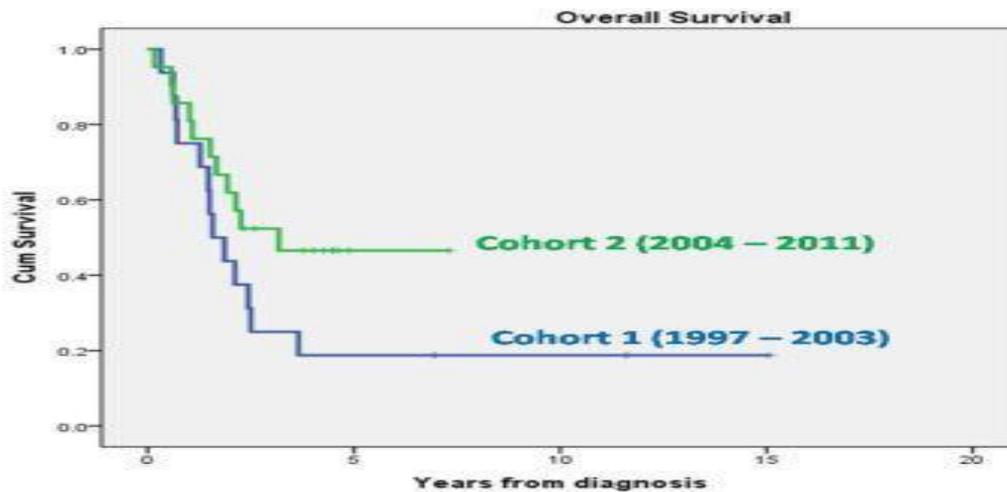
High-risk neuroblastoma patients in Singapore are treated with chemotherapy, surgery, myeloablative therapy (MAT), radiation and cis-retinoic acid maintenance. We retrospectively reviewed characteristics, treatment practices and outcome of high-risk patients seen at KK Women's and Children's Hospital (KKH), the largest pediatric unit in Singapore.

Methods

The study was approved by Singhealth Centralized Institutional Review Board. We included patients who were (1) INSS stage 4 and over 12-months-old at diagnosis, or (2) stage 2/3/4S with *NMYC*-amplification, and treated at KKH from 1997 to 2011 (15 years). We excluded patients who came for second opinion or surgery only. We divided patients into earlier (1997 – 2003, cohort 1) and later cohorts (2004 – 2011, cohort 2) for comparison.

Results

There were 37 high-risk patients – 16 in cohort 1; 21 in cohort 2. The median age at diagnosis was 34.5 months (range 12.2 months to 9.9 years), and 23 (62%) were boys. Majority (92%) had stage 4 disease; 3 had *NMYC*-amplified stage 3 disease. Changes in management were identified. *NMYC* status was available for 7/16 (44%) patients in cohort 1, and all in cohort 2. The chemotherapy was OPEC/OJEC before 2008, and modified N7 from 2008. MAT conditioning consisted of cisplatin, teniposide, doxorubicin and melphalan, with/without TBI (modified VAMP-TBI); TBI was omitted from 2009. 20/37 (54%) patients underwent MAT - 44% of cohort 1; 62% of cohort 2. 12/16 (75%) patients from cohort 1 and 10/21 (48%) from cohort 2 died of disease. Two died from sepsis. The 3-year overall survival was 18.8% (cohort 1) and 46.6% (cohort 2).



Conclusions

Although numbers were small, the trend was encouraging, and could be explained by multiple factors - regimes, surgery, supportive care, dedicated teams, uniform practices. We hope results will continue to improve with the availability in future of immunotherapy, MIBG therapy, novel agents or other modalities.

EP-370

Neuroblastoma

THE ROLE OF P53/MDM2 PATHWAY ABNORMALITIES IN NEUROBLASTOMA PROGNOSIS

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Objectives

Abnormalities in p53 pathway are present in 30-40 % of neuroblastoma (NB) cases at diagnosis and occur predominantly by MDM2 hyperexpression and p14ARF inactivation. The aim of our study was to estimate the role of p53/MDM2 pathway abnormalities in neuroblastoma prognosis.

Methods

The case group comprised 84 patients with histologically confirmed NB (median age: 39.6 month; range: 1.5 – 204 months; I-II stages: 15; III-IV stages: 69; MYCN-amplified tumors: 27 %). Patients were treated according to a risk groups under the international standard protocols. Primary tumor tissue obtained from patients at diagnosis was used for molecular-genetic analysis. TP53 deletion and MYCN gene amplification were detected by FISH method. The MDM2 gene expression level was analyzed by TaqMan real time RT-PCR.

Results

Deletion of TP53 was observed only in one case of NB (1.2 %). MDM2 expression level increases proportionally to the stage of the disease ($p=0.02$) with maximum value in stage IV. MDM2 expression level was higher in MYCN-amplified tumors than in those without MYCN amplification ($p=0.02$). Primary resistant tumors had significantly higher levels of MDM2 gene expression compared to chemotherapy sensitive tumors ($p=0.001$). ROC analysis revealed that MDM2 expression level is an important marker which is associated with event-free survival (EFS) of primary childhood NB patients (Se=85.7 %; Sp=61.0 %; AUC=0.75; $p=0.002$). Tumors were categorized into two groups (high or low MDM2 expression) based on cutoff point - optimal criterion, that was determined by ROC analysis. High MDM2 expression was associated with reduced EFS in NB patients. The 2-year EFS rate for NB patients with high MDM2 expression was 35 % compared to 81 % for patients with low MDM2 expression ($p=0.001$).

Conclusions

Our results suggest the possibility that MDM2 is involved to the clinical behavior of NB. Inhibition of MDM2 can restore p53 activity and sensitize NB cells to chemotherapy-induced apoptosis.

EP-371

Neuroblastoma

CLINICAL FEATURES AND TREATMENT OUTCOMES IN NEUROBLASTOMA PATIENTS: A SINGLE CENTER EXPERIENCE FROM TURKEY

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Objectives

Neuroblastoma is the most common extracranial solid tumor in childhood. Prognostic factors such as age, stage and cytogenetic profiles are used for risk stratification and treatment assignment.

Methods

In this study demographic data and clinical outcome of 129 neuroblastoma cases were evaluated and within those, therapeutic results of treated with the IPOG (before 2003) and TPOG (after 2003) protocol were compared.

Results

Median age was 24 months(1-106 months) (29.6±23). Primary localization were abdomen in 102 patients(most localization in surrenal 92), mediastinum in 15, cervical in 5, paraspinal in 7. According the INSS system, 13(10%) patients were classified as stage I, 16(12%) stage II, 29 (22.5%)stage III, 65(50.5 %) stage IV, 6(5%) stage IVS. Most frequent sites of metastasis were bone marrow, bone and liver.

Patients in advanced stage, received chemotherapy (26% patients modified 6-in-one chemotherapy, 12% patients OPEC, 50% patients Turkish Pediatric Oncology Group-TPOG Protocol, 12% patients no chemotherapy) ± radiotherapy (13%) .

Five and 10 year general survival were found to be 64 and 52 % and disease free survival was 64 and 52% with 63±73 months follow-up (1-272 months). Relapses were detected in 42 (33%) patients. The 5 year general survival was 43 %, 5 yr EFS was 43 % in ICOG group and 62%,62% in TPOG group. Event free survival was 67% under 18 months old and 47% upper 18 months old. There was significant diferantiation between these two groups (p=0.023) Survival differed according to stage. Ten year general survival in stage I,I,III,IV was 100,100, 48, and 23 % respectively. Ten year event-free survival in stage I,I,III,IV was 100, 100, 43, 23 respectively.

Conclusions

In conclusion; survival rates of neuroblastoma have improved over the last decade in our center.

EP-372

Neuroblastoma

SIMULATION OF SPECT/MR ATTENUATION CORRECTION DEMONSTRATES POTENTIAL FOR UPTAKE QUANTIFICATION IN NEUROBLASTOMA

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Objectives

Neuroblastoma is an extremely heterogeneous neuro-endocrine cancer which requires a multitude of diagnostic tests, including imaging with ¹²³I-mIBG scintigraphy and MRI. An audit of RHSC mIBG clinical reports from 2013 suggested that quantification of radionuclide uptake would have been useful in 69% (18/26) of cases. One major confounder of accurate uptake quantification is photon attenuation. This can be corrected using non-uniform attenuation correction (AC) derived from SPECT/CT. However, CT introduces an additional radiation burden. An alternative approach would be to derive AC from MRI data. In PET/MR, Dixon-based sequences enable segmentation of soft tissues but lack the ability to discriminate cortical bone. The purpose of this study was to simulate and evaluate Dixon-based MRAC for SPECT, using a readily available SPECT/CT dataset; adult bone scans.

Methods

Eleven sequential bone SPECT/CT scans were selected from the GRI Nuclear Medicine database. Each CT dataset was segmented into five tissue types; air, lung, water-based soft tissue ('water'), adipose tissue and cortical bone. Adipose tissue and 'water' were assigned population averaged Hounsfield Unit values. Cortical bone was assigned the same value as 'water' to simulate a morphological filling process. Each MRAC SPECT reconstruction was then compared to the corresponding CTAC SPECT by visual assessment and voxel value analysis.

Results

Visual assessment identified no clinically significant changes in MRAC SPECT datasets. Voxel value analysis showed that SPECT uptake was reduced by 11% on average compared to CTAC.

Conclusions

MRAC produces qualitatively similar SPECT images to CTAC with an average reduction of radionuclide uptake of 11%. 10% is quoted in PET/MR literature as the threshold of clinical significance. In practice the use of more sophisticated atlas- or sequence-based approaches should enable the average voxel error to be further improved. Based on this study, MRAC is feasible for SPECT reconstruction and should provide a superior baseline SPECT scan for quantification of neuroblastoma without additional patient dose.

EP-373

Neuroblastoma

LOCALLY ADVANCED CERVICAL NEUROBLASTOMA PRESENTING IN THE PRENATAL PERIOD

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Objectives

To describe a locally advanced neonatal cervical neuroblastoma first detected on an antenatal ultrasound.

Methods

Congenital cervical neuroblastoma is extremely rare, representing less than one percent of all neonatal cases¹. Most neonatal cases are stage 1 or stage 4S with small abdominal primaries. We describe a congenital cervical neuroblastoma identified on antenatal ultrasound at 29 weeks gestation and ultimately proven to be stage 2B.

Results

Postnatal urinary VMA (vanillylmandelic acid) was high at 117 mg/g (normal 27 mg/g) as was uHVA (homovanillic acid) at 78 mg/g (normal 42 mg/g). Postnatal ultrasound showed a 4.7 cm solid mass with calcifications. An MRI showed a mass extending from the thoracic inlet to the base of the skull. The mass compressed and involved surrounding structures including the carotid artery, trachea, thyroid and parotid gland (Figure 1). A complete resection with lymphadenectomy was performed. The tumor completely effaced and partially encased the common carotid artery (greater than 50 percent), carotid bifurcation, and internal and external jugular veins (75 percent). It displaced and compressed the trachea medially and elevated the parotid gland superiorly. The vagus nerve was encased but was preserved by capsular incision and meticulous neurolysis. Five lymph nodes were positive. The MKI (mitotic karyorrhetic index) was low, the DNA index was greater than one, and *N-myc* was non-amplified. A postoperative MIBG scan revealed asymmetric uptake in the left neck, felt to represent a salivary gland rather than metastatic disease. The tumor was classified as low risk and the infant will be followed by serial labs and examinations.

Conclusions

This represents a unique case of a locally advanced neonatal cervical neuroblastoma that was successfully treated with surgical excision without the need for chemotherapy.

EP-374

Neuroblastoma

IRINOTECAN AND TEMOZOLAMIDE AS EFFECTIVE SCHEDULE IN PROGRESSIVE AND THERAPY RESISTANT NEUROBLASTOMA – EXPERIENCE OF POLISH PEDIATRIC SOLID TUMORS GROUP

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Objectives

Irinotecan/temozolamide (IT) chemotherapy (Kushner 2006) was evaluated as a possible therapy schedule in progressive or therapy resistant neuroblastoma (NBL) in patients treated in the centers of Polish Pediatric Solid Tumors Group.

The endpoints of the study were the best response to IT, overall and progression-free survival (OS, PFS), side effects and quality of life.

Methods

Patients treated from 2000-2012 were included (n= 697). Therapy failure was diagnosed in 194 (28%). IT was employed in 46 patients (1 stage 1, 1 stage 2, 5 stage 3, 1 stage 4s and 38 stage 4 at diagnosis), age 1-189 months at diagnosis. All patients were treated with previous chemotherapy. Seven patients had primary resistant disease, 28 the first and 11 at least second therapy failure. Four patients with additional vincristine were excluded. The objective response was observed in 38 patients (11 CR, 8 PR and 19 SD).

Results

The number of IT cycles in responding patients was 1-39 (median 6); 15 patients are alive (5 with CR, 3 with PR and 7 with SD). All received additional chemotherapy, 17 patients received HSCT (autologous in 9 and allogeneic in 8 cases, 7 of them with MIBG therapy), 10 – radiotherapy, 5 – 13-cis RA cycles and one immunotherapy. Mean OS was 44 months (12-172,7) and PFS from IT employment – 8,3 months (0,2-54 months).

Adverse events were observed in 31 cases (67%). Diarrhea was present in 19 (41%) patients, cured with loperamid (only in 1 case atropine was necessary) and hematologic toxicities. Only 12 (26%) of patients required modifications in drugs dosage or frequency, all of them heavily pre-treated or with bone marrow involvement.

Conclusions

The chemotherapy was accepted by all patients and parents. Generally, patients did not require hospitalization between the cycles.

We found IT as effective therapeutic option both as intensive and palliative treatment.

EP-375

Neuroblastoma

CLINICAL FEATURES AND PROGNOSTIC FACTORS IN CHINESE CHILDREN WITH NEUROBLASTOMA

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Objectives

To explore the clinical features and prognostic factors in Chinese children with neuroblastoma (NB).

Methods

One hundred and three NB patients were registered in our hospital from Jan. 2007 to Dec. 2013. Their clinical data and prognostic factors were retrospectively analysed. Kaplan-Meier was used for survival analysis.

Results

Ninety-two newly diagnosed NB children were enrolled in this study. Their median age at onset was 32.3 months (2.0~159.8 months), male to female ratio was 1.5. The median follow-up time was 32 months (12~80 months). Five-year overall survival (OS) was 64.4%±5.6%, and event-free survival (EFS) was 53.4%±6.0%. Total fourteen recurrent cases were observed. The median interval from initial diagnosis to relapse was 13 months (4~27 months) and 3y- OS after relapse was 42.9%±13.2%. The patients whose recurrent time was later than 18 months from diagnosis had a higher 3y-OS than those relapsed within 18 months (83.3%±15.2% vs 12.5%±11.7%, P=0.007). Among 29 deaths, the leading cause was severe chemotherapy -related infection (17/29, 58.6%), followed by death due to tumor progression (10/29, 34.5%). Univariate analysis revealed that the INSS stage III and stage IV, high-risk and very high-risk, LDH >500 U/L, bone metastases , N-MYC amplification were negative prognostic factors. Multivariate analysis suggested that only INSS stage and N-MYC amplification were independent prognostic factors.

Conclusions

INSS stage and N-MYC amplification were independent prognostic factors for Chinese Children with NB. Death caused by severe chemotherapy-related infection should be paid more attention. The patients who relapsed within 18 months after diagnosis had inferior prognosis, but patients with stage I or II or recurrence in situ could acquire a long-term survival after being treated timely.

EP-376

Neuroblastoma

EFFICACY OF MEK1 INHIBITION IN NEUROBLASTOMA

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Objectives

Mitogen-activated protein kinase (MAPK) signaling cascades are key pathways involved in the regulation of cell proliferation and survival, and aberrant MAPK pathway signaling contributes to the pathogenesis of a number of different malignancies. However, the role of MAPK pathway activation and signaling in neuroblastoma tumor cells is poorly understood. We hypothesized that RAS/MAPK pathway inhibition would be effective against neuroblastoma tumor cells.

Methods

We evaluated expression and activity of RAS/MAPK pathway members in a panel of neuroblastoma tumor cells and tumors using Western blots and neuroblastoma tumor cell viability after inhibition of MAP2K (MEK1) using MTT assays. Analyses were performed for changes in RAS/MAPK pathway activity after treatment with inhibitors.

Results

Responses of neuroblastoma tumor cell lines to MEK1 inhibition were variable, with some cell lines being very sensitive and others being resistant. IC50 values for sensitive cell lines ranged from

Conclusions

Inhibition of MEK1 in neuroblastoma tumor cells results in cell death in sensitive cell lines. Resistant neuroblastoma tumor cell lines displayed increased MEK1 phosphorylation in response to MEK1 inhibition, suggesting a possible feedback loop leading to treatment resistance. Inhibition of MEK1 represents a potential new therapeutic strategy for neuroblastoma, and further preclinical studies of MEK1 inhibitors in neuroblastoma models are warranted.

EP-377

Neuroblastoma

REPORT ON LONG-TERM FOLLOW-UP OF STAGE 4 NEUROBLASTOMA

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Objectives

To evaluate the long-term outcomes of childhood stage 4 Neuroblastoma (NB) and its correlative prognostic factors.

Methods

Comprehensive protocols including tumor resection, intensive chemotherapy, radiotherapy, ABMT and 13-cis-retinoid were designed and put into practice. Total 112 NB stage 4 patients in Shanghai Children's Medical Center collected from June 1998 to December 2010 were treated according to comprehensive protocols. The clinical features, therapeutic effects over different periods, long-term outcomes and prognostic factors were analyzed.

Results

Among 112 patients, 12 patients didn't complete treatment because of the parents' decision although the patients turned to become better. The rest completed the protocols, in which 62 cases (62.0%) achieved very good partial remission (VGPR), 20 cases (20.0%) achieved partial remission (PR), but another 18 cases (18.0%) progressed during the treatment. The efficiency rate (including VGPR+PR) of treatment was 82.0% (82 cases). The median follow-up period was 78 months (39-153). 13 cases of patients were lost after a median follow-up of 16 months. The 2-, 3-, 5 year event free survival (EFS) of all patients was 56.2%, 40.8%, 21.1%, respectively. Age (>18 months), poor curative effect (fail to achieve VGPR at the end of treatment), high levels of LDH (> 5-times the normal value), bone marrow involvement were poor prognostic factors. ($\chi^2 = 12.01, 13.66, 6.29, 5.44$, all $P < 0.05$). As to the multivariate estimates of hazards, age, poor curative effect, high levels of LDH were associated with a worse survival ($OR = 3.44, 3.32, 1.76$, all $P < 0.05$). Brain metastasis predicted a worse outcome with 100% death rate. Compared to the traditional chemotherapy, Topotecan included chemotherapy could not improve the efficiency (52.6% vs 63.2%, $P = 0.416$) and long-term outcome (2 year EFS 42.1% vs 56.4%, $P = 0.487$) of stage 4 NB.

Conclusions

The prognosis for neuroblastoma of stage 4 remains poor. Age (>18 months), poor curative effect, high level of LDH (> 5-times the normal value), bone marrow infiltration were associated with worse prognosis. Brain metastasis predicted the worst with 100% death rate. Topotecan included chemotherapy could not be proved more effective in this study.

EP-378

Neuroblastoma

CLINICAL EFFICACY ANALYSIS OF 16 CASES OF INFANT NEUROBLASTOMA

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Objectives

The purpose of this paper is the analysis of clinical characteristics and clinical efficacy of Nb less than 1-year old.

Methods

16 cases of infant Nb confirmed and diagnosis using pathology or / and imaging from February 2007 to August 2013. 10 cases of male and 6 cases of female. The median age was 9.5 months. 1 case of 1 stage, 7 cases of 4 stage, 8 cases of special 4s stage. Combining chemotherapy and operation. Statistic Analysis of the primary site, and the first symptom characteristics, and the level of serum NSE, and the chemotherapy efficacy, and the prognosis.

Results

(1) 5 cases of less than 3 months old accounting for 31.25%; 2 cases of 3-6 month old, accounted for 12.5%; 9 cases of 6-12 months old, accounting for 56.25%. (2) In all of patients, 15 cases of middle risk group accounted for 93.75%, 1 cases of high risk group accounted for 6.25%. (3) all of 16 cases were higher than normal while diagnosis, reached 100%, and the median of the level of serum NSE was 59.95mg/dl (17.48~264mg/dl). After the treatment, 3 cases of slightly higher than the normal accounting for 18.75%, 1 case of decreased significantly accounted for 6.25%, 12 cases of decreased to normal level accounting for 75%. (4) follow up to February 2014, except for 1 case of treating, 15 cases for followed-up. In 15 cases, 14 cases achieved complete remission (CR) and accounted for 86.67%, and 2 cases achieved partial remission (PR) and accounted for 13.33%. Overall survival rate was 100% (15/15).

Conclusions

Infant Nb sensitive to chemotherapy. the disease incidence rate of stage 4S in infant Nb is high. Remission rate and prognosis of infant Nb after comprehensive treatment was high.

EP-379

Neuroblastoma

CHROMOSOME ANALYSIS OF NEUROBLASTOMA IN CHILDREN

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Objectives

To study the clinical features and prognosis of 55 children with neuroblastoma according to their chromosome status in our hospital, and analyze the relationship between the chromosome status and characteristics and the short-term curative effect. Improving the understanding of neuroblastoma with chromosomal abnormalities.

Methods

The clinical characteristics, treatment and survival status of 55 children with neuroblastoma were retrospectively analysed, and with review of literature.

Results

There was a total of 5 patients with chromosomal abnormalities among 55 cases which were adopted in our hospital, including 4 cases with 17q gain, 1 case with both 17q gain and 1p deletion, and no abnormalities were found in the rest. Tumor markers in 5 cases with chromosomal abnormalities were elevated in different range, Serum NSE was $280\pm 18\text{ng/ml}$, which was higher than $125\pm 12\text{ng/ml}$ in neuroblastoma children with normal chromosome; All 5 cases with chromosomal abnormalities had MYCN gain; During treatment, 1 case was lost of follow-up, 2 cases progressed, 1 case died, the rest one with both 17q gain and 1p deletion was complete remission after regular chemotherapy, surgery and autologous peripheral blood stem cell transplantation, followed-up with 33 months in out-patient. The different EFS rate was found in patients with different chromosome status, a 2-year EFS rate was higher in normal chromosome group than abnormal group, P value <0.05 .

Conclusions

Based on our cases and relevant literatures shows that: 17q gain and 1p deletion were risk factors in neuroblastoma, there was certain clinical significance in the diagnosis and evaluation of prognosis in neuroblastoma. But in our research, the positive rate of abnormal chromosome with conventional detect method is lower than previous report, it is considered to be related with methodology which needs further improvement.

EP-380

Neuroblastoma

THE LEVEL AND CLINICAL SIGNIFICANCE OF TH1/TH2 CYTOKINES IN SERUM OF CHILDREN NEUROBLASTOMA

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Objectives

To study the levels of Th1 and Th2 in children with neuroblastoma(NB) and their relation to clinical stages, to provide the basis for immunomodulatory and supportive therapy in the NB chemotherapy.

Methods

The study enrolled children with the new NB patients treated in our hospital from November 2011 to December 2012. The level of Th1 type cytokines include interleukin-2(IL-2),interferon- γ , (IFN- γ),tumor necrosis factor- α (TNF- α) and Th2 include interleukin-4(IL-4),interleukin-6(IL-6),interleukin-10(IL-10).Th1/Th2 cytokines in serum were detected by flow fluorescence immunomicrobeads assay (FFIA) from 66 children of high risk and 22 children of low and medium risk with NB.

Results

The level of Th1 type cytokines such as IL-2 were significantly lower in patients of high risk than low and medium risk with NB($P<0.05$). IFN- γ were lower in patients of high risk than low and medium risk with NB,but there was no statistically significant differences($P=0.076$).The level of TNF- α were significant higher than low and medium risk with NB patients($P=0$).The level of Th2 type cytokines such as IL-4 and IL-6 were higher in patients of high risk than low and medium risk with NB,but there was no statistically significant differences(IL-4, $P =0.058$.IL-6, $P=0.078$). The level of IL-10 patients were significant higher than low and medium risk with NB patients($P<0.05$).

Conclusions

Th1/Th2 was imbalance in children with NB.Th1 type cytokines were inhibited and Th2 type cytokines were relatively enhanced,so Th1/Th2 shift to Th2.With the increase of risk, the trend was more obvious. Serum levels of Th subsets may be related to immune functions of lung cancer patients and be a good sign of prognosis.

EP-381

New Drugs/Experimental Therapeutics

EFFECTS OF ZEBULARINE ALONE OR IN COMBINATION WITH THE HISTONE DEACETYLASE INHIBITOR SAHA ON MEDULLOBLASTOMA CELLS

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Objectives

Medulloblastoma (MB) is an aggressively growing tumor, arising in the cerebellum, and is the most common malignant one in children. Current treatment cures reaches about 50-80 % of patients however approximately 40% of children experience tumor recurrence, and 30% will die from their disease. Thus new approaches are urgently needed. Drug combination using inhibitors of DNA methyltransferases (iDNMTs) and histone deacetylase (iHDAC) have shown antineoplastic effects in different tumors. Zebularine (ZB) blocks DNA methylation by inhibiting DNA methyltransferases activity and exhibits minimal cytotoxicity both *in vitro* and *in vivo*. However, its effects on MB have not been previously reported. This study aimed to investigate the anti-cancer efficacy of ZB alone or in combination with SAHA *in vitro* using MB cell lines.

Methods

The effects of ZB alone or in combination were evaluated by cell viability, clonogenic and apoptosis assays on MB cells UW402 e UW473. Combined-effects analyses were conducted according to the median-effect principle established by Chou and Talalay. Drug combination analyzes using two different schedules of administration (simultaneous and sequential) were performed. Statistical analysis was performed by one- and two-way ANOVA and Bonferoni post-hoc.

Results

ZB decreased cell proliferation and clonogenic capacity in all cell lines in a time- and dose-dependent manner, respectively ($P < 0.05$). The drug increased apoptosis rate. The combination index values of the ZB and SAHA treatments were all greater than 1, indicating that the two agents induced antagonistic effects on the MB cells, independently of the schedule used.

Conclusions

Administered alone, both ZB and SAHA exert anti-tumoral activity on *in vitro* MB cells. The ZB and SAHA combination treatment produces antagonistic, rather than synergistic, effects. Further studies are being conducted with different drug combination schedules, aiming to better characterize the effects of this combination.

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EP-382

New Drugs/Experimental Therapeutics

SIROLIMUS FOR THE TREATMENT OF VASCULAR ANOMALIES

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Objectives

Vascular anomalies (VA) are heterogeneous group of benign disease which require multidisciplinary treatment approach. "Mammalian target of rapamycin" (mTOR) inhibitor Sirolimus has been recently used in the treatment of VA and successful results have been reported. In this study, clinical characteristics and outcome of patients with VA treated with Sirolimus were evaluated.

Methods

Files of 21 patients with VA who was treated with Sirolimus were analyzed retrospectively for clinical features and treatment results. The patients were diagnosed either radiologically or histologically after biopsy.

Results

The median age of 14 boys and 7 girls at diagnosis was 5 years (ranged 3 days - 13 years). Patients were given Sirolimus at a median age of 8 (ranged 2 months - 13 years). The subtypes were venolymphatic malformation in 7, lymphangioma in 6, vascular malformation in 3, venous malformation in 2, Gorham Stout syndrome in 2 and Blue rubber bleb nevus syndrome in 1 patient. Most of the patients (18/21) received at least one previous treatment. Sirolimus were given for 1 to 24 months (median 6 months). The most frequent clinical responses were improvement in pain, feeding and exercise capacity, reduction in hospitalizations, tracheostomy closure and extubation. Clinical and radiological response was between 50-90% in 7 patients and less than 50% in 8 patients. There was no response in 6 patients radiologically. Five patients had oral aphthous lesions and 4 patients had hyperlipidemia during treatment. Both side effects were mild and reversible.

Conclusions

Sirolimus can be used effectively and reliably in patients with VA who were refractory to previous therapies with acceptable toxicity.

EP-383

New Drugs/Experimental Therapeutics

PROMISING USE OF SIROLIMUS IN PROLIFERATIVE DISORDERS

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Objectives

Mammalian target of rapamycin (mTOR) signaling stimulates cell growth and is inhibited by rapamycin, a naturally occurring antifungal compound first discovered on Easter Island. Rapamycin (or Sirolimus) has been used as an immunosuppressant in kidney transplants but is also known recently to reduce proliferative tumours on hamartoma syndromes and refractory vascular anomalies, with few serious adverse side effects.

We describe our experience in the use of Sirolimus in a variety of proliferative disorders.

Methods

Five patients were put on Sirolimus according to an institutional protocol from June 2012. The latest patient was recruited in January 2014. The diagnoses were Gorham's disease (2), metastatic haemangioendothelioma, lymphangiomatosis and extensive inflammatory myofibroblastic tumour (IMT). All patients had failed a variety of therapies before they were offered Sirolimus. Monthly Sirolimus blood levels were kept between 5 to 15 ng/ml. Monthly full blood counts, renal panel, liver function, fasting lipids and urinary total protein were monitored. Prophylactic cotrimoxazole was given.

Results

Out of the 5 patients, 1 (metastatic haemangioendothelioma) showed near complete response, 1 (Gorham's) showed good response, 1 (Gorham's) showed stable disease, 1 (extensive IMT) showed possible partial response while the latest patient recruited cannot be assessed as yet. Their ages range from 1.2 to 16.8 years at the time of treatment.

Interestingly the patient with IMT also had chronic ITP which responded to Sirolimus with platelets normalising after 3 months. Two patients had transient hypercholesterolaemia and 1 had transient proteinuria. One patient had mucositis which, together with cost issues, caused her to stop treatment after 9 months. Treatment was otherwise well tolerated. As of 28th February 2014, the duration of treatment ranged from 2 to 20 months.

Conclusions

Sirolimus shows promising results in the treatment of proliferative disorders refractory to other therapies. It is well tolerated, however long term effects on young children have not been determined.

EP-384

New Drugs/Experimental Therapeutics

ANTITUMOR ACTIVITY OF A NOVEL S1P₂ ANTAGONIST AB1

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Objectives

The bioactive lipid sphingosine-1-phosphate (S1P) and its receptors (S1P₁₋₅) play critical roles in many pathological processes including cancer. The S1P axis is becoming a potential therapeutic target. JTE-013 is a literature standard S1P₂ antagonist with potential instability *in vivo*. Through its structure modification, we try to develop more specific and more stable JTE-013 analogs.

Methods

FLIPR assay was conducted to assess the agonism/antagonism of JTE-013 analogs against S1P₁₋₅. Pharmacokinetic analysis was performed to detect their blood concentrations in mice over different time. Migration assay in glioblastoma (GB) and neuroblastoma (NB) xenograft model were utilized to compare the biological efficacy between JTE-013 and its analogs. Western blot and real-time PCR were performed to compare their efficacy on modulating the expression of S1P₂ downstream molecules such as p-Akt, p-ERK, VEGF and CTGF.

Results

One of the JTE-013 analogs, AB1, exhibited better S1P₂ antagonism effect compared to JTE-013, with an IC₅₀ of 3.5 nM versus 11 nM of JTE-013. Intravenous pharmacokinetics showed that the blood concentration of AB1 in mice remained higher than that of JTE-013 over 12 hours, indicating better stability or slower clearance of AB1 *in vivo*. Migration assay in GB showed that AB1 was more potent than JTE-013 to either reverse S1P-mediated cell migration inhibition in S1P₂-predominant U118 cells or further enhance S1P-stimulated cell migration in S1P₁-predominant U87 cells. In a NB cell line SK-N-AS, AB1 displayed at least the same potency as JTE-013, in reversing S1P-mediated p-Akt inhibition and inhibiting S1P-mediated p-ERK activation, and in inhibiting S1P-induced VEGF and CTGF expression. Further, in SK-N-AS cell-based xenograft tumor model, AB1 displayed stronger tumor inhibition effect compared to that of JTE-013.

Conclusions

AB1 has improved potency and intravenous pharmacokinetics, better cellular activity, and displays stronger anti-tumor activity compared to JTE-013 in NB, and may have enhanced clinical applicability.

EP-385

New Drugs/Experimental Therapeutics

DATABASE OVERVIEW FOR INFORMATION RETRIEVAL OF EXPRESSION LEVELS FOR THE BRIC 7 GENE IN TUMORS :NEUROBLASTOMA , MEDULLOBLASTOMA, RHABDOMYOSARCOMA, EWING-SARCOMA AND LEUKEMIA

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Objectives

Newcastle disease virus (NDV) is an avian paramyxovirus that has a potential selective oncolytic effect on human tumors.

It is shown that Newcastle virus (NDV-HUJ, a one-cycle replicating virus), overcomes the resistance to apoptosis of melanoma primary cultures that over express the Livin protein. In contrast, melanoma tumor cells that do not express Livin are relatively resistant to NDV-HUJ treatment. NDV-HUJ is a potent inducer of apoptosis that can overcome the antiapoptotic effect of Livin and allow cleavage of Livin into the proapoptotic tLivin.

The over expression of Living protein in tumor can predict the oncolysis effects of Newcastle virus protein.

Methods

We have searched Gene Expression Database GEO for microarray experiments which description contains the name of one of the requested cancer types: Neuroblastoma, medulloblastoma, Rhabdomyosarcoma and EWING-sarcoma.

The retrieved experiments were searched for the BIRC7 gene, and the gene expression profile was either taken from the pre-calculated "GEO profiles" (if available), or calculated and visualized using the GEO2R tool.

Results

Medulloblastomas (from children ages 3 to 16 years): 24 of 72 expressions of the gene were above the background and only 3 of 72 have very high expression.

In Neuroblastoma cell line: One of 4 cell lines has expression of brich 7 gene.

In Glioblastoma(GBM):10 of 27 with expression of the gene.

Rhabdomyosarcoma in(mice): Only 1 of 4 has expression of the gene.

Ewing sarcoma family: 10 of 44 with expression of the gene.

Leukemia in children: More than 600 patients were checked for the gene. Most children with good risk leukemia (etv6-runx1) with higher expression of the gene

Conclusions

Higher expressions of Bric 7 gene in brain tumors frequently in GBM than other tumors.

All higher expressions resulted in good prognosis in leukemia

We are currently investigating the gene expression in children who contracted the Newcastle virus.

EP-386

New Drugs/Experimental Therapeutics

THE VECTORIZED ANTI-CANCER DRUG F14512 DEMONSTRATES A HIGHER PRECLINICAL ACTIVITY IN NEUROBLASTOMA THAN IN PEDIATRIC GLIOMA CELL LINES: FIRST DATA IN PEDIATRIC ONCOLOGY.

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Objectives

The prognosis of children with high grade glioma (HGG) and high risk neuroblastoma remains poor despite aggressive multidisciplinary therapeutic approaches. F14512 combines an epipodophyllotoxin core-targeting topoisomerase II with a spermine moiety introduced as a cell delivery vector. This spermine moiety facilitates selective uptake by tumor cells *via* the Polyamine Transport System (PTS) and reinforces topoisomerase II poisoning.

Methods

F14512 was evaluated in three pediatric HGG and four neuroblastoma cell lines. PTS activity and specificity were evaluated by confocal microscopy and flow cytometry using the fluorescent probe F17073 which contains the same spermine moiety as F14512. Cytotoxicity of F14512, alone or in association with cisplatin, carboplatin, melphalan, and radio-sensitizing effects were investigated *in vitro*. The antitumor activity of F14512 was assessed *in vivo* using a bioluminescent liver-metastatic neuroblastoma model.

Results

An active PTS was evidenced in all tested pediatric cell lines, providing a specific and rapid transfer of spermine-coupled compounds into cell nuclei as assessed in three neuroblastoma cell lines. Competition experiments with spermine confirmed the essential role of the PTS in the cell uptake and cytotoxicity of F14512. This cytotoxicity appeared greater in neuroblastoma compared to HGG cells but seemed independent from the PTS activity levels. Interestingly, F14512 presented a significant higher cytotoxic effect than etoposide (lacking the spermine chain). *In vivo* evaluation confirmed an important and prolonged antitumoral effect in neuroblastoma. The combinations of F14512 with cisplatin and carboplatin were found to be often synergistic, and combinations with melphalan appeared various. Finally, we demonstrated the significant radio-sensitizing potential of F14512 in the MYCN-amplified Kelly cell line.

Conclusions

F14512 appears more effective than etoposide in pediatric tumor cell lines, with a higher efficacy in neuroblastoma cells. The synergistic effects observed with platinum compounds and its radiosensitizing effect could lead to a great potential development in pediatric oncology.

EP-387

New Drugs/Experimental Therapeutics

RESVERATROL INDUCES APOPTOSIS OF MEDULLOBLASTOMA CELLS WITHOUT AFFECTING ASTROCYTES AND NEURONS

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Objectives

Medulloblastoma is a lethal pediatric brain malignancy due to aggressive growth and frequent recurrence. Adjuvant therapies are employed to prevent cancer relapse but cause long term side effects. Resveratrol in 100mM and 150mM induces differentiation and leads medulloblastoma cells to growth arrest and apoptosis. This study aims to further prove the practical values of resveratrol by evaluating the effects of resveratrol on normal brain cells.

Methods

The glial cells and neurons were isolated from the fetal rat brains after getting the permission of Experimental Animal Warfare Committee of Dalian Medical University. They were separately cultured under optimal conditions for 7 days and then treated by 100mM or 150mM resveratrol for 96 hours. The morphology of the treated cells was checked in 12 hour intervals and the cell bearing coverslips were collected at each of observation points for immunocytochemical, MTT and TUNEL analyses. Resveratrol-treated UW228-3 medulloblastoma cells were cited as control.

Results

Unlike UW228-3 cells, rat glial cells and neurons have little response to resveratrol treatment because the proliferation rates and/or morphology of resveratrol-treated cells are similar with that of their normally cultured counterparts. STAT3 is expressed in both glial cells and neurons but lack of nuclear translocation and its level is not altered by resveratrol. Nuclear labeling of STAT3 is evidenced in UW228-3 cells and becomes diminished upon resveratrol treatment accompanies with extensive apoptosis.

Conclusions

The safety of the effective anti-medulloblastoma doses of resveratrol for rat glial cells and neurons is confirmed, presumably due to the inactivated status of resveratrol targeted STAT3 signaling in those cells. Therefore, this non-toxic compound would be useful in the clinical treatment of medulloblastomas.

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EP-388

New Drugs/Experimental Therapeutics

DHMEQ IN PEDIATRIC MEDULLOBLASTOMA CELL LINES

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Objectives

Medulloblastoma is a pediatric cancer of the central nervous system, highly invasive, of embryonic origin, located in the cerebellum. The most common treatments are surgery and chemotherapy, and radiotherapy is only to children older than 3 years old due to its side effects. NF- κ B is a key transcription factor in the regulation of immune response and inflammation process, and it is involved in the transcriptional regulation of a large number of genes related to the tumorigenesis process, and constitutively active in many types of cancer, being an important potential therapeutic target. DHMEQ (Dehidroximetilepoxiquinomicina) is a drug that inhibits the translocation of NF- κ B from the cytoplasm to the nucleus, thus inhibiting its activity as a transcriptional activator. Several studies have shown the antineoplastic effects of DHMEQ in numerous tumor types, however, there is no surveys that have tested their effects in medulloblastoma.

Methods

The present study evaluated the effects of DHMEQ in UW402, UW473 and ONS-76 pediatric medulloblastoma cell lines through proliferation, clonogenic capacity, apoptosis, invasion and migration assays, besides drug combination and radio sensitization assays.

Results

The proliferation test results demonstrated a significant decrease in the cell growth, strongly inhibition of the clonogenic capacity and the migration and cell invasion in the three medulloblastoma cell lines. Additionally, increased the level of apoptosis, it was synergistic in combination with other chemotherapeutic agents in most combination points, and radiosensitization strongly the three cell lines.

Conclusions

The results are congruent with the potential antitumor effect of DHMEQ and pointed clearly the possible use of it as new therapeutic agent to medulloblastoma treatment.

EP-389

New Drugs/Experimental Therapeutics

ROLE OF WNT/ β -CATENIN PATHWAY IN THERAPY RELATED MYELOID NEOPLASMS (T-MDS/T-AML) WITH 5Q DELETION: A NEW THERAPEUTIC TARGET

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Objectives

Successful therapy for pediatric malignancies has led to rise in incidence of t-MDS/t-AML. Del(5q) is a recurring cytogenetic abnormality in approximately 25% of pediatric t-MDS/t-AML. With current therapies 5 yr survival is only 25%. Del(5q) is associated with haplo-insufficiency of APC gene in hematopoietic stem cells (HSCs) which leads to MDS-like disease in mice. APC regulates the function of HSCs through β -catenin dependent mechanisms. Our objective is to show effects of Wnt/ β -catenin pathway blockade on del(5q) leukemia.

Methods

The expression of β -catenin is higher in UoCM1 [human myeloid leukemia cell line with del(5q)] versus REH [lymphoid line without del(5q)]. We treated UoCM1 and REH cells with 100uM Indomethacin. Lentiviral particles expressing a control empty backbone or β -catenin targeting inhibitory shRNA were transduced into UoCM1 and REH and β -catenin knockdown achieved. The cells were analyzed for effects on growth, cell cycle and apoptosis. In vitro colony forming assay was performed.

Results

UoCM1 cells showed significant more growth inhibition compared to REH with Indomethacin ($p < 0.05$). β -catenin inhibition with treatment was confirmed. UoCM1 cells transduced with β -catenin shRNA showed 60% growth inhibition compared to control vector. In contrast, REH demonstrated comparable growth in control and β -catenin shRNA transduced cells. There was a decrease in the S and G2/M fractions and increase in apoptosis ($p < 0.05$) in UoCM1 cells with β -catenin inhibition compared to control. REH showed no difference in distribution in cell-cycle and similar frequency of apoptosis in inhibited and control cells. Decrease in colony formation was observed in UoCM1 cells with β -catenin inhibition.

Conclusions

5q del leads to up-regulation of β -catenin. Blockade of Wnt/ β -catenin pathway suppresses cell growth and induces apoptosis in a myeloid leukemia cell line with del(5q). This discovery paves the way for new therapeutic strategies targeting β -catenin and improving survival in del(5q) t-AML/MDS.

EP-390

New Drugs/Experimental Therapeutics

DECITABINE ENHANCES CYTOTOXIC EFFECT OF OTHER ANTI-LEUKEMIC AGENTS SYNERGISTICALLY IN ACUTE LYMPHOBLASTIC LEUKEMIA CELL LINE

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Objectives

We examine the combined effects of decitabine (DAC) and anti-leukemic agents such as clofarabine (CLO) and etoposide (ETO) on the Acute Lymphoblastic Leukemia (ALL) cell line CCRF-CEM.

Methods

We measured *in vitro* drug sensitivity of DAC, CLO, ETO, DAC+CLO and DAC+ETO on CCRF-CEM, using MTT assay. The combination Index (CI) was produced with CalcuSyn® software. We also assayed with caspase-3/7 to detect apoptosis. Using RQ-PCR in CCRF-CEM cells, we examined mRNA expression levels for the pro-apoptotic genes *BAK*, *BID*, *BAX*, *BAD*, *BIM*, *PUMA*, *ATM*, *TP53*, and *NOXA*, as well as those for the anti-apoptotic genes *BCL2*, *BCL2L1*, and *XIAP*. The expression level of each target gene was calculated by normalizing it to *GAPDH*. We then analyzed the methylation status of these genes after 48 hours incubation with or without DAC.

Results

IC₅₀ for ETO, ETO+DAC, CLO, and CLO+DAC was 3.36, 0.625, 4.96, and 1.92, respectively. The CI was 0.026 for ETO+DAC and 0.431 for CLO+DAC. We observed greater caspase-3/7 activity with DAC + CLO and DAC + ETO than with CLO and ETO. We observed DAC increased mRNA expression levels of *BAX* and *NOXA*, but decreased those for *BAK*, *BID*, *PUMA*, *BCL2L1*, *ATM*, *TP53*, and *XIAP*. Methylation status of *BAK*, *NOXA*, *BCL2L1* and *XIAP* incubation with DAC was 1.3%, 3.3%, 2.5% and 72.9%, respectively and incubation without DAC was 1.9%, 3.6%, 0.7% and 92.3%, respectively.

Conclusions

Our results showed that DAC synergistically enhances CLO and ETO cytotoxicity, and this cytotoxic effect depends on caspase-3/7 activity. We found that DAC decreased some pro-apoptotic genes, such as *BAK*, *BID*, *PUMA*, *ATM*, and *TP53*. Our results show that DAC did not demethylate the CpG of *BAK*, *NOXA*, *BCL2L1*, or *XIAP*. Thus, DAC must demethylate the CpG of other genes. Nevertheless, many genes are involved in apoptosis, and it remains unclear which genes are demethylated by DAC.

EP-391

New Drugs/Experimental Therapeutics

ANTITUMOR ACTIVITY OF INDISULAM ON PEDIATRIC AND ADULT GLIOBLASTOMA CELL LINES AND XENOGRAFT TUMORS

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Objectives

Glioblastoma (GBM) is the most aggressive form of brain cancer, with a dismal prognosis in children and adults. Carbonic anhydrases isoforms 9 and 12 (CA9/12) are highly overexpressed in many types of cancer including GBM. The aim this study was to evaluate the effects of inhibition of the CAs 9/12 by Indisulam (a novel anticancer drug with potent inhibition of CAs) *in vitro* and *in vivo* models.

Methods

In this study, we investigated the effects of the inhibition of CA9/12 by Indisulam on cell survival in 9 pediatric and adult GBM cell lines. The cell lines were cultured in conditions of hypoxia (1%) and proliferation, cell cycle, apoptosis were evaluated. The *in vivo* antitumor and chemo-sensitizing effects of Indisulam were assessed in Swiss nude mice (n=6 by group) inoculated with the GBM cell line U-87. Indisulam was administered by different treatment approaches. Tumor growth and potential treatment toxicity were monitored.

Results

CA 9/12 inhibition *in vitro* significantly reduced proliferation in dose-time dependent ($p < 0.05$) with G2/M arrest when compared with control and increased apoptosis upon hypoxia exposure. Moreover, concurrent combination with temozolamide (TMZ) inhibited cell growth in all cell lines, as determined by proliferation. Results of animal tests using human tumor xenograft indicated that Indisulam significantly reduced the growth of tumors (66-84%, $P < 0.05$). Pretreatment with Indisulam equally sensitized cells to chemotherapy with TMZ and leads to 96-98% reduction in xenograft tumor volume ($P < 0.05$). No differences were observed with TMZ alone when compared with controls.

Conclusions

This study provides evidence of the therapeutic potential of Indisulam as a chemo-sensitizing agent in drug-resistant tumor cells and might, therefore, be an attractive treatment strategy in GBM.

EP-392

New Drugs/Experimental Therapeutics

SUCCESSFUL MANAGEMENT OF LYMPHATIC MALFORMATION OF THE TONGUE USING SIROLIMUS

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Objectives

Lymphatic malformation is a congenital malformation and can lead to significant disfigurement from soft tissue hypertrophy and skeletal overgrowth, bony abnormalities, and/or infection. Treatments for removal include surgical resection and a variety of sclerosing agents. In this report, we present a novel approach to treatment of lymphatic malformation of the tongue using sirolimus.

Methods

One year old girl admitted with the complaint of macroglossia. She was born at term to a 23 years old woman by vaginal delivery with a birth weight 3000 gram. She had macroglossia. She hadn't any further significant antenatal, maternal medical or family history. On physical examination she had scabbed ridges on the tongue and the dimensions of the tongue were diffuse elevated. She couldn't chew so she had been fed only with liquid nutrients. MR imaging revealed a heterogeneous hypervascular solid/cystic mass with unclear borders that mainly localized at anterior 2/3 of the tongue. Chest x-ray and abdomen USG were normal. Laboratory examinations including chromosomal microarray testing and testing for metabolic disorders were also normal.

Results

The patient began treatment with sirolimus which is a mammalian target of the rapamycin inhibitor. Initial dosing was 0.04/mg/kg/day, administered oral, twice daily. Subsequent dosing adjustments were made in order to maintain a goal drug trough level of 10-15 ng/ml. She continued on a therapeutic dose of sirolimus for nine months without any adverse effects. She was able to close her mouth and eat everything.

Conclusions

Sirolimus therapy offers a promising treatment option for lymphatic malformation in children.

EP-393

New Drugs/Experimental Therapeutics

PYRROLE-IMIDAZOLE POLYAMIDES TARGETING KCNQ1OT1 INDUCE APOPTOSIS IN WILM'S TUMOR CELL LINE (G401)

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Objectives

KvDMR is one of imprinting control regions assigned to chromosome 11p15.5 in human. Since KvDMR is located on the promoter of *KCNQ1OT1*, genomic alteration of this region, such as deletion, paternal UPD, and de-methylation in maternal allele lead to over-expression of *KCNQ1OT1*. The non-coding RNA *KCNQ1OT1* is known to suppress circumjacent genes, including tumor suppressor gene *KIP2*, and over-expression of *KCNQ1OT1* accompanied with down-regulation of *KIP2* has been reported in several tumors. De-methylation of KvDMR is frequently observed in Beckwith-Wiedemann syndrome (BWS), and around 10% of BWS patients develop embryonal tumor (Wilm's tumor, Hepatoblastoma). Based on these facts, we hypothesize that suppression of *KCNQ1OT1* could show anti-tumor effect.

Methods

Pyrrole-Imidazole polyamides (PIPs) are small synthetic chemicals composed of the aromatic amino acids and recognize a specific DNA sequence. PIPs designed against transcription factor binding site can suppress the expression of downstream genes. We generated PIPs targeting *KCNQ1OT1* promoter and investigated their anti-tumor effect on human BWS fibroblast (BWS6, 9) and G401.

Results

It was clearly shown by real-time PCR that the expression level of *KCNQ1OT1* was significantly reduced in BWS6, 9, G401 treated with PIPs compared to the control cells. Induction of KIP2 protein in G401 cells after treatment with PIPs was detected by Western Blotting. WST8 assay revealed that G401 cells treated with PIPs showed significantly lower viability than that of the control cells. And we found the higher number of cells undergoing apoptosis in the PIPs treated group than in the control group by FACS analysis.

Conclusions

Our current data strongly suggested that PIPs induce apoptosis in G401 by suppressing *KCNQ1OT1* expression, followed by the up-regulation of KIP2 protein. We believe that the PIPs targeting *KCNQ1OT1* have possibility to be new therapeutic agents for tumors harboring de-methylated CpG island on *KCNQ1OT1* promoter.

EP-394

Nursing

SUPPORT FOR WOMEN SURVIVORS OF CHILDHOOD CANCER: A LITERATURE REVIEW

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Objectives

As the cure rates of childhood cancers continue to improve, more long-term survivors are living with the late effects of treatment. Support for women survivors of childhood cancer has not been sufficiently studied thus far, particularly in regard to women of childbearing age. We therefore conducted a literature review to clarify the current status of women survivors of childhood cancer and the support they receive.

Methods

MEDLINE and CINAHL were searched for articles published from 2004 to 2013 on adult childhood cancer survivors. Included studies focused on issues specific to women survivors of childhood cancer or compared these women with their male counterparts.

Results

Women survivors of childhood cancer had lower quality of life than their male counterparts and a higher risk of posttraumatic stress disorder. The women were concerned about their reproductive health and felt uncertainty about the future.

Conclusions

The results indicate that further support is needed for childhood cancer survivors, particularly women.

EP-395

Others

ROLE OF INTERLEUKINS IL10, IL12 AND IL23 IN PREDICTING TUMOR AGGRESSIVENESS AND RESPONSE TO THERAPY IN PEDIATRIC MALIGNANCIES

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Objectives

Upon contact with tumor cells when co-cultured *in vitro*, human monocytes become unresponsive to re-stimulation and demonstrate decreased production of IL-12 and enhanced IL-10 secretion. Clinically, deregulated serum level of IL10 and IL12 and their reciprocal balance have been stated in many cancers. On the other hand, IL-23 dampens directly tumor growth *in vitro* and *in vivo* through the inhibition of tumor cell proliferation and induction of apoptosis. We aimed in our study to detect the pretreatment serum level of IL10, IL12, their ratio and IL23 in pediatric hematological malignancies as well as solid tumors, and correlate them with the chemotherapy response.

Methods

Pre treatment serum level of IL10, IL12 and IL23 are detected in blood samples of 20 children diagnosed with different types of malignancies and 20 healthy peers using ELISA. A correlation between serum level of these Interleukins and disease severity and patients' response to chemotherapy is conducted.

Results

Median IL-10 and IL-12 levels were significantly higher in cancer diseased children than in healthy controls, while median IL23 level was significantly decreased. Elevated IL-10 and IL-10/IL-12 ratios and decreased IL-12 and IL23 correlated with poor-risk histology, poor response to therapy, relapse and death from cancer.

Conclusions

Pre-treatment serum levels of IL-10, IL-12, IL-10/IL-12 balance and IL23 in children with cancers may be of value as additional prognostic tools to predict the response to therapy. Our analysis potentiate the theory of the anti tumor effect of IL23 and the possibilities of its use as a candidate novel drug in resistant malignancies.

EP-396

Others

ASSESSMENT OF MYOCARDIAL FUNCTION IN CHILDREN BEFORE AND AFTER AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION

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Objectives

More interest is focused on the long-term adverse effects of bone marrow transplantation. Subclinical cardiac involvement appears to be common in adults, but only a few reports concern pediatric patients.

Methods

A Prospective case-control study performed on 19 children with normal cardiac function undergoing autologous hematopoietic stem cell transplantation (HSCT). Tissue Doppler imaging (TDI) and echocardiographic measurements were obtained according to guidelines of the American Society of Echocardiography.

Results

Lateral mitral annulus before HSCT showed significant reduced mitral systolic annular velocity ($p < 0.0001$), early diastolic annular velocity ($p < 0.0001$), late diastolic annular velocity ($p = 0.02$) and prolonged isovolumetric relaxation time ($p < 0.0001$) in comparison to control. Significant reduced mitral systolic annular velocity ($p < 0.0001$), early diastolic annular velocity ($p = 0.0005$) and Em/Am ratio ($p = 0.004$), with higher late diastolic annular velocity ($p = 0.02$) and prolonged ICT ($P = 0.003$) and IRT ($P = 0.002$) after HSCT were observed. Study of lateral tricuspid annulus showed nearly similar results as the lateral mitral annulus. LV and RV Tei indices were found to be higher before HSCT in comparison to control and remain higher after HSCT.

Conclusions

TDI could detect the subtle abnormalities in the systolic and diastolic functions before and after HSCT which can imply that conditioning regimen may affect cardiac function.

EP-397

Others

ACTIVE DRUG CONCENTRATION OF GENERIC VINCRIStINE FORMULATIONS IN SOUTHEAST ASIA

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Objectives

Availability of generic drugs aid the rising cost of healthcare especially in developing countries. These are more affordable than the innovator product however there is public perception they may be of inferior in quality. There are established guidelines ensuring pharmaceutical quality, but many countries do not have resources to implement them. In Asia, there are numerous cases of fake and substandard generic medicines such as anti-malarials and anti-microbials. Few studies have evaluated generic chemotherapy formulations; and low active drug levels, contamination and increased toxicity have been reported. For old agents such as Vincristine, only generic brands are available in Asia. The purpose of this study is to determine the active drug concentration of Vincristine among different brands available in Southeast Asia.

Methods

Generic vincristine formulations were obtained from Southeast Asian countries, including India, and transported in cold storage to National University Singapore. Vincristine levels were measured using high performance liquid chromatography and compared to Vincristine lab standard (Sigma), as modified from US Pharmacopeia methodology.

Results

Ten generic Vincristine formulations were obtained from Malaysia, Sri Lanka, Vietnam, Indonesia, India, Philippines and Singapore. Two brands had 4 samples each; 5 brands had 2 samples each; and 3 brands had a sample each. These were manufactured in India, South Korea, Netherlands and Hungary; and were within prescribed shelf life. The mean Vincristine levels obtained per brand all fell between 90-110 % of the control; values ranged from 92.07% to 109.6 %.

Conclusions

Selected generic vincristine formulations from Southeast Asia and India have acceptable active drug levels between 90-110 % of the lab standard. The presence and quantity of impurities which may be clinically significant were not tested in this study.

EP-398

Others

CHILD TUMORS IN THE AFRICAN ENVIRONMENT: DIFFICULTIES IN MANAGEMENT AND ADVOCACY FOR HEALTH SCREENING AND CARE

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Introduction:

Childhood cancer is a complex. The aim of this study was to discuss the difficulties of managing children with cancer in eastern DR Congo, to bring awareness of the problem and advocate for policy change.

Patients and methods:

The study was conducted in the city of Bukavu, eastern DR Congo. A questionnaire was administered to caregivers working in various health care facilities.

Results:

The Wilms tumor was the most common followed by leukemia, retinoblastoma and malignant lymphomas. The clinical diagnosis was supported by ultrasound and histopathology. Treatment however was limited, by the high cost (the middle cost is 600\$ USA) and lack of inventory. Cyclophosphamide, Methotrexate and Prednisolone are the available drugs most used in the two general reference hospitals in Bukavu meeting the criteria for the management of childhood cancers, meaning the presence of qualified staff (Pediatrician, Surgeon, and Pathologist), a laboratory capable of determining tumor markers and a pharmacy capable of providing the anticancer drugs.

Conclusion:

Childhood Cancer is a serious problem in eastern DR Congo. With the current challenges in diagnosis and treatment, a unit capable of caring for childhood cancer is essential. It will also begin addressing the popular misconception that "childhood cancer always ends in the cemetery."

EP-399

Others

ABDOMINAL TUMORS IN CONGOLESE CHILDREN: DIFFICULTIES IN THE MANAGEMENT OF 16 CASES

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Introduction:

Abdominal tumors in children are many diagnostic and therapeutic challenges, especially in developing countries such as DR Congo. The aim of this study is to determine the frequency of abdominal tumors in children and to describe the therapeutic modalities in a country with limited resources.

Patients and methods:

It's a retrospective study for five years (2008-2012) in our department of Pediatric Surgery. All children 0 to 15 years old presenting to Hospital with an abdominal mass were followed. Epidemiological, clinical and therapeutic parameters were documented and analyzed.

Results:

Females made up a higher percentage of children presenting with an abdominal mass (56.2%), the average age was 7.5 years. The age group of 5 to 10 was most affected (37.5 %). The clinical diagnosis was supported by ultrasound in 98%. Wilms Tumor was the most common tumor (50%), followed by genital tumors (25%), neuroblastoma (18.7 %) and pancreatic tumors (6.25%). 98% of cases underwent surgery. The postoperative course was uneventful (81.1%). There were no deaths; however, 3 children were released under palliative care.

Conclusion:

Abdominal tumors in children represent 50% of childhood tumors. Diagnosis is primarily clinical, however, ultrasound is an important tool. Surgical treatment but must be complimented by chemotherapy, however, it is not always available in our community.

EP-400

Others

THE ROLE OF A PARENT GROUP IN AWARENESS CREATION OF CHILDHOOD CANCERS

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Objectives

To raise awareness of childhood cancers in Ghana

Methods

A high profile launching of the Ghana Parents' Association for Childhood Cancers (GHAPACC) in 2009 with publicity about challenges faced by children affected by cancer and their families. Awareness creation, fundraising walk organised during the International Childhood Cancer day in 2010. Coverage was by national TV. Needs of children affected by cancer and their parents made public through articles in the national daily papers. Members of the parents' group have participated in radio and television talk shows. Family funfair organised during Easter 2011 was used as an avenue for awareness creation. In September 2011 a media meeting was organised by GHAPACC. 35 media houses were involved to disseminate the early warning signs on television, radio and the print media.

Results

Nationwide publicity about childhood cancers ongoing. Over 5000 posters distributed by GHAPACC including schools and churches. Several organisations made substantial contributions directly towards childhood cancer treatment and many NGOs have sprung up as result. We are currently about to launch a project to construct a 30 bed hostel for families of children on admission at the hospital.

Conclusions

Level of awareness of childhood cancers in Ghana has improved but more needs to be done. Superstitious beliefs and stigmatization by society are some of the hindrances to early reporting of cases to health facilities. More education through the media would be an effective way for continued awareness, help get better access to care and improve outcomes for childhood cancer.

EP-401

Others

IMPROVING THE STAGING OF INFECTION RISK IN CHILDREN WITH FEBRILE NEUTROPENIA BY MULTIPLEX VIRAL PCR AND CYTOKINE DETERMINATION

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Objectives

Respiratory viral infections (RVI) are a common cause of febrile neutropenia (FN) episodes in children with cancer. We present a cohort of children with FN evaluated for RVI by multiple-PCR in conjunction with cytokine profile in order to describe the incidence, clinical outcome, and potential early biomarkers of RVI.

Methods

Children with FN admitted to the hospital between Oct'10 and Dec'13 were prospectively enrolled. On admission, children were evaluated for 16 RV in nasopharyngeal wash by multiple-PCR, and cytokine profile was determined in blood by flow cytometry. Children with RVI were compared to children with bacterial infection (BI) by analyzing risk staging on admission, clinical outcome, laboratory parameters and cytokine profile.

Results

A total of 130 episodes of FN in 45 children were enrolled (56.2% female, median age 5.6 years [3.1-13.8]). On admission, 16.9% were classified as low risk of BI(LRBI) according to our own protocol. Overall, microbiologic confirmation was obtained in 49.2%. RV were identified in 28.3% episodes, being 4.6% mixed RV-BI. BI were detected in 24.6%. Rhinovirus was the most common virus (n=21), followed by parainfluenza (n=4), RSV (n=2), coronavirus (n=2), influenza B (n=2) and adenovirus (n=1). RV were more common in children with LRBI compared to high risk (40.9% vs. 25.7%, p=0.1). On admission, children with RVI presented lower median PCT (0.2[0.1-0.5] vs. 0.7[0.3-5.1]; p=0.01), IL12 (1.8[0-50.6 vs. 188.2[5.4-1117.8];p=0.04) and TNFa (0 vs. 94.8(0-1593);p=0.06) compared to children with BI. The outcome of children whose only isolation was a RV was favorable regardless of the risk established on admission.

Conclusions

In our cohort of children with FN, RV were the infectious agents most frequently isolated. Early detection of RV by multiple-PCR in conjunction with low PCT, TNFa and IL12 levels on admission may enhance the identification of these patients, improving the risk staging of children with FN.

EP-402

Others

CLOSTRIDIUM DIFFICILE-ASSOCIATED DIARRHEA IN CHILDREN WITH HEMATOLOGICAL MALIGNANCY

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Objectives

Clostridium difficile associated diarrhea (CDAD) is now considered to be one of the commonest causes of nosocomial diarrhea worldwide. Gastro-intestinal infection in the form of diarrhea and dysenteric illness are the leading causes of infection in pediatric oncology patients in BSMMU, Dhaka, Bangladesh. The study was conducted to see the frequency of Clostridium difficile infection by EIA among diarrheal children with hematological malignancy in BSMMU.

Methods

This prospective observational study was conducted from april 2012 to march 2013 to see the rate of Clostridium difficile infection in children with hematological malignancy. A total of 58 diarrheal episodes experienced by 51 children with different hematological malignancies were consecutively included if developed diarrhea at any point of hospitalization. Fecal samples were sent to ICDDR B laboratory EIA for C. difficile , aerobic culture for common bacteria and PCR for common parasitic infection.

Results

Among the total 58 diarrheal episodes 22.4% samples were positive and 77.6% samples were negative for GDH antigen by EIA test. But None of the fecal samples were positive for toxin A and/ or B by EIA. Potential pathogenic bacteria were isolated from 5.2% sample by aerobic stool culture. Different parasites were identified from **70.4%** samples by PCR and most frequently identified protozoa was Giardia lamblia (**68.5%**) . During episode 81% children were neutropenic and severe neutropenia had significant corelation with GDH positivity. Usage of Imipenem , high dose cytosar and omeprazole had significant correlation with GDH positive diarrheal episodes.

Conclusions

The study found colonization rate of Clostridium dificile 22.4% but none was toxigenic among diarrheal children with hematological malignancy . Parasitic infections were seen more frequently in children with malignancy.

EP-403

Others

MALIGNANCIES IN INFANTS IMPLEMENTS METASTATIC POTENTIAL AS TUMORS REACH THE PEAK OF ITS GROWTH RATE

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Objectives

To rate kinetic characteristics of growth embryonic tumor in relation with the terms of implementation metastatic potential of the primary tumor.

Methods

A retrospective analysis of the primary malignancies by ultrasound diagnosis in 109 children aged 1-366 days both sexes (with nephroblastoma - 31, 58 - with retroperitoneal neuroblastoma neuroblastoma and adrenal gland, 20 - with hepatoblastoma) was made. The point of maximum velocity (inflection point) for the Gompertz model was calculated based on the vanishing of the second derivative of the Gompertz. ROC-analysis was used to determine the threshold age at which the disease goes to prognostically unfavorable stage.

Results

Median of actual volume of abdominal tumor at the primary imaging was 176 (40-355) cm³. Was obtained Spearman rank correlation ($\rho = 0.53$; $p < 0.0001$) between the tumor volume at the time of initial diagnosis and age. Based on the evaluation of the Gompertz model parameters was calculated the point of maximum rate of tumor growth - T_{max}. Its value corresponded to 124 days since birth and was indicating at critical change in the growth rate of malignancies in the first four months of life. According to the results of ROC-analysis was found threshold of exceeding of age at which the chances of malignancies diagnosis at an advanced stage in sick infants are increased 4.35 fold (95% CI 1.7-11.5) . This threshold was 129.5 days (51% specificity (95% CI 39-63), the sensitivity of 81% (95% CI 69-91), AUC=0.61 (95% CI 0.49-0.71).

Conclusions

Thus, on the clinical data of the cohort of infants was modeled a situation where in the first 4 months life occurs the greatest intensification the process of malignancies growth realizing metastatic potentials when reach the peak of its growth rate.

EP-404

Others

INVESTIGATING HEPATITIS B IMMUNITY IN CHILDREN PRESENTING TO A PAEDIATRIC HAEMATOLOGY AND ONCOLOGY UNIT IN SOUTH AFRICA

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Objectives

Hepatitis B is an important public health issue in South Africa. The hepatitis B vaccine was introduced into the South African Expanded Programme of Immunisation (EPI) in 1995, without any catch-up programme. The duration of protection after hepatitis B vaccination is unknown, and waning of vaccine-induced immunity leaves children at risk of hepatitis B infection in a setting where the prevalence is high and horizontal transmission is likely. The aim of this study is to assess the immunity to hepatitis B in patients at first presentation to a paediatric oncology unit.

Methods

A retrospective audit was done of all new patients seen in the unit from January 2012 to December 2013. None of these patients had received previous immunosuppressive therapy. A total of 210 patients' results were available for review. Patients were classified as immune (anti HBs >100mIU/mL), low immune (anti HBs 10-100mIU/mL) and not immune (anti HBs <10mIU/mL).

Results

Of the 210 patients included (median age 6.5 years), 84 (40%) had no immunity to hepatitis B despite presumed vaccination as part of the EPI schedule. Six patients tested positive for hepatitis B core antigen (anti-HBc) consistent with previous infection. No patients had active hepatitis B infection (hepatitis B surface antigen positive). Most of the patients with HIV infection were not immune (80%).

Conclusions

A significant number of children are not immune to hepatitis B despite vaccination being part of the South African EPI. Revaccination should be considered for all oncology and haematology patients where the opportunity exists for exposure to hepatitis B virus. Consideration should also be given to offering booster vaccination to the population as a whole.

EP-405

Others

WATER QUALITY CHARACTERIZATION IN 4 CHILDREN'S HOSPITALS IN SANTIAGO, CHILE

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Objectives

Good water quality in a hospital is critical for mitigating risks in immune-compromised children. In order to understand the reality in the Santiago, Chile metropolitan area, we conducted an investigation of our local hospitals' water supplies at PINDA (National Antineoplastic Drugs Children's Program) Centers. The samples were taken in the Santiago, Chile metropolitan area during the months of April, July, November 2013, and January 2014.

Methods

The Microbiology and Mycology Program of the Faculty of Medicine of the University of Chile conducted analyses of bacteriological, fungal, and parasitological presence were conducted. The statistical analyses employed a non-parametric test, where the response variable was the microbiological load of each hospital.

Results

We identified the presence of at least one microorganism at 90.32% of the locations tested. *Microsporidia spp.* was the most prevalent, with a 37% presence in the samples. In decreasing order, we identified the following organisms: *Pseudomonas fluorescense*, *Enterobacter cloacae*, *Pseudomonas aeruginosa*, *Pseudomonas oleovorans*, *Pseudomonas putida*, *Stenotrophomonas maltophilia*, *Pseudomonas stutzeri*, *Alcaligenes faecalis faecalis*, and also a unidentified bacterium (a gram negative non fermentative bacilli), and fungus.

Although quantitative analyses showed there was a presence of microorganisms, there was not a consistent enough presence in the samples to detect statistical differences ($P > 0.05$) among the 4 hospitals tested.

Conclusions

We have discovered generalized water quality deficiency in the tested hospitals. Thus, as these hospitals treat immunocompromised patients, the present data suggests it necessary to take specific measures to ensure the health of each child treated at hospitals in the Santiago, Chile metropolitan area.

EP-406

Others

ROLE OF THE PEDIATRIC SURGEON ONCOLOGIST WITH ACUTE PANCREATITIS IN CHILDREN WITH LEUKEMIA TREATED WITH ACUTE LYMPHOBLASTIC L - ASPARAGINASE. EXPERIENCE IN THE NATIONAL INSTITUTE OF PEDIATRICS .

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Objectives

Pancreatitis is an inflammatory disease of the exocrine pancreas, self-digestion of the tissue by its own enzymes. The aim of this paper is to evaluate the role of de oncology pediatric surgeon in management of acute pancreatitis

Methods

This is a retrospective study analyzing cases of patients with ALL who had acute pancreatitis induced by L -asparaginase treated at the National Institute of Pediatrics (INP) in the Department of Surgical Oncology for a period of 11 years. In order to establish the role of the pediatric surgeon oncologist in the management of patients with acute pancreatitis by L - Asp. The clinical records of 120 patients admitted to the surgical oncology with acute pancreatitis during the period 2002 to 2013 , of which 30 patients had acute pancreatitis induced by L - Asp were reviewed. Clinical and biochemical data , ultrasound, computed tomography , treatment, complications and intensive care stay were analyzed.

Results

Patients who had acute pancreatitis by L - Asp, the mean age was 12 years , gender was found with a ratio of 12 male patients (40 %) and 18 female (60%). All patients had abdominal pain, nausea, vomiting and elevated pancreatic enzymes lipase and amylase. CT pancreatic necrosis was found in 3 patients (13 %), 2 patients underwent peritoneal drainage catheter and patient Tenckhoff I performed necrosectomy . 8 died (26 %) patients, only one due to toxicity of the pancreas .

Conclusions

L - Asp is an effective drug for the treatment of ALL, but because of its toxicity requires close monitoring due to the main complication is pancreatitis in order to start treatment as soon as possible. Surgery in acute pancreatitis is limited to removal of infected necrotic pancreatic tissue, so that the role of the surgeon is of paramount importance to determine the window of opportunity and timely management.

EP-407

Others

POEM (PEDIATRIC ONCOLOGY EXERCISE MANUAL): A KNOWLEDGE SYNTHESIS TO IMPROVE AWARENESS ABOUT PHYSICAL ACTIVITY BENEFITS DURING AND AFTER CHILDHOOD CANCER

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Purpose

To promote physical activity (PA) in children with cancer, thereby improving their overall quality of life (QOL). The Pediatric Oncology Exercise Manual (POEM) and its website will be distributed among clinicians, fitness professionals and educators (CFEs) and well as to families. Specifically, this project seeks to increase the awareness of the benefits of PA during cancer treatment by equipping CFEs and families with tools, resources and evidence-based information.

Methods

We convened an internationally (Spain, Germany, The Netherlands, USA, and Canada) acclaimed panel of experts in pediatric oncology to develop the first worldwide evidenced-informed PA manual for children with cancer. The manual has been developed in both professional and lay versions. Highlighted topics include general evidence on the benefits of PA and cancer, recommendations, and precautions in survivors experiencing late-effects. The POEM will be distributed along with educational sessions. An online platform is being created to: (a) evaluate quality of POEM; (b) provide ongoing resources; (c) foster ongoing international collaborations; (d) further develop an online training to create global capacity in this area.

Results

The dissemination of the POEM across Alberta will begin in Spring 2014, with planned expansion nationally, throughout Canada and then internationally, to contributors' countries. Finally, a plan to disseminate POEM to low-income countries is being developed. Dissemination of the manual will be tracked, along with use of website resources. Survey results will be analyzed and incorporated into yearly quality improvement cycles, ensuring the best evidence-to-practice translation occurs.

Conclusion

The creation of the POEM along, with the online support, will enhance awareness about the role of PA in pediatric oncology in an economically sustainable manner. Increased PA levels results in enhanced QOL for pediatric cancer survivors and diminished risk of developing comorbid conditions in survivorship.

Acknowledgements

Canadian Institute of Health Research, Alberta Children's Hospital and the POEM Contributors.

Keywords

Exercise, physical activity, pediatric, cancer, guidelines, quality of life

EP-408

Others

DEVELOPMENTAL DELAY IN A CHILD WITH AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME

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Objectives

Autoimmune lymphoproliferative syndrome (ALPS) is an inherited lymphoid disorder, attributed to a defect in apoptosis, characterized by non-malignant lymphoproliferation, autoimmunity and cytopenias with raised circulating double negative T cells (DNT). Developmental Delay (DD) has not been reported with this condition. Here we describe a girl with ALPS who had developmental delay.

Methods

A detailed analysis of the child's history, examination, laboratory investigations along with review of literature of the two conditions has been done.

Results

A 9-year-old girl presented with intermittent fever and repeated hospitalization for the same for last 3-4 years. On physical examination she had splenohepatomegaly and developmental delay. She was evaluated for infections (malaria, kala-azar), leukaemia, lymphoma, inborn error of metabolism (glycogen storage disorders) and connective tissue disorders.

Investigations revealed neutropenia, hypergammaglobulinemia. Chest X ray was normal and Mantoux was negative. Almost all infectious causes were ruled out by serological tests. ANA was negative. Bone marrow examination was normal. In view of persistent neutropenia (> 6 months) which was non-infectious non-malignant with splenohepatomegaly possibility of ALPS was thought and flow cytometry done which revealed 4.18 % double negative T cells (CD3+ CD4-CD8-) confirming ALPS. She had resolution of neutropenia after starting of prednisolone. She was also started on sirolimus so as to decrease the organomegaly. Though no improvement occurred in her developmental milestones

Conclusions

ALPS should be suspected in a child with isolated persistent neutropenia and organomegaly for which common causes like infection, malignancy and autoimmunity have been ruled out. To our best knowledge, developmental delay has not been reported with ALPS. We report this to make paediatric oncologists aware of this rare association.

EP-409

Others

DEFICITS IN CLINICAL TRIAL ENROLLMENT AMONG ADOLESCENTS AND YOUNG ADULTS WITH CANCER TREATED AT AN ACADEMIC MEDICAL CENTER

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Objectives

Improvement in survival for adolescents and young adults (AYAs, age 15-39) with cancer is worse compared to children and older adults. This trend may be partly due to poor accrual to clinical trials. We determined clinical trial enrollment at an academic medical center and compared the proportion of AYAs enrolled with children (age \leq 14) and older adults (age \geq 40) and between institutions within the center.

Methods

The California Cancer Registry provided data on patients diagnosed with cancer 1/2008-12/2012 and treated at a University of Southern California (USC) Cancer Center institution. At USC, oncology care is delivered in 3 settings: a children's hospital, an adult cancer hospital and a county-run facility, which provides care to children and adults. Patients identified by the registry were matched to institutional databases that track trial enrollments. Differences in enrollment were determined by the chi-square test.

Results

Overall, 174 of 793 children (22%) were enrolled on therapeutic clinical trials compared to 104 of 1699 AYAs (6%) and 518 of 9311 of adults (6%) ($p<0.01$). Enrollments among AYAs were higher at the children's hospital (29/191, 15%) compared to either the adult cancer hospital (10/320, 3%, $p<0.01$) or county facility (65/1188, 5%, $p<0.01$). However, within the children's hospital, the proportion of AYAs enrolled on therapeutic trials (29/191, 15%) was significantly lower compared to children (174/761, 23%, $p<0.01$).

Of the 10 most frequent AYA diagnoses, 7 had clinical trials available, compared to 10 of 10 in children and 9 of 10 in adults.

Conclusions

The proportion of AYAs and adults enrolled on therapeutic trials is low, suggesting administrative barriers to enrollment. Within a children's hospital, lower enrollment among AYAs suggests other age-related barriers. Trial availability may also contribute. However, reasons for non-enrollment are not routinely captured, which prevents further analysis of the causes of low enrollment, and should be documented prospectively across treatment settings.

EP-410

Others

CYSTEINE CATHEPSINS, CYSTATIN C AND VEGF IN TUMOR VASCULOGENESIS

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Objectives

Studying activity of cysteine proteases - cathepsins B, L, H, and their endogenous inhibitor cystatin C, vascular endothelial growth factor (VEGF) in the blood serum of children with infantile hemangiomas before and after propranolol-therapy compared with the control.

Methods

Studying the activity of cathepsins B, L, H and the concentration of cystatin C and VEGF in blood serum from 24 healthy children and 80 children with infantile hemangiomas treated with propranolol: 64 (group 1) with good response and 16 (group 2) with relapse after discontinuation of propranolol by using standard methods.

Results

Serum level activity of VEGF and cathepsins B, L and H in patients with hemangiomas significantly higher than that in the serum of healthy children. VEGF serum concentration is higher in the group 1 comparing to the control ($p = 0.008$) and have gradually normalizing during the course of treatment. VEGF concentration was not different from control in the group 2. There was the activity of cathepsins B, L and H in the group 2 before treatment more comparing to the control (p-levels: 0.001, 0.000 and 0.003) and to the Group 1 (p-levels: 0.000, 0.000 , and 0.003); have not reached the level of healthy children with the severe propranolol-induced involution of hemangiomas. There was not pattern of level cystatin C concentration.

Conclusions

Unfavorable and aggressive course of hemangiomas associates with the elevated concentrations of VEGF and the activity of cathepsins B, L and H in the blood serum. Understanding the role of cysteine ??cathepsins in tumor vasculogenesis could lead to the development of more efficacious therapies.

EP-411

Others

UNTANGLING THE CORD: A POLICY ANALYSIS OF NATIONAL PUBLIC UMBILICAL CORD BLOOD BANKING IN CANADA

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Objectives

Recognition of the value of cord blood has prompted widespread efforts at its collection and banking, both privately and publicly. Until recently, Canada was the only Group of 8 country without a national public cord blood bank. The explanation for Canada's relative delay in developing a national cord blood banking (CBB) program is unclear, and has received almost no scholarly attention.

Methods

Data for this analysis derive from searches of the published and grey literature on CBB. Sources of data include academic articles, governmental and non-governmental documents, media sources, organizational and industry websites, and online media. To map the determinants of CBB policy in Canada, we employ an analytic framework developed by Jonathan Lomas that considers the manner in which information, values and institutions configure the context for policy decision-making.

Results

Our analysis highlights the predominance of institutional structure as a determinant of policy stasis on CBB. Structures of blood system governance conditioned the use of values and information to influence problem definition, agenda-setting, and decision-making on CBB in Canada. Diffusion of agenda-setting roles hampered early and sustained stewardship of CBB policy. Disjuncture between the political responsibility for, and ambit of, national CBB policy slowed the development of a national cord blood bank.

Conclusions

Our analysis suggests that locating greater responsibility for agenda-setting and funding at the federal level would facilitate coordinated national responses to the policy challenges that emerge as stem cell science evolves. Explicit frameworks for policymaking on cord blood and other rapidly evolving areas of blood system policy would provide transparent blueprints for decision-making. Formal efforts at public consultation, through deliberative processes or otherwise, could help plait public perceptions with evolving scientific evidence, and align broadly held moral intuitions with the ethical principles justifying policy choices.

EP-412

Others

OUTCOME OF ACUTE GUT GVHD POST STEM CELL TRANSPLANT IN CHILDREN – IMPORTANCE OF NUTRITIONAL STATUS

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Objectives

Acute Graft-versus-host disease (aGvHD) after allogeneic hematopoietic cell transplantation is associated with considerable morbidity and mortality. Gut aGvHD remains the most difficult to manage and the morbidity and mortality increases with malnutrition. This study was undertaken to report outcome of gut aGvHD in children at a tertiary care center in India and the effect of malnutrition on morbidity and mortality.

Methods

It was a retrospective, observational study reporting the outcome of 15 patients (age 4 – 18 years) with gut aGvHD out of which 8 were grade IV and 6 were steroid refractory. Nine children (60%) were malnourished at the time of starting conditioning regimen (weight for age less than 25th centile of CDC standards).

Results

Nine children had matched sibling donor; 4, 1 and 1 had matched unrelated, haploidentical related and one antigen mismatched related donors respectively. Source of stem cells was peripheral blood in 10 patients and bone marrow in five. Mean CD34+ cell dose was 6.62×10^6 /Kg/L. Mean time of appearance of symptoms was 20.9 days. The mortality was 46.66% in our cohort and most common immediate cause of death was gram negative sepsis secondary to immunosuppression. Four patients (66.66%) with steroid refractory gut GvHD did not survive (P < 0.05). Five out of 7 malnourished children succumbed (P < 0.01).

Conclusions

Outcome of children with malnutrition and gut aGvHD is worse and steroid refractory gut aGvHD holds to have a very poor outcome.

EP-413

Others

BREAST DISEASES IN CHILDREN AND ADOLESCENTS: RISK FACTORS FOR BREAST CANCER

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Objectives

To analyze the breast diseases in children and adolescents and to estimate the risk factors for breast cancer.

Methods

317 patients 0-19 year old, with breast diseases were treated (surgery and non-surgery treatment) between 1990 and 2013 in the Institute of Oncology Bucharest. We were looking for the risk factors for breast cancer, family history of breast, ovarian malignancies, diet and the outcome of disease. Surgical treatment (164 pts): lumpectomy, tumorectomy. 82 pts. received drug therapy. In 71 cases of small tumors (<2 cm) the choice was expectancy.

Results

There were 8 cases of male patients. The highest incidence was between 15 - 21 year old (55%). Types of breast tumors: fibro-adenomas 68%, Phyllodes tumor, ductal papilloma. 23% of the mammary disorders were fibrocystic changes. Signs and symptoms: physiologic swelling and tenderness (212 pts.), nodularity (82 pts.), breast pain (289 pts.), palpable breast lumps (244 pts.). Family history events were found in 76% of patients: mothers or relatives with benign mammary lesions, breast and/or ovarian cancer (15%). 64% pts. have had symptomatic high serum estrogen levels (menstruation disorders, ovarian cysts, early menarche). Excessive carbohydrates diet, overweightness and obesity were presented in 58% of cases. 5- 10 years follow up for 65. with small tumors (<2cm) has revealed that 30% of them became smaller, 18% kept the same size and 52% became larger.

Conclusions

A significant number of children and adolescents with breast benign tumors and fibrocystic changes have risk factors for breast cancer. Effective and accurate counseling for adolescents and their parents regarding breast cancer prevention should be a routine component of preventive health

EP-414

Others

WORKING TOGETHER ON ETHICS: ETHICAL DELIBERATIONS INVOLVING PROFESSIONALS AS WELL AS PATIENTS' AND PARENTS' REPRESENTATIVES. LESSONS AND RESULTS FROM THE EU-FP7 ENCCA PROJECT.

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Objectives

In the ethics work-package (WP18) of the European Network for Cancer research in Children and Adolescents (ENCCA), the use of validated methodologies for ethical evaluation and deliberation aimed at making a state of the art review of relevant ethical issues in paediatric oncology research and at balancing the perspectives of professionals and of patients' and parents' representatives.

Methods

European representatives from the International Confederation of Childhood Cancer Parent Organizations (ICCCPO) and professionals involved in ENCCA were invited to participate in ethical deliberations on clinical trials and on bio-banks. These deliberations were conceived as a means to get the stakeholders' expert conclusions on ethical issues by making them participate in "a game of giving and asking for reasons" in which they had to justify their stances by sound arguments. By their ability to (dis)agree, stakeholders became the very "scorekeepers" in this game. Ethical deliberation is fully inclusive of all views.

Results

From the scope and nature of (dis)agreements, three kinds of results could be distilled, namely 'like-mindedness' (e.g. the value of research participation), 'rallying' (e.g. "community equipoise" in clinical trials), and 'discrepancies' (e.g. re-consent after 18 in bio-banks). Voluntary participation and exclusive membership ('ENCCA partners') found these deliberations a meaningful scoping exercise that have allowed design of ethics interventions and identification of empirical and normative research avenues relevant for the paediatric oncology community as a whole (professionals and lay people).

Conclusions

Ethical deliberation is not a consensus-forming process and does not preclude disagreements. Therefore, why is it important to develop "a more exhaustive balancing of perspectives"? Two answers are to be made to this question. One relates to the value of pluralism for biomedical research and for ethical knowledge. Another consists of feed-back presented by a patients' representative on the value of ENCCA's experience in ethics.

EP-415

Others

JENECEE PLACE: A HOME AWAY FROM HOME WHERE FAMILIES CAN STAY WHILE UNDERGOING MEDICAL TREATMENT

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Objectives

The purpose was to build a home for families who needed a place to stay in Victoria while undergoing medical treatment. The home would provide a warm, safe, and inviting environment for pediatric families and hopefully eliminating stresses during their stay. To also raise approximately 10 years of operational costs, eliminated the need for fundraising in the early years of operation.

Methods

Using my personal story of overcoming medical challenges and my past history of raising over a million dollars in pennies for Variety, The Children's Charity, secured me the recognition, and support of notable partners, such as TELUS, The Children's Health Foundation and Norgaard Foundation. These corporate sponsors donated very large amounts of money and the rest was donated by the island communities. Securing donations in kind from the contractors and securing 6 figure donations from various local corporate sponsors, to name a room helped us achieve our goal in a very short period of time. Media coverage was paramount.

Results

From the first shovel in the ground to finish, Jeneece Place was built in 9 months, a 10,000 square foot home, to accommodate 10 families. We raised more than projected goals and built Jeneece Place significantly under budget due to in kind donations from the contractors. A first time accomplishment for this 20 year old young lady.

Conclusions

Jeneece Place has been open for 2 years now and has served over 700 families. Over 96% of the families that visit Jeneece place come from Vancouver Island and the Gulf Island but few have come from as far away as France, there by serving its purpose of helping BC families.

EP-416

Others

PROTOCOL FOR THE ABDOMINAL COMPUTED TOMOGRAPHY FOR REDUCTION OF IONIZING RADIATION IN PEDIATRIC ONCOLOGY PATIENTS.

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Objectives

Dose reduction of ionizing radiation in pediatric oncology patients, changing the protocol of computed tomography scanning to stage only with intravenous contrast, “early portal phase” described.

Methods

30 patients were selected who underwent computed tomography (CT) examination of the upper abdomen, lower abdomen, for the total period of November 12, 2012 until August 23, 2013, was described “Old Protocol Group” and 30 patients who underwent CT during the period of September 23, 2013 until January 31, 2014, was describe “New Protocol Group”. From the total dose, average total dose equivalent was done for each group.

Results

Based on the average equivalent dose of CTs there was a reduction of more than 50% of the radiation dose for all patients of the “New Protocol Group” compared to the “Old Protocol Group”. Moreover, the protocol change did not cause damage to diagnostic imaging.

Conclusions

The principal objective of this work was to verify the results of the reduction of the total equivalent dose in CT examination, within the possible limits is based on the principle of ALARA (Radiation Safety Manual University of Washington's Radiation Safety).

EP-417

Others

MISDIAGNOSIS AND REFERRAL OF PATIENTS WITH A NON-MALIGNANT DISORDERS TO A PEDIATRIC ONCOLOGY UNITS

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Objectives

To evaluate patients who were wrongly misdiagnosed and referred to a Pediatric oncology unit with initial suspicion of cancer to evaluate the size of this problem in one large Cancer institute in a developing country.

Methods

A retrospective analysis was performed on all patients referred to the pediatric oncology department, South Egypt Cancer Institute (SECI) between 2006 and 2010.

Results

For all available data of the 712 patients who were admitted in SECI 570 (80.1%) were suffering from malignant tumors, 19 (2.7%) referred/escaped/lost before full diagnosis, 21 (2.9%) died early after admission before reaching a final diagnosis and 102 (14.3%) proved to have a non-malignant disease, of them 25 (24.51%) were benign tumors, 24 (23.53%) were benign hematological diseases, 24 (23.53%) were infections, 22 (21.57%) were inflammatory cases, 2 (1.96%) were metabolic diseases, and 5 (4.90%) have other different diagnoses.

Conclusions

Misdiagnosis of cancer in children is a problem that should be excluded before starting of therapy in pediatric oncology units, especially in developing countries where diagnostic facilities are restricted.

EP-418

Others

STRATEGIES TO PREVENT TREATMENT ABANDONMENT IN CHILDHOOD CANCER IN RIO DE JANEIRO, BRAZIL

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Objectives

Abandonment of treatment in childhood cancer has been considered one of the major limitations to achieving high cure rates in developing countries. The aim of the study is to describe the impact of a simple strategy to prevent treatment abandonment.

Methods

The study period was 08/01/2012 to 02/28/2014. Patients younger than 18 years, diagnosed and treated with solid tumors at the Instituto Nacional de Câncer- Rio de Janeiro- Brazil were prospectively monitored for adherence to appointments. Daily, one health care professional registered all patients that missed the scheduled oncology consultation. Family members were contacted within 24 hours of the missed appointments by phone call and/or telegram. The primary physician was informed as well as the multidisciplinary team. Interventions addressing lack of resources as travel expenses, lodging, transportation, food basket, were provided to all families. Abandonment was defined as 4 weeks of missing appointments during active treatment.

Results

During the study period 2056 patients had 8570 scheduled oncology consultations and 201 (9.8%) patients missed at least one. All families were contacted by the data manager. The number of absences on diagnostic investigation or 'on treatment' was: 109/201(54.2%) and the number of absences by pt was: n=1 in 85(78.0%); n=2 in 16(14.6%); n=3 in 3 (2.8%); n=4 in 3 (2.8%); n=5 in 1 (0.9%) and n=6 in 1 (0.9%) pt. One hundred and five (96.3%) pts returned to treatment, but 4 pts abandoned treatment despite all efforts. In 92/201(45.8%) the absences occurred in pts 'off treatment'.

Conclusions

Monitoring missing appointments, early intervention to address the issues associated with them and providing resources to help families during treatment is associated with very low abandonment rates.

EP-419

Others

EARLY DIAGNOSIS OF CHILDHOOD CANCER IS CHALLENGE IN DEVELOPING COUNTRIES

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Introduction:

In developed countries the cure rate of cancer children exceeds 75%, this reality is far from being achieved in Brazil and the main reason is the difficulty that health professionals have to diagnose the disease early. The Cancer Hospital of Cascavel - UOPECCAN in partnership with the Ronald McDonald Institute through the early diagnosis of cancer children and adolescents program, train professionals of health and pediatrics of the municipalities of Parana-Brasil.

Objective:

Train professionals of health and pediatricians to contribute to the early identification of cancer in children and adolescents, reducing the time between the onset of signs and symptoms and diagnosis in a specialized center providing an increase of the probability of cure.

Methodology:

Health professionals from 16 cities were trained from April / 2008 to Dec/2013, received basic information about children cancer and adolescents (Epidemiology; signs and symptoms of suspicion; care needed for the attention to children and adolescents with cancer). The groups were formed with 40 professionals, 20 hours / course.

Results:

1007 professionals, 63 doctors, 117 nurses, 162 technicians / nursing assistants, 475 community health agents, 81 upper level and 88 medium-level professionals or auxiliary.

Comments:

Among the diagnosed cases of cancer in children in Brasil, many are referred to treatment centers with the disease at an advanced stage. One goal of the campaign is to encourage educational and preventive actions, becoming known to more people about symptoms and signs of disease. This program was performed in 86 Brazilian cities, showed a reduction in the time course in weeks (13 to 5) for the arrival of children at a referral center in the regions trained. Shortening the time between the suspicion of cancer and early diagnosis and treatment, will certainly contribute to the increasing expectations of cure in developing countries.

EP-420

Others

DILUTION OF VINCA-ALKALOIDS IN PEDIATRIC ONCOLOGY: FROM GUIDELINES TO PRACTICAL APPLICATION

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Objectives

Since 1968, cases of accidental intrathecal injections of vinca-alkaloids have been reported worldwide and are responsible for severe and irreversible neurological disorders. In order to avoid those adverse events, several Health Authorities have published recommendations. Among them is the dilution of vinca-alkaloids. In 2013, 4,370 chemotherapies were produced for our pediatric unit, among which 792 preparations of vinca-alkaloids. Our purpose was to study the feasibility of implementation of these guidelines.

Methods

We analyzed 11 international recommendations (France / WHO / USA / Canada / England / Ireland / Spain / Australia / Hong Kong). The use of mini-bags is mainly recommended (n=7) in adults and pediatrics. Four guidelines recommend the use of syringes only in pediatrics. In our pediatric oncology unit, 3 vinca-alkaloids are prescribed: vinblastine, vincristine and vinorelbine. We worked together with pediatricians to dilute these chemotherapies in mini-bags.

Results

We managed to dilute vinorelbine in minibags. The main issue was the total administered volume (dilution and flush of the infusor), sometimes too large for smaller children. As a consequence, we couldn't do the same for vincristine and vinblastine (shorter administration time) for which a dilution in large syringe (60mL) was implemented. The aim of this kind of preparation is to reduce the probability of accidental intrathecal administration. Larger volumes on a short period could lead to cardiovascular adverse effects.

Conclusions

In pediatric oncology, recommendations made to secure the use of the vinca-alkaloids are difficult to apply. We still have to use luer syringes for some preparations. The only way to efficiently secure the use of the vinca-alkaloids would be the use of non-luer devices for intrathecal injections (not yet available in France). The spread of these devices would be a major step.

EP-421

Others

IDENTIFICATION OF INSTRUMENTS USED TO EVALUATE SYMPTOMS IN CHILDREN AND ADOLESCENTS WITH CANCER - SYSTEMATIC REVIEW

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Objectives

A systematic literature review to identify instruments used to assess the symptoms of children and adolescents with cancer .

Methods

Review carried out in PUBMED database using the keywords : (' Questionnaires ' [Mesh] OR scale OR OR instrument OR questionnaire inventory) AND (' Symptom Assessment ' [Mesh] OR pain OR ' pain ' [MESH] OR ' fatigue ' [MESH] OR fatigue OR weakness OR lack of energy tiredness OR OR ' depression ' [MESH] OR depression sadness OR sleepiness ' Sleep Stages / complications ' [Mesh] OR ' dyspnea ' [MESH] OR dyspnoea dyspnea OR lack of air nausea OR* vomit ' anxiety ' [MESH] OR anxiety OR constipation OR ' constipation ' [MESH] OR drowsiness) AND (' neoplasms ' [MESH] OR cancer OR tumor OR tumor OR neoplasm) AND * pediatric. Inclusion criteria were : titles and abstracts in English, Portuguese and Spanish, without restriction period that addressed single or multiple symptoms scales, questionnaires or pediatric instruments.

Results

481 articles were found. 343 were excluded after review of these, 49 addressed instruments of quality of life and symptoms after completion of treatment , 10 scales of mucositis and the other 284 dealt with other themes and population. Thus, 138 articles, of which , 62 were excluded were analyzed , all deleted , 1 occurred in adults, 3 in follow up, 3 were related to the critical instruments , one on communication , 2 on systematic review , 4 on other pathologies , 1 side Effects, 15 addressed interventions to improve quality of life , 7 reported experiences of patients undergoing cancer treatment , 8 discussing pharmacological interventions on pain and 16 the perception of parents or staff about treatment. Thus, 76 studies were analyzed.

Conclusions

It was possible to identify that there is shortage of instruments to assess symptoms in pediatric patients . Likewise , it happens for pediatric oncology . Therefore , it's necessary to the development and validation of instruments to assess symptoms of children with cancer.

EP-422

Others

USE OF INTERACTIVE PLAY WITH CHILDREN IN A 3RD WORLD COUNTRY, WHERE ACCESS TO SCHOOLING HAS BEEN DISRUPTED THROUGH DIAGNOSIS AND SUBSEQUENT TREATMENT

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Objectives

Based on this premise of UBUNTU we provide basic interactive play for the hospitalised young person allowing them the opportunity to interact with each other, as well as adults, learn new skills and ultimately reintegrate into society. With limited to no schooling owing to their age or circumstance, CHOC fills the gap with interactive play whilst on treatment.

Methods

Power Point Presentation with a discussion. Interactive packs prepared for each delegate in order to achieve 2/4 activities

Results

To create a personal experience that can be duplicated in any country with diminished resources.

Conclusions

We do not advocate Interactive Play as a replacement for schooling. Interactive play fulfils a social, emotional, cognitive and interactive function. Our role is to close the gap so that a child with cancer can reintegrate into society painlessly having learnt skills that they can incorporate into their schooling. We want to impart tried and tested skills.

EP-423

Others

MICROBIOLOGICAL PROFILE OF INFECTIONS IN CHILDREN WITH SOLID TUMORS RECEIVING ANTICANCER TREATMENT IN ONE CENTER

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Objectives

One of the most common complications of anticancer treatment are infections. Neutropenia, mucositis, prolonged hospitalization, central venous catheters are the main risk factors. Changing pattern of microbiological agents responsible for serious infections and growing antibiotic resistance warrant continuous epidemiological and microbiological monitoring. The aim of the study was to assess the type and frequency of etiological agents of infectious complications in children with solid tumors treated at a single institution.

Methods

During 2 years (2012-2013) 5849 chemotherapy related hospitalizations (treatment and complications) were registered in our Department. Each year about 400 children aged 0 to 18 years of age are treated. Blood, urine, stool and other specimens were collected and cultured in all cases of neutropenic fever and in all non neutropenic patients from sites corresponding to symptoms of infection. Analysis of type of microbiological agents and its resistance to antibiotics was performed.

Results

Out of 5694 microbiological studies performed, 889 (15.6%) were microbiologically positive, of which 232 (26%) correlated with clinical symptoms of infection. Gastrointestinal infections were the most common: in 61 (26%) episodes *Clostridium difficile* was identified, in 53 (23%) - rotaviral infection. Bacterial central venous catheter-related infections were confirmed in 55 episodes, 33 with Gram positive agent, 19 with Gram negative. The most common Gram positive bacteria were *Staphylococcus* spp - 94 % .There were 3 episodes of candidaemia (CVC) and 3 episodes of *Candida* spp cultured in urine specimens

Conclusions

In our material etiological agent was identified in 15% of specimens only. *Clostridium difficile* was most frequently identified which can be attributed to broad spectrum antibiotics administered in children undergoing anticancer treatment. In case of fever targeted treatment is often not possible, as the cultures are usually negative. Gram positive agents remain the most frequent etiology of CVC-related infections.

EP-424

Others

RESULTS OF PARENT SUPPORT GROUP AND HEALTH PROFESSIONAL SURVEYS ON KNOWLEDGE ABOUT AND ACCESS TO ESSENTIAL MEDICINES IN LOW/MIDDLE INCOME COUNTRIES (LMICS)

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Objectives

To gauge knowledge about and identify barriers to access of drugs on the WHO Essential Medicines List from health professionals and parents

Methods

Two surveys were delivered last year, one to SIOP Members, the other to The International Confederation of Childhood Cancer Parents' Organizations (ICCCPO) Members

Results

From SIOP, 82% of respondents (n=65) were from low and low middle income countries.

74% of respondents knew about the WHO Essential Medicines list (EML) but only 28% were certain that their Government used the EML to guide purchasing of drugs. In 82% of respondent said that drugs were sourced from a combination of Government and NGO's. In the past year, 2/3 of respondents had to delay or cancel treatment due to drug unavailability with 39% experiencing this on a weekly or monthly basis. 45% felt that drug cost was always a barrier, and 42% felt was sometimes a barrier to access. 59% felt that the price charged to families for drugs was a significant barrier.

From ICCPO, 69% of respondents (n: 48) were from low and low middle income countries. 67.5% of respondents believe there are problems with shortages and delays in their country. Shortage problems are most pronounced in Low- to Middle-Income countries. Delays in medications are due largely to too much bureaucracy. In Low- to Middle-Income Countries, the main reasons for patients/doctors requesting medications is that health insurance companies and government do not supply medications 77% of respondents from L/LMIC budgeted for the purchase of medicines/drugs and 50% of respondents from HIC provide medication.

Conclusions

Access to medicines remains a significant concern in LMICs with Cost/Price, unavailability and beaurocracy being major barriers in delivering treatment.

EP-425

Others

A SUPPORT SYSTEM FOR CHILDHOOD CANCER SURVIVORS WITH JOB-HUNTING DIFFICULTY

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Objectives

There are many childhood cancer survivors (CCSs) launching themselves in various fields because of increasing cure rate. Some CCSs, however, have to struggle with hardship to work. Although the government delivers disability certificates as a social welfare service for handicapped people, there are quite a few CCSs with some problems who are not covered by it. Even in the case of brain tumor CCSs with higher brain dysfunction, only 10 % of them can be covered. The handicapped person's employment law gives an opportunity for disable people to find employment. But, again, it is not applied to almost all CCSs who may face with the job-hunting difficulty. We started a project to improve this circumstance.

Methods

We sent out questionnaires to 672 CCSs to grasp their employment situation and 240 answered. We found out some CCSs, even in their late twenties to forties, financially depend on their family .

Results

Last April, we opened a tearoom and hired 5 CCSs. The aim is job-training and the ultimate goal is getting them hired by business society in future. They learn how to communicate people working at the tearoom as waiters/ waitress and simple paper working on the computer, as well. They also have opportunities to learn something they want, like getting certified for some special skills. We also assign them to keep daily work description to find what they are not good at and how they overcome it by themselves.

Conclusions

Now it has passed a year since opening the tearoom. The hired CCSs are confident in themselves and positive as a member of society who pays tax. One of them has got married and expects a baby soon. Other one has got hired by a company and started a new life.

EP-426

Others

CLOFARABINE IN CHILDREN WITH RELAPSED ACUTE LEUKEMIA: ISTANBUL EXPERIENCE

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Objectives

Although Clofarabine is known as an effective novel agent in relapsed acute leukemia, optimum combination and time to use remain a challenge. Aim of this study is to evaluate a clofarabine based protocol in children with multi-relapsed acute leukemia.

Methods

We retrospectively analyzed data of twelve children treated with CLOVE protocol for third or greater bone marrow relapsed acute leukemia between 2009 and 2013. Seven of 12 patients were ALL, 5 of them were AML. Patients with relapsed ALL were treated with one or two cure of FLAG after performing BFM-95 REZ protocol and relapsed AML were treated with two cure FLAG after MRC protocol. The cases with no response to at least two relapsed protocol were received CLOVE protocol in one or two cure.

Results

Clofarabine was effective to induce remission in six patients and half of them had hematopoietic stem cell transplantation (HSCT) (Table 1). All of them relapsed after the HSCT, one of them also relapsed after the second HSCT. Although clofarabine was effective to induce remission, overall survival was poor in our study. The 3-month and 12-month overall survival rates from start of CLOVE protocol were 45.5% and 9%, respectively (Figure 1). The most common adverse event was prolonged neutropenia. Although only one patient died from severe infection, all of the patients had severe bacterial and invasive fungal infections. Also, we observed elevated liver enzymes in 92% of the patients. One patient with refractory AML needed pediatric intensive care due to severe hepatotoxicity and VOD after clofarabine therapy.

Conclusions

All of the patients except one died from relapsed/refractory leukemia even though four of them had HSCT. Although we have provided longer lifetime using the CLOVE for multiple relapsed acute leukemia, subsequently the patients died from uncontrolled leukemia. Therefore, we suggest that clofarabine can be used at the first relapse in leukemia with MRD determination to obtain better results. The main question remains if better outcomes could be obtained with earlier Clofarabine based chemotherapy.

EP-427

Others

INFECTIONS WITH RESPIRATORY VIRUSES IN CHILDREN WITH CANCER IN ISTANBUL

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Objectives

Respiratory virus (RV) infection can cause significant morbidity and mortality in pediatric cancer patients. The aim of this study is to identify the RV infections in children with cancer presenting with signs and symptoms of respiratory tract infection.

Methods

During January1-March 15 2014, all children with cancer presenting with signs and symptoms of respiratory tract infection were assessed for RV with algorithms and molecular techniques (rRT-PCR) suggested by CDC and WHO in the reference Virology laboratory, of Istanbul University.

Results

Samples in 34 episodes of 31 children with cancer were evaluated. The following 20 RV were identified in 17 episodes: influenza A (H3N2) 5, Influenza B 1, Respiratory Syncytial Virus 4, Rhinovirus 4, Coronavirus 3, Metapneumovirus 2 , Bocavirus 1. Five patients had lower respiratory tract infection (Influenza A 2, RSV 1, a patient with Coronavirus had also pleural effusion). Fever, cough, nasal discharge and sore throat were the most common symptoms. Systemic antibiotics were also given in febrile neutropenic episodes. Patients with influenza were treated with oseltamivir. All except 2 (1 Rhinovirus, 1 Metapneumoniae + parainfluenza), required hospitalization. All recovered with specific and/or supportive treatment. Chemotherapy had to be delayed for 3-7 days in most episodes.

Conclusions

It should be kept in mind that viruses are a major cause of respiratory tract infections in children with cancer. Oseltamivir is effective in treatment of influenza in children with cancer. Since there are no effective antiviral agents for some respiratory viruses, precautionary infection control and early diagnosis is important to prevent the infection spread. In most cases, hospitalization and supportive care is needed to reduce morbidity and avoid mortality.

EP-428

Others

IMPROVED OUTCOME OF INVASIVE FUNGAL DISEASE IN PEDIATRIC CANCER PATIENTS: LOCAL INSTITUTIONAL EXPERIENCE OVER 21 YEAR

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Objectives

Background: Increased incidence of invasive fungal disease (IFD) due to increasing intensity of various chemotherapy. IFD are a common cause of morbidity and mortality in immunocompromised patients. Available many antifungal agents have an impact on outcome.

Objectives: to find type of cancer infected with IFD, types of IFD and study outcome of pediatric cancer patients with IFD and impact on survival.

Methods

Retrospective review of pediatric cancer and hematological malignancies who developed during their illness proven or probable IFD from 1993-2013. We reported at ASCO 2008 abstract No.10046 overall survival 33/61=54%, mortality due to cancer 18/61=30% and due to IFD 10/61= 16%. We will report types of cancers, type of fungal disease, overall survival and mortality whether due to primary disease or IFD.

Results

over this period 180 patients registered, 108 with ALL = 60% (21/108= 20% relapsed ALL), 28 AML 16%, 13 NHL, 8 NBL, 4 RMS, 4 WT, 2 for each OS, LCH, HD, Chediak Higashi synd., MBL and aplastic anemia; 1 for each ES, CML, HLH. 49 pts. proven aspergillosis 24/49=49% Survived and 25 died (19 from primary disease, 6 from IFD. 49 pts. with candidiasis 28/49=57% survived and 21 died (14 from primary dis., 4 fungal and 2 sepsis). 76 pts. considered probable IFD 68/76=89%survived, 8 died of primary disease. 6 mucormycosis, 2/6=33% survived (2 died of primary disease after cure of cutaneous and pulmonary mucormycosis, while 2 died of mucormycosis). Overall survival 122/180=68%, mortality primary disease 43/180=24% and mortality IFD 14/180=8%

Conclusions

comparing with our previous abstract showed local improved outcome of IFD due to proper timing of starting empirical antifungal, C T fungal diagnostic approach. Surgical debridement of cutaneous lesion, sinuses and lung lesion once indicated, choosing appropriate antifungal agent according to each patient clinical and functional status

EP-429

Others

PATIENT-REPORTED MEASUREMENTS OF ORAL MUCOSITIS IN CHILDREN WITH CANCER

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Objectives

Aim of this study was to evaluate the administration of the Patient-Reported Oral Mucositis Symptom (PROMS) scale among pediatric cancer patients, to compare PROMS-derived data with dental surgeon assessed oral health measures and to establish the adverse impact of OM on quality of life (QoL).

Methods

Seventy-five children with cancer (19 boys, 46 girls; age 12.0±4.3 yrs) were investigated between January, 2011 and December, 2012. Hungarian version of PROMS self-administered scale was used. Participants filled in the questionnaire according to the severity of symptoms ("items") on a visual analogue scale on admission and weekly (Days 7, 14, 21, 28 and 35). The sum of item scores gave the total PROMS score. OM was diagnosed by a dental surgeon using the WHO score. Cariological and periodontal conditions, WBC, anticancer drugs and antiinfective supportive therapy were registered.

Results

OM was observed in 53/75 (71%) patients. Total PROMS score increased gradually by Day 21 followed by a transient decrease on Day 28 and a 2nd peak on Day 35. In contrast, patients with ALL, the largest homogenous subgroup of patients (No. 44) exhibited a monotonously decreasing tendency of the total PROMS score from Day 21, i.e. by concluding induction therapy. We found significant associations ($p < 0.05$) between PROMS item scores and WHO OM score and its components. Significant correlations ($p < 0.05$) were observed between item and total PROMS scores and WBC. There were no significant associations between cariological and periodontal indices and the total PROMS score and item scores.

Conclusions

PROMS questionnaire is an easy-to-use and suitable measure of OM in pediatric patients. Characterizing the incidence and severity of OM by PROMS may allow to develop a comprehensive program to reduce this highly distressing side-effect of cancer treatment in children.

The study was **supported** by the TÁMOP 4.2.1./B-09/1/KONV-2010-0007, TÁMOP-4.2.2.A-11/1/KONV-2012-0025, OTKA K108885 projects.

EP-430

Others

RELATIONSHIP OF CYP3A5 EXPRESSION AND VINCRISTINE NEUROTOXICITY IN TURKISH CHILDREN WITH MALIGNANCY

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Objectives

Vincristine is a widely used chemotherapeutic agent in the treatment of childhood malignancies. Neuropathy which can be a combined onset of peripheral, progressive, motor, sensorial and autonomic components is not only the most common adverse effect of vincristine treatment, but also is the leading cause of dose modifications. However vincristine dose that will cause neuropathy in a particular patient can not be decisively anticipated. CYP3A4 and CYP3A5 enzymes of cytochrome p450 enzyme system are responsible in vincristine metabolism. CYP3A5*3, which is the most common allele encodes for an abnormally spliced mRNA with a premature stop codon, resulting in decreased expression of CYP3A5. CYP3A5*1, which is the most common allele in African-American people, can provide high expression rates of CYP3A5 and fast metabolism of vincristine which leads to lesser neurotoxicity. In this study, distribution of CYP3A5 alleles among Turkish children with malignancies, relation between CYP3A5 genotype and neurotoxicity rates, and severity, duration of neuropathy and total vincristine doses were investigated.

Methods

Files of 115 patients (age 1 - 17 years) who were treated with vincristine consisting chemotherapy protocols were retrospectively reviewed for neurotoxicity and CYP3A5 genotypes were analyzed. Neurotoxicity was graded according to National Cancer Institute Common Terminology Criteria for Adverse Events Scale.

Results

Neurotoxicity occurred in 20.8% of patients. Combined sensorial and motor neuropathy was the most common form. Although it was found to occur more frequently after the 4th dose of vincristine and rates were higher in the low dose vincristine group suggesting other contributing factors. While neurotoxicity rate in the CYP3A5*1/*3 genotype was 17.6%, it was 21.6% in the CYP3A5*3/*3 genotype and the difference was not statistically significant ($p < 0.05$).

Conclusions

In conclusion, this study suggested that vincristine related neurotoxicity is dose-independent and genotype is not the only causative factor in the occurrence of neurotoxicity in these patients.

EP-431

Others

OUT-OF-POCKET COSTS CAN LEAD TO FINANCIAL CRISIS IN FAMILIES OF CHILDREN WITH CANCER THAT COULD BE AVOIDED WITH THE PROVISION OF BASIC FINANCIAL SUPPORT

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Families of children with cancer experience numerous out-of-pocket expenses that create additional emotional stress and financial challenges that can seem insurmountable. The provision of basic financial assistance lessens the financial burden on families and helps reduce the number of those who face financial crisis and other longer-term economic implications.

Input, feedback and ongoing dialogue with families and healthcare providers consistently identified areas of need (parking fees, gas costs, meal expenses incurred for parents at hospital, childcare), which were addressed by Candlelighters through the provision of programs that have genuine impact in a family's financial situation. An on-line survey was conducted in February 2014 to evaluate the significance of these programs in the childhood cancer journey.

82% of those surveyed reported having experienced financial hardship as a result of having a child with cancer. Of the 95% of responding families who have benefitted from Candlelighters' initiatives, 74% of them reported that their family would have experienced a financial crisis without Candlelighters assistance. (Financial crisis* defined as the need to request additional financial assistance beyond what is provided to all families by Candlelighters). 91% of the survey respondents reported that they believe every family who has a child diagnosed with cancer, regardless of race, religion, culture or socioeconomic status should be eligible for this basic funding, with the knowledge that additional funding could be accessed based on additional need. 61% feel that there is enough financial assistance available for families, in large part due to the services provided by Candlelighters. There is no avoiding the inevitable out-of-pocket costs that result when a child is diagnosed with cancer. Providing much needed financial support for "everyday" expenses results in a more stable financial situation and has a positive effect in a family's overall financial position when coping with childhood cancer.

Document not received

EP-432

Others

RESULTS OF TRACKING WILMS TUMOR PATIENTS IN KENYA

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Objectives

Review of the Kenyan Wilms Tumor (WT) Registry and tracing calls revealed an estimated 2 year overall survival (OS) of 36 percent for patients diagnosed between 2008 and 2011 due to in-therapy mortality and treatment abandonment. We report preliminary results of tracking efforts for WT patients at Moi Teaching and Referral Hospital.

Methods

In January 2013, a trained research nurse called parents who had abandoned treatment or off therapy follow up for their children between 2008 and 2012 to determine vital status and encourage return to therapy. In 2013, she tracked all patients previously and newly diagnosed after each missed visit.

Results

Patients diagnosed with WT between 2008 and 2012 (n=56) had a 28.6 percent in-therapy mortality rate and a 17.9 percent mortality rate from treatment abandonment. The abandonment rate was 39.3 percent, of which 27.3 percent were alive (one patient returned to therapy), 27.3 percent were not contactable and 45.5 percent died. Nine percent of patients were lost to follow up after termination of treatment, of which one patient returned after the tracing call. OS was estimated at 41 percent. While patients diagnosed in 2013 (n=26) are still in therapy, there is preliminarily a 27 percent in-therapy mortality rate. One patient abandoned treatment and returned after the tracing call.

Conclusions

Results are preliminary due to documentation lag time and time short of 2 years. In-therapy mortality remains high. Tracking after missed visits results in potentially less treatment abandonment, but false beliefs and financial constraints still exist. Standardized treatment protocols, supportive care, education and financial support will be crucial to improve survival from WT in Kenya.

EP-433

Others

SHUT IN, SHUT OUT, SHUT UP: CAREGIVERS OF LONG-TERM PAEDIATRIC BRAIN TUMOR SURVIVORS

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Objectives

What can a weblog for caregivers of paediatric brain tumor (PBT) survivors contribute to the current state of knowledge about their caregiving work? How might an online blog address the silencing isolation these caregivers experience? What can be learned about their needs and lifestyles? In what ways does their informal, unpaid work constrain their quality of life? How has the health of caregivers been impacted given decades of unpaid work for their child/youth/adult?

Methods

Material: More and more PBT survivors are living into adulthood, but most are unable to gain self-sustaining employment or maintain friendships, and given their health and social vulnerabilities, they require the daily supports provided by parents, particularly mothers. For the past 31 years, I have been the caregiver for my son, who had a malignant, inoperable PNET brain tumor diagnosed at age 6. Radiotherapy calcified his invasive tumor, but long-term effects continue to disable him progressively, with declines typical of the demographic: hearing and sight losses, impaired speech, endocrine issues, mobility factors, cognitive speed, and strokes. I am both a researcher *and* a research subject in a new weblog project to create knowledge and interconnect 4,000 Canadian caregivers for PBT survivors.

Methods: Using anonymous weblog data, I hope to assess the current state of caregiving knowledge for PBT survivors, including unmet needs. Qualitative narrative inquiry and post-modern standpoint theories will help assess issues of social isolation, invisibility and silencing, and economic loss. Research project and ethical approvals are now in process.

Results

Your venue will help inform caregivers about this new Canadian project, by a PBT survivor's caregiver and doctoral student.

Conclusions

It is hoped this research will identify personal, social and economic barriers faced by caregivers of PBT survivors. It is also hoped that themes for future advocacy work will also be identified.

EP-434

Others

CHEMOTHERAPY MEDICATION ERRORS ON THE PEDIATRIC ONCOLOGY CLINIC AT THE NATIONAL CANCER INSTITUTE OF COLOMBIA

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Objectives

To establish and classified the chemotherapy medical error at our Outpatient Clinic There is worldwide a potential increase in the number of errors related to prescriptions due to the increase of new drugs on the market and the clinical practice. As well know the medication errors in oncology services is about 9% and many of them causing all kind of lesions over the patients like a disability lesions, even the death. In many of cases this errors go in unobserved and start from the prescription, preparation until administration over the patient.

Methods

It was a cross sectional study and we established a sample size for analyzing the chemotherapy prescriptions in the oncology pediatrics service care. There was a review of chemotherapy orders at the National Cancer Institute-Colombia Pediatric Oncology Outpatient Clinic during the period six months between July 2012 to December 2012. Errors types were classified using the **National Coordinating Council for Medical Error Reporting and Prevention Index for Categorizing Medication errors**

Results

In a six months period there were about 1100 chemotherapy prescriptions for oncology, hematology and pediatric oncology. The pediatric oncology sample size was 85 and we found 19 medication errors (22.4%). The most frequent errors were mainly related with the dosage and with the omission of some medications. There weren't any death or disability secondary by medication error

Conclusions

In the analysis period none of these errors led disabilities or deaths over any patient, therefore doesn't know in the future. We don't know how many errors were potentials and how many errors not were related with the prescription and how many were corrected at the administration time. With the introduction of new medications to the clinical practice it's necessary to develop a program to avoid errors related with the prescription, dosage and identification of the patients

EP-435

Others

ADOLESCENTS AND YOUNG ADULTS (AYA) PROGRAM IN BARRETOS, BRAZIL

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Objectives

Adolescent and Young adult oncology is an ongoing science. As NCI recognizes, this population ranges from 15 to 39 years old, and has its own characteristics and demands. This age group has been underrepresented in clinical trials and it could be the reason for the lack of improvement in survival rates over the last 30 years. Different organization models drive pediatric oncology and medical oncology. Adult cancers are resistant to chemotherapies, exactly the opposite is seen in pediatric oncology. They should receive a different model of care. Current opinion says that training pediatric and medical oncologists in all the skills needed to manage a multidisciplinary AYA treatment strategy is the best way.

Methods

Several attempts at AYA comprehensive programs are in development all over the world. One of them is taking place in Barretos' Cancer Hospital, in Brazil. In order to improve the communication and cooperation between pediatric oncologists and medical oncologists, we designed an integrated model of care. A pediatric oncologist composes the adult sarcoma/melanoma team and a patient-focused approach has taken place. Patients under the forties enter in the pediatric clinics, where a team of pediatric and clinical oncologists is trained to recognize their specific demands.

Results

The AYA program in Barretos, Brazil, has initiated recently with a very good acceptance.

Conclusions

Pediatric and adult oncology groups come from different backgrounds and have different priorities even when they deal with similar diseases, different practices tend to be homogenized in this model of care and it improves the institutional treatment. In 2011 and 2012, a total of 2,148 patients between 15 and 39 years old were treated in our institution. It represents almost 10% of the total patient population. The numbers are expressive and, in 2013, a differentiated model of care came to answer the specific questions and demands of the AYA patients.

EP-436

Others

PATTERN OF BONE MARROW METASTASIS IN PAEDIATRIC SOLID TUMOURS-A RETROSPECTIVE ANALYSIS AT A REGIONAL CANCER CENTRE IN KASHMIR, INDIA

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Objectives

Though bone marrow involvement is a common occurrence in leukemias and lymphomas, solid tumours may also spread to bone marrow especially the ones which metastasize via the blood stream. Aim of the present study was to review the clinical characteristics and the pattern of bone marrow infiltration in various solid tumours in paediatric population.

Methods

This retrospective study was carried out at the Department of Medical and Paediatric Oncology, Regional Cancer Centre, Sher-i-Kashmir Institute Of Medical Sciences, Srinagar, Jammu and Kashmir, India. The clinical, hematological and pathological data of the patients was reviewed over a two years period from January 2012 to December 2013.

Results

Out of 6232 cancer patients registered during the study period, 860 (13.79%) were hematological and lymphoreticular malignancies while as 5372 (86.21%) were solid tumors. The frequency of adult and paediatric solid tumors were 94.64% (5084) and 5.36% (288) respectively. In the paediatric solid tumors, the bone marrow infiltration was observed in 41 cases (14.23%). The commonest among was Ewings sarcoma/PNET 5.90% (17 cases) followed by Neuroblastoma 3.81% (11 cases), Rhabdomyosarcomas 2.08% (6 cases), Wilms tumor 1.73% (5 case), and Retinoblastoma 0.34% (1 case). There was a unique case of Hepatoblastoma in a 2 years male child with bone marrow secondaries (0.34%). Bone marrow biopsy was complementary to aspiration in all cases and helped in diagnosis making in 5 patients (1.73%). The common symptoms include fatigue, low appetite, fever and bleeding. Anaemia was commonest hematological finding (72.5%), followed by thrombocytopenia (63.9%) and neutropenia (12.8%).

Conclusions

The metastasis of bone marrow by the solid tumors is a sign of advanced stage of disease and poor prognosis. Bone marrow aspiration is an easy and cost effective method of reporting of metastasis in a very short span of time. Moreover a clue to the primary site can also be suggested if it is unknown.

EP-437

Others

PEDIATRICS ONCOLOGY NETWORK DATABASE (POND): A USEFUL ADJUNCT IN SETTING UP OF A NEW PEDIATRICS HEMATO-ONCOLOGY UNIT AND CANCER REGISTRY IN THE DEVELOPING WORLD

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Objectives

A nationwide registry is lacking for paediatric cancer patients in India. Pediatric Oncology Network Database (POND) is a useful adjunct to create or supplement cancer registry. It is a free online database provided by St.Judes Children's Hospital,USA to pediatric oncologists in the developing countries. Here we describe the usefulness of POND in registering data of all new patients in first one year after setting up of a new pediatric hematology-oncology (PHO) and bone marrow transplant (BMT) unit.

Methods

All new patients registered in PHO unit in the first one year were included. Their data regarding diagnosis, treatment and outcome was prospectively entered by an experienced data base manager in POND.

Results

We had 293 new patients registered in our unit with blood and cancer disorders and their data was entered in POND. Malignant hemato-oncology- 75 patients (Acute lymphoblastic leukemia- 48, Acute myeloid leukemia-7, Chronic myeloid leukemia-5, Hodgkin lymphoma-7, Non-hodgkin lymphoma-8). Solid tumor- 28 patients (Brain tumor-7, Wilms tumor- 8, Neuroblastoma-5, Adrenocortical carcinoma-1, Rhabdoid tumor-1, Teratoma-2, Ewing's sarcoma-3, Retinoblastoma-1. Benign hematology –190 patients (Immune thrombocytopenic purpura-24, Aplastic anemia-15, Thalassemia-40, Sickle cell anemia-10, LCH-7, Hemolytic anemia-8, Megaloblastic anemia-2, Pure red cell aplasia-4, Hemophilia-4, Hemophagocytic lymphohistiocytosis-2, Primary immunodeficiency- 12, Congenital dyserythropoietic anemia-1, Sideroblastic anemia-1, Congenital neutropenia-1, Protein C deficiency-1, others diseases- 58. Hematopoietic stem cell transplant (HSCT) was performed in 17 patients. Autologous were 5 (NHL-1, Medulloblastoma-3, AML-1) and 12 were allogeneic (Aplastic anemia-2, Thalassemia major-4, Sickle cell anemia-3, Primary Immunodeficiency-2, Myelodysplastic Syndrome-1).

Conclusions

POND is a useful adjunct in maintaining hematology-oncology patients' database. We recommend this in each PHO unit in India to create a registry.

EP-438

Others

BEABA: FROM PATIENT TO TRANSFORMING AGENT - INFORMATION AS MEDICATION TO DESMYSTIFY CANCER

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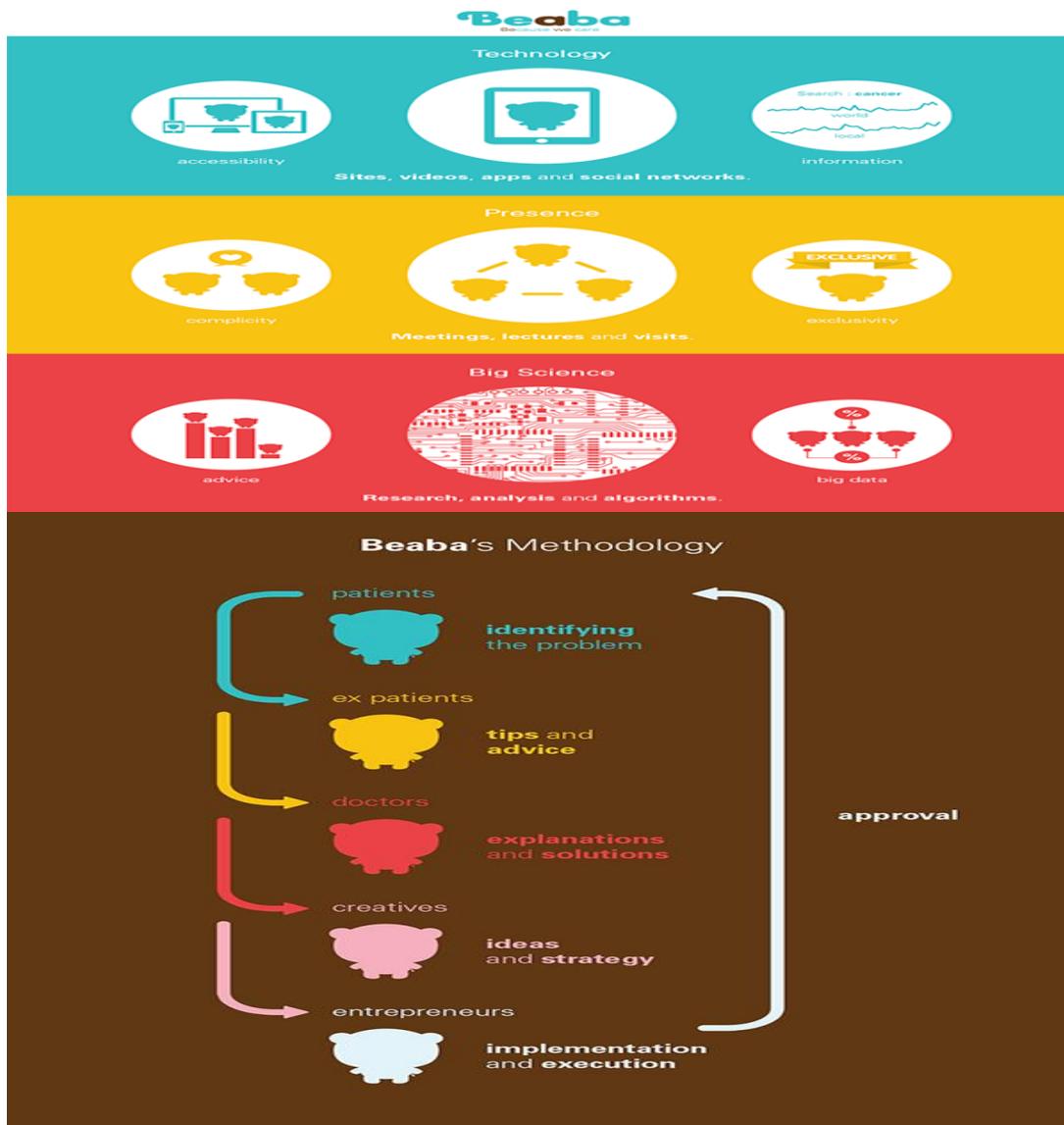
Objectives

The oncologic world is a particular universe. Each child and their family who debuts in this environment are impacted by new experiences, complex terms and meanings that are frightening. Our mission is to demystify this environment, presenting information about cancer and its treatments in a way that is clear, objective and optimistic.

Methods

Beaba is a nonprofit organization composed of young patients, ex-patients, doctors, creatives and entrepreneurs. Our difference is in the design methodology where the young patients are the ones responsible for creating the briefings. They pinpoint everything that bothers, frightens or is unknown to them. After the data is collected, they then proceed to discussions with former patients, who also give their suggestions and opinions. Then come the doctors, who are responsible for the knowledge that assesses and validates everything. With all the information at hand, the creative team figures out the best strategy to meet the little patients' needs and, after their approval, the entrepreneurs execute the idea. The material that is produced ranges from a wide variety of products, such as 'The Etiquette Manual' for society learn how to treat cancer patients and 'Personal Workshops', where small patients and ex-patients will teach the newcomers.





Results

The result was an increase in self-esteem of these young patients who, in addition to feeling the importance of being responsible for the entity's activities, realize that they actually became role models for other children. The little patient turned from a passive individual to an active one, coordinating the learning process of innumerable children and thus, promoting the exponential growth of Beaba.

Conclusions

Information still is the best way to save lives. Whether it is used for early diagnosis, to relieve symptoms or ease fears, it relaxes and invigorates the little cancer patients.

EP-439

Others

SYMPTOMATIC THROMBOSIS IN LEBANESE CHILDREN WITH CANCER TREATED AT A TERTIARY CARE CENTER

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Objectives

To study the prevalence and potential risk factors for thromboembolism (TE) in children with cancer.

Methods

A retrospective chart review of children (<21 years) between 2002 and 2013 who developed symptomatic TE.

Results

914 patients were treated at CCCL over a period of 11 years; all had central venous lines (CVL). 49(5.4%) patients developed symptomatic TE, mean age was 10.3 years (Range, 2 months-20 years). 30 were males. 19(39%) patients had evidence of CVL dysfunction. 15 patients (30.6%) either died or are alive with recurrent end-stage disease, while 34 remain alive and disease free (ADF). Of 213 ALL patients, 18(8.4%) developed TE. All CNS TE occurred while receiving steroids and L-asparaginase concomitantly. 17 remain alive. All received anticoagulation. Nine patients with sarcoma had TE. All had tumors >5cm. Six had metastatic lung disease. Seven developed disease recurrence; 2 are ADF. Eleven lymphoma patients (8.3%) developed TE; 7 had bulky mediastinal disease. Three died, 8 are ADF. 4(2.5%) patients with brain tumors developed symptomatic TE; 3 died. 3(6.4%) AML patients had TE; 2 are ADF. The 2 patients with neuroblastoma were infants <6 months old; both are ADF. Children with solid tumors and thrombosis had worse outcome than those without thrombosis. 31 patients were tested for inherited thrombophilia: 3(9.7%) had heterozygous Factor II mutation and 8(25.8%) had heterozygous Factor V Leiden.

Conclusions

Prevalence of symptomatic TE was 8.4%, 8.3% and 5.1% for patients with ALL, lymphomas and sarcomas, respectively. Patients with TE were older compared to children with the same cancer diagnosis. More than 30% had CVL dysfunction. One third of patients with TE died or reached end stage recurrent disease. Factor V Leiden was prevalent. Duration of anticoagulation was variable (mean, 10 months/patient). Brain tumor patients had low incidence of thrombosis. Solid tumor patients with thrombosis had worse outcome.

EP-440

Others

CORRELATION OF PET-CT AND IMAGE GUIDED BIOPSY RESULTS IN CHILDREN

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Objectives

To evaluate our early experience in the correlation of PET-CT with image guided biopsy (IGBx) results in a pediatric population, to better understand the role PET-CT may play.

Methods

This is a single centre retrospective case series. Patients who underwent IGBx and PET CT scan between January 2007 and December 2012 were analyzed. Inclusion criteria were those whose IGBx occurred within 6 weeks of their PET-CT scan (prior to or post biopsy). Clinical, demographic, imaging and pathology reports were collected using RedCap and correlated. Descriptive statistics were employed.

Results

45 patients (23 male and 22 female) were included, aged 4-17 years (median 10.5 years). Twenty-patients had known malignancy. Coaxial technique was used in 36/47, with ultrasound guidance in 40, CT in 6, and fluoroscopy in 1. Biopsies involved soft tissues (43) and bone (4). There were 3 minor and 1 major complication (bleed requiring transfusion). 39/47 PET scans were positive and 8/47 PET scans were negative. Of the 39 positive scans, biopsy in 19 showed a malignant diagnosis, 13 a benign diagnosis (infection/inflammation), 1 normal tissue and 6 were inadequate. Of the 8 negative PET scans a benign diagnosis was found in 5 and malignant in 3 (interval chemotherapy had been given). Concordant results between biopsy and PET was obtained in 32/47 and discordant results were obtained in 15/47. Sensitivity of PET was 80% and PPV 82%.

Conclusions

PET-CT can play a valuable role in directing image guided biopsies in children.

EP-441

Others

CHEMOTHERAPY ADMINISTRATION IN PEDIATRIC ONCOLOGY : DILUTION IS NOT THE SOLUTION

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Objectives

Due to the young age of some of our pediatric patients (4,370 chemotherapies in 2013), administration of high volumes during a short time could be responsible for adverse effects (mainly cardiovascular). Dilution volume associated with chemotherapy rinsing volume was designated as problematic by pediatric oncologists. So our aim was to reduce these volumes to optimize medicinal treatments.

Methods

By consulting protocols used in our hospital, we have identified different doses prescribed for each anticancer drug. In cooperation with pediatric oncologists, we took care about factors affecting terms of dilution (weight, dose, route of administration: peripheral or central line infusion, risk of extravasations, physicochemical stability of molecules linked to final concentrations and infusion rates). We have based our research on our anticancer drugs thesaurus (n=24).

Results

An adaptation of anticancer drugs dilution volumes was done for the 24 pediatric anticancer drugs prescribed. In most protocols drug doses were determined according to patient's weight, or according to body surface area. We decided to define three subgroups of patients (less than 10kg, 10 to 30 kg and over 30kg). A summary table was made and approved by pediatric oncologists, summing up dilution volumes for each subgroup of patients. Most anticancer drugs are diluted in mini-bags (78%). In 86% of cases, volume is less or equal to 100 mL. For patients less than 10kg, infused volumes are less than 50mL in 66% of cases.

Conclusions

This multidisciplinary approach has succeeded to reduce volumes infused to children and adapt our practices to pediatric specificities. Through this improvement, we have optimized care for our patients. Due to the overfilling of industrial mini-bags, the use of empty bags should be promoted in most cases.

EP-442

Others

CONDOM-USE PERCEPTION BY ELDERLY PEOPLE: A BIG CHALLENGE TO HIV/AIDS MITIGATION IN HIGH RISK URBAN SLUMS IN AFRICA

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Objectives

As HIV/AIDS continues to pose a public health challenge in Africa, the pandemic cut-across borders. It affects every age group including old persons, despite engagement in risky sexual activities which increases HIV/AIDS infection. However, limited attention is paid to this sub-group in mitigating the pandemic. This study therefore examined condom-use and perceived HIV/AIDS infection among old people in Africa.

Methods

The study was cross-sectional in design. A multi-stage sampling procedure was used to select 400-geriatrics. Pre-tested questionnaire developed, using information obtained from 10 Focus Group Discussion (FGD), was used to collect information. FGD data were analyzed thematically, while questionnaire data were analyzed using descriptive and statistically.

Results

Twenty-five percent of the participants had extra-marital sex since they attained elderly age. However, among this subgroup that had extra-marital sex, few (6.8%) used a condom. More males (5.3%) than females (1.5%) used condom during the last extramarital sex. Low level of condom-use was attributed to condom not worthwhile (34.5%) and opinion (50.0%) condom not made for the elderly. Moreover, FGD participants viewed sex could not lead to pregnancy and majority (60.3%) posited patronizing traditional healers and few (10.3%) use of herbs/concussion could prevent HIV/AIDS. Similarly, non-condom use was due to confidence in traditional herbs, perceived to protect against STIs including HIV/AIDS.

Conclusions

Engagement in risky activities among elderly is a growing HIV/AIDS challenge. Condom-use is misconstrued probably due to knowledge gap. Without urgent measures to enable them protect themselves, development efforts will be in jeopardy. Investing in geriatric SRH is cost-effective intervention in mitigating HIV/AIDS pandemic.

EP-443

Others

MALIGNANCIES IN PRIMARY IMMUNODEFICIENCIES: SINGLE CENTER EXPERIENCE

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Objectives

The overall risk for developing malignancy in children with primary immunodeficiency (PID) is estimated at 4-25%. Non-Hodgkin's lymphomas predominate, accounting for 60% of cases. The PIDs known to be associated with increased incidence of malignancy are: common variable immunodeficiency (CVID), IgA deficiency, and DNA repair disorders. During recent years other types have also been included, such as severe combined immunodeficiency (SCID) and Wiskott Aldrich syndrome (WAS). Here, we aimed to study the histopathological characteristics of malignancies in PIDs and to report results from a single reference center at middle Anatolia in Turkey.

Methods

We presented eight patients (1 boy, 7 girls) with PIDs which were evaluated at the Pediatric Hematology-Oncology Department of Medical Faculty, Erciyes University between 1996 and 2013. The age at diagnosis of PIDs, age at diagnosis of malignancies, histopathological characteristics of malignancies, and clinical courses of patients were analyzed.

Results

In a 17-year study period, there were 8 patients with malignancies associated with PIDs.

The patients ranged from 5.5-20 years of age with the mean age of 11,75 years (SD \pm 5,55 years) at the diagnosis of malignancies. Histopathologically, five patients were with diffuse large B cell lymphomas, 3 of those with idiopathic CD4 deficiency, and 2 of those with DNA repair immunodeficiencies (Ataxia-telangiectasia, Nijmegen Breakage Syndrome). The remaining 3 patients had Hodgkin's Lymphoma with ataxia-telangiectasia, Osteosarcoma with Bloom's syndrome, and Gastric Signet Ring Carcinoma with ataxia-telangiectasia, respectively.

Conclusions

Here, we want to underline again that PIDs are genetic disorders which predispose patients to malignancies as well as to severe infections and autoimmunity.

EP-444

Others

MEETING THE NEEDS OF AT-HOME SIBLINGS OF PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) PATIENTS

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Objectives

At-home siblings of pediatric cancer HSCT patients report lack of information, lack of inclusion, family separation, and additional responsibilities during the family's transplant experience (1). Although resources currently exist to help these siblings, these children may benefit from personal attention and information. The purpose of this study is to identify strategies for helping at-home siblings. We propose a novel cyber-intervention implemented by Certified Child Life Specialists.

Methods

We conducted a secondary semantic analysis of qualitative interviews completed with family members of pediatric HSCT patients, coding the data for strategies the family used during the cancer experience. We also interviewed HSCT healthcare team members regarding current resources for at-home siblings and suggested additional interventions.

Results

42 family interviews were coded and 15 healthcare workers were interviewed, including Certified Child Life Specialists(CCLS), inpatient nurses, midlevel providers, psychologist, social worker, and physician. The most frequently used strategies were meetings with a member of the healthcare team, sharing all information with the child, using phone calls or Skype to communicate more often, having parents split time between hospital and home, attending sibling support groups or workshops, giving the sibling a special role, having the sibling visit the hospital, and having a special day or event for the sibling. Twelve(80%) healthcare workers expressed concern about at-home sibling distress not addressed by current support which requires travel, 11 about lack of sibling inclusion, and 5 about lack of information. All 15 nominated CCLS to intervene with these siblings via Skype to address the needs felt by at-home siblings.

Conclusions

Existing resources are inadequate to meet the needs of at-home siblings of children undergoing HSCT. These children may benefit from personal information and support delivered through a variety of strategies by both family members and healthcare workers. A novel CCLS virtual intervention may help alleviate siblings'unmet needs.

EP-445

Others

CHILDREN WITH CANCER AND INTELLECTUAL DISABILITIES: DID WE SPARE TREATMENT? A MONOINSTITUTIONAL EXPERIENCE AT FONDAZIONE IRCCS ISTITUTO NAZIONALE TUMORI, MILANO

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Objectives

To report our experience in treating children with cancer and intellectual disability.

Methods

From 1999 to 2013, we treated 41 children with intellectual disability and cancer. Patients affected by neurofibromatosis were not included in the series.

Results

We treated 41 children, 18/41 female, median age 5.8 years with different tumors. The observed disabilities are listed in table 1.

Early diagnosis was made in 5 children with Wilms Tumor (WT) and in 4 with hepatoblastoma thanks to scheduled screenings.

In 5 patients with severe disabilities a 'treatment sparing' was adopted in order to minimize toxicity: a 4-year-old child with post partum asphyxia and medulloblastoma (MBL) didn't receive radiotherapy (RT) but high dose thiotepa. In 1 patient with mitochondrial encephalopathy and testicular germ cell tumor, bleomycin and lung metastasectomy were omitted to avoid lung toxicity. In 1 pt with Down+West syndrome and WT, vincristine was omitted due to potential neurotoxicity. In 1 pt with autism spectrum disorder and refractory HD, subtotal-nodal RT and standard, non high-dose chemotherapy (CT) was delivered. One child with structural chromosomal aberrations and pPNET received personalized CT excluding vincristine and ifosfamide because of potential neurotoxicity. In 4 patients with WT hemi-nephrectomy was performed to preserve kidney function. 3/17 pts (5, 6 and 8 years old) who received RT required sedation due to insufficient compliance.

Two patients with relapsed MBL received palliative oral CT and 1 relapsed PNET only supportive care.

We found no statistically significant correlation between relapse or death and 'therapeutic sparing' (?² test).

Five years OS and EFS were 79% and 66% respectively (median follow-up 62 months). Two patients developed a second malignancy, both died.

Table 1

Autism spectrum disorders	6
WAGR	3
Down	2 (1 Danys-Drash + West)
Costello	2
Beckwith-Wiedemann	2
Danys-Drash	2
Kabuki	2
mitochondrial encephalopathy	2
Other chromosomal anomalies	2
CHARGE	1
Klinefelter	1
Rubistein-Taybi	1
post partum asphyxia	1
tuberous sclerosis	1
corpus callosum agenesis	1
Undefined	12

Conclusions

We observed therapeutic sparing only in severe disabilities, OS is in line with survival of children without intellectual disability.

EP-446

Others

**USE OF RASBURICASE IN CHILDREN WITH HEMATOLOGICAL MALIGNANCIES:
EXPERIENCE FROM A PEDIATRIC HEMATO ONCOLOGY CENTRE IN SOUTHERN
INDIA**

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Objectives

Rasburicase rapidly reduces plasma uric acid (PUA) and thus markedly decreases the risk of renal failure in tumor lysis syndrome (TLS). However, there is very limited data on its use in India because of limited use due to high-cost. This study analyses use of rasburicase in a resource limited setting.

Methods

This retrospective study looks at the efficacy and safety of rasburicase in 41 children with hematologic malignancies treated over a period of 42 months. Male:Female was 32:9. Thirty-four had laboratory TLS and 7 were at risk for TLS. Diagnoses: T-cell ALL, 19; Pre-B ALL, 18; T-NHL, 2; B- NHL in 2 cases. Rasburicase was given at doses of 0.08 - 0.24 mg / kg. No one was screened for G6PD deficiency.

Results

Initial PUA: median, 8.5 mg/dl (range, 4.3 to 45.5). Six had creatinine levels of > 2 mg/dl; and 10 had peak phosphate levels of >10 mg/dl. Only one patient required dialysis. Dose of rasburicase used: median, 0.12mg/kg (range, 0.08 – 0.24). Median reduction in PUA at 6 hours: 80% (range 40% to 98%). Twenty-seven needed only one dose; 12 needed 2 or 3 doses; and two needed 5 doses each. None died of TLS. None developed anaphylaxis or significant hemolysis.

Conclusions

Rasburicase is safe and effective even in lower doses ranging from 0.1 to 0.2 mg/kg, and it markedly reduces the risk of renal failure from TLS in Indian children with hematological malignancies.

EP-447

Others

ETOPOSIDE INFUSION-RELATED REACTIONS IN PEDIATRIC ONCOLOGY PATIENTS

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Objectives

Etoposide is a common chemotherapy agent used to treat childhood cancer. Over the past year, the rate of etoposide associated reactions was perceived to be higher than expected at our institution, prompting a review of the nature of these reactions.

Methods

A retrospective chart review was conducted at a single institution. Patients aged 0-18 years who received IV etoposide from October 2012 to June 2013 were eligible for this study.

Results

114 patients received etoposide during the study period. Ninety-seven patients met inclusion criteria. Thirty-nine patients (40%) had a reaction to etoposide. The average rate of infusion of etoposide did not differ between patients who had experienced a reaction and those who did not. Reactions occurred shortly after the start of etoposide infusions, with a mean time to adverse event of 13.3 minutes (range 2-95 minutes). Most reactions occurred during the patient's second dose of etoposide (range 1 to 6). These reactions were associated with a variety of symptoms including mucocutaneous (n=37; 38%), respiratory (n=25; 26%), gastrointestinal (n=11; 11%), and hypotension (n=6; 6%). Of the patients who displayed reactions, 20 (78%) tolerated subsequent etoposide doses given with premedication (antihistamine or/and steroid) and/or infused at a slower rate. The remaining 19 patients completed therapy with etoposide-phosphate. Two of these patients experienced a subsequent reaction; the first patient developed lip swelling and the second experienced persistent vomiting. Both patients were able to tolerate further doses with premedication.

Conclusions

An infusion-related reaction rate to etoposide of 40% was observed. Although the exact mechanism of these events is unclear, the natural history is consistent with a type I hypersensitivity reaction. Patients who developed reactions can be safely rechallenged with etoposide if given premedication. Further investigations into possible etiologies of these reactions, including examination of infusion devices, are ongoing.

EP-448

Others

TO TELL OR NOT TO TELL CHILDREN ABOUT THEIR CANCER?

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Objectives

This study was designed to provide research-based evidence on how to inform children of their cancer diagnosis so as to minimize the negative psychosocial effects of the cancer experience on survivors.

Methods

Childhood cancer survivors (now adult) (N=99). completed a structured questionnaire to evaluate a) the information given them as children about their diagnosis, and (b) their current mental pain, mental pain tolerance, quality of life and perception of their childhood cancer experience -- apparently the first application of this methodology.

(Table 1: age at diagnosis, age today and time since the end of treatment (in years) (N=91)

	Mean	Std Dev	Minimum	Maximum
Age at diagnosis	11.47	5.134	1	23
Age today	25.5	5.8808	18	43
Time since the end of treatment	12.84	7.153	1	38

Results

The sample's overall mean score for their perception of their cancer as children was moderately positive 3.31 (out of 5; SD=0.54). Analysis of gender and age separately generated a statistically significant interaction between age and past mental pain (F(1,86)=8.26, Eta²=.09). The younger group (up to 12 years at diagnosis) who received 'not good information' reported higher levels of past mental pain than those who got 'good information'. Surprisingly, members of the older group who got 'good information' reported higher past mental pain than those who got 'not good information'.

Table 2: study groups by information: gender and diagnosis

	values	good 'information' % N	not good 'information' % N	² ?
gender	male	54.8 23	55.1 27	.00
	female	45.2 19	44.9 22	
prognosis	leukemia	42.9 18	46.9 23	.43
	lymphoma	26.2 11	20.4 10	
	other	31.0 13	32.7 16	

Conclusions

'Good information' is critical to survivors' quality of life. We have to aspire to make survivors psychosocially as well as physically healthy. Current practice is not based on research-based evidence.

EP-449

Others

USING A CHANGE IN METHODOLOGY TO IMPROVE PATIENT FLOW AND BED USAGE: EFFECT OF ALTERING THE METHOTREXATE ASSAY SERVICE

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Objectives

Delayed discharge outside working hours frustrates children and families, means less safe and effective use of beds and can delay treatment.

We identified delay in receiving methotrexate assays from another hospital as contributing to this problem.

Methods

Plan: An in house assay for serum methotrexate levels was set up. Flexibility was agreed to produce the results in a timely manner without overburdening the lab service.

Do: Regular meetings of pharmacists, doctors, nurses and laboratory scientists addressed any issues that developed. Several steps from the old system were eliminated (batching of specimens, transfer by courier, processing in a different hospital, telephoning of results after office hours)

Results

Check: Complaints about missing results disappeared.

Patients receiving High Dose Methotrexate (HDM) who are discharged when safe levels are reached include those with acute lymphoblastic leukaemia (ALL) and patients with osteosarcoma. We compared length of stay (LOS) before and after the change in assay for 15 and 14 ALL and 14 and 15 osteosarcoma admissions. A reduction in length of stay after HDM for those patients who are discharged on the 3rd day for ALL ($p = 0.02$) and 4th day for osteosarcoma ($p = 0.05$) was noted. No difference was found in patients with prolonged excretion of methotrexate in either group, as would be expected. Importantly more than half patients were now discharged during office hours after the introduction of the local assay.

Conclusions

Act:

The expense of setting up a new assay service has been offset by improvements in discharge. We plan to undertake value stream mapping to identify further aspects of admission which prolong stays occur and use PDCA cycles do help eliminate delays. We are also going to use patient level costing to measure the economic benefits realised by this and future changes.

EP-450

Others

THE EVOLUTION OF HUMANITY AND VENOUS ACCESS: A HISTORICAL ANALYSIS

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Objectives

Throughout the mankind time it has steadily continued its evolution that led to the constant changes in all spheres of science.

Methods

1. 2 million years ago - the emergence of ancient man - archanthropines.
2. 200 thousand years ago - the formation of the second feature of hominid triad: a hand with a thumb, which contributed to fine manipulation of labor - the emergence of paleanthropines.
3. 40 thousand years ago - Formation of Homo sapiens, which, along with the second feature of the hominid triad had two more different: bipedal locomotion and large highly developed brain. The first surgical procedures - craniotomy was performed
4. 255 years BC - Erasistratus invented the catheter for drainage of cavities
5. 1519 - da Vinci injected vessels with wax
8. 1657 - Wren - the first intravenous injection through a bird feather
9. 1663 - Boyle - a blood transfusion from animal to animal
10. 1667 - Lower performed sheep blood transfusion to Coga - first recipient
11. 1832 - Latt performed intravenous infusion of saline to cholera patients through the canula
14. 1853 - Pravaz invented syringe
16. 1929 - Frossmann introduced a catheter through a peripheral vein in the hands to the right atrium, for which in 1956 was granted the Nobel Prize
17. 1945 - the emergence of a flexible peripheral catheter inserted on the needle
18. 1946 - Huber invented a "non-cutting" needle
19. 1953 - Aubaniac described percutaneous puncture of the subclavian vein, and Seldinger - vein catheterization through a conductor
20. 1956 - Murdoch invented a plastic disposable syringe
21. 1964 – A BD company started production of sterile disposable venous catheters
22. 1968 - Hickman invented tunneled venous catheter
23. 1973 - in the US a community of nurses involved into intravenous injections was established
24. 1975 - Invention of PICC
25. 1989 - Woodburn patented venous port

Results

Treatment becomes more effective and safer.

Conclusions

But not in all countries. At what point of the evolution have Russia stopped?

EP-451

Others

ON THE SELECTION OF VENOUS ACCESS SYSTEMS AND PROFESSIONALS INVOLVED IN THEIR INSTALLATION

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Objectives

Treatment of cancer is impossible without venous access. But who must be responsible for its choice, and who – for direct provision? There should be an integrated approach involving oncologists, surgeons and anesthetists.

Methods

In 2010 - 2013 years we conducted a training on "Selection and installation of venous access for 150 doctors of various specialties: 71 oncologists (47.4 %), 67 anesthesiologists (44.7 %) and 12 interventional radiologists (7.9 %). The training included practicing in operating theatres with demonstration of subclavian venous catheters and venous ports installation technique together with the theoretical course or some theoretical exercises only. In addition, we analyzed experience of 7 oncology clinics in Russia in approaches to provide venous access.

Results

Only 11 physicians (7.4 %) have fully mastered the technique, the majority - interventional radiologists (7 physicians), 3 and 1 anesthetist surgeon. In all seven clinics the problem of choice of venous access was not considered. In 4 clinics peripheral veins were used for chemotherapy provision. Only after serious complications they began to apply subclavian catheters. In 3 clinics subclavian catheters were used from the beginning of treatment. All clinics insertion of subclavian catheters involved anesthesiologists. While in 50% of cases due to the complications caused by incorrect installation and operation of subclavian catheters a cancer treatment program was interrupted.

Conclusions

A comprehensive and targeted training of doctors directly in the field of venous access is necessary as doctors of any of the existing specializations do not have all the necessary skills for this procedure. Anesthesiologists have difficulty in section and suturing tissue, surgeons and interventional radiologists - when puncturing blood vessels. The optimal training of such specialists is among interventional radiologist, as most of them are not only proficient in general surgical skills, but also able to use intraoperative fluoroscopy effectively.

EP-452

Others

MODERN RUSSIA – A HERITOR OF ANCIENT TRADITION OF BABYLON: THE TRAGIC STORY OF CENTRAL VENOUS CATHETERIZATION

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Objectives

A lot of health problems in Russia are not given attention. Only a few clinics in the country with a population of 140 million people are paying attention to vascular access.

Methods

In Russia 2,995,566 cancer pts are recorded, there are 6539 oncologists (458.1 pt to the doctor) and 125 cancer clinics. Among them, only 7 clinics (5.6%) practice implantable venous port system for the treatment of not more than 10% of their pts. In the remaining pt clinics each pt undergoes central vein catheterization at least 5 times over the period of treatment. More commonly peripheral veins are used. Thrombophlebitis and pneumothorax are routine complication. From 6539 oncologists not more than 150 people (2.3%) are aware of the existence of venous ports and not more than 30 (0.45%) know a method of implantation. In all Russian clinics (including non-cancer ones) there are only 147 X-ray surgical operation theatres, that's the reason of the impossibility of the widespread introduction of port systems.

Results

From 1991 tens of thousands of pts' lives were ruined by the actions of illiterate health workers. The reason for its the totalitarian regime, lack of education, lack of adequate health care financing and pervasive corruption that penetrates into all spheres of daily life. Many of the complications being a consequence of negligence, however, are taken as inevitable. The exact number of complications associated with errors in the provision of vascular access and catheter associated bloodstream infections have not taken into account. According to the conservative estimates at least 40% of central venous catheterization is accompanied by the development of severe complications. Level of catheter associated bloodstream infections is not less than 35%.

Conclusions

In ancient Babylon authorities executed patients. Medical Service of the Russian Federation often does the same.

EP-453

Others

**RISK FACTORS OF LONG-TERM CENTRAL VENOUS CATHETERS (CVCS)
COMPLICATION IN CHILDREN WITH HEMATO-ONCOLOGICAL DISORDERS**

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Objectives

To identify risk factors for long-term CVCs complications for understanding the optimal CVC managements.

Met

hods

Complications were analyzed retrospectively for 275 catheters which were implanted in 208 patients between June 2003 and February 2014 at St. Luke's International Hospital.

Complications included centralline associated blood stream infection (CLABSI), obstruction, dislocation andrupture. Multivariate logistic regression was conducted to adjust for several potential confounders.

Results

The total number of CVC days was 64,427. The overall rate of complications was 1.4/1000 CVC days. Age at CVC insertion ≤ 3 , double lumen catheter, and betadineskin preparation (vs chlorhexidine) were significant predictor of CVC complications($p=0.01$).

Conclusions

CVC complication rate was decreased dramatically with the use of chlorhexidine instead of betadine. Proper aseptic techniques by well-trained staff are recommended for the further progress not only for young patients but also for those who require double lumen catheters.

EP-454

Others

INCIDENCE OF FEBRILE NEUTROPENIA IN ACUTE LEUKEMIA CHILDREN IN INDIA USING UK PROTOCOL

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Objectives

Assesing febrile neutropenia episodes and mortality related to it, in Acute Leukemia children in India using UKALL 2003 and AML 15 protocols.

Methods

A prospective study performed in a tertiary care children hospital from March 2012 to May 2014, in children between 6 months to 15 years

Results

Total 72 children analysed, 51/72 are boys (71.83%), remaining girls. Out of 72, 59 are (81.9%) Acute lymphoblastic leukemia (ALL), 13 are Acute Myeloid Leukemia (AML). CALLA +ve B cell ALL were 54, 5 T cell ALL. Total 129 episodes of febrile neutropenia (F.N) observed in 72 patients. 106/129 in ALL, 23/129 in AML. In ALL, F.N episodes commonly observed in Consolidation (67.1%) followed by Reinduction- I (22.6%), then in Induction (10.3%). In AML, F.N episodes were commonly observed in 1st and 3rd month (37.5% each) followed by 2nd & 4th month of chemotherapy (12.5% each). Respiratory complaints seen in 40% of episodes followed by Genitourinary (22%) & Gastrointestinal (20%). Fever Without Focus in 18%. Cultures positive in 66 episodes (53.2%). Common site of isolation was Urine (66.6%), followed by Blood (33.3%). Gram negative bacteria commonly seen (86.3%) followed by Gram positive. Escherichia coli was common (67.2% cases) among gram negatives followed by Pseudomonas aeruginosa (20%) & then Klebsiella (12%). Most of them sensitive to amoxyclav, piperacillin tazobactam and carbapenems. In Gram positives, Staphylococcus was common (83%) followed by Pneumococcus (16%). Episodes responded to first line antibiotics 21.9% of times (Cefipime+ Amikacin), 78.1% episodes needed upgradation of Antibiotics. Antifungals used in 40.4% cases, 84% treated empirically & 16 percent had evidence of fungal infection. Mean duration of hospital stay 6.7 days. 5 children died in the study, 3 had relapse and 2 due to Febrile neutropenia (2.7%).

Conclusions

With good supportive care western protocol can be used in developing countries without increasing febrile neutropenia related mortality and morbidity.

EP-455

Others

VARIED SPECTRUM OF NEUROLOGICAL COMPLICATIONS RELATED TO DISEASE AND THERAPY IN CHILDHOOD MALIGNANCIES

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Objectives

To describe neurological complications in children with cancer and their short term outcome

Methods

Neurological problem as presenting feature or part of therapy related complications in childhood malignancies, identified and reviewed from november 2008 to december 2013, 4 years prospective and 14 months retrospective

Pre existing neurological problems, CNS tumors & post chemotherapy cognitive dysfunctions excluded.

Results

44 children, 3 months to 15 years of age had neurological problems . Acute lymphoblastic leukemia(ALL) 20/44, neuroblastoma 9/44(Opsoclonus Myoclonus syndrome in 4/9).

Neurological problems in Ewings /PNET seen in 4. Histiocytic disorder with CNS deposits in 3 cases. Four had Acute myeloid leukemia(AML), one was Hodgkins lymphoma, one was diffuse large B cell lymphoma, one germ cell tumour and one Rhabdomyosarcoma.

Tumor related neurological problems: seen in 27. 22 /27 directly related to tumor, 4/27 were paraneoplastic Opsoclonus myoclonus secondary to neuroblastoma.

Cord compression-12,(NBL-4, Ewings/PNET-4, Germ cell tumor-1, RMS-1,AML-1,Hodgkins Lymphoma-1). Five presented with seizures(ALL-3,AML-1,Histocytosis-1). Two had Encephalopathy with seizure(1 histiocytosis,1 AML). Two had facial nerve palsy with tumor infiltration as presenting feature(one AML/one DLBL). One Ptosis(with intracranial neuroblastoma extension) and 1 primary HLH presented with head ache and vomitings secondary to CNS deposits.

Therapy related problems seen in 17 ALL cases. Stroke like presentations seen in 7children with Methotrexate . Seizures in 6(post methotrexate-4/2 with cortical venous thrombosis secondary to PEG Asparganise). One had ventriculitis while on Induction. One child had post MTX chemical meningitis. One had Posterior reversible Encephalopathy syndrome secondary to hypertension(Steroid) and one had vincristine induced acute flaccid paralysis. Two cases in disease related group and 3 in treatment related had mild neurological disability.

Conclusions

Therapy related neurological complications seen only in ALL children. spinal cord compression was common neurological presenting feature. Early recognition of neurological complication either disease or treatment related is essential to control mortality & morbidity.

EP-456

Others

INVASIVE FUNGAL INFECTIONS IN CHILDREN WITH CANCER

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Objectives

The assessment of clinical course of IFI in neoplastic children according to the diagnostic and therapeutic difficulties, based on our institution experience.

Methods

To this study were enrolled 28 children with cancers diagnosed as having IFI. We analyzed the clinical course of IFI based of the initial symptoms,diagnostic difficulties, therapy clinical course of IFI,diagnostic difficulties, therapy and treatment results

Results

All of 28 pts developed IFI during deep neutropenia period with characteristic persistent fever. In 28 pts IFI were located in lungs, in 4 pts additionaly in CNS, in 1 pt in the liver. Diagnosed fungi pathogens were: Candida albicans, Candida tropicalis, Aspergillus, but in 9 pts pathogen was not identified. In all group IFI were diagnosed as a probable (18pts), possible (8 pts) and proven(1pts) infection.

Conclusions

Invasive fungal infections are serious cancer treatment complication because ofthe diagnostic and therapeutic difficulties , and subsequent result as delay in the therapy.Deep neutropenia play the funamental role in the development of IFI .

EP-457

Others

THE COST OF CHILDHOOD CANCER TREATMENT IN AFRICA

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Objectives

Annually more than 50.000 African children will suffer from cancer.

Information on the costs of care of childhood cancer in Africa is missing, making it impossible for policy makers to adopt affordable interventions. The aim of this study is to estimate the health systems costs of cancer care in Africa and to propose a more effective approach to investigations and treatment for the most common cancers.

Methods

The costs of cancer were estimated using administrative data for the different period of time (2008-2012) in different African units. We derived direct and indirect financial and economic costs from a health systems perspective. Costs included drugs, personnel and annuitized capital costs. The diseases analysed included nephroblastoma, retinoblastoma, Burkitt lymphoma and HIV associated malignancies (Kaposi sarcoma and NHL).

Results

The cost of treating nephroblastoma varied between EUR 650 for stage 1 and 5 times more for stage 4 (EUR 3325). Treating one patient with nephroblastoma averted more than 32 DALYs. The cost of treating BL was 591 Euros for group B and 2220 for group C. The first line treatment of KS cost EUR 800 and the paclitaxel salvage regimen EUR 1232. The retinoblastoma cost was estimated at less than 1000 EUR for advanced disease.

Conclusions

Treating childhood cancers in Africa is cost effective. Key policy points from our research are the need for 1) recognition of childhood cancer as a health problem by African governments 2) improving awareness and early diagnosis 3) adapted protocols for local resource limited conditions 4) affordability of treatment.

EP-458

Others

BLOODSTREAM INFECTIONS AND PREDICTORS OF MORBIDITY AND MORTALITY AMONG CHILDREN LIVING WITH CANCER IN RURAL SETTINGS IN UGANDA

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Objectives

Bloodstream infections (BSI) are a common cause of admission, morbidity and mortality among pediatric patients with malignancy worldwide. The impact of antibiotic resistance and other co-infection (e.g. HIV infection, TB) on treatment outcomes in many rural developing settings are not well known.

Methods

We conducted prospective multicenter study to evaluate the incidence of BSI and risk factors among children treated due to cancer in 6 rural settings in Uganda. There were observed 176 consecutive admissions of children with signs of systemic infectious disease. Blood was taken for serological tests, culture and malaria microscopy, when indicated. There were recorded data on clinical findings, underlying diseases, antimicrobial drug used before and on admission, microbial agent findings and outcome.

Results

The incidence of laboratory confirmed bloodstream infection was 37% from admitted children with systemic infectious signs. More than 96% of the patients received during prior admission at least one course of antimicrobial therapy and 58% antimalarial therapy, prior a blood culture. The most frequent isolates were Klebsiella spp., E. coli, Salmonella, enterococci, Staphylococcus aureus, Streptococcus spp. 16% of the pediatric patients had a malaria, 21% HIV infection and 4% Tuberculosis. 34% of the children with laboratory confirmed bloodstream infection died in comparison to 72% of those with clinical +/-lab presentation of infection from files evaluation. 43% of the microbial agents had confirmed resistance at least to one of the common antibiotic agents.

Conclusions

Bloodstream infections were less common than malaria in our settings but were responsible for more death among children with cancer. The frequent use of antimicrobial drugs prior blood culture may have crucial impact on detection of the micro-organism, antibiotic testing and susceptibility to commonly used antibiotics. The findings that antimicrobial resistance, co-infection and malnutrition predict fatal outcome calls for renewed efforts and recommendations on national but also local level.

EP-459

Others

EFFECTIVE MODES OF FINANCIAL AIDS FOR SUPPORTING THE TREATMENT OF PEDIATRIC CANCER PATIENTS IN RESOURCE POOR SETTING

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Objectives

Treatment of any form of cancer in children poses a significant financial burden on the family in resource poor countries like India. In these circumstances, abandonment of treatment is a common event. Financial aid from the Government as well as Non-Government Organizations (NGO) help such patients to complete treatment. We attempted to analyse the effectiveness of various modes of financial aids available to the families that helped them to continue with the treatment.

Methods

A retrospective analysis of patients with Acute Lymphoblastic Leukemia (ALL) diagnosed at our centre between Jan 2012-Dec 2013 was carried out. All patients were treated as per the BFM 95 protocol. The source of financing the treatment of each patient was assessed by a questionnaire.

Results

During the study period, 71 patients were diagnosed with ALL at our centre. Of these, 4 patients (5.6%) were lost to follow up and 22 patients (30.9%) opted for treatment at an alternate centre. Of the remaining 45 patients, 18 patients (40%) sought financial assistance for the completion of treatment. Of these 18 patients, parents of 12 patients (66.6%) completed treatment of their child with the help of insurance available through their employment agencies. 6 patients (33.3%) sought monetary aid from the Prime Minister's Relief fund (Government Support). They also got support from a NGO in the form of 'free of cost' medicines. Of these 6 patients, 2 patients (11.1%) also received aid from the Support Group formed by the parents of children treated of ALL in the past.

Conclusions

In resource poor country like India, many patients diagnosed with ALL need financial assistance for treatment. For financially constrained families, insurance grant from the parental employment agencies and an ascertained financial aid from the Government play a major role in decreasing the rate of treatment abandonment.

EP-460

Others

FEBRIL NEUTROPENIA IN OUR PEDIATRIC MALIGNANCY PATIENTS

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Objectives

The aim of this study was to determine the clinical features, microbiological pattern and antimicrobial susceptibility in febrile neutropenia in children with cancer.

Methods

Isolated microorganisms and antimicrobial susceptibilities of all febrile neutropenic episodes in patients hospitalized at Department of Pediatric Hematology and Oncology between August 2011 –October 2013 were evaluated retrospectively in this study.

Results

In 69 patients, 232 episodes of FN were reported. Primary malignancies were leukemia in 99 episodes (42.7%) and solid tumors in 133 episodes (57.3%). Mean absolute neutrophil count was $150.86 \pm 156.81/\text{mm}^3$, mean duration of hospitalization was 9.25 ± 10.03 days and mean fever time was 3.03 ± 4.69 days. Of the 232 episodes, 50 (21.6%) were microbiologically documented. The most common sites of clinical documentation were the mucosa and skin. Of isolated microorganisms, 53.5% were gram-negative bacilli, 41.9% gram-positive cocci and 4.7% Candida spp. E.coli (15/27; 55.5%) and Staphylococci (13/14; 92.8%) were the most common isolates among Gram-negative and Gram-positive bacteria, respectively. In antimicrobial susceptibility testing among isolated microorganisms, resistance was found 18.7% (3/16) for piperacillin-tazobactam and 21.4% (3/14) for cefepime that the most frequently used antimicrobial agents in empiric therapy. No cefoperazone resistance was identified. A total of 136/232 (58.6%) febrile neutropenic episodes improved with first-line antimicrobial therapy, while modification was required in 96 episodes (41.4%). In leukemia duration of fever and discharge from the hospital were longer and CRP was higher than in the solid tumors. There were a total of 3 deaths (1.3%).

Conclusions

The most suitable and rationalist approach to decrease the mortality and morbidity is to start rapidly empiric therapy in febrile neutropenic patients according to results of frequencies and susceptibility patterns of isolated microorganisms in local epidemiologic data and if necessary to make modification in therapy according to culture results and clinical situation.

EP-461

Others

INCIDENCE AND SEVERITY OF ADVERSE REACTIONS ASSOCIATED WITH ANTHRACYCLINES IN PAEDIATRIC PATIENTS

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Objectives

To determine the incidence and severity of adverse reactions associated with anthracyclines in paediatric patients.

Methods

A retrospective cohort of patients treated with anthracyclines treated at Children's Hospital of Mexico Federico Gomez and the Pediatric Hospital of Centro Medico Nacional Siglo XXI. To identify adverse reactions, Intensive pharmacovigilance method was performed, analysis of causality was performed using the Naranjo test and severity of adverse reactions was determined according to Official Mexican Standard 220-SSA1-2012 called Installation and operation of the pharmacovigilance.

Results

A total of 33 patients were included in the study. Found total of 431 adverse events which 292 (68%) were associated with anthracyclines. The incidence of adverse reactions associated with anthracyclines was 82 %, 79 %, 48 %, 45 %, 30 % and 3% for neutropenia and fever, vomiting, mucositis, thrombocytopenia, anemia and cardiotoxicity, respectively. According to the severity of adverse reactions associated with anthracyclines 155 (53%) were severe, 90 (31%) were mild and 47 (16%) were moderate.

Conclusions

Anthracyclines have a high rate of adverse events, some even fatal. Intensive pharmacovigilance is an effective method to determine the incidence of adverse events, which is necessary for the timely identification of potential risks in patients with cancer.

EP-462

Others

THE FIRST PEDIATRIC ONCOLOGY HOSPITAL IN MEXICO A NEW MODEL OF CARE

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Objectives

To report the planning and opening of the first hospital specially designed for children with cancer in Mexico

Methods

We review the process of planning and the design of the hospital as a innovative model of care.

Results

The construction of the 17500m² Hospital Infantil Teleton de Oncología (HITO) started in 2012 and finished by november 2013. The medical model is based in 5 axis: Diagnostic accuracy, modern treatment, prevention of complications, quality of life, housing (Teleton House)

Teleton foundation designed this campus with hospital and Teleton house to treat children with cancer in an integrated model of health care exclusively for children suffering cancer.

Conclusions

This is a new model of pediatric oncology care, a proposal for a change in health care with focus in the special needs of cancer patients, expecting solve the main problems that affect results.

EP-463

Others

CHEMOTHERAPY SURVEILLANCE WITH CANCER PATIENTS FROM THE NATIONAL INSTITUTE OF PEDIATRICS, MEXICO

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Objectives

Chemotherapy surveillance is a fundamental tool in pediatric oncology to evaluate with a long term follow up the efficacy and security of treatments. The aim was to describe the severe adverse events (SAE) secondary to chemotherapy in the oncology department at the National Institute of Pediatrics.

Methods

We realized a prospective study registering all grade 3 and 4 SAE according to the World Health Organization from February 2013 to February 2014. We analyzed diagnosis and outcome according to the Naranjo algorithm.

Results

We included 178 patients who presented 874 SAE. The more frequent was grade 3 and 4 neutropenia (60%), anemia (13%), thrombocytopenia (10%), neutropenic colitis (3%), mucositis (3%), anaphylactic shock (3%). The more frequent diagnosis was acute lymphoblastic leukemia (54%) acute myeloid leukemia (8%), osteosarcoma (18%), Ewing sarcoma (7%), retinoblastoma (5%), medulloblastoma (5%), germ cell tumors (3%). Ifosfamide was the more frequent chemotherapeutical agent associated with SAE. Mortality was 10%.

Conclusions

Chemotherapy surveillance in pediatric oncology must be a systematic action in order to establish causality, assess the security of chemotherapy and generate new strategies to reduce the severity and mortality of SAE.

EP-464

Others

EXPERIENCE WITH HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR ACQUIRED SEVERE APLASTIC ANEMIA IN A DEVELOPING COUNTRY LIKE INDIA

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Objectives

To assess the role of Haploidentical Hematopoietic Stem Cell Transplantation (HHCT) for Acquired Severe Aplastic Anemia (SAA) as an alternative to Matched unrelated donor (MUD) transplantation in a resource limited country like India.

Methods

Study design: retrospective study.

Study period: January 2011- February 2014.

Setting: B L Kapur Superspeciality Hospital, Delhi.

Inclusion criteria: Two children aged between 10 to 15 year who showed no response to Immunotherapy were included.

Conditioning regimen included Fludarabine (30 mg/m² from day-6 to -2days), Cyclophosphamide (14.5 mg/kg on day -6 and -5), and TBI (200cGy on day-1). Prophylaxis against GVHD was cyclophosphamide (50 mg/kg on days +3 and +4), Tacrolimus (0.06mg/kg), and Mycophenolate Mofetil (10mg/kg q8h).

Absolute Viable CD34 positive Cell Count varied between 3 x 10⁶ to 6 x 10⁶ per kg of recipient body weight.

Results

One of our patient experienced early graft rejection but she received a second HHCT and achieved sustained engraftment. One of our patient developed acute GVHD grade II which was managed with steroids. Both the children are having sustained complete donor chimerism and normal peripheral blood counts.

Conclusions

HHCT using high-dose post transplantation cyclophosphamide for T cell depletion is a reasonable treatment option for children with acquired SAA and is feasible in developing countries, with limited availability of matched unrelated donors.

EP-465

Others

A SKIN PROTECTANT REGIMEN FOR THE MANAGEMENT OF DIAPER SKIN COMPROMISE IN PEDIATRIC ONCOLOGY PATIENTS

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Objectives

Severe diaper dermatitis is an extremely challenging side effect of treatment among infants with leukemia. It is likely due to multiple factors including chemotherapy leading to chemical burns, hyper hydration with increased urine and stool output, looser stools, with suspected higher concentrations of enzymes, decreased immune function, and decreased healing capacity resulting in severe morbidity. The institutional current practice of a liquid barrier film and a topical barrier cream were not sufficiently effective. The objective was to determine the effectiveness of a regimen consisting of a substantive liquid skin protectant plus a zinc-based ointment with daily sitz baths and frequent diaper changes to minimize/prevent irritant diaper dermatitis throughout multiple chemotherapy cycles.

Methods

Infants receiving high dose chemotherapy (e.g., doxorubicin, cyclophosphamide, vincristine, prednisone, L-asparaginase, intrathecal therapy, and high-dose methotrexate and cytarabine) and diapered patients receiving methotrexate, alkalinization and hyperhydration, were enrolled upon hospitalization in the IRB approved study. The liquid protectant was applied to the diaper regions upon resolution of open wounds, evaluated daily and reapplied as necessary throughout multiple chemotherapy and recovery cycles. The zinc ointment was applied liberally at every diaper change. The skin was assessed for erythema and rash using a validated scale and standardized digital images taken to quantify area of involvement and erythema. Absolute neutrophil counts, urine and stool output and frequency, and medications were tracked with skin grades and images over time.

Results

Twenty patients were enrolled and followed for 7 – 240 days. There was no severe diaper dermatitis and only mild perineal irritation was observed over multiple chemotherapy cycles despite being neutropenic or on multiple antibiotics for fevers. There was no delay in chemotherapy due to severe skin breakdown.

Conclusions

The regimen is effective in delaying and lessening skin compromise among infants receiving chemotherapy relative to the hospital standard of care.

EP-466

Others

DEVELOPING A SERVICE CAPABILITY FRAMEWORK: A GUIDE FOR HEALTH SERVICES PROVIDING CARE TO CHILDREN AND ADOLESCENTS WITH CANCER

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Objectives

Achieving best outcomes in paediatric cancer care requires a coordinated, timely, multidisciplinary approach, with active collaboration between health services. To support this approach, the Paediatric Integrated Cancer Service has developed a Service Capability (SCF) for the State of Victoria, Australia. Its purpose is to define the minimum requirements for providing sustainable, coordinated and safe paediatric oncology care across a variety of health networks including regional and urban settings.

Methods

A literature review was undertaken to gather evidence to guide the rationale and recommendations within the SCF. An expert steering group was established, with wider consultation from other disciplines. The SCF was endorsed by the Victorian paediatric tertiary referral centres, as well as the Victorian State government's Risk Management and Insurance Group

Results

The SCF presents four levels of care for health service participation, including an algorithm of risk factors that may escalate the level of care required. The levels are defined according to complexity of care, patient critical mass and the level of paediatric oncology services available. Services vary across Victoria from outreach centres providing supportive care, through to specialist tertiary/quaternary referral centres. Levels are also defined across critical time points in the patient's care, supporting clinical decision making and referral processes. Each level describes the necessary infrastructure, workforce, education, research, quality, clinical governance and service networking required. The framework also describes minimum requirements in speciality areas such as clinical trials, laboratory services, imaging, multidisciplinary team meetings, nursing, pharmacy, psychosocial and psycho-oncology care, radiation oncology, surgery and management of late effects

Conclusions

The SCF supports health services to plan and develop a paediatric cancer service within an agreed scope of practice. The SCF supports health services to deliver a level of care that meets the needs of their local community whilst maintaining patient safety, efficacy and a confidence in referring shared care

EP-467

Others

BETA BLOCKER TREATMENT IN HEMANGIOMAS: EXPERIENCE IN 344 CASES IN A SINGLE INSTITUTE

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Objectives

Efficacy and safety of beta blockers, especially propranolol had been approved in infantile hemangiomas. Aim of our study was to analyse efficacy and safety of systemic and topical beta blockers in a large population after preliminary experiences in our institute.

Methods

Between September 2009 and January 2014, medical records of 344 patients diagnosed with hemangioma were retrospectively investigated at Baskent University Department of Pediatric Oncology. Basal complete blood count, serum biochemistry were obtained in all patients with systemic beta blocker treatment. Cardiac evaluation was made to all patients, with echocardiography in selected ones. Starting dose of propranolol ranged from 2-4 mg/kg/day. Steroid was added to propranolol in majority of cases. Local timolol ointment was used in a minority of cases with tiny cutaneous hemangiomas. Treatment response was recorded both by early and late response criteria in both groups. Retrospective records of vital signs during initial treatment and recorded adverse events were examined. Re-growth of lesions and secondary treatment was also evaluated.

Results

There were 244 girls. Median age was 4.7 months (0.3-108 months). The gestational age of was under 37 weeks in 22%. Indications for treatment were rapid growth, ulceration, infection, cosmetic issues, bleeding, breathing, feeding and ocular problems and compartment syndrome. Early response was seen in 80.8 % of the cases. The response at the end of treatment was 75.3 %. Adverse events resulting in interruption or cessation of treatment were detected in 7.8% of cases. Favorable results were obtained in several locations and phenotypic variants of hemangiomas. Local treatment with timolol was of limited use.

Conclusions

Experience in hemangiomas revealed satisfactory results in several cases with specific locations and phenotypic variants. We believe that early use of beta blockers would be associated with less complications in course of a benign disorder.

EP-468

Others

PROPRANOLOL IN TUMORS EXCEPT INFANTILE HEMANGIOMAS: PRESENTATION OF FOUR CASES

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Objectives

There is no more debate in use of propranolol in infantile hemangiomas but there is some question in efficacy in some of vascular lesions like tufted angioma, Kasabach Merrit syndrome, and hemangioendothelioma. On the other hand improved survival had been published in adult cancers with incidental use of beta blockers for other indications. Herein four cases with lesions other than infantile hemangiomas were presented with beta blocker treatment with interesting results.

Methods

An 9 year-old girl with metastatic hemangioendothelioma to liver and bones; a 2 year-old boy with Noonan syndrome and progressive hypothalamic chiasmatic low grade glioma, a 4 month-old girl with a giant retroorbital plexiform neurofibroma with neurofibromatosis type 1, and 22 months-old girl with recurrent giant cell granuloma of the jaw were presented. The parents of the patients with metastatic hemangioendothelioma and progressive glioma refused standard treatment after relapse. In recurrent giant cell tumor, the lesion was inoperable after three operations and steroid injections and the treatment was offered during the period for the procurement of calcitonin from the health care system. In all patients, propranolol 2-3 mg/kg and prednisolon 1-2 mg/kg were used after informed consents were all obtained. Prednisolon duration was differed between patients.

Results

The patient with metastatic hemangioendothelioma responded well to propranolol and prednisolon with failure free survival of 25 months after relapse. The patient with progressive glioma showed prominent neurocognitive development and radiological regression of the tumor. In case of plexiform neurofibroma, MRI displayed regression of the retroorbital mass in the first three months of treatment and a stabile course thereafter. Giant cell tumor responded to treatment in approximately three weeks after the third relapse. No side effect was detected with prolonged use.

Conclusions

Anti-angiogenesis is the probable mechanism in four different cases with borderline tumors. Acceptable responses to treatment with propranolol were achieved.

EP-469

Others

ABDOMINAL INFLAMMATORY MYOFIBROBLASTIC TUMORS: GREAT MIMICKER, HOW IMAGING CAN HELP IN DIAGNOSIS

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Objectives

Inflammatory myofibroblastic tumor (IMT), is a quasineoplastic lesion that most commonly involves lung and orbit, but it has been reported to occur in nearly every site in the body. IMT has been reported mainly in the children and young adults. Variations in the clinical presentation of IMT have confounded its diagnosis. Because of IMT's rarity and because the lesions often mimic sarcoma, lymphoma, and metastasis, IMT can often be clinically misdiagnosed as a malignant tumor. The features of IMT on the imaging studies are variable but manifest most often as a soft tissue mass. Our objective is to evaluate the imaging features of the pathologically confirmed ten cases of abdomino-pelvic IMT .

Methods

We retrospectively reviewed imaging studies of ten cases of pathologically confirmed IMT of abdomino-pelvic region.

Results

Ten patients, 7 males and 3 females with abdomino-pelvic IMT were studied, their age ranged from one to 17 years. Mesentery was the commonest location ($n = 5$) followed by liver ($n = 4$) and urinary bladder ($n = 1$). US of all ten patients were reviewed and showed non-specific hypo-echoic soft tissue mass lesion with no definite specific sonographic criteria for IMT. CT of all ten patients were reviewed and showed heterogeneously hypo dense masses with evident enhancement; calcification was encountered in only one case, small cysts were noted within 3 cases. The mesenteric lesions did not cause any secondary effect, i.e intestinal obstructions. MRI was reviewed in 2 cases, one hepatic and the urinary bladder case, the most significant feature was hypointense T2WI signal of the IMT masses.

Conclusions

IMT is a rare and usually benign neoplasm that mimics several malignant tumors both radiologically and clinically. The radiologist should be familiar with this entity and its presentations to facilitate accurate diagnosis and help avoid unnecessary radical surgical resection.

EP-470

Psychosocial

INITIATION AND IMPLEMENTATION OF ART AND CRAFT ACTIVITIES BY CHILD LIFE SERVICES DEPARTMENT FOR UNDERPRIVILEGED PEDIATRIC ONCOLOGY PATIENTS TO IMPROVE QUALITY OF LIFE

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Objectives

Child life services (CLS) is an offshoot of the psycho-oncology department, created in 2013 to improve quality of life of hospitalized children. In view of the parental concerns regarding loss of normalcy in child's life, due to the long hospital stays during chemo and other long-term cancer treatments; an art and craft project was initiated with the children. It is an intervention based on the belief that the creative process involved in the making of art is healing and life enhancing.

Methods

Volunteers were initially trained in the basics of child/client centered therapy and art work. They were then sent to engage children in different art and craft activities i.e. hand and face painting, collage, origami, cut and paste, drawing and coloring. They worked with groups of 8 to 10 children (approx 100 children), age range from 4 to 14 years, in in-patient, out-patient and daycare units. Observational study method was used where volunteers provided their written observations pre and post activity along with the feedback of hospital staff and parents.

Results

Response to intervention was observations by staff, parents and volunteers which yielded similar results. Intervention helped in alleviating the mood and stress of children, it created responsiveness, group work, enthusiasm, interest, sharing and release of boredom. Further it helped in producing compliance with food and medicine and also aids in distraction during invasive procedures.

Conclusions

Emotional health and wellbeing of children suffering from cancer is crucial for child development as well as the treatment itself. Implementing such interventions in an underprivileged, charity organization is a challenge in itself due to the scarcity and limitation of material as well as human resources. Also the family's unswerving and unfounded beliefs on faith healers compounds the problems faced by doctors in treating the patients.

EP-471

Psychosocial

QUALITY OF LIFE FROM THE PERSPECTIVE OF PEDIATRIC CANCER PATIENTS AND SURVIVORS: “THERE ARE GOOD THINGS AND THEN THERE ARE BAD THINGS”

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Objectives

The systematic assessment of quality of life (QOL) is necessary within pediatric oncology research and clinical practice. Research and intervention initiatives require a theoretical framework that is founded on a clearly defined construct of QOL; however, given the multidimensional nature of QOL, it remains unclear which domains and concepts are most important to children with cancer. The purpose of our study was to inform the theoretical underpinnings of QOL from the perspective of pediatric cancer patients and survivors through a qualitative study, guided by interpretive description.

Methods

Study participants were recruited from four Canadian academic pediatric hospitals. Data collection was completed through in-depth, one-on-one, semi-structured interviews. Transcripts were examined line-by-line for common themes and patterns and reviewed continuously as interpretative understanding was considered within the context of clinical practice and current knowledge in the field. Themes were refined through team consensus until saturation was reached.

Results

A total of 37 children participated (19 female; 51%) who were diagnosed with varied cancer types or identified as a cancer survivor (median age 13; range 8-18 years). Participants acknowledged the presence of positive and negative aspects within their cancer experience and expressed that it was necessary to take ‘the good with the bad’. This perspective was illuminated across three prominent themes: 1) Doing what one is able, but not always what one wants; 2) Feeling isolated within a new closeness of family and friends; and, 3) Developing positivity amidst anger, sadness, and lingering worry.

Conclusions

Exploration of these themes highlighted the participants’ interwoven experience of QOL and demonstrated its potential to be dynamic within contextual variables. Future steps include considering whether QOL instruments are a representative assessment of how QOL is experienced within a pediatric population with cancer. A developing theoretical framework will be refined within the context of current findings.

EP-472

Psychosocial

LONGITUDINAL CHANGES IN HOPE IN PARENTS OF CHILDREN WITH CANCER OF POOR PROGNOSIS: THE EFFECT OF DIAGNOSIS

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Objectives

To date, no studies have used standardized instruments to prospectively document parental hope when a child is treated for cancer with poor prognosis. **Objectives:** To use a standardized instrument to longitudinally examine parental hope over the first year post-diagnosis and the effect of cancer diagnosis on hope.

Methods

Thirty-five parents of children diagnosed with cancer of poor prognosis in a large pediatric cancer centre participated. Institutional approval was obtained for the study and participants signed consent to participate. Parents completed the Hearth Hope Index (HHI), in reference to their child's condition, upon enrollment (3 months post diagnosis, T1), 3 months (T2), six months (T3), nine months (T4) and 12 months (T5) later. HHI was standardized with adults with chronic or advanced disease. Based on the child's diagnosis, parents were stratified into three groups: leukemia/lymphoma (LL; 41%), solid tumors (ST; 31%) and brain tumors (BT; 28%). For analyses, repeated measures ANOVAs and t-tests were conducted. Effect sizes are presented.

Results

Overall, parents' scores of hope were significantly higher than normative data at each of the time intervals assessed (T1: $d=1.21$; T2: $d=1.28$; T3: $d=1.39$; T4: $d=1.07$; T5: $d=1.11$). At T3 there was significantly more hope in the BT group than the ST ($d=0.74$) and in the LL group compared to the ST group ($d=0.60$). In the BT group, parental hope significantly increased from T2 to T3 ($d=-0.62$). In the ST group, hope significantly decreased between T1 and T3 ($d=0.60$). Hope did not alter over time in the LL group.

Conclusions

Fluctuations in parental hope over time seem to be related to their child's diagnosis, likely depending on the child's response to treatment. These results suggest the importance of addressing parental hope during the child's treatment as part of psychosocial care

EP-473

Psychosocial

TO ASSESS THE CONTINUED IMPACT OF THE HOLISTIC CARE, PROVIDED AT ST. JUDE INDIA CHILDCARE CENTRES, ONCE THE CHILD RETURNS HOME AFTER TREATMENT

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Objectives

To understand the impact that St. Jude has had on the quality of life of the patient- families, analyze the problems that families face at home. To measure the impact of these families as “change agents” in their communities and to use the findings to further support these families, and improve our model.

Methods

A pilot study was conducted with 30 families at the Centre to establish the parameters of the study. A random selection of 37 families who have returned home, who agreed to participate in the study were interviewed, photographs of the home and complete checklist completed of items observed.

Results

There is a change for the better for the entire family, when the daily routine, cleanliness of the home, eating habits change. More than 70% of the families have managed to keep their houses clean.

Children learn these good habits and pass them on to others in the family.

Many families have tried to improve the way they live at home. Some have renovated their homes to provide proper facilities,

Out of the 13 (or 34.21%) of the 37 families have relocated for better homes and schools.

The conditions at their home differ substantially from those at the centre. Tables show some details of our findings.

Table 1: Family Income

Range (per month)	No. of Families	%
500-3000	27	72.97
3000-6000	6	16.22
6000 +	4	10.81
Total	37	100.00

Table 2: Type of house

Types	No	%
Apartment	5	13.51
Cemented old homes	11	29.73
Standalone pucca homes	6	16.22
Mud house	5	13.51
Chawl	5	13.51
Brick house thatched roof/temporary	5	13.51
Total	37	100.00

Conclusions

All the families agreed that they have learnt: cleanliness, discipline, control over daily life, to live harmoniously in a community, positive thinking and a feeling of empowerment and confidence.

EP-474

Psychosocial

EXPLORATION OF PSYCHOSOCIAL ASPECTS OF PAEDIATRIC ONCOLOGY: PERSONALIZED LIFEBOOKS INITIATIVE ILLUSTRATING PSYCHOSOCIAL EXPERIENCES OF PATIENTS AND FAMILIES WITH PAEDIATRIC CANCER IN SINGAPORE.

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Objectives

Lifebooks, as a therapeutic tool, have been reviewed in elderly with dementia and the terminally ill, but not yet in children. The process of exploring experiences and their meaning facilitates reflection and holds potentially tremendous psychosocial benefit. This is especially pertinent in acute lymphoblastic leukemia patients and families, who, despite the increasing rates of remission (>90%), still face many psychosocial challenges. Lifebooks also serve as an inspiration, provide advice to others, and help as a coping mechanism for families should their child not survive.

Methods

Patients and families are recruited based on their willingness to have a lifebook. Informed consent was done. Formal open-ended interviews are conducted, audiotaped and transcribed. Transcripts are re-organized into smooth-flowing storylines. Patients and families are involved as much as possible, encouraged to contribute content and design ideas, and provide any materials like photos. Drafts are created with a publishing company, reviewed with the families, doctors-in-charge, and social workers. Complimentary printed copies are given to patient and family.

Results

The production of lifebooks is a long-term ongoing project. Current recipients and healthcare professionals found it very beneficial and therapeutic. Children's Cancer Foundation (CCF) Singapore – a key non-profit organization supporting children with cancer and their families – is supporting this project. We aim to eventually benefit all National University Hospital (NUH) paediatric oncology patients and families.

Conclusions

Besides being therapeutic, the full spectrum of experience narrated in lifebooks uniquely supplement the perspectives of healthcare professionals. Future directions include compiling an advice booklet, publishing a compiled lifebooks coffee-table book, creating a lifebooks library in NUH wards/clinics and launching a lifebooks online platform. Our project is promising in shedding light on how to improve paediatric oncology psychosocial care in the Singapore and Asian setting.

EP-475

Psychosocial

HELP CANCER SURVIVORS TO REGAIN THEIR WELL-BEING BY FACING THE CHALLENGE OF A THERAPEUTIC ADVENTURE EXPEDITION

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Objectives

The adolescents living with cancer are not only threatened in their physical integrity, but they are often affected in their self-esteem, their quality of life and their relationship with family and friends. Since 1996, On the Tip of the Toes Foundation is organizing outdoor therapeutic adventures for young cancer survivors from 14 to 20 years old from all across Canada. Our mission is to help those young people living with cancer to regain their well-being by overcoming new challenges, by being in contact with nature and being part of a group with individuals who has been through the same problematics. The purpose of this presentation is to explain the approach of On the Tip of the Toes Foundation. With their specific program objectives, they help the participants to surpass themselves, to become aware of their strength, to develop their sense of autonomy and responsibility, to create an experience based on social inclusion after going through the sickness and treatments. This adventure programming allows an holistic healing process in the remission period.

Methods

A Powerpoint will be used to present the organization, the program and the results. Some pictures of the trips and a short video will be presented.

Results

The preliminary result of the five years study of The impact of the therapeutic expedition on the quality of life of adolescents living with cancer (PAQUETTE L., University of Quebec in Chicoutimi) will be presented.

Conclusions

The presentation will give a better understanding of the approach and the program developed by On the Tip of the Toes Foundation and the results on adolescents.

EP-476

Psychosocial

BALANCING GRIEF AND SURVIVAL: EXPERIENCES OF CHILDREN WITH BRAIN TUMOURS AND THEIR PARENTS

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Objectives

While researchers have explored many important aspects of living with childhood cancer, including the multitude of strains on family members and their reactions, very little is known about the experiences of children with brain tumours and their parents. To this end, our research team conducted a qualitative study guided by grounded theory methods to explore the unique and shared elements of the experiences of childhood brain tumours, from the perspectives of these children and their parents.

Methods

Semi-structured interviews were conducted with twelve children with brain tumours who were between the ages of 6 and 14 years, and one of each of their parents, for a total of 24 participants.

Results

Woven throughout their stories were expressions of grief and uncertainty related to the tumour and its effects on their lives. Children and parents described efforts and strategies that they used to try to maintain a positive outlook and a sense of normalcy, in order to cope and to adapt to the struggles and the changes in their lives.

Conclusions

A substantive theory of Balancing Grief and Survival was developed, offering a lens through which to view the children's and parents' complex experiences, struggles and coping strategies as integrated, dynamic processes. This presentation will introduce participants to this theory, illustrated by quotes and insights shared by the children and their parents. Implications for future research and clinical practice will also be discussed.

EP-477

Psychosocial

SINGLE SESSION GROUP INTERVENTION FOR GRIEVING RELATIVES

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Objectives

The purpose of this intervention is to give emotional tools and strategies to the participants for a healthy elaboration of their grief process.

Methods

For this intervention, 39 relatives of 16 patients who died because of an oncological disease were gathered at the National Unit of Pediatric Oncology (UNOP) to take part in a series of activities led by the Psychology department and with the aid of Social Work, Child Life and Palliative Care. These group activities are focused in the development of emotional skills for the participants to cope with the loss of someone close.

Results

At the end of the activity, the participants had a secure environment for the emotional catharsis and can name at least 4 conducts they can introduce into their everyday life for the appropriate grieving process.

Conclusions

This semi-annual intervention offers an opportunity for the participants to guide their own emotional resources to a healthy resolution of their grieving process.

EP-478

Psychosocial

COGNITIVE FUNCTION OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA UNDERGOING CHEMOTHERAPY: DEVELOPING COUNTRY PERSPECTIVE

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Objectives

There are few studies on cognitive function of patients of acute lymphoblastic leukemia (ALL) while on therapy. Majority of the studies have focused on long term survivors. Data from developing countries is even scarcer as the emphasis is still on cure rather than quality of life after completion of therapy. Present study was carried out to assess cognitive function of children with ALL who were still on treatment.

Methods

Cognitive function of 30 children with ALL during maintenance phase of chemotherapy was assessed using Malin's Intelligence Scale for Indian children, an adaptation of Weschler Intelligence scale. Children were divided into standard and high risk groups based on age at diagnosis, initial white cell count, immunophenotyping and cytogenetics. High risk group received more intensive chemotherapy including cranial irradiation. 40 children with non-hematologic chronic disease served as controls.

Results

Median age of patients was 9 years. 15 of 30 (50%) children with ALL scored an IQ of less than 90 as against 6 of 40 (15%) in the control group. Mean IQ score was 89.7 ± 7.93 and 95.9 ± 5.86 in study and control groups respectively ($p < 0.001$). Patients had poor scores in all areas but it was statistically significant in areas of information, comprehension, arithmetic, digit span, picture completion, block design and coding. In subgroup analysis, mean IQ score in high risk and standard risk group was 86.5 ± 7.07 and 93.8 ± 7.23 respectively ($p < 0.01$). High risk patients scored lower in comprehension, arithmetic, block design, object assembly and coding.

Conclusions

Children with ALL undergoing chemotherapy had lower scores on verbal, performance and overall IQ. The difference was more marked in the high risk group. Early identification of at risk patients for poor neuro-developmental outcome will help in better rehabilitation of these patients.

EP-479

Psychosocial

PSYCHOLOGICAL PROBLEMS OF HEALTHY SIBLINGS IN PEDIATRIC ONCOLOGY

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Objectives

Childhood cancer significantly affects the entire family making considerable impact on daily functioning, emotional condition of healthy siblings who are particularly vulnerable to competently deal with the family crisis. The study purpose is to explore psychological problems, Self-concept and coping resources of healthy siblings. Participants comprised 35 children aged 7 to 17. 15 were pediatric oncology patients in remission; 20 - their healthy siblings, 4 of them grieving the loss of elder sisters from leukemia.

Methods

The study was conducted in rehabilitation camp and city family club for two years, including diagnostics and therapy, individually, in sibling pairs and in groups. Diagnostic projective tests: "House-Tree-Person", "My family". Diagnostic and therapy methods: guided phantasy after V. Oaklander; play therapy after T.D. Zinkevich-Evstigneeva; Sandplay.

Results

Outcomes revealed that healthy siblings have no less but often more long-lasting emotional and behavioral problems than their sick brothers/sisters. Self-concept of healthy siblings: low self-appreciation, diffidence, passive vital position, high or lack of self-control, early "adult status". They feel flooded with complicated emotions: anger, offence, fear of death, jealousy, guilt, sadness, abandonment, coexisting with care and concern for the sick, which leads to emotional conflict and high anxiety. In response siblings demonstrate behavior and syndromes known as defense mechanisms, or maladaptive coping: autoaggression, closeness, acting out, dependent/deviant behavior, hyperactivity or retardation, school failure, psychosomatic disorders, depression etc. Healthy siblings suffer losses which could not be openly acknowledged and mourned: parents' love and safety, confidence in the future, usual way of life etc. – up to possible loss of a cancer sibling.

Conclusions

Healthy siblings should be involved in rehabilitation programs right after cancer is diagnosed in the brother/sister. Family system therapy is the core element of rehabilitation program. Families can help their healthy children cope, sharing with them information, feelings, care for the sick, love, attention.

EP-480

**Psychosocial
REHABILITATION CAMP PROGRAM.**

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Objectives

Russian camp program has been conducted in Moscow twice a year since 2006 by ANO "Children" with scientific and methodological support from D. Rogachev Federal Research Center of Pediatric Hematology, Oncology, Immunology. The purposes are to attain psychosocial rehabilitation and adaptation of disabled children and healthy siblings, to help them overcome social deprivation, to promote the family's effective social integration.

Methods

Over 400 children aged 6 to 18 received care within the program - 20% siblings, 5% receiving maintenance chemotherapy. Our camp program is based on the following principles: siblings are accepted during hospital treatment of their brothers/sisters; there are no restrictions on the number of arrivals; when a child is 18, he (she) can work as a camp leader assistant; children are co-authors of the program; individual and group psychotherapy is the core element of camp program. Multidisciplinary specially educated team of oncologist, psychologists, art therapist, teachers and camp leaders work in the camp.

Results

Camp program for children with cancer is a highly effective rehabilitation technology in pediatric oncology. Its long-lasting rehabilitation effects depend on the several conditions: camp is not independent, but complimentary program with a city family club; children should be involved for the long period in both programs with the same staff.

Conclusions

Camp program is an essential element of rehabilitation system for children with cancer, parents, healthy siblings and the entire family. Our experience shows that permanent development of the camp program is a result of effective collaboration of a non-profit organization, parents' club, Federal Center and commercial structures.

EP-481

Psychosocial

CROSS-SECTIONAL ANALYSIS OF HEALTH-RELATED QUALITY OF LIFE IN SURVIVORS OF CHILDHOOD CANCER: A STUDY FROM TURKEY

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Objectives

To evaluate the health related quality of life (HRQoL) in Turkish childhood cancer survivors and assess the influence of demographic and medical characteristics on HRQoL.

Methods

This cross-sectional study was conducted with 76 cancer survivors whose ages were between 3 and 18 at the beginning of their treatments and their treatments were stopped at least 5 years ago and 138 healthy controls with the same characteristics in terms of age, gender and socio-economic conditions. While "Pediatric Quality of Life Inventory (PedsQL) 4.0 TM, Generic Core Scale" was used for survivors aged 8-18 years and their parents, "WHO Quality of Life-BREF Survey" was applied for the survivors over the age of 18.

Results

Comparison of total scores between survivors and controls of 8-18 age revealed lower points in HRQoL scores of survivors ($p=0.04$). Survivors who were older than 8 years at the time of diagnosis had reported significantly worse HRQoL scores ($p<0.01$) than controls. Survivors of 8-18 age group had worse scores of HRQoL in physical and social subscales ($p=0.02$ and $p<0.01$, respectively). Evaluating physical subscale, the scores of the survivors among the parameters for "walking" ($p=0.01$), "running" ($p<0.01$), "exercising" ($p<0.01$), "daily house work" ($p=0.04$) and "fatigue" ($p<0.01$) were found to be lower than those of the control group. Similarly, scores of survivor group among social parameters for "others not wanting to be friend" ($p=0.04$), "not able to do things that others can do" ($p<0.01$), "keeping up when playing with other kids" ($p=0.04$), were found to be lower than those of control group. "Working capacity" and "concentration" scores were worse in survivors who are older than 18 years old than control group ($p<0.01$ and $p=0.03$, respectively).

Conclusions

Our study provides crucial clues on the HRQoL in pediatric cancer survivors. These clues should be leading in post-treatment rehabilitations.

EP-482

Psychosocial

THE JORDAN RIVER VILLAGE: CAMP PROGRAM FOR CHILDREN WITH CANCER IN ISRAEL

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Objectives

Cancer diagnosis and treatment causes significant stress leaving the children at increased risk of psychological problems. The Jordan River village-the 14th and newest member of the Newman chain of camps is located in the Lower Galilee region of Israel and is the only camp of its kind in the Middle East.

Methods

The Jordan River village seeks to be play-land for kids with chronic illnesses in the broader Middle East and to enrich the lives of Jewish, Muslim and Christian children in the region.

Results

The village opened two years ago, 1736 children with chronic diseases came from Israel and Palestine without their parents, 296 diagnosed with cancer (19%) age 9-18 years old (mean 13 years). The staff included volunteers physicians, nurses, therapists, counselors, clowns and social workers. The program offered 24-hour medical supervision during a week of swimming and drama, sports and arts in a 61-acre setting in the Upper galilee. The children are under constant supervision, with one counselor (Arabic and Hebrew language) assigned to every two campers, attending to their needs during the day and sleeping in the same room at night, and with specially trained staff overseeing each of the daily activities. Staff doctors and nurses, as well as many volunteer medical personnel, provide the necessary medical supervision. Leading hospitals and voluntary disease-oriented organizations have partnered with the Jordan River village recognizing the importance of such a village and its benefit to thousands of children.

Conclusions

By creating free, fun- filled, memorable and medically safe camping experiences, the Jordan River village is one of the best model of therapeutic recreation programs for children with cancer giving them an opportunity for independence independently of their cultural differences.

EP-483

Psychosocial

RECENT EMPLOYMENT TREND OF CHILDHOOD CANCER SURVIVORS IN JAPAN: A CROSS-SECTIONAL SURVEY

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Objectives

Previous research has shown that some adult childhood cancer survivors (CCSs) have experienced employment difficulties. However, the actual employment status of CCSs in Japan has not been studied.

Methods

The participants were selected from the membership directory of Heart Link mutual-aid health insurance and recruited by the Childhood Cancer Patients' Network. We conducted a cross-sectional survey (a self-rated questionnaire on employment) via postal mail or an e-mail communication with a link to an Internet website. We explored the association between the characteristics of CCSs who require disability qualification and having experienced unemployment. The adjusted odds ratios (ORs) for the factors with an outcome of interest were estimated with logistic regression analysis.

Results

In total, 44 CCSs indicated that they had a disability qualification. The significant independent factors related to needing a disability qualification were late effects [OR 12.3; 95 % confidence interval (CI) 3.37–45.2], brain tumors (OR 9.55; 95 % CI 1.90–48.0), and being a high school graduate (OR 9.86; CI 2.67–36.4). The unemployment rate was 15.9 % among CCSs, excluding homemakers and students. Approximately 70 % of unemployed CCSs had some late effects and reported having experienced some job difficulties because of childhood cancer; independent factors related to unemployment were late effects (OR 6.22; 95 % CI 1.80–21.40), dropping out of school (OR 8.46; 95 % CI 1.66–43.10), and brain tumors (OR 2.73; 95 % CI 0.83–8.96). Seventy four % of the unemployed CCSs reported wanting to work if their employers understood CCSs better.

Conclusions

The unemployment rate is not high in Japan, but some CCSs need extended disability qualification. The independent factors related to unemployment were late effects and dropping out of school. Most unemployed CCSs were likely to seek work, despite their health problems.

EP-484

Psychosocial

FATHER AND SURVIVOR RETREAT: EXPLORING FATHER/SURVIVOR ROLES, COMMUNICATION AND RELATIONSHIPS IN THE AYA BRAIN TUMOR COMMUNITY

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Objectives

While research has indicated that the father's also experience increased distress levels both during treatment and in survivorship (Sloper, 2000), there have been few clinical interventions designed to address distress. The father's level of distress has a greater impact on the vulnerability a child feels than a mothers distress level has on the child (Robinson et al, 2007). Fathers of survivors are less likely to be connected to others in a similar situation than mothers. Peer mentoring and community building have been shown to reduce distress. Sloper, P. (2000). Predictors of distress in parents of children with cancer: A prospective study. *Journal of pediatric psychology, 25*(2), 79-91.

Robinson, K. E., Gerhardt, C. A., Vannatta, K., & Noll, R. B. (2007). Parent and family factors associated with child adjustment to pediatric cancer. *Journal of Pediatric Psychology, 32*(4), 400-410.

Methods

To address the relationship and communication issues for fathers and survivors, a pilot weekend intervention was explored. Father focus groups were conducted to determine program objectives, which indicated concerns around communication and age appropriate developmental markers (careers, relationships, independence). Survivors were also surveyed on interests. Both fathers and survivors indicated a desire for team building activities. Activities and discussion groups were created to meet both the researched and identified needs.

Results

Families were recruited from the tri-state area with twelve brain tumor survivors and their fathers' attending a three day retreat. Increased levels of communication between father and survivor was seen and an increase in father involvement at community events held by Children's Brain Tumor Foundation.

Conclusions

This poster will discuss program creation, implementation and outcomes of our retreat. The impact on father/survivor relationships and communication will be looked at as well as future implications and further steps to evaluate the effectiveness of this intervention.

EP-485

Psychosocial

PEDIATRIC ENHANCING CONNECTIONS: AN PARENTING INTERVENTION FOR MOTHERS OF CHILDREN WITH CANCER

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Objectives

Parents of children with cancer face incredible demands including disruption in normal functioning, anxiety, trauma, depression and other negative psychosocial outcomes. Therapeutic interventions are needed to help parents cope with the ongoing stresses and enhance their resilience in response to their child's diagnosis.

The purpose of this study was to evaluate the feasibility of adapting the Enhancing Connections program, a multi-component, manualized educational counseling program for mothers with breast cancer and their school age children to a **Pediatric** Enhancing Connections (PEC) program for mothers and children during the acute phase of the **child's** cancer diagnosis and treatment.

Methods

Qualitative in-depth semi-structured interviews were used to inquire about how the modified intervention resonates with mother's (n=7) experiences with their child's cancer. The thematic analysis of the data involved identification of common threads that represented participant's experiences. Themes were identified that describe reactions of the mothers to the intervention materials, and how they perceive the intervention as meeting the needs of their family.

Results

Results indicated a desire for support specific to the unique experience of parenting a child with cancer. Mothers described the availability of psychosocial support for their children, but a lack of support for their own emotional needs, specifically parenting concerns. Mothers described feeling guilt and lack of confidence in their parenting skills in regards to their child's illness. Mothers expressed a desire for other parents in similar situations. Finally mothers described barriers faced in relation to self care.

Conclusions

Mothers of children with cancer have clear suggestions for adaptation of this evidence-based intervention to meet their needs. Findings suggest a need for parenting interventions for mothers faced with childhood cancer.

EP-486

Psychosocial

CANCER IN CHILDREN AND THE SOCIOECONOMIC RESOURCES OF PARENTS. HOW CAN NON GOVERNMENTAL ORGANIZATIONS SUPPORT FAMILIES?

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Objectives

Cancer in children influence the entire family. Parent's work situation may be affected.

Methods

Parents of 50 children with cancer were evaluated in regard to number of siblings, the living environment, parental employment. . All hospitalization and medication of all children were reimbursed by the government.

Results

Ten families did not have a home in Istanbul. They stayed in the houses of their relatives, so that two or three families lived in the same house, most of the time having two rooms per house. Twenty families had two or more siblings. Twelve fathers did not have a regular job, they were either unemployed, or had to quit their job to care for their child. Thirty had a very low income. Most mothers were housewives. About 30 % tried to gain some income for the family by doing housework such as cleaning. All hospitalization and medication of all children were reimbursed by the government. Nevertheless, the family had extra financial needs for transportation to and from the hospital, food and clothing.

Conclusions

In addition to the psychological burden of cancer in children, poor socioeconomic resources of the family increase the burden of the family. Non governmental organizations (NGO) may provide some support for these families.

EP-487

Psychosocial

DEVELOPMENT OF PEDIATRIC PSYCHO ONCOLOGY IN AN ENVIRONMENT WITH LIMITED RESOURCES

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Objectives

In Serbia around 350 children are diagnosed with cancer yearly. Most of them are treated at the Hemato-oncology Department at The Mother and Child Health Care Institute of Serbia 'Dr Vukan Cupic' (MCHCIS). In Serbia there is no formal education program, nor hospital volunteering for psycho-oncologists. Great support in this matter is given by local Childhood Cancer Parent Organization 'Zvoncica' (CCPO), where my professional practice started from. Before my introduction to the Hemato-oncology Ward in July 2013, there were several unsuccessful attempts and during that period it is recognized that psycho-social needs of children and families were not adequately met.

Methods

Psychological support has been provided in the form of individual interviews with children and families, play therapy, medical play and psychological counseling and psychotherapy.

Results

Approximately six hundred psychological interventions were provided to approximately one hundred children in first six months. Children's and families' feedback shows that such help was necessary and that their life quality was improved during long term hospitalization and treatments.

Conclusions

Experience shows that pediatric psycho-oncology support should continue to exist. Our future efforts will be to develop and provide better professional support, to improve professional skills in order to meet children's and families psychological and social development. Our goals are: contributing to children's recovery, preserving of patient's and families mental health, helping them to get through all the challenges of cancer treatment in order to continue their lives once the hospitalization is over. With the medical staff recognition of the necessity of professional psychological support and close cooperation with CCPO, we are on the right track to achieve this.

EP-488

Psychosocial

**DEVELOPMENT AND IMPLEMENTATION OF THE PSYCHO-ONCOLOGY DEPARTMENT
IN CHILDREN CANCER HOSPITAL USING INTEGRATIVE MEDICINE:A
MULTIDISCIPLINARY APPROACH**

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Objectives

In order to meet the psychosocial needs of the pediatric population of Children Cancer Hospital, the Psycho-oncology department was started in January 2013 which included Child Life and Spiritual Counseling services.

Methods

The Psycho-oncology model of care by the Government of Western Australia, Department of Health was used as a benchmark for practice. For assessment the Distress Thermometer, Cross-Cutting Symptom Measure (DSM-5), Human Figure Drawing test and a comprehensive interview schedule are used. Tiered intervention model (Hutchison, Steginga and Dunn, 2006) is used for individual and group therapy. SPIKE protocol for delivering unpleasant information is employed. Interventions such as play, art, music assisted therapy; integrative medicine practices such as meditation, aromatherapy, reiki, touch, dream work, mindfulness based stress reduction, are used to address distress and cognitive disturbances. The legacy project was initiated to ease the dying process. Condolence visit is arranged to give emotional support to family. Child Life specialists employ art and play therapy to ensure optimum quality of life for patients. The Spiritual Counselor, trained in person-centered and cognitive behavioral therapy addresses the patients' and family's existential crises.

Results

Psychosocial care which is available throughout the cancer journey ensures better quality of life and treatment compliance from the patient through reduction of stress/distress associated with illness. Up till now more than six thousand sessions have been given by the Psycho-oncology department to patients and their families.

Conclusions

Further challenges are resource limitations which include human, space and technological; language barrier, poverty, and lack of education and awareness of the patients and their families regarding the disease and its psychosocial impact. Another challenge is the stigma associated with getting psychological help. Further training is required in the field as there is no specialization in Pakistan pertaining to Psycho-oncology.

Document not received

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Psychosocial

BENEFITS OF FUNCTIONAL ACTIVITY TOYS IN RECREATIONAL THERAPY FOR CHILDREN WITH CANCER

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Objectives

FUNctional Activity Toys positively effect the patients' quality of life when used in recreational therapy for children with cancer.

Methods

UDOO produces therapeutic play products that are also functional clothing items.

NewDo hats simulate the activity of hair styling in a fun and creative way. The fleece dreads can be braided, tied or knotted, and can be worn up or down. The hats come in four (4) different colors that mimic natural hair - blonde, brunette, red and black. A range of hair accessories can be added.

BooDo hats make it easy and fun to change and rearrange features on the hat, to express different fantasy faces.

PuppMittz are functional mittens that keep hands warm, and have four (4) different characters in each mitten. Children and caregivers can flip the mitt and flop the top, to reveal different looks and emotions. PuppMittz can tell stories, and kids can express experiences and feelings through the characters.

FUNctional Activity Toys were used in interactive, live theatre performances at BC Children's Hospital, Vancouver, Canada. FUNctional Activities were also added before and after the shows. Based on the results, UDOO PLANET LTD. created a line of FUNctional Activity products particularly suitable for Recreational Therapy.

Results

The results were very promising; the patients exhibited a high level of involvement with the product, and with their peers. The kids were delighted to play, and to act like just kids. There was a clear positive impact on children who participated; they were more engaged and felt better.

Conclusions

UDOO products were enthusiastically received by a facilitated focus group of twenty children at the BC Children's Hospital in Vancouver. Bright colors and tactile fabrics engage children and encourage creativity.

EP-490

Psychosocial

EXPERIENCES OF PARENTS OF PAEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) TWO MONTH AFTER THE COMPLETION OF TREATMENT

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Objectives

The completion of pediatric cancer treatment is considered a difficult and anxiety producing time for families. The transition from active to follow-up care is believed to be exceedingly stressful as families have spent years living with the demands and uncertainty of cancer treatment. Despite growing recognition of families' emotional stress, uncertainty, vulnerability and decrease in health related quality of life, there exists a paucity of research about parents' experiences during this crucial time. Further exploration of parents' experiences during this transition was needed. The purpose of this study was to capture the lived experiences of parents of pediatric ALL patients two months after completion of cancer therapy, with an ultimate objective of examining the need for end of treatment and post treatment supports.

Methods

This was an open exploratory study of experiences related to the child's illness and treatment, as well as lingering effects of health care experiences and treatment delivery. Qualitative methodology was employed using McCracken's in-depth interview method as well as an interview guide containing open-ended, semi-structured questions. Interviews were audio taped and transcribed verbatim. Transcriptions were entered into NVivo 9 and analyzed using the long interview method of qualitative data analysis.

Results

Findings from the analysis identified a range of themes including elation to guilt and fear of relapse. A sense of decreasing priority, an abrupt end of treatment, uncertainty, dealing with a new normal, and a lack of preparedness for transitioning from active care to follow-up were also identified. Results suggest that a greater understanding of, and sensitivity to the experiences of these families is essential.

Conclusions

The results of this study highlight the need for significant changes to the current practice for therapy completion, to better promote positive long-term psychosocial coping and adjustment. Next steps are to formulate and implement a consistent and comprehensive end of therapy plan.

EP-491

Psychosocial

THE POSITIVE IMPACT OF CANCER SURVIVORS AND THEIR MOTHERS IN PROVIDING SUPPORT TO PEDIATRIC CANCER PATIENTS AND THEIR MOTHERS

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Objectives

Research shows that mothers of pediatric cancer patients are more involved on a daily basis with their child's treatment course and therefore have more influence on how he and the rest of the family cope with the illness. (Frank et al, 2001).

Adolescents diagnosed with cancer often lose hope more easily, and a success story of a surviving peer may help improve his mental state and bring hope into his life.

Methods

The research involves qualitative questionnaires that check the positive influence of the support the mothers of children who have survived the cancer give families who are at the first stages of treatment and asks their experience, their feelings, and insights after having met the mothers of surviving children, and how it helped them deal with the ongoing treatment.

Results

Mothers in support of mothers: Up till now there were 20 individual meetings between mothers whose children have recovered and mothers whose children are receiving treatment.

Interviews with mothers of children under treatment reported satisfaction from the meetings. They felt encouraged and understood that it was possible to deal with the difficult period of treatment. They also felt the supporting mothers were able to pinpoint their weak spots and empathize with them.

Survivors in support of patients: Up till now there were 25 individual meetings between survivors and adolescent patients.

In interviews conducted with the adolescent patients they reported feelings of hope and optimism and said that listening to other success stories has given them energy to continue the battle. They felt that the survivors understood them and felt a closeness with them, even more so than with their peers.

Conclusions

The outcomes of the interviews point out that these projects are important and necessary. They promote feelings of optimism and hope among the patients.

EP-492

Psychosocial

MARITAL RESILIENCE OF PARENTAL COUPLES FACING STEM CELL TRANSPLANTATION (HSCT) IN CHILDREN WITH CANCER

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Objectives

Research on the effects of childhood cancer on the parental couple has showed conflicting results with negative and positive effects being described. In order to articulate previous results, we focus on a new model on marital resilience combining the two core elements of common couple's identity and collaborative behaviors. Such a model is necessary to help reinforce parental couples in order to support future family rehabilitation. The purpose of this study is to describe the experience of couples facing HSCT and the cancer of their child, in order to identify perceived factors of couples' resilience.

Methods

We collected cross-sectional qualitative data in twelve couples who experienced HSCT of their child following cancer. Parents were asked to talk about their couple in general and how they both reacted as a marital unit to the cancer and the HSCT of the child. Interviews were video-recorded and coded with an open coding agenda grouping concepts retrieved in previous researches on the subject, and the We-ness Coding Scale, usually used in couple therapy to measure in each partner their individual sense of identity to their couple. They also coded their sense of intimacy on the Inclusion of Other in the Self Scale.

Results

Parents identified several factors of major importance for their marital resilience, including cohesion within their couple, capacity to work as a team when facing adversity, and open communication. The results support the idea that experience of we-ness is a major predictor of resilience.

Conclusions

The importance of collaboration within well-adjusted couples, and especially the maintenance and development of communication and emotional support between parents, suggests that resilience could be encouraged. The results can be translated into a set of recommendations to apply into practice by transplantation teams to strengthen parental couples.

EP-493

Psychosocial

PSYCHOSOCIAL RISK IN BRAZILIAN FAMILIES OF CHILDREN WITH CANCER: TWO MOMENTS OF THE TREATMENT

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Objectives

Psychosocial risks associated with the cancer diagnosis must impact on adjustment of children and adolescents to the treatment, besides their future adaptation. This research aimed to describe the psychosocial risks of families of children with cancer in the moment of the diagnosis (Time 1= T1) and after two months from the beginning of the treatment (Time 2= T2).

Methods

Nine patients aged 6-12 years (M= 7,8) attending in the Onco-Hematology Service of a Children hospital in Espirito Santo, Brazil, were included in the study. Their parents provided information about psychosocial risk through the Portuguese language version of Psychosocial Assessment Tool (PAT) and about their social economic level (Brazilian Economic classification criteria). Clinical characteristics were obtained from the patient medical documents. Data were analyzed by descriptive statistics, and considering the tool standards.

Results

Most of the patients received the diagnosis of Leukemia (55.5%) and Lymphons (33.3%) and presented high risk gravity of cancer (55.5%). The socioeconomic level of the families were C2, indicating vulnerability in this aspect. The patients families maintained the psychosocial risk classifications in the levels Clinical (T1=66.7% and T2=55.6%) and Targeted (T1=22.2% and T2=44.4%), and in T2 any family exhibited the Universal classification. The subscales analysis showed that Family Problems (T1=0.50 and T2=0.35) and Problems with the Children (T1=0.50 and T2=0.40) were highlights as source of risk, but in T2 the domain of Stress Reactions showed the greated average risk (M=0.41).

Conclusions

The psychosocial risk found in T1 remained after two months, showing that these families are under the impact of cancer diagnosis even when the treatment goes on. It is recognized that these families must be assessed during the recent diagnosis and continuously over time, directing intervention proposals that promote adaptative outcomes over the cancer course and in the children's survival.

EP-494

Psychosocial

PARENTAL SUPPORT REQUIRED BY HEALTHY SIBLINGS OF PEDIATRIC CANCER PATIENTS

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Objectives

Siblings of pediatric cancer patients have a higherrisk of developing emotional problems. Especially during the patients' hospitalization,the siblings would receive less attention from their mothers. We investigate thesupport by mothers to the siblings and further identify the support required bythe siblings.

Methods

The participantswere 20 mothers of pediatric cancer patients and the patients' siblings and 11siblings. The mothers were asked to complete the support scalewhich measures how much support the mothers provided to the siblings. Thesiblings answered another support scale which measures how muchsupport they received from their mother.

Results

A chi-square test indicated that there were significant differencesbetween the mother and thesiblings about 'telling the siblings by the mother which treatmentwill work for the patient'($\chi^2=5.77, p\leq.05$)and 'going on a holiday with their mother' ($\chi^2=7.37, p\leq.05$).

Conclusions

The results suggest thatthe siblings require the information about the patient's treatment.

EP-495

Psychosocial

THE PAIN MAY BE SINGULAR, BUT THE SUFFERING IS PLURAL: A QUALITATIVE ANALYSIS OF THE IMPACT OF CHILDHOOD CANCER ON THE SENEGALESE FAMILY

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Objectives

It is assumed that the diagnosis of childhood cancer will agitate the family. We aim to explore numerous families' testimony to understand their experience and find out how they undergo it.

Methods

This is a qualitative analysis of thirty focus groups with 387 parents of hospitalized children. We address their journey before they reach the only pediatric oncology unit, the hardships during hospitalization, the strain on the family equilibrium, and we discuss the resources they mobilize to manage the cancer experience.

Results

Parents report delays in diagnosis because they have wasted time seeking traditional treatment and were not suitably referred in the medical system. They discussed the financial burden of treatment fees but mostly the struggle to balance the cost of living in the hospital with the expenses at home. Parents report feelings of powerlessness and frustration when not informed sufficiently by the medical team or when their child's health degrades. Mothers testify being distressed by the lack of understanding from their spouses or in-laws who blame them of voluntarily staying in the hospital. Regardless, parents are grateful for the quality of care and the reassuring improvement of their child's health. They also value the support from other parents and from some medical team members. Mostly, they are impressed by their own strength and the emotional resources they mobilize for their children and never knew they possessed.

Conclusions

The intrusion of cancer in a child disturbs the family's homeostasis. Parents are fragile since they are separated from their supporters, they have to reorganize their structure and mobilize sparse resources. They report a highly stressful period in which they must be resilient and perseverant to support their children when they are themselves overwhelmed and lonely. Yet they fight, for giving up on their child is never an option.

EP-496

Psychosocial

A NORDIC PLATFORM FOR CLINICAL ETHICS IN PEDIATRIC ONCOLOGY

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Objectives

The purpose of this presentation is to present the development, activities and achievements of the NOPHO/NOBOS Working Group on Ethics (WGE) 2008-2013.

Methods

A joint working group on ethics, consisting of pediatric oncology nurses and physicians, was constituted during the NOPHO/NOBOS Annual Meeting in 2008. The intention was to create a Nordic competence group addressing ethical questions within pediatric oncology. The WGE has 14 members (7 nurses and 7 physicians) with at least two representatives from each of the Nordic countries. The group meets yearly at two 1-day-meetings and one 3-day-workshop. Meetings are organizational and educational. Members are educated through international courses and conferences in clinical ethics, and are trained facilitators in moral case deliberation.

Results

All WGE members participate in, or have initiated, formalized clinical ethics projects at their pediatric departments, hospitals, regions or countries. Most clinical projects provide deliberation on ethically difficult cases on a regular basis as an integrated part of daily work in pediatric oncology. Ten members are active in local clinical ethics committees. Two members have initiated or supervise research projects on ethical matters. Two members teach ethics to nursing or medical students. One is a board member in a national society for clinical ethics.

Conclusions

To the best of our knowledge, WGE represents the first specialized working group on ethics within the framework of an international study group for pediatric oncology (NOPHO) and the first joint working group of NOPHO and NOBOS. It has proved beneficial to combine pediatric oncology nurses and physicians from different countries for this work. Through collaboration and education we have created a common Nordic platform for developing clinically applied ethics. Importantly, the WGE has inspired and enabled all members to initiate or engage actively in projects locally, regionally and nationally, thus increased the focus on clinical ethics.

EP-497

Psychosocial

CAREGIVER SELF-ADMINISTERED FINANCIAL EXPENDITURES (C-SAFE) FOR PEDIATRIC CANCER: ADAPTING AN ESTABLISHED INSTRUMENT

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Objectives

To adapt the Caregiver Self-Administered Financial Expenditures (C-SAFE) instrument for use in the pediatric cancer context. The C-SAFE will be used to measure the longitudinal financial burden among caregiver's of pediatric cancer patients and to identify the characteristics of those financial burdens.

Methods

Focus group methodology was used to evaluate the face validity and understandability of C-SAFE in pediatric cancer. 16 individuals were invited to review the current C-SAFE instrument in a face-to-face meeting. Participants included a diverse group of health care professionals and parents of children diagnosed with cancer. In advance of the focus group, participants evaluated each item with regard to importance of each item related to costs; and understandability. During the focus group, an independent facilitator worked question-by-question probing participants with regard to the essential nature of the concept, understandability, face validity and appropriate use of examples. The revised C-SAFE was provided for additional comments to participants.

Results

All 16 invited participants provided pre-meeting evaluations of the C-SAFE. A total of 9 participants attended the face-to-face meeting. The focus group responses provided clarity in three main areas: recall timeframe, concept clarity and the need for more overall explanation and specific examples. The C-SAFE was then restructured. An introduction that describes the focus of each section along with definitions used throughout was generated. Each question was revised to focus recall to the past 4 weeks. The format, wording and examples for each question were revised based on feedback.

Conclusions

Utilization of a multi-disciplinary focus group to help in the adaptation of an established instrument for a new, but unique, population provided invaluable insight. The focus group participants drove a thoughtful re-design of the instrument, ultimately resulting in an instrument that is more focused, easier to understand and provides clear instruction and examples.

EP-498

Psychosocial

MEASURING LEVELS OF MEDICAL TRAUMATIC STRESS IN PARENTS OF CHILDREN WITH CANCER WHO HAVE RECENTLY COMPLETED TREATMENT

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Objectives

The transition to off-therapy follow-up is a stressful event for parents and/or primary caregivers (henceforth referred to as parents) of children with cancer. The psychosocial needs of parents after therapy have received limited attention in the United States with only 3 published quantitative studies, the largest with 35 parents, and as a small academic center without a formal off-therapy program we wanted to investigate and address these needs. We recruited a transition care coordinator (TCC) to quantitatively screen parents at end of therapy and to develop supportive interventions.

Methods

After informed consent, a standardized questionnaire, the Psychosocial Assessment Tool (PAT) was administered to parents at therapy completion (T1) and 6 months later (T2). The TCC provided "universal" intervention to all families with an end of therapy binder containing a treatment summary, follow-up roadmaps, information on late effects, and survivor scholarships. Based on their PAT scores, some parents were provided intervention specific to symptoms (targeted intervention) or referred to a behavioral health specialist (clinical intervention).

Results

PAT was administered to 14 parents; at T1 women (n=10) scored 54% higher than men (n=4). Parents experienced worry and anxiety (71%) and sadness/depression (50%). In addition, they reported post-traumatic stress symptoms of re-experiencing (29[v1] %) and hypervigilance (36%)[v2] . A substantial proportion (29%) were found to warrant targeted or clinical intervention for psychosocial need, facilitated by the TCC.

Conclusions

This pilot study was initiated in October 2013 at a small academic center using a TCC and PAT screening tool. Emerging statistics suggest greater stress on mothers after therapy, and that a substantial proportion of parents have symptoms of PTSS after therapy. We anticipate gathering data on 40 parents to confirm these findings.

EP-499

Psychosocial

LINKING COMMUNITY RESOURCES TO SUPPORT ADHERENCE TO TREATMENT APPOINTMENTS AND REDUCE ABANDONMENT IN CHILDHOOD CANCER IN EL SALVADOR

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Objectives

Abandonment of treatment is a major cause of treatment failure and deaths for children with cancer in developing countries. Our purpose was to gain insight into reasons of Salvadoran parents for missed appointments and abandonment to be able to establish their need for support. The study formed part of a newly introduced tracking system for early detection and improvement of adherence to treatment appointments, which resulted in a substantial decrease of abandonment rates.

Methods

Nearly 500 patients who missed one or more appointment were tracked and qualitative data were gathered through 374 interviews varying from short phone conversations to semi-structured interviews at the hospital.

Results

Most of the reasons for absences were practical, and local resources such as health clinics and municipalities in the patient's community were contacted, to assist in supporting the families to adhere to treatment. This consisted mostly of money or transportation for attending appointments. This confirms that parents' decision making is not only dependent on medical considerations regarding risks and benefits of the treatment, but also on practical resources. We also asked parents' experience of the support they received. Their answers suggest the added importance of socio-emotional benefits of both the tracking and the interventions resulting from it. Giving practical support in the direct daily environment of patients reduced feelings of isolation and helplessness and thus had a positive influence on the predisposition of parents towards the treatment of their children.

Conclusions

The hospital can reach the patients' community and have an impact on decisions about treatment by putting together resources ready to be used in the patients' daily environment. The participation of community institutions brought economic relief to the families and to the cancer program. We propose that unexpected social emotional benefits helped enhance the effects of the intervention.

EP-500

Psychosocial

IN THEIR OWN WORDS: AN ANALYSIS OF WEBLOGS POSTED BY PARENTS OF CHILDREN WITH CANCER

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Objectives

To identify psycho-educational needs of parents of children with cancer distilled naturalistically from blogs posted on the Internet.

Methods

Blog posts were identified using StoryUpgrade, a program that searches weblog posts using a fictional prototype story. We sought posts from 3 time points: diagnosis, active treatment, and after treatment completion. Using the Family Adjustment and Adaptation Response (FAAR) model as a conceptual framework, a team of 3 content experts independently reviewed blog entries, coding them into themes/sub-themes. Reviewers' coding differences were resolved through discussion to achieve consensus.

Results

Through analysis of 90 posts on 40 blogs, key themes previously identified in focus groups and structured interviews (Patterson et al. 2004; Miedema et al. 2010) were verified. Strains most often noted were illness related to treatment (*cancer-related*), strong emotions and loss of normal life/activities (*child*), strong emotions and loss of normal family life (*family*).

Resources most frequently mentioned were child's strengths (*child*), religious beliefs, parental competence and extended family support (*family*), support from parents' friends/co-workers (*community*), competent/caring doctors and support from nurses/social workers (*health care system*). Coping strategies most often cited were being positive/maintaining hope, religious faith, pride in child/strength from child, and living and focusing on the present (*appraisal-focused*); being normal/seeking normality, balancing family needs, advocating for child, being organized/planning ahead, seeking information about cancer (*problem-focused*); and humor/fun/celebrating, seeking/giving support (*emotion-focused*). Blog analysis also discovered several themes not previously identified: cancer-related pain (strains); gratitude, altruism (coping); and general community support, tangible support (resources).

Conclusions

Weblog analysis yielded confirmatory and new evidence of parents' psycho-educational needs, supporting use of the Internet for such research. Findings may be useful in guiding clinical care and fostering access to vetted e-health resources (e.g., searchHOPE.chla.org) based on parents' collective lived wisdom.

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EP-501

Psychosocial

EXPERIENCE OF USING SICK CARD AND OTHER PATIENT EDUCATION MATERIAL TO IMPROVE OUTCOME OF CHILDHOOD CANCERS

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Objectives

Parents of children undergoing treatment for childhood cancers are under stress and extreme anxiety. Many of them are from distant places. The aim was to provide details of disease, side effects of treatment, information on care of children with cancer, opportunities available from government and non governmental sources for treatment to the families. We have also constructed a sick card which carries all information regarding the patient's disease, the medications for common ailments with doses and first line management for febrile neutropenia. This is made in the local language too besides English.

Methods

A questionnaire to 25 parents was provided based to assess their understanding of the patient education material

Results

Parents were aware of various forms of patient education materials prepared for them. Details of them will be provided. This helped in their ability to understand disease better. Details of various laboratories and investigation rooms will be provided. They found the sick card particularly useful as it carries information of intravenous drugs that may be used as first line treatment for febrile neutropenia, out telephone contact number, e mail of the support group that is made for parents of children undergoing cancer treatment. Details of support group 'Sambhav' will be discussed

Conclusions

Patient education material plays an important role towards improved treatment outcomes
Document not received

EP-502

Psychosocial

CAMP TRILLIUM – CANCER CAMP FOR CHILDREN WITH CANCER AND THEIR FAMILIES IN ONTARIO, CANADA

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Objectives

For over 30 years Camp Trillium has been providing camp experiences for children with cancer and their families. Both summer and year-round camping programs are very popular for children with cancer and their families in Ontario. Recent findings suggest camping programs help children and families cope with childhood cancer and help improve quality of life.

We aim to describe the scope of the programs and number of campers attending the programs offered by Camp Trillium and to increase the awareness of its existence. Camp Trillium has been considered a leader in oncology camping and has been actively involved in collaborating with national and international programs to enhance the cancer camp experience.

Methods

A qualitative approach was taken including: gathering historical and current documents about Camp Trillium and interviewing current staff and board members of Camp Trillium.

Results

In the summer of 2013, 587 families participated in camp programs. Of these families 24% of were on active cancer treatment, 68% were off cancer treatment and 8% were bereaved families. Camp Trillium works with all 5 pediatric treatment centres. Of the 587 summer families in 2013 38% were patients at the Hospital for Sick Kids in Toronto, 17% were patients of Children's Hospital of Western Ontario, London, 18% from McMaster Children's Hospital, Hamilton, 18% from the Children's Hospital of Eastern Ontario, Ottawa, 7% from Kingston Regional Cancer Centre, Kingston and 2% unknown clinics. Interactions with board of directors and year staff conclude that the mission of Camp Trillium has demonstrated positive impacts to families of children with cancer.

Conclusions

This abstract aims to raise awareness of Camp Trillium and oncology camping programs which supports children with cancer and their families.

EP-503

Psychosocial

A CANADIAN MODEL: THE CANCER CAMP MOVEMENT – NATIONAL COLLABORATION OF ONCOLOGY CAMP BEST PRACTICES

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Objectives

The Canadian Association of Pediatric Oncology Camps, was formed in 2006 to ensure that the cancer camps pediatric oncologists were referring their patients to were safe. The clinic directors from across Canada (C17) encouraged leaders in cancer camps to examine all oncology camp programs in Canada. As a result a set of guidelines were adopted and developed as a baseline for best and standard practice. The implementation of an annual standards review process has led 13 member camps across Canada being given the Gold Star for practicing at the highest level.

We aim to describe the evolution and role of the Canadian Association of Pediatric Oncology Camps (CAPOC) and to increase the awareness of its existence and need for best practices in camping programs.

Methods

A qualitative approach was taken including: gathering historical and current documents about CAPOC and interviewing current board members of CAPOC.

Results

Together with its board of directors, medical committee, CAPOC has worked to develop a comprehensive set of guidelines for oncology camps. Several resources and networking opportunities already exist including peer – peer visits that occur every three years resulting in Gold Star Membership. These visits allow other members to see camp in action, to share ideas and verify the camps commitment to safe camp operations.

Conclusions

This abstract aims to raise awareness of CAPOC and therefore, enable future work around the development of pediatric oncology camping guidelines, resources and sharing of best practices world-wide. The oncology camper requires attention and expert knowledge about their needs, prior to, during and after the camp experience. The safest cancer camps consider the medical and psychosocial supervision and supplies that are needed to care for a sick child, as well as the meeting or exceeding of the provincial camp standards to ensure camp contributes to a positive experience for the child.

EP-504

Psychosocial

ADDRESSING THE PSYCHOSOCIAL NEEDS OF THE HOSPITALIZED CHILD: THE ROLE OF THE CHILD LIFE PROGRAM

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Objectives

Kythe Foundation Inc., a Philippine based organization, established hospital-based child life programs (CLP) to address the psychosocial needs of chronically ill patients, providing developmentally appropriate interventions that minimize the stress and anxiety experienced and assuring continued optimal growth and development. Kythe undertook this study to look into the role the CLP plays in lowering the negative emotions experienced by chronically ill children.

Methods

The study was conducted at the Hematology and Oncology Department of the Philippine Children's Medical Center that adapted the CLP in December 2012. As evidence of the value of the CLP, children's drawings through the Child Drawing: Hospital (Clatworthy, 1999), an instrument designed to measure the emotional status of hospitalized children, were obtained from 30 hema-onco pediatric patients, ages 6-13 years old, prior to the implementation of the CLP. The same instrument was administered six months into the implementation of the CLP to ascertain whether changes in the children's drawings were seen. A statistician was hired to analyze the data.

Results

Results show a significant difference in the scores between the pretest and posttest drawings, indicating an alleviation of the negative emotions experienced by the children.

Conclusions

Child life programs are integral in the hospital setting as these focus on the social and emotional impact of illness and hospitalization on children and strive to promote a positive hospital experience for them. The goal is to minimize the stress and anxiety as much as possible and to provide an environment where children can gain a better understanding of the hospital, their illness and medical treatment.

EP-505

Psychosocial

WORKING WITH TEENAGERS AND YOUNG ADULTS (TYA) WITH CANCER TO DEVELOP BETTER APPROACHES TO CARE: A CO-CREATION APPROACH

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Objectives

Service user questionnaires, used for clinical service evaluation/improvement, often represent the knowledge/insights of professionals who construct them. Responsibility for solutions also tends to lie with professionals so that services are re-designed around, rather than with patients. Co-creation methodology shifts the focus from professionals delivering care to one in which patients become central not only to the re-design of services but also in continuous development, to co-create better health experiences/outcomes. The likely success of this approach in a TYA population was unknown.

Methods

A convenience sample of patients attending a regional TYA centre was invited to participate in exploratory work based around the development of a patient questionnaire: 27 expressed interest and 7(26%) fully engaged. A combination of techniques (1:1 interviews, email exchanges, focus group) was used over a period of several months to ascertain views about the construction of a questionnaire (content, design/face validity, communication preferences) for distribution to a larger patient cohort. Respondent validation ensured congruence between team records and patient experience/perspective.

Results

Unanimous agreement was reached about areas for inclusion: Physical wellbeing/health; Peer support; Information provision; Psychological/emotional support; Family/friends; Education/employment; Education/training about TYA cancer for others; along with design suggestions and ideas for ongoing communication with TYA patients. The questionnaire was subsequently distributed to 108 TYA patients with whom the team had had no prior contact: 42/108(39%) were returned; 28/42(66%) indicated an interest in continuing to work with the team.

Conclusions

Using co-creation, patients engaged creatively in the development of a TYA friendly questionnaire with satisfactory response rates. Subsequent work has involved TYA in prioritising themes for service development interventions based on the questionnaire findings. Their participation has included: agreeing content and delivery of wellbeing days; selection of mentors for a work mentoring programme; and defining content, design and functionality of a psychological support website.

EP-506

Psychosocial

BENEFIT-FINDING IN ADOLESCENTS WITH CANCER: A SIX MONTHS FOLLOW-UP STUDY DURING THE FIRST YEAR AFTER DIAGNOSIS

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Objectives

Despite the fact that benefit-finding (BF) has been promoted as one of the potential mechanisms underlying resilience in adjustment to pediatric oncology, few studies have examined BF in youth with cancer. Furthermore, research on BF during the early phase of the cancer trajectory is almost absent. This study aimed to investigate (1) the temporal dynamics (time of onset, pattern of change over time), and (2) impact of BF on psychological outcomes in adolescents with cancer during the first year post-diagnosis.

Methods

Thirty-three newly diagnosed adolescents with cancer (mean age=14.1, SD=1.7; 55% female; all types of cancer; 88% >60% chance of survival) completed measures of BF, anxiety, depression and quality of life at 6 and 12 months post-diagnosis.

Results

Six months post-diagnosis (T1) all adolescents experienced BF at least to some degree. BF at T1 ($M=34.5$, $SD= 5.5$) did not differ significantly from BF at 6 months follow-up (T2) ($M=35.2$, $SD= 6.7$, $t(29)=0.64$, $p<.05$). BF at T1 was significantly positively associated with the physical functioning quality of life subscale at T1 and T2, but not with anxiety, depression or other aspects of quality of life. BF at T2 was unrelated to all outcomes (all p 's>.05).

Conclusions

The finding that patients report a similarly high level of BF at both assessment points suggest that BF already occurs within the first 6 months after diagnosis. Future research with a longer follow-up should determine whether levels of BF remains stable or decrease during the (long-term) survival phase. BF was not associated with any of the psychological outcomes measured in this study. Thus, the question whether BF is adaptive for youth with cancer requires further investigation.

EP-507

Psychosocial

PREDICTORS OF BACTERIAL INFECTION AMONG PEDIATRIC CANCER PATIENTS AND SINGLE CENTER EXPERIENCE

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Objectives

Children with cancer undergoing chemotherapy develop many common complications. A bacterial infection (BI), especially blood stream infection (BSI) is usually commonly observed during treatment course. Presentation can be different from case to case, with or without neutropenia, fever and clinical signs of sepsis.

Methods

We conducted a prospective, single-center study to identify predictors for invasive bacterial infection or culture negative sepsis in children cancer patients in Slovakia. There were enrolled 140 patients who met inclusion criteria. It was taken sample for investigation of bacterial inflammation e.g. IL-6, IL-10, TNF alpha, procalcitonin, C-reactive protein and presepsin. Independent predictors at clinical presentation were analyzed using multiple regression models.

Results

Patient's median age was 7.24 years; 62% had an underlying diagnosis of leukemia. Independent predictors of bacterial infection were ANC less than 500, temperature at presentation $\geq 39.0^{\circ}\text{C}$, central venous catheter insertion and underlying diagnosis of ALL. All markers except CRP and procalcitonin correlated with predicting of bacterial infection. The highest values were observed among those who developed blood stream infection or serious bacterial invasive infection. More common were hospital-acquired infection (83%).

Conclusions

This study identifies predictors of infection/complications and confirmed predictive value of new markers in pediatric patients with bacterial infection. This work highlights the importance of the new inflammation markers which can be successfully used in different cancer pediatric patients. These prediction models warrant prospective validation.

EP-508

Psychosocial

EXPLORATION OF THE PSYCHOSOCIAL ASPECTS OF PAEDIATRIC ONCOLOGY: A QUALITATIVE STUDY OF THE PSYCHOLOGICAL, SOCIAL AND EMOTIONAL EXPERIENCES OF PATIENTS WITH PAEDIATRIC CANCER IN SINGAPORE

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Objectives

Acute lymphoblastic leukemia (ALL) – the commonest childhood cancer – had dismal 10-20% survival rates in the 1960s. However, with extensive biomedical advances, >90% now enter complete remission and 80-90% are cured. Yet, with countless physical, emotional and psychosocial implications of childhood cancer, the question of whether quality matches up to quantity of life remains unanswered. This study aims to identify, collate, analyze and classify significant psychosocial issues from patients to improve the holistic care, patient-family education, and lay down a good foundation for further research.

Methods

17 semi-structured 1-3-hour-long interviews were done with 17 pairs of caregiver and patient. Interviews were kept open-ended and conversational using Seidman interviewing techniques. Audio-recordings were transcribed and analyzed using Smith's interpretative phenomenological analysis (IPA). All subjects had no relapses/transplants, and were under Ma-Spore ALL 2010 protocol.

Results

An organized over-arching hierarchy was conceptualized to logically encompass the wide-range of psychosocial issues raised by subjects. Out of many themes and subthemes, significant ones were: Adverse impact on academic pursuits; Deteriorating relationships with peers and siblings; Fear of medical settings, personnel and procedures attributable to impressions from caregiver and healthcare professionals; and Increased maturity of child.

Conclusions

Important psychosocial issues highlighted by this study will help guide healthcare professionals in providing psychosocial care to patients and caregivers. Further research could delve deeper into reasons and ramifications of these issues, and their exact significance to quantifiable health-related quality of life.

EP-509

Psychosocial

**DECISION-MAKING FOR CHILDREN FOLLOWING A CANCER DIAGNOSIS–
PRELIMINARY FINDINGS FROM A QUALITATIVE STUDY WITH PARENTS AND
ONCOLOGISTS**

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Objectives

To investigate decision making processes for children undergoing curative cancer treatment from the perspective of parents and oncologists.

Methods

Semi-structured interviews were conducted separately with 12 dyads of parents and oncologists in Switzerland and Romania. The study was approved by Research Ethics Committees in both countries and written informed consent was obtained from each participant before starting the interview. Participants were asked to discuss their experiences at the time of their child's cancer diagnosis and treatment. Interviews were transcribed verbatim and thematic coding with MAXQDA was used to elicit major topics.

Results

Parents describe the time of their child's diagnosis as overwhelming and catastrophic. They identify a myriad of constraints that limit their ability to make decisions regarding treatment: their lack of medical knowledge and understanding, time pressure, unfamiliarity with the hospital setting, information overload, and emotional turmoil. Hence most of the time they follow physicians' lead in decision making but feel equally responsible for the decision. Parents highlight a loss of control that is somewhat regained by focusing on starting treatment immediately. Physicians report to grapple with this need by gearing discussions towards starting treatment while also customizing information to parents' reactions. In interactions with parents, physicians tend to seek compliance to treatment which they perceive as following the best interest of the child.

Conclusions

Decision making in pediatric oncology around the time of diagnosis is a complex and partially understood process. A better understanding of parents' needs in these difficult situations can facilitate communication at diagnosis and address constraining factors impinging on decision making.

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Psychosocial

PERCEPTIONS OF YOUNG ADULTS WITH CANCER OF THE "VENTURING OUT PACK PROGRAM" AS A SOURCE OF TANGIBLE SUPPORT

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Objectives

Within the cancer community, young adults (YAs) with cancer have been increasingly recognized as a distinct group with unmet supportive care needs. 'Venturing Out Beyond Our Cancer' is a non-profit community agency committed to providing YAs with tangible support services to address their cancer-related needs. One of these services, called the 'Venturing Out Pack (Vo-Pak) Program', provides backpacks containing three resource kits to help YAs throughout their cancer journey. The study objectives were to: (a) explore the needs of YAs newly diagnosed with cancer; (b) discuss with them the extent to which Vo-Pak helps them meet their practical, psychosocial and informational needs; and (c) explore with them how the Vo-Pak could be further enhanced.

Methods

A qualitative descriptive study was conducted with a purposive sample of 12 YAs treated for cancer at a university-affiliated tertiary hospital in Montreal, Quebec, Canada. One-time, audio-recorded, semi-structured interviews were conducted, transcribed, coded and thematically analyzed.

Results

Overall, YAs positively perceived the Vo-Pak as a welcoming, ready-to-use, timely package to meet their cancer-related needs. The Hospital Comfort Kit was seen as a 'hands on' resource that helped in comforting them during their hospital stay. The Venturing Out Kit was viewed as a catalyst for connecting with similar others and offering them 'guilt-free' complimentary outings. The Friends of Lara Information Kit was commended for its relevance as a dispatcher to important support resources. Participants recommended delivery of the Vo-Pak two month after diagnosis and broader awareness and dissemination of the program.

Conclusions

Enhancing the Vo-Pak program by increasing awareness and promoting networking among YAs with cancer is critical in meeting their needs. More systematic dissemination of programs such as this one would add to the overarching goal of providing comprehensive person-centered cancer care to an underserved segment of the cancer population.

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Psychosocial

EXISTENTIAL ANXIETY AND GROWTH IN CHILDREN WITH CANCER

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Objectives

To date, there has been minimal research that details the experience of children diagnosed with cancer in their existential predicament. The purpose of this presentation is to describe findings that speak to the existential challenges experienced by children living with cancer.

Methods

An interpretive, descriptive qualitative research design was used. Thirteen children (8-17 years) undergoing treatment for cancer participated in the study. Two main sources of data collection were utilized. First, children had the opportunity to journal their experiences via a computer diary created by the first author. Additionally, the computer diary had a drawing tool for children to express how they were feeling. The second source of data involved children taking part in open-ended individual interviews. Data analysis occurred concurrently with data collection using the constant comparative method of data analysis.

Results

Within the cancer world children moved between feelings of anxiety (generated by existential worry, existential longing, and the existential vacuum) and existential growth. As children worked within the drawing tool, a portal to their inner worlds was opened, which allowed them to explore their anxiety through drawings. In many of the children's drawings the intimate connection between the physical symptoms and the emotions that defined their existential challenges were clearly evident. connection between the physical symptoms and the emotions that defined their existential challenges were clearly evident.

Conclusions

This research provides evidence that the active engagement of children's imaginations through the use of a computer-drawing tool may have significant therapeutic value for assisting children with cancer to explore, understand, and manage their physical suffering, as well as the associated anxiety they live with. The use of symbolic forms of communication including drawing, offer health-care professionals new possibilities for enhancing the therapeutic conversations and interactions they have with ill children and their families.

EP-512

Rare Tumours

CASE REPORT OF MALIGNANT SMALL ROUND CELL TUMOUR OF UNKNOWN HISTOGENESIS : A DIAGNOSTIC DILEMMA

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Objectives

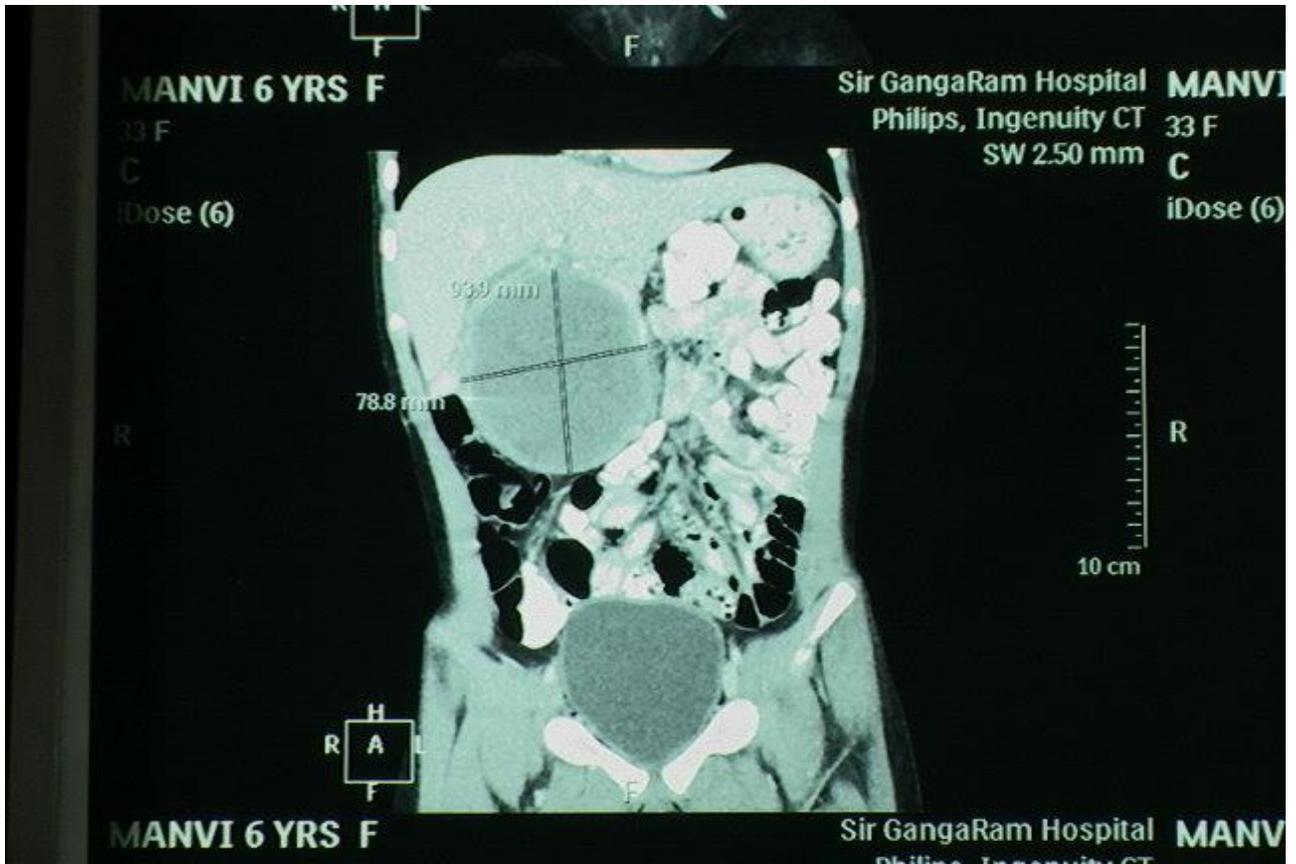
Malignant small round cell tumors with extensive necrosis such that its histogenesis could not be delineated are rare lesions which have occasionally been reported from India. The exact incidence, etiology and histogenesis of such tumors are unknown because of its rarity

Methods

We report a patient of abdominal mass in whom despite a comprehensive evaluation no tumor defining histopathologic, immunocytochemical, ultrastructural, cytogenetic, features could be identified.

Results

A 6 years old girl presented with fever- 6 days duration and a mass per abdomen-4 days with difficulty in breathing-1 day. USG showed a large retroperitoneal heterogeneous mass lesion with areas of hypoechogenicity suggestive of necrosis. CECT showed a hypo-dense mass in C loop of duodenum, head of the pancreas not defined from the lesion. For further evaluation PET scan was done, revealed a large lobulated FDG avid peripherally enhancing solid cystic mass lesion with hyper-dense areas suggestive of hemorrhage, abutting the liver, gall bladder and duodenum. She underwent exploratory laparotomy, frozen sections on histopathology were found to be necrosed and no viable tumor cells were available for reporting. Repeated attempts to obtain the tissue also revealed only necrotic tissue, which was verified at multiple centers in INDIA. IHC - low Ki 67 activity and negative for LCA, Synaptophysin, CD 99, MPO, CK and PLAP. She was given VAC regimen following which the tumor shrunk in size making it amenable for surgical resection. She underwent Whipple's procedure (Isolated loop) which again revealed extensive ischemic necrosis with outlines of round cell tumor. However the patient is stable without recurrence on 6 months of follow up.



Conclusions

This diagnostic nightmare due to non availability of viable tumour was a peculiar finding in our case. However she responded to standard treatment modality. The exact nature of the tumor is still a mystery and can be a spectrum of yet unidentified category of tumors.

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Rare Tumours

SYSTEMIC SYMPTOMS OF ANGIOMATOID FIBROUS HISTIOCYTOMA ARE CAUSED BY EWS-CREB1 FUSION-INDUCED EXCESSIVE IL-6 PRODUCTION

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Objectives

Angiomatoid fibrous histiocytoma (AFH), a rare soft tissue neoplasm with intermediate biologic potential, often arises in the extremities of children and young adults. However, the etiopathogenesis of AFH remains unclear. In this study we describe a 7-year-old Japanese girl with a tumor of the left upper extremity which appeared on magnetic resonance imaging as a heterogenous lobulated mass (low intensity on T1-weighted images, high intensity on T2-weighted images, and low enhancement with contrast) measuring 55 x 41 x 28 mm. Moreover, the patient had systemic symptoms such as weight loss continued intermittent fever. Laboratory data showed anemia, thrombocytosis, and high level of inflammatory reactive markers. After complete resection of the tumor, both the patient's general condition and the laboratory data markedly improved. We studied the molecular etiopathogenesis of AFH.

Methods

The resected tumor was studied immunopathologically and molecular genetically. Blood samples obtained before and after the operation were subjected to cytokine analysis by using Bio-Plex multiplex assay (Bio-Rad laboratories).

Results

The tumor was diagnosed as an AFH on the basis of pathological findings and *EWS-CREB1* fusion gene detected with fluorescent in-situ hybridization and reverse-transcriptase polymerase chain reaction (RT-PCR). Direct sequencing of the RT-PCR-amplified product showed that exon 7 of the *EWS* gene was fused on exon 7 of the *CREB1* gene. The cytokine profiles of serum samples demonstrated postoperative decreases in interleukin-6 (IL-6), MIP-3a (CCL20) and the chemokine superfamily fractalkine. Immunopathological study showed that the resected AFH cells were positive for IL-6 and phosphorylated STAT3 (Tyr705).

Conclusions

The *EWS-CREB1* fusion gene leads to continuous activation of the *CREB1* gene, resulting in IL-6 production. Excessive production of IL-6 might play a pivotal role in the etiopathogenesis of AFH. Our results, therefore, provide the rationale for the development of IL-6 target therapies for AFH.

EP-514

Rare Tumours

OLFACTORY NEUROBLASTOMA IN CHILDHOOD

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Objectives

Olfactory neuroblastoma (esthesioneuroblastoma) is a rare, slow growing and locally aggressive tumor derived from olfactory neuroepithelial tissue. Symptoms are not prominent before tumor reaching bigger size. Total surgical resection is the mainstay of the treatment. But literature supports the combined treatment approaches with surgery, neoadjuvant chemotherapy and radiotherapy. In this study, it was aimed to evaluate clinical characteristics and treatment results of patients diagnosed with olfactory neuroblastoma in our department.

Methods

Olfactory neuroblastoma (esthesioneuroblastoma) is a rare, slow growing and locally aggressive tumor derived from olfactory neuroepithelial tissue. Symptoms are not prominent before tumor reaching bigger size. Total surgical resection is the mainstay of the treatment. But literature supports the combined treatment approaches with surgery, neoadjuvant chemotherapy and radiotherapy. In this study, it was aimed to evaluate clinical characteristics and treatment results of patients diagnosed with olfactory neuroblastoma in our department.

Results

Three patients aged 3, 9 and 13 were diagnosed as olfactory neuroblastoma. All had nasal obstruction at diagnosis. All three tumors were at sinonasal region. Bone destruction, intracranial or intraorbital extension was also present. Patients had stage III disease according to Kadish staging system. Endoscopic tumor excision was performed in 2 patients after neoadjuvant chemotherapy. First patients died due to metastatic disease. Second patient have been followed up in remission for 3 years. Third patient had craniotomy and partial tumor excision craniotomy adjuvant radiotherapy and chemotherapy for third patient; he has been followed up in remission for 6 years.

Conclusions

The best treatment approach is surgery in olfactory neuroblastoma however it is difficult to perform total resection because of the tumor localization. Literature supports the chemosensitivity of the tumor. Combining surgery with neoadjuvant chemotherapy and radiotherapy might increase the resectability and outcome.

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Rare Tumours

HISTIOCYTIC SARCOMA IN A 15 MONTHS-OLD FEMALE: A CASE REPORT

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Objectives

Histiocytic sarcoma (HS) is an exceedingly rare tumor especially in children and an aggressive malignant neoplasm showing morphologic and immunophenotypic evidence of histiocytic differentiation. The vast majority of previously reported HSs are recognized to be initial misdiagnosis.

Methods

We describe a pediatric patient with HS who presented with lymphadenopathies and pulmonary nodules. Her tumor progressed during chemotherapy designed for Langerhans' cell histiocytosis (LCH) and sarcoma.

Results

A healthy 15 months-old girl experienced isolated fibroelastic lymph nodes in the left inguinal region. Most lymph nodes measured less 10 mm, the largest measuring 27 by 21 mm. A biopsy was made and the results were suggestive of LCH. Node volume quickly increased and evolved to a large vascularized swelling bleeding on contact. LCH-based therapy was started. Because her condition was deteriorating a new biopsy was performed.

Morphological and immunohistochemical alterations were compatible with HS.

Immunophenotyping confirmed the histiocytic lineage by positive expressions of the CD 163, CD68 and lysozyme, and negative for CD1a, CD3, CD20, CD30, and Melan A, EMA, ALK.

Chemotherapy according to MMT98 sarcoma protocol was started. Under treatment CT scan showed evolution with mediastinal lymph nodes and pulmonary nodules. Because of disease spread and poor response to therapy the patient received ICE chemotherapy. Condition deteriorated and the child died.

Conclusions

Few reports of bona fide HS exist, mostly involving adults. We describe an unusual clinical presentation. The diagnosis is mainly based on immunohistochemical techniques and on molecular genetic methods excluding other malignancies with epithelial, melanocytic and lymphoid phenotypes. Poor prognosis is a common finding (because of disease spread and poor response to therapy). We report a similar poor response to LCH- and sarcoma-based chemotherapy. The rarity of HS continues to make its management and recommended therapy challenging for young children.

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Rare Tumours

MALIGNANT SOLID TUMORS IN CHILDREN WITH DOWN SYNDROME: REPORT OF THREE CASES AND DISCUSSION

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Objectives

Children with Down syndrome (DS) have decreased incidence of solid tumors. We report three patients, two with rhabdomyosarcoma and one with periosteal osteosarcoma.

Methods

Description of three recent cases with DS seen at SOLCA Hospital: AE, a 5 years-old boy with trisomy 21 and metastatic embryonal rhabdomyosarcoma in relapse, referred from another hospital two years after diagnosis. He had a history of hematuria and a bladder tumor; received chemotherapy and relapsed during treatment. In our hospital we found pelvic and bladder tumors, pulmonary and hepatic metastasis. He received second-line chemotherapy, developed renal failure and tumor progression, and went into palliative care.

AM is an 18 months-old boy with DS and agenesis of the right kidney. He presented at 13 months of age with pedunculated perianal lesions, the largest was 9 x 6 cm in diameter. He also had inguinal metastasis. The biopsies confirmed an embryonal rhabdomyosarcoma. He is undergoing chemotherapy with frequent infectious complications.

YN, 12 years-old girl with DS and a 24 months history of a slowly growing left tibial mass. MRI of left leg showed a 13 x 5.4 cm tumor with soft tissue involvement. CT scan of thorax disclosed multiple metastasis. Bone biopsy was diagnostic of periosteal osteosarcoma. She received two cycles of cisplatin and doxorubicin with resolution of lung metastasis. Local therapy was not accepted by the parents and abandoned therapy.

Results

Occurrence of solid tumors, specifically rhabdomyosarcoma and osteosarcoma, is very unusual in patients with DS. Only few reports of embryonal and bone tumors have been recorded in the medical literature

Conclusions

It is speculated that tumor suppressor genes, increased levels of S-100 b protein and decreased hormone and endostatin serum levels protect children with DS against solid tumors. Treatment related toxicity constitutes a formidable challenge in these cases.

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Rare Tumours

BILIARY RHABDOMYOSARCOMA, A RARE TUMOR IN CHILDHOOD - A CASE REPORT

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Objectives

Rhabdomyosarcoma is a malignant tumor of mesenchymal origin, most often occurs in children and adolescents, corresponding to 4% of cancers in children. Common sites are the head and neck, genitourinary tract and retroperitoneum. Biliary location is rare (0.8%), but is the most common cause of malignant obstructive jaundice in this age group. The average age of presentation is 3 years. They can present obstructive jaundice in 60-80% of cases and they can be accompanied by fecal acholia and hepatomegaly. Pain, nausea, vomiting and fever are uncommon. The histology of the biliary tract is only the embryonic type. Current treatment includes surgical resection, radiotherapy and chemotherapy, usually a highly chemosensitive tumor and commonly used medications are: actinomycin , vincristine , cyclophosphamide or ifosfamide with or without doxorubicin.

Methods

Because of this rarity we report the case of a child, male, 2 years and 11 months old, who was admitted to abdominal distension , jaundice, acholic stools, choluria and hepatomegaly . With hyperbilirubinemia, elevated liver enzymes, negative hepatitis serology and normal Alpha-fetoprotein. Abdominal ultrasound and TC scan of the abdomen showed a large mass liver heterogeneous, well-defined limits, located on segments III, IVa, IVb, V and VIII, involving portals and hepatic vessels, causing mild dilatation of bile ducts, measuring 7.0 x 8 6 x 5.9 cm. Percutaneous biopsy and histological examination showed biliary embryonal rhabdomyosarcoma. Immunohistochemical examination positive vimentin, Alfa1T, S100, HHF35, desmin, myogenin and C99 confirmed the diagnosis.

Results

Chemotherapy with vincristine, actinomycin and cyclophosphamide was made. After week 5 patient developed progression of disease, even with chemotherapy rescue with irinotecan and vincristine the tumor was refractory and the patient died.

Conclusions

In conclusion, our patient had an unfavorable outcome compared to the few reports in the literature.

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Rare Tumours

CERVICAL SPINE RHABDOID TUMOR : CASE REPORT AND LITERATURE REVIEW

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Objectives

To report a retrospective case of an atypical spinal malignant rhabdoid tumor (MRT) in a 14 years old girl .

Methods

A retrospective case report of spinal pediatric rhabdoid tumor (SPRT) in a 14 years old girl with a family past history of a first degree consanguineous marriage.

Results

The patient presented first with cervicobrachial neuralgia that rapidly progressed into tetraparesis .The MRI showed a right latero-vertebral tumor localized in the right scalenus lodge at the level of C5 , with vertebral invasion and spinal canal extension. Surgery was performed with residual disease .

In immunohistochemistry , the tumor cells were positive for EMA ,Pan CK , vimentin ,CD99 and NSE, and negative for LCA , desmin and myogenin. INI1 was not practiced (not available) .

Despite postoperative radiotherapy followed by chemotherapy ,we only obtained the stabilization of the tumor then the patient died 11 months after initial diagnosis .

Conclusions

This is in our knowledge the 8th case of PSRT . The prognosis remains poor . More cases are needed to determine effective treatment .

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Rare Tumours

SUCCESSFUL LONG-TERM USE OF SORAFENIB IN PROGRESSIVE PULMONARY METASTASES IN PEDIATRIC PAPILLARY THYROID CARCINOMA

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Objectives

Sorafenib has been studied in adult patients with advanced thyroid cancer and prolonged their progressive-free survival. Reports on the use of this substance in the pediatric population are scarce.

Our objective is to present a young girl with progressive pulmonary metastases due to RAI-resistant PTC who achieved stable disease with few side-effects with long-term use (3 years so far) of Sorafenib in the adult dose (2 x 400 mg).

Methods

A twelve year old girl had been diagnosed with PTC 6 years previously. (TNM 2002) pT3N1bM1(pul). She underwent thyroidectomy, neck dissection, and 8 courses of radioactive iodine, the final 3 courses after retinoids. But pulmonary metastases progressed, thyroglobulin increased and signs of pulmonary insufficiency developed. Off-label use of Sorafenib was initiated in 5/2011, 200 mg once daily and step-wise increased to twice 400 mg after 6 months. Hematologic side-effects were minimal, also cutaneous side-effects were mild (grade 1 hand/foot syndrome). Due to cramping, diarrhea and weight loss, therapy was decreased to once daily 400 mg after a year and increased again to the full dose after 5 months. Thereafter minor reductions of the dose were necessary for a further few months, but for one year now the patient has tolerated the full dose of 2x 400 mg with hardly any side-effects. Thyrotropin-suppressive therapy, calcium and calcitriol therapy were continued as before.

Results

One month after initiation of sorafenib the extensive pulmonary metastases showed a mild reduction, thereafter no further decline was observed with MRI and CT, but also no progression. Thyroglobulin levels and thyroglobulin antibodies have remained elevated without significant decrease due to fluctuating values (thyroglobulin 200 ng/ml-75 ng/ml).

Conclusions

In a case of pediatric PTC with progressive pulmonary metastases and no further RAI option Sorafenib can help to stabilize the disease and can be given in the adult dose of 2 x 400 mg without severe side-effects.

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Rare Tumours

CHILDREN WITH RET PROTOONCOGENE CODON 634 MUTATION

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Objectives

We would like to present our treatment experience in children with RET protooncogene codon 634 (c634) mutation.

Methods

Medical records of patient is summarized.

Results

A 7 years old girl admitted to our center without any complaint. Her medical history was unremarkable. Her mother was 30 years old and had 3rd pregnancy. Mother had been diagnosed as medullary thyroid carcinoma (MTC), and treated six years ago. Heterozygous mutation of the RET proto-oncogene at c634(c.1901 G>T) had been detected in her mother. There was no history of malignancy in mother's family. Her father and 9 years old sister were healthy. The RET protooncogene analysis was normal in 9 years old sister. The RET protooncogene analysis showed heterozygous mutation at c634(c.1901 G>T) also in our patient. Physical examination was unremarkable. Thyroid ultrasonography revealed no abnormalities. Thyroid function test resulted in normal fT3: 4,12pg/mL (2.5-3.9) fT4: 0.96pg/mL (0.50-1.51), TSH: 0.73µIU/mL (0.34-5.6). Serum levels of antimicrosomal and antithyroglobulin antibodies were normal (Anti-TPO: 0,2 IU/mL (0-35), Anti TG <0,9 IU/mL (0-40). Serum calcitonin level was found minimal elevated at two times (Calcitonin: 37.9 pg/mL, and 26,2 37.9 pg/mL (0-11.5)). Parathormone (PTH: 52,4 pg/mL) and carcinoembryonic antigen (CEA:2,21 ng/mL) levels were normal. Prophylactic thyroidectomy and sampling of cervical lymph nodes were performed. Histopathologic examination of thyroid revealed hyperplasia in C cells, and examination of lymph nodes revealed reactive lymphadenopathy. There was no MTK.

Conclusions

The risk of MTC has been reported 100% through the life for patients who had RET proto-oncogene mutation, and prophylactic thyroidectomy is proposed for these patients. It has been reported that particularly patients with c634 mutation had more risk for occurrence of metastatic and progressive/recurrent MTC, rather than patients who had c804, v618, c620 mutation. Prophylactic thyroidectomy and cervical lymph node dissection before 5-years-of-age should be proposed for patients with c634 mutation.

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Rare Tumours

PRIMARY PULMONARY PNET/EWING'S SARCOMA WITH ADRENAL METASTASIS

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Objectives

Extraskeletal Ewing's sarcomas are exceptionally rare tumors and primary extraskeletal Ewing's sarcoma/PNET of the lung is even rarer and very few cases have been reported in the literature. Retrospective study of extraosseous PNET from 2009-2013 and describe a case of primary pulmonary PNET lung with adrenal metastasis in an 11 year girl child.

Methods

To study with the clinical, pathological and radiological profile of a primary pulmonary PNET and review the literature

Results

Of the total 5 cases of Extraosseous Ewing's sarcoma, treated between 2009-2013 only one case of Primary pulmonary PNET was detected with adrenal and bony metastasis

Conclusions

Primary pulmonary PNET is a very rare tumor with usually a very poor outcome especially in cases where it presents with metastasis and emphasises the importance of early evaluation of any metastasis.

EP-522

Rare Tumours

SURGERY OPTIONS AND RESULTS OF TREATMENT OF CHILDREN WITH SOLID PSEUDOPAPILLARY TUMORS OF THE PANCREAS

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Objectives

Solid pseudopapillary tumor (SPT) of the pancreas are rare neoplasms with low malignant potential, first described by Franz in 1933 and less than 3% of the tumors. It is extremely rare in children.

Methods

In scientific research institute of Children's oncology and hematology from 2005 to 2012 9 children with the diagnosis a solid pseudo-papillary tumor of a pancreas are operated. We analysed clinicodiagnostic data, operation volumes, and results of treatment and observation time.

Results

All patients were girls age from 9 to 15 years (a median 13y.o.). As a rule, the disease is asymptomatic and discovered incidentally, but the two children experienced pain in the epigastric region, 1 patient had nausea and vomiting. According to the study at 4 patients the tumor was located in the tail of the pancreas, 2 - in the body, and 3 - in the head.

The maximum size of the tumor was 8.3 x7, 4x8, 5 cm and was located in the head of the pancreas. In 4 children underwent laparoscopic distal pancreatectomy, 2 - gastropancreatoduodenal resection, and 1 case performed distal subtotal resection of the pancreas, enucleation of the tumor resection wall duodenum, resection of the body of the pancreas. Complications occurred in 5 patients: in 2 cases - postoperative pancreatonecrosis, in the other - pancreatic fistula, bleeding from the pancreatic branch of the splenic artery and pneumonia.

The observation period of the patients was from 1 month to 6 years. All patients are alive without evidence of disease recurrence.

Conclusions

Solid pseudopapillary tumor (SPT) of the pancreas is a rare disease in children, which usually occurs in girls of pubertatny age. The main method of treatment is surgery, however there is a high risk of complications because of tumor localization

EP-523

Rare Tumours

SURGICAL TREATMENT OF PANCREATIC TUMORS (ONE CENTRE EXPERIENCE)

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Objectives

Solid pancreatic tumors are the rare pathology at the young age. The surgical treatment for this group of patients is technically complicated. A surgical treatment experience is not sufficiently advanced in a modern literature.

Methods

10 patients (9 girls and 1 boy) were given the surgical treatment of pancreatic tumor for the last 15 years. The average age of patients was 10.7 years (children from 1 till 15 years old). The following operations were carried out: one patient received pancreatic tumor enucleation, two patients – splee-preserving distal pancreatectomy, four patients – radical antegrade modular pancreatosplenectomy, one patient – radical antegrade modular pancreatosplenectomy with left adrenalectomy, two patients – pancreaticoduodenectomy with duct-to-mucosa pancreatojejunostomy and author's method of totally isolated Roux-en-Y pancreaticobiliary tract reconstruction with microjejunostomy and microgostomy (patient age was 1,10 year old).

Results

Pathology conclusion of operation materials shown as follows: in four cases tumor was verified as a solid pseudopapilloma pancreas cancer (all female patients), three cases - a malignant neuroendocrinological tumors (G3), one case - a malignant paraganglioma (G3), next one - as an adenocarcinoma and another one - as a mature teratoma with involving to a head of pancreas. The average time of surgery is 250 min., the average hemorrhage was 156 ml (max was 300 ml). During the postoperative period one patient had an abscess which was success treated via US drainage. Three patients have been treated with adjuvant chemotherapy. One patient died because of metastatic recurrent, nine patients - still alive, without signs of disease.

Conclusions

Surgical treatment of solid pancreatic tumors is a complicated method that provides long term survival.

EP-524

Rare Tumours

ALPHA-FETOPROTEIN PRODUCING RIGHT ADRENOCORTICAL ADENOMA IN A TEN-YEAR OLD BOY: CASE REPORT

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Objectives

We report a case of adrenocortical adenoma with an elevated level of serum alpha-fetoprotein(AFP)

Methods

Case report

Results

The patient was a ten-year-old boy. He consulted a family doctor because of diarrhea and abdominal pain, and incidentally a right adrenal gland tumor was diagnosed by ultrasonography. He was referred to our hospital for further treatment. The adrenocortical function was normal by blood test, and all tumor markers were negative except for serum AFP (234 ng/ml). Abdominal CT showed the tumor mass in the right upper retroperitoneum. The size of the tumor was 36 x 48 x 52 mm with homogeneous texture(CT index was low, around 40-50). Radiological findings strongly suggested the tumor to be an adrenocortical carcinoma.

The patient underwent right adrenalectomy. No lymph node swelling around the tumor was detected. The final pathological diagnosis was adrenocortical adenoma. Serum AFP decreased to the normal level after the operation.

Conclusions

Adrenocortical tumor is rare in children. Furthermore AFP producing adrenal tumor was extremely rare, only one adult case had been reported before in English literature. This is a first pediatric case of AFP producing adrenocortical adenoma.

EP-525

Rare Tumours

MALIGNANT ATYPICAL RHABDOID TUMOR OF PELVIS: CURE IS STILL A DISTANT DREAM

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Objectives

Extra renal extra cranial malignant rhabdoid tumor is highly lethal, rare tumor with poor prognosis with an incidence of 0.15 per million in children. No definite treatment has been defined. Here we describe course and outcome of malignant atypical rhabdoid tumor (MATRT) in a child.

Methods

A seven year old girl was admitted with us in view of bleeding per vaginum for 2 weeks duration. Her rest general and systemic examination was normal. On further evaluation MRI of pelvis showed a mass of 65 x 43 x 45 mm in the pelvis without any metastasis, suggestive of rhabdomyosarcoma. Histopathological report of transrectal trucut biopsy of mass showed high grade poorly differentiated malignant tumor of pelvis. Immunohistochemical stains were positive for vimentin but negative for desmin and myogenin. Finally diagnosed as MATRT. A PET-CT scan showed an FDG avid heterogeneously enhancing cystic mass localized to pelvis with no other FDG avid distal metastasis.

Results

Repeat MRI of whole abdomen with contrast after 6 weeks of VAC (Vincristine, Actinomycin and Cyclophosphamide) showed a mass of almost same size. She underwent surgery with gross total resection and colostomy. Histopathology and immunohistochemistry was compatible with viable MATRT (expressed EMA and vimentin but negative for desmin and myogenin). She received 6 courses of alternating VDC/IE chemotherapy (vincristine, doxorubicin, cyclophosphamide, ifosfamide, etoposide) with concomitant radiotherapy (50.4 Gy) after 3 courses of IE/VDC. Repeat MRI and PET scan showed no evidence of disease. After six cycles of mentioned chemotherapy, spino-meningeal relapsed occurred. She was given high dose methotrexate (5gm/m²) and cyclophosphamide to relieve her symptoms. She was planned for autologous stem cell transplant but finally died at home.

Conclusions

Cure is still a distant dream for ATRT. A newer and aggressive multimodality approach is required in near future to cure this fatal disease.

EP-526

Rare Tumours

NEONATAL SOLID TUMORS. 5 YEARS EXPERIENCE IN THE RICARDO GUTIERREZ CHILDREN HOSPITAL ONCOLOGY DEPARTMENT

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Objectives

Neonatal solid tumors (NST) are rare neoplasms in children: 0.5% to 2%. Their histology, low incidence, tumor behavior and response to treatment differ from tumors found in older children. To describe clinic and epidemiological features, histological type, treatment and outcome of NST.

Methods

Retrospective descriptive study of patients (p) with NST admitted in the Oncology Department of Ricardo Gutierrez Children Hospital between 2008 and 2014.

Results

n: 27 p, histology: benign 40% (11p), malignant 60% (16p). Prenatal ultrasound diagnosis 22% (6p). Signs and symptoms at birth: 26% (7p). Tumor types: neuroblastoma (NBT) 26% (7p), 4s 2p; low grade fibrosarcoma 3.5% (1p); myofibromatosis 7.5% (2p); retinoblastoma (RTB) 11% (3p), bilateral 2p; hepatoblastoma 3.5% (1p); mesoblastic nephroma 3.5% (1p); primitive neuroectodermic tumor 3.5% (1p); teratoma 19% (5p), 4 mature, in central nervous system (CNS) 1p, sacrococccigeal 3p; other CNS tumors: anaplastic ependymoma 1p, low grade glioma 3p, papyloma 1p; adrenocortical tumor 3.5% (1p). Diagnosis: 70% (19p) required biopsy; 4 NBT clinic and image diagnosis, all RTB with ocular fundus and 1 brainstem glioma with image. Metastatic at diagnosis: 15% (4p), 3 NBT and 1 myofibromatosis. Treatment: 44% (12p) received chemotherapy and 85% (23p) require surgery, 12p alone and the rest combined with other therapy. 2p with RTB received local radiotherapy. 63%% achieved complete remission. Only 1p relapsed (bilateral RTB). 4p (15%) died: 1 NBT due to surgery complication and the rest for tumor progression. Sequelae: 22% (6p)

Conclusions

The majority of p evaluated had malignant disease (the most frequent tumor type was NBT), a quarter of the p presented symptoms at birth and few prenatal diagnosis. The surgery was an important mainstay of treatment. High rate of complete remission was observed and low relapse rate and mortality. The data obtained were similar to those reported in the world literature.

EP-527

Rare Tumours

A NOVEL ALK REARRANGEMENT A2M-ALK IN A NEONATE WITH FETAL LUNG INTERSTITIAL TUMOR

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Objectives

Fetal lung interstitial tumor (FLIT) is a recently-reported pathological type of congenital lung lesion comprising solid and cystic components. The pathological features include unique interstitial mesenchyme-based cell proliferation, and differ from other neoplasms represented by pleuropulmonary blastoma or congenital peribronchial myofibroblastic tumor. FLIT is extremely rare and its gene-expression profile has not yet been reported. Here we first report a novel chromosomal rearrangement resulting in α -2-macroglobulin (*A2M*) and anaplastic lymphoma kinase (*ALK*) gene fusion in a patient with FLIT.

Methods

Surgically-resected tumor specimen was reviewed pathoimmunohistochemically and examined to identify the tumour specific translocation using fluorescence *in situ* hybridization (FISH) and 5'-rapid amplification of cDNA ends (5'-RACE).

Results

The tumor cells contained the t(2;12)(p23;p13) translocation and were mesenchymal in origin (e.g., inflammatory myofibroblastic tumors), suggesting the involvement of *ALK* in this case of FLIT. Break-apart FISH demonstrated chromosomal rearrangement at *ALK* 2p23. Using 5'-RACE, we further identified a novel transcript fusing exon 22 of *A2M* to exon 19 of *ALK*. The corresponding chimeric gene was subsequently confirmed by sequencing, including the genomic breakpoint between intron 22 and 18 of *A2M* and *ALK*, respectively.

Conclusions

Discovery of *A2M* as a novel *ALK* fusion partner, together with the involvement of *ALK*, provides new insights into the pathogenesis of FLIT, and suggests the potential for new therapeutic strategies based on *ALK* inhibitors.

EP-528

Rare Tumours

EXTRARENAL RHABDOID TUMOR: “RARE BUT CLINICIANS SCARE”

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Objectives

Malignant rhabdoid tumors are rare. The central nervous system is the commonest extra renal site reported , while extra renal and extra cranial sites are extremely rare with few isolated case reports in literature. Keeping this scarcity of literature in to prospective we report our experience as a case series with an aim of providing greater insight in to management of this rare entity.

Methods

A retrospective audit of all the patients with histologically confirmed diagnosis of extrarenal rhabdoid tumor presenting to the pediatrics division of our hospital in the year 2013 was done. Only patients with complete follow up details and who were treated at our hospital were included in this review.

Results

There were 5 patients in our study, of which 3 were males and other 2 were females. The site of origin included axilla, cervicothoracic , liver and groin. All the patients were less than 10 year age at the time of diagnoses. Loss of INI1 was found in our all cases on IHC. Vincristine and Adriamycin based chemotherapy was given to all of our patients and was not found to be very effective. None of our patients benefitted from radiotherapy. Two of our patients had succumbed to their disease within 6 months of the diagnoses, while one patient had a recurrent disease at local site post treatment and died within 2 months of disease recurrence. Two of our patients are alive with disease and are on metronomic therapy.

Conclusions

Rarity of these tumors makes it impossible for any institute to gain solid experience and formulate management guidelines , thereby making it imperative for the clinicians to review the literature available in form of case series and derive appropriate inferences to guide treatment and improve the dismal prognosis of these rare but scary tumors.

EP-529

Rare Tumours

USE OF VANDETANIB IN METASTATIC MEDULLARY CARCINOMA OF THYROID IN A PAEDIATRIC PATIENT WITH MULTIPLE ENDOCRINE NEOPLASIA 2B

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Objectives

We aim to present the first case of a paediatric patient with multiple endocrine neoplasia (MEN) 2B and unresectable metastatic medullary carcinoma of thyroid (MTC) treated with vandetanib, together with a positive response to treatment. Vandetanib is a novel tyrosine kinase inhibitor selectively targets transfection (RET) gene, vascular endothelial growth-factor receptors 2 and 3, and epidermal growth-factor mediated signalling.

Methods

A 12 year old boy presented with locally advanced and metastatic inoperable MTC associated with MEN2B. Genetic studies confirmed mutation of rearranged during transfection (RET) gene. He was started on vandetanib, 100 mg daily.

Results

He has demonstrated a good clinical response with a fall in calcitonin levels from 15400 ng/l to 1200 ng/l within 2 months and a reduction in size of the primary thyroid malignancy, lymph nodes and pulmonary metastases on repeat CT scan. He has now been on vandetanib for over 18 months with stable disease and calcitonin levels.

Conclusions

Vandetanib has a role in the treatment of patients including children with inoperable locally advanced and metastatic medullary carcinoma of thyroid. More information is needed on its use in children and long term outcome.

EP-530

Rare Tumours

NASOPHARYNGEAL CARCINOMA IN CHILDHOOD. REPORT OF THREE CASES AND DISCUSSION

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Objectives

During the past seven years we treated three adolescents with Nasopharyngeal Carcinoma (NPC) in the Service of Pediatric Oncology. This tumor is rare in children; therefore the management is derived from adult treatment protocols.

Methods

Review of medical records of three patients with NPC treated from 2007 to 2012 and analysis.

Results

A 17 years-old boy presented with cervical pain, fever, weight lost and dysphagia. The CT scan reported a 7.3 cm mass obliterating 80% of the nasopharynx. A non-keratinizing NPC Stage III was diagnosed. He received Radiation therapy (RT) (66.6 Gy), chemotherapy with 5-fluorouracil and cisplatin. He relapsed after 5 years; received second line chemotherapy with gemcitabine and carboplatin and is in complete remission.

The second patient is a 16 years-old boy who presented with weight loss, fever and bilateral cervical and supraclavicular lymphadenopathy. CT scan showed a mediastinal mass, initially misdiagnosed as germ cell tumor received BEP with excellent response; after pathological review a NPC Stage IV was confirmed and started 5-fluorouracil and cisplatin. He had progressive disease and a partial response was obtained with second-line chemotherapy.

The third patient is 10 year-old boy with a 5 months history of cervical lymphadenopathy and suspicion of tuberculosis. The biopsy reported NPC Stage III. He received radiotherapy 66.6 Gy, eight cycles of chemotherapy with 5-fluorouracil and cisplatin and remains in remission 8 months after completion of therapy.

These results evidence male predominance, advance stages and systemic symptoms such as weight loss and fever. The diagnosis was established by lymph node biopsies. Initially, two patients had a complete response followed by relapse, the three patients are alive.

Conclusions

Nasopharyngeal carcinomas are rare in children. There is a male sex predominance, which cannot be completely explained by known risk factors. A cooperative study is needed in order to standardize the treatment options.

EP-531

Rare Tumours

MALIGNANT PLEURAL MESOTHELIOMA IN A CHILD

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Objectives

Herein, we describe successful treatment of malignant pleural mesothelioma in a child. There is a scarce body of literature pertaining to childhood mesothelioma, and most practices are guided by data from adult literature. Our objective is to add to the paediatric literature in order to improve outcomes in the treatment of the childhood entity.

Methods

An eight year old child found to have a right sided chest mass measuring roughly 11 x 8 x 8 cm is the basis of our report. After an inconclusive needle biopsy, an open lung biopsy was done. Unfortunately, frozen section specimens were inconclusive, and were further reviewed in Boston and Vancouver. A diagnosis of malignant pleural mesothelioma - epithelioid type - was made. We decided to surgically resect the tumour, and intra-operatively found that the tumour appeared to originate from the visceral pleura of the horizontal or oblique fissure. It extended into the lung parenchyma to involve all three lobes of the right lung. Right pneumonectomy was performed. Unfortunately, the child developed a right chest wall recurrence and the chest wall, including ribs four through eight were resected. Following surgery, the child underwent 8 cycles of chemotherapy with Pemetrexed and Cisplatin.



Results

The child is now 20 months from pneumonectomy and 14 months from chest wall excision. There appears to have been complete response to therapy with no definite recurrence of disease. Functionally, the child is well and able to attend school.

Conclusions

Childhood malignant pleural mesothelioma is an extremely rare tumour in the paediatric population that carries a dismal prognosis. Although additional work is needed to develop a standard of care for the disease, we have documented successful treatment with pneumonectomy followed by chest wall excision, and chemotherapy with Pemetrexed and Cisplatin.

EP-532

Rare Tumours

AMG 900, AN AURORA KINASES INHIBITOR, ENHANCES THE CHEMOSENSITIVITY TO TOPOISOMERASE II INHIBITORS AND MODULATES GENE EXPRESSION IN H295A ADRENOCORTICAL TUMOR CELL LINE

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Objectives

Pediatric adrenocortical tumors (ACT) are rare malignancies and in advanced disease the treatment has a small impact on overall survival. Previous study from our group suggests that AURKA and AURKB overexpression in pediatric ACT may be related to more aggressive disease. These genes are involved in the maintenance of the genome integrity during cell cycle division and they have been considered as new targets to cancer treatment. The present study shows the results of the effects of the new aurora kinase inhibitor AMG 900, associated or not with standard chemotherapeutic agents, on adrenocortical carcinoma cell line H295A.

Methods

Cell proliferation was assessed by Giemsa staining and apoptosis was performed by flow cytometry. Drug combination analysis was made on the basis of Chou-Talalay method. Hormones dosage assay was performed to evaluate the effects of the aurora kinases inhibitor on hormone secretion. Microarray experiments were carried out using the Agilent Human microarray.

Results

Treatment with AMG 900 caused inhibition of proliferation, increased apoptosis and sensitized the cells to topoisomerase II inhibitors (doxorubicin and etoposide) whereas combination with cisplatin led to an antagonistic response. Additionally, the AMG 900 reduced hormone synthesis and modulated the expression of genes involved in this activity. Finally, aurora kinases inhibition altered the expression of genes associated with G1 cell cycle phase regulation and affected the Notch signaling pathway target genes.

Conclusions

These data suggest that aurora kinase inhibition by AMG 900 may be a new therapeutic approach to adrenocortical carcinoma treatment.

EP-533

Rare Tumours

EXTRA-CRANIAL MALIGNANT RHABDOID TUMOR IN CHILDREN: A SINGLE INSTITUTE EXPERIENCE

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Objectives

Malignant rhabdoid tumor (MRT) is a rare and highly aggressive tumor that affects young children. Due to its' extreme rarity, most of the available data is based on retrospective case series. To add to the current knowledge of this disease, we reviewed the patients treated for extra-cranial MRT in our institute.

Methods

A retrospective medical record review was done on children treated for pathologically confirmed extra-cranial MRT at Seoul National University Children's Hospital between January 2003 and May 2013.

Results

Eleven children (7 boys, 4 girls) were diagnosed with extra-cranial MRT at median age of 9 months old. Six patients (55%) had renal MRT, and 5 (45%) had soft tissue MRT in submental, paraspinal, retrosternal or coccygeal area. Ten patients were evaluated for loss of *INI1* and 9 patients (90%) had loss of *INI1* staining. The 1 patient whose specimen had retained *INI1* staining was showed late presentation during adolescence. Five patients (45%) had metastasis at diagnosis. The entire cohort (100%) received chemotherapy, and 4 patients (36%) underwent additional high dose chemotherapy with autologous stem cell rescue (HDCT & ASCR) with melphalan, etoposide, and carboplatin (MECb). Eight patients (73%) had surgery, and 6 patients (55%) received therapeutic radiotherapy. Five patients (45%) progressed or relapsed. The overall survival of the cohort was 51.9% with median follow-up duration of 17.8 months (range, 2.3 to 112.3 months), and the event free survival was 50.0% with median follow-up duration of 11.9 months (range, 0.9 to 112.3 months).

Conclusions

Extra-cranial MRT is still a highly aggressive tumor in young children. But the improved survival of our cohort is promising. Surgical resection, therapeutic radiotherapy, and HDCT & ASCR with MECb may be promising treatment options.

EP-534

Rare Tumours

COLORECTAL CARCINOMA IN CHILDREN AND ADOLESCENTS, SINGLE CENTER EXPERIENCE

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Objectives

Colorectal carcinoma (CRC) is one of the most common tumors in adults, but is extremely rare in childhood. This study retrospectively reports on a group of six patients < 18 years old, treated at the Department of Pediatric Hematology and Oncology, Prague, Czech Republic between 1993 and 2013.

Methods

There were 3 girls and 3 boys among the children/adolescents with CRC (median age 15.8 years, range 12.9-17.6), all had unfavorable CRC histiotypes (Signet cell or mucinous adenocarcinoma) and all had advanced disease (1x stage IIB, 1x stage IIIB, 4x stage IV) at the time of disease onset. Initial surgical resection was complete in 3/6 cases, 5 patients received postoperative chemotherapy (Xelox, Folfox) with/without targeted therapy. Tumor predisposition syndrome was confirmed in two patients (Lynch sy., CMMR-D sy.).

Results

Four patients had tumor progression or relapse and all died of their tumor, overall survival (OS) was 21% at 5 years. Two patients are alive, one with stage IIB CRC is a long term survivor, now over 19 years from the time of disease diagnosis.

Conclusions

This study confirms the rarity, advanced stage, aggressive biology and poor prognosis of CRC in children and adolescents, Surgery remains the mainstay of treatment, chemotherapy with targeted therapy had no impact on disease control in metastatic childhood CRC.

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EP-535

Rare Tumours

PEDIATRIC MALIGNANT SOLITARY FIBROUS TUMOR OF KIDNEY: CASE REPORT AND REVIEW OF THE LITERATURE

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Objectives

Renal solitary fibrous tumors are unusual spindle cell neoplasms originating from mesenchymal cells and were originally discovered in the pleura.

Methods

Ten year old boy, previously healthy was admitted to our hospital with macroscopic hematuria and dysuria. He had low grade fever and abdominal pain, without palpable mass and normal blood pressure. Laboratory tests showed mildly elevated white blood cell count and normal renal function tests. Urine analysis showed numerous white and red blood cells, with normal culture results.

Results

Abdomen Ultrasonography revealed well-defined, lobulated soft tissue mass in the right kidney with hyperechoic appearance, measuring 40x42 mm. Enhanced CT scan of the abdomen revealed 40x42 mm, hyperdense mass, located within the pelvis of the right kidney with focal ectasia. The radical right nephrectomy was performed.

Macroscopically the specimen measured 7x6x5 cm, located in the pelvis with renal parenchymal infiltration, without hemorrhage and necrosis. Microscopically, the cells and nuclei were from round to oval to spindly, hyperchromatic with eosinophilic cytoplasm and mild coarse chromatin. Tumor cells frequently had mitoses 5–6 or more per 10 high power fields. Tumor was classified as malign group due to hypercellularity, cytologic atypia and mitotic activity histopathologically. The neoplastic cells were diffusely positive for CD34 and vimentin. They showed rare positivity for SMA and were negative for bcl-2, S-100 protein, EMA, desmin, CD 68 and pancytokeratin. Nuclear positivity with Ki-67 was detected 3-25% of the cells.

Conclusions

After the total resection of the tumor, there wasn't any recurrence or metastasis within the 15 months follow-up without any chemotherapy. In our knowledge, this is the first reported case of malignant solitary fibrous tumor of the kidney in pediatric age. Further clinical trials are needed to follow-up the malignant forms of tumor and clarify the benefit of chemotherapy.

EP-536

Rare Tumours

DENOSUMAB TREATMENT OF GIANT-CELL TUMOR OF MAXILLA IN A 9-YEAR-OLD GIRL

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Objectives

Giant-cell tumor of bone (GCTB) is primarily seen in young adults and comprises 5% of primary bone tumors. GCT are rarely seen in childhood, only in 1.7% of all cases of GCTB. It is usually a benign tumor but frequently recurs locally after surgical resection. Metastatic disease at presentation is uncommon. A 9-year-old girl presented in March 2010 with a facial mass causing a swelling on her left side. Family history revealed her father being diagnosed as GCTB at 7 years of age. Her brother, was diagnosed as GCT of maxilla at the age of 14, was successfully treated with intralesional steroids and calcitonin in our center.

Methods

The patient was treated with intralesional steroids and calcitonin, developed cellulitis, was hospitalized with broad spectrum antibiotics, surgical drainage and curettage. After she was discharged, she was lost to follow up for 3 years, finally she admitted in February 2013 with a left maxillary huge mass completely filling the oral cavity, dacryocystitis and fistula. She was put on subcutaneous IFN-Alpha2A 3million U/m²/d every other day and Imatinib mesylate 400mg/day orally. Two months later she was seen at outpatient clinic, maxillofacial surgeons performed intralesional steroids/ weekly, for a month then every other month. In May 2013, Denosumab treatment was planned because there was no satisfactory regression of the tumor. She was subsequently started on denosumab with induction dosing of 120mg subcutaneously/ weekly for 3 weeks, followed by 120 mg denosumab subcutaneously per month.

Results

She is currently 10 months into treatment. The patient has required 4,000 IU/ day of oral vitamin D and 40mg/kg/day elementary Calcium supplementation because of developing hypocalcemia from decreased bone turnover during her treatment, her most recent calcium level was 9.1mg/dl. The tumor showed shrinkage, the reconstructive surgery is planned.

Conclusions

She is the first pediatric patient treated with Denosumab for GCTB in Turkey.



EP-537

Rare Tumours

ARE THYROID CANCERS INCREASING IN YOUNG ADOLESCENTS

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Objectives

We believe that the incidence of a rare tumor, differentiated thyroid cancers in children, are increasing following The Chernobyl Nuclear catastrophe. The most common presenting findings of thyroid cancers are thyroid nodules and cervical lymphadenopathy. Positive family history and neck irradiation are risk factors for development of thyroid carcinoma.

Methods

Between 1990- February 2104, 22 cases of thyroid carcinoma have been diagnosed. Sixteen were females, 6 were males with an age range of 15.8+3.2 years. One had cranial RT for

ALL, one had neck irradiation because of HD, one patient who had lived in Kiev, had family history in both parents. Histopathologically 13 cases had differentiated papillary thyroid carcinoma, 7 had papillary thyroid variant, 1 follicular and 1 medullary thyroid carcinoma. In 3 of the cases thyroid nodules were

Results

Following surgery, there was lymph node infiltration in one case, whereas in one, there was distant - lung metastasis. Three patients experienced hypoparathyroidism, in one case there was vocal chord problems. All patients received adjuvant radioactive iodine therapy and were put on thyroid hormone replacement therapy. B-RAF 600 mutation studies were carried out in case of adding targeted therapy i.e sorafenib to metastatic recurrent cases. The patients are monitored by measuring serum human TG levels and by ultrasound for recurrences.

Conclusions

Although the treatment modality in children with thyroid cancers is still controversial, total thyroidectomy together with lymph node sampling / dissection represent the dominant method of surgical treatment, enabling the success rate of RAI therapy and provide a longer disease free survival.

EP-538

Rare Tumours

AGGRESSIVE FIBROMATOSIS IN CHILDREN: A SINGLE CENTER EXPERIENCE

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Objectives

To determine the clinical features and treatment results of children with aggressive fibromatosis treated in a single institution.

Methods

The records of 11 patients with aggressive fibromatosis treated between 1972 and 2013 were analyzed retrospectively. Demographic characteristics and tumor locations were recorded. If possible, surgery was performed. Radiotherapy (RT) and/or chemotherapy were used for treatment. Tamoxifen, interferon, rocaltrol, vincristin+actinomycin-D+cyclophosphamide+adriamycin, or vinblastine+methotrexate regimens were used according to relapsed or disease condition.

Results

There were three males and eight females with a median age of 8 years (range, 4-16 years). Tumors were located in the lower limb (n=4), upper limb (n=3), gluteal region (n=3), and neck (n=1). The largest tumor diameter ranged from 5 to 20 cm (median 14 cm). Five patients had undergone a subtotal resection at the time of diagnosis, while six had only undergone a biopsy. Seven patients who all had progressive disease were followed-up without any treatment after surgery. Two out of the 11 patients received RT, and they achieved stable disease without need for any further treatment. Two patients received RT and chemotherapy, one with rocaltrol and the other with tamoxifen+vincristin+actinomycin-D+cyclophosphamide+adriamycin. These cases also had stable disease and did not require any further treatment. The patients who had progression after follow-up were treated with RT and/or chemotherapy. Three of them were only treated with RT, and one received RT and rocaltrol, two only received rocaltrol, and one received vinblastine+methotrexate. One patient treated with RT + rocaltrol and one with only treated with RT achieved stable disease, while another treated with RT alone developed progressive disease.

Conclusions

Aggressive fibromatosis is a rare tumor, and treatment can be problematic. Although our series was small; we can conclude that RT may enable a stable disease course in some patients.

EP-539

Rare Tumours

PARAOVARIAN ENDOMETROID CYSTOADENOCARCINOMA IN AN INFANT WITH PROTEUS SYNDROME: A CASE REPORT AND REVIEW OF LITERATURE

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Objectives

Ovarian and paraovarian malignant neoplasms are uncommon in children; mainly germ cell tumors and least frequently, epithelial tumors. There is an association between genital tract tumors and Proteus syndrome, a rare, sporadic and progressive entity, characterized by a postnatal overgrowth of several tissues in a mosaic pattern caused by a mutation in the AKT gene.

Methods

We describe an infant with Proteus syndrome who developed a paraovarian cystoadenocarcinoma. Clinical presentation, histological features and clinical outcome were examined. A PubMed/Medline search was performed to collect all cases of adnexal masses in Proteus syndrome.

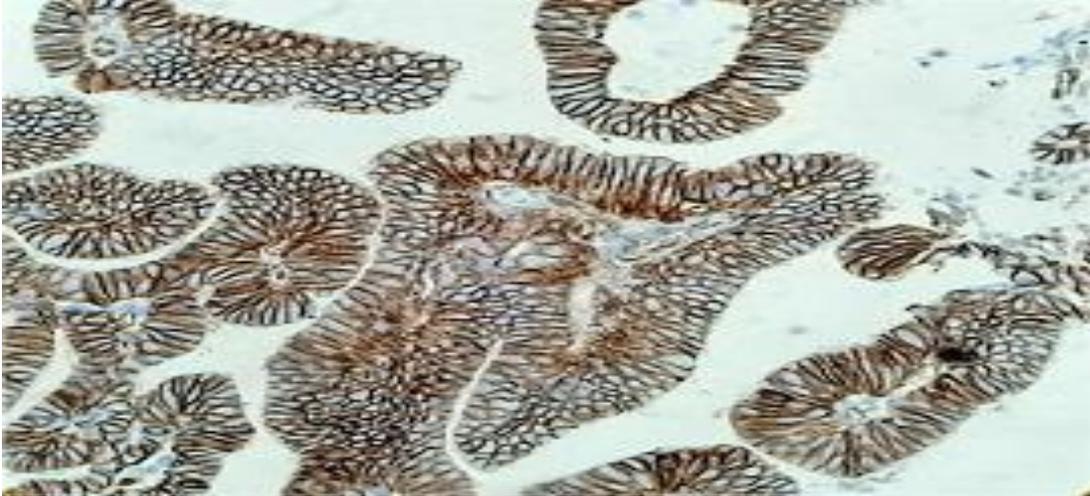
Results

A 20-month-old asymptomatic girl with Proteus syndrome was diagnosed of an unilateral paraovarian mass in a routine ultrasound. Classical criteria for this syndrome like connective tissue nevus and disproportionate overgrowth of limbs and fingers was found.





There was no evidence of distant metastasis at onset. She underwent complete resection of the tumor, taking samples of omentum, lymph nodes and peritoneum. The pathology was an endometrioid cystadenocarcinoma, stage IC.



She received adjuvant chemotherapy with paclitaxel 175 mg/m² in a 3h infusion at day 1, 8 and 15 and carboplatin AUC 6 at day 1, for 3 cycles with no evidence of disease after seven months of follow-up. A total of nine patients have been described with tumors of female tract and Proteus syndrome, which mostly includes bilateral ovarian cystadenomas and other benign masses.

Conclusions

A paraovarian neoplasm is extremely rare in children and could be included as a criterion for Proteus syndrome. This is the youngest patient with this rare syndrome and a malignant adnexal tumor so far reported in the international literature. Staging and treatment of these tumors is not well standardized; however, most authors conclude that these neoplasms must be treated as their ovarian counterparts.

EP-540

Rare Tumours

SMALL CELL LUNG CANCER IN A 13-YEAR-OLD MALE

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Objectives

Small cell lung cancer (SCLC) is exceedingly rare in children.

Methods

We herein report a pediatric case of extensive-stage SCLC.

Results

A 13-year-old male was admitted to our department with a three-month history of cough. Thoracic CT and MRI showed two large masses, one was a 5.8 × 4.3 × 3.9 cm primary tumor close to the right middle lobe bronchus, and the other was a 2.8 × 4.0 × 4.5 cm subcarinal lymph node. Systemic PET-CT revealed multiple bone metastases. In the serological analyses, the levels of pro-gastrin releasing peptide (pro-GRP) and neuron-specific enolase were high, at 4,075 pg/mL (normal, ≤ 81 pg/mL) and 52.3 ng/mL (normal, ≤ 16.3 ng/mL), respectively. We diagnosed the patient with SCLC based on the histopathological findings of biopsy specimens which were obtained endoscopically from the tumor partially exposed on the bronchial wall. We started treating him with cisplatin and irinotecan (PI), because this combination therapy is one of the recommended regimen for adult patients. After the first course of PI combination therapy, there was both a reduction in the tumor volume and a decrease in the levels of some biomarkers. Therefore, we plan to administer several courses of PI therapy.

Conclusions

The long-term prognosis of adult SCLC patients is generally poor, even if desirable initial treatment responses are obtained. In order to improve their prognosis, new trials with other anti-cancer agents, such as topotecan and amrubicin, should be performed. Bevacizumab, an anti-vascular endothelial growth factor (VEGF) monoclonal antibody which is effective against non-SCLC, is an intriguing candidate molecular target drug that should be evaluated for SCLC. Because the value of VEGF in the present patient's plasma was high, we consider that early administration of bevacizumab in combination with the effective PI therapy may be an intense treatment for the patient, and may improve his prognosis.

EP-541

Rare Tumours

A PEDIATRIC NEUROENDOCRINE TUMOR WITH HEPATIC METASTASES

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Objectives

Neuroendocrine tumors (NETs) are heterogeneous group of malignancies that arise from neuroendocrine system. NETs in pediatric population are extremely rare and primarily involve the gastrointestinal tract and lungs. These tumors can be either non-functioning tumors with symptoms related to mass effects and malignant tumor disease or functioning tumors with specific hormones secreted to induce specific clinical syndromes. Although the majority of tumors are malignant, they are relatively slow-growing neoplasms and most of NETs classified as well-differentiated tumors due to tumor's histology. Metastatic tumors are more frequent than localized NETs and often they present with liver metastasis. In this paper we aimed to present a pediatric NET with hepatic metastases at initial diagnosis.

Methods

Thirteen years old boy admitted with the complaint of abdominal pain. On physical examination he had erythematous eruption on the face, neck and trunk. Also he had epigastric mass. Radiological examinations revealed solid masses in all segments of the liver which had cystic and necrotic components. Pathological report of tru-cut biopsy of liver revealed diagnosis of well-differentiated neuroendocrine tumor, WHO Grade 2. The level of 5-hydroxyindoleacetic acid in 24-hour urine collection was elevated. Gastrointestinal system endoscopy and biopsies were normal. Somatostatin receptor scintigraphy revealed only the liver lesions. Octreotide and everolimus treatment were given for one year. Severe tricuspid valve regurgitation developed and treatment was discontinued. Somatostatin receptor-targeted radionuclide therapy administered two months ago and any side effects were observed.

Results

Systemic treatment options for a child with neuroendocrine liver metastases who is not a candidate for surgical resection were rather limited. Our patients' symptoms resolved and liver lesions regressed with the combination of somatostatin analogs and everolimus. But we had to terminate this therapy because of severe cardiac side effects due to everolimus.

Conclusions

Somatostatin receptor-targeted radionuclide therapy offers a promising treatment option for NETs in children.

EP-542

Rare Tumours

MANAGEMENT CHALLENGES IN A YOUNG CHILD WITH THREE CO-EXISTING TUMORS: A COMPLEX CASE OF LI-FRAUMENI SYNDROME

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Objectives

Li-Fraumeni-Syndrome (LFS) is an autosomal dominantly inherited cancer predisposition syndrome associated with heterozygous germline mutations in the *TP53* gene. LFS-related cancers generally occur in children or young adults and survivors have an 80-fold increased risk for multiple primary cancers. Knowledge of the genetic status of the *TP53* gene in these patients is critical not only due to the increased risk of malignancies, but also because of the therapeutic implications, since a higher rate of radiation-induced secondary tumours in these patients has been observed.

Methods

We describe a 2 year old child with LFS harbouring a maternally inherited heterozygous *TP53* germline mutation (Glu294fs). who was affected by three synchronous malignancies at the age of 2: an anaplastic alveolar rhabdomyosarcoma (RMS) of the right orbit (diagnosed at age 19 mnths), right adrenocortical carcinoma (ACC) (at age 27 mths) and a right orbit low grade osteosarcoma (OS) (at age 28 mths). Radiological treatments and a surveillance program were adjusted according to recommendations for LFS patients.

Results

He was treated as per Children's Oncology Group (COG) protocol ARST0331 for the RMS. In order to avoid radiation, local control was achieved by an orbital exenteration. During routine LFS surveillance, the ACC and orbital low grade osteosarcoma were diagnosed. Following two cycles of chemotherapy/mitotane as per COG ARAR0332, complete resection of the ACC was achieved. Optimal management strategy of the OS is being evaluated.

Conclusions

Management of tumour treatment options for patients with LFS is complex due to both theoretic and actual risks of treatment-related and de novo secondary tumors. The concurrent presentation of three distinct cancers in our case highlights the challenges of management, the potential for development of cancers even while on therapy, and the importance of surveillance imaging for presymptomatic tumor detection.

EP-543

Rare Tumours

DESMOPLASTIC SMALL ROUND CELL TUMOR: A CASE REPORT

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Objectives

Desmoplastic Small Round Cell Tumor (DSRCT) is a rare disease in all age groups. Less than 200 cases have been reported worldwide till now. Presentation in infancy is rare. Because of the rarity of this disease, little is known about optimal treatment and outcome. We try to present our findings of the course of the illness of a patient diagnosed with DSRCT at our institute.

Methods

A step wise approach to identify the etiology of the illness was adopted for the patient who presented with symptoms of abdominal distension.

Results

An 8 months old male child, presented with progressively increasing abdominal distension since 1 month. There was no history of altered bowel habits, fever, bleeding, jaundice, loss of weight or hematuria. His β -HCG and AFP levels were normal. CT Scan revealed a retroperitoneal large heterogeneous soft tissue mass lesion. Subsequently, biopsy was done which revealed malignant small round cell tumour (SRCT) but the exact nature of the disease could not be delineated. In view of lack of specific diagnosis, a repeat biopsy was done which showed a malignant round cell tumor with expression of Mic 2, epithelioid markers Cytokeratin, EMA (focal) and an occasional cell expressing desmin. Also, the tumor cells were immunonegative for Synaptophysin, WT-1, LCA and Myogenin, thus confirming it to be DSRCT. After the diagnosis, the child was given Inj Vincristine, Cyclophosphamide and Doxorubicin. However, the response could not be assessed as the parents abandoned treatment post 2 cycles of chemotherapy for the lack of resources.

Conclusions

DSRCT is a rare tumor that requires a high index of suspicion and multidisciplinary approach. In spite of rarity of the occurrence of such tumors, DSRTC should be kept in mind as a differential diagnosis in an infant presenting with intra-abdominal mass.

EP-544

Renal Tumours

THE PROGNOSTIC SIGNIFICANCE OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) EXPRESSION IN WILMS' TUMOR AND ITS RELEVANCE TO WT1 EXPRESSION

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Objectives

Angiogenesis plays an important role in wilms tumor progression and metastatic spread. Vascular endothelial growth factor (VEGF) is an angiogenic factor found in genitourinary neoplasms. VEGF is a direct, WT1 target gene.

Methods

VEGF and WT1 expression was determined immunohistochemically in 30 Wilms' tumor specimens

Results

All cases (100%) expressed VEGF and WT1 . A significant positive correlation was detected between WT1 and VEGF expression and a significant negative correlation was detected between WT1 expression and tumor stage.

A significant association was found between poor outcome on one hand and advanced tumor stage and high risk pathological group on the other hand.

Conclusions

WT1 expression, advanced tumor stage and high risk pathological group are poor prognostic factors in Wilms' tumor. VEGF and WT1 significant positive correlation implicate them in tumorogenesis and further support the postulated regulatory influence of VEGF over WT1 expression.

EP-545

Renal Tumours

NEPHROBLASTOMA INFILTRATION OF TRICUSPID VALVE IN A 4 YR OLD BOY

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Objectives

Introduction

Nephroblastoma is the commonest childhood renal cancer and its spread into the heart without pulmonary involvement is unusual.

Methods

A 4yr old boy referred with a 2 month history of dyspnoea, progressive abdominal mass, weight loss, anorexia and weakness. No cough or contact with Tb patients.

On examination, no dysmorphism, has wasting of muscles with stunted growth (WHZ, HAZ <-2). Dyspnoeic and tachypnoeic, (RR=48/min), pallor, mild dehydrated, had generalized lymphadenopathy, no splinter haemorrhage; Normal eyes. Temperature 37.2°C, BP 114/74mmHg, HR142/min. There was ascites as well as hepatomegaly (4cm) with a hard mass in right lumbar region crossing the midline and extending superiorly to the right hemi thorax. Normal bowel sound.

Apex beat was located at 5th ICS anterior axillary line. PSM 4/6 was audible at LLSB. CXR showed cardiomegaly with >65% cardio-thoracic ratio. Right lower lobe collapse of the lung was also noted. Echocardiogram detected the presence of tricuspid vegetation which extends to the pulmonary valve area.

Haematuria (3+) and proteinuria (2+) observed on urine dipsticks. Blood culture for bacteria was negative. Haemoglobin was 7.6 g/dl and ALT was normal (28u/l).

Blood urea and creatinine were normal (1.3mmol/l and 26µmol/l respectively). LDH level was high (3216 u/l). VMA, HVA and NSE were negative. MIBG was negative. CT abdomen revealed a huge right renal mass invading inferior vena cava and Para aortic lymph nodes . Stage IV nephroblastoma diagnosed with tricuspid valve involvement and heart failure. He had pre-op chemotherapy, nephrectomy and got post-op chemo and radiotherapy. Valvular lesions regressed with residual tumor which was planned to be removed by cardiothoracic surgical unit but he collapsed and died while awaiting cardiac operation.

Results

see images

Conclusions

The prognosis of nephroblastoma with cardiac involvement in children appears to be altered negatively especially in poor resource countries.

EP-546

Renal Tumours

CAN IMPLEMENTATION OF STRONG SOCIAL SUPPORT IMPROVE SURVIVAL OF RENAL TUMORS IN A DEVELOPING COUNTRY? CHILDREN'S HOSPITAL LAHORE EXPERIENCE

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Objectives

Children's Hospital Lahore is a tertiary government centre receiving over 500 new cancer patients from all over Pakistan and across the border per year. The purpose of this study was to analyze management and outcome of children with renal tumors and to discuss the role of effective social support in improving the survival of these patients.

Methods

Retrospective review of 120 patients enrolled between January 2011-January 2014 was done. Data regarding their age, stage, histopathology, risk stratification, treatment, outcome and impact of social support was analyzed. Patients were treated according to UKCCSG WT 2001 02 protocol.

Results

Total 120 patients with age ranging from < 1 to 10 years (mean age=3.43) were included. M: F Ratio was 1:1. 101/120(93%) presented with advanced stage, 43/120(36%) stage IV and 68/120(57%) stage III and only 9/120(7%) stage II (p-value=0.014). 105/120(87%) wilm tumor, 8/120(7%) CCS, 6/120(5%) had Round blue cell tumor. Total 50/120(42%) have completed treatment, 27/120(23%) are on treatment, 21/120(17%) got LAMA and 14/120(12%) expired due to metastatic and progressive disease. 67/120(56%) received preoperative chemotherapy and 36/120(30%) had upfront nephrectomy done and 17/120(14%) are on preoperative chemotherapy. Four patients(3%) relapsed during their course of therapy. 92/120(77%) travelled >100 km for day care visits. 68/120(57%) fathers had monthly income <100USD (p-value=0.050). 75/120(64%) of moms have had only primary education. 67/120(58%) patients had malnutrition (p-value=0.013). By providing more social support and patient tracking system LAMA rate decreased from 27% to 17% and treated patients increased from 37% to 42% (comparing the SIOP DATA 2012- PUB 406).

Conclusions

Survival of these patients can be significantly improved by strengthening the social support services and public awareness to seek early and complete treatment. Mortality of 12% can be reduced by early diagnosis and treatment and effective infection control practices. The abandonment rate can be decreased by efficient tracking and follow-up services in the day care center.

EP-547

Renal Tumours

GROWTH RATE OF RENAL TUMORS IN INFANTS

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Objectives

To establish the growth rates of malignant kidney tumors in infants.

Methods

The twenty infants were surveyed (median age 7.6 months) with malignant tumors of the kidney (established prospectively: nephroblastoma -17, rhabdoid tumor-2, sarcoma-1). The prenatal diagnosis in terms of 32-37 weeks of gestation in fetus and ultrasonography in infants with suspected malignant tumor of the kidney were completed.

Results

There were no patients diagnosed with a kidney tumor by the prenatal diagnosis data. Nevertheless postnatal volume of the tumor was 317 ml (218-498 ml) at the primary diagnosis time point. How can we explain this? Established volume of the tumor 317 ml consists of 30 embryonic of doublings. According to the published data the rate doubling of cell culture of nephroblastoma have 7-8 days. Hence, fetal tumor growth of the visual-detectable volume beginning at 1 ml can be formed during 210-240 days (30.0-34.3 weeks). Given the start time favorite of the excretory system, we can determine the gestational age visualization reference between 33.5-37.8 weeks. However, controversy this findings, we found that in the group of sick infants the tumor grew at least for 2.3-3.5 months, but at different speed. So, the number of doublings for all stages of the tumor was 8.30 (7.70-8.68). But in infants with III-IV stages of disease the doubling time of the tumor was 11.19 days (10.24-23.91) and age of 93 (91-132 days)) that is much less than those in group I-II, V stages (31.42 (24.83-38.11) and 231 (185-303) days) (p <0,05).

Conclusions

The natural history of tumor growth remains poorly understood. It is not possible or possible in isolated cases only to continuously track down the growth of native human tumors. Received data have required to study the pathophysiological aspects of tumor growth and establishment of the screening intervals of ultrasonic testing in infants.

EP-548

Renal Tumours

APPRAISAL OF EFFECTS OF APPLYING UH-1 CHEMOTHERAPY REGIMENT TO PEDIATRIC TOUGH WILMS TUMOR

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Objectives

The preliminary effects of applying COG UH-1 chemotherapy regiment to pediatric tough Wilms Tumor in our hospital in recent years were summarized and analyzed.

Methods

In reference to NWTSG standard diagnosis synthetic appraisal by stage and texture pathological pattern, preliminary summary and analysis were done of applying COG UH-1 chemotherapy regiment and synthetic radioactive therapy to tough children Wilms' Tumor in our hospital between April 2009 and May 2013.

Results

All the patients who have been kept contact for 5 to 43 months were all survived. The overall survival (OS) rate and disease-free survival rate (DFS) were 100% and 87.5%, respectively. No serious reaction occurred except acute myelosuppression. In comparison with the previous 3-year overall survival rate and 3-year disease-free survival of treatment ? stage of metastasis or recurrent Wilms Tumor, 37.5% and 12.5%, respectively, the 3-year OS and DFS of unfavourable prognosis pathological pattern(UFH+CCSK+RTK)were 77.27% and 59.08%.

Conclusions

Applying UH-1 chemotherapy regiment to pediatric tough Wilms Tumor is safe and significantly effective.

EP-549

Renal Tumours

MULTILOCLAR CYSTIC NEPHROMA: A RARE BENIGN RENAL NEOPLASM

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Objectives

Multilocular cystic nephroma (MLCN) is a relatively rare, benign tumor of uncertain etiology. We have increased the awareness of this type of renal tumor.

Methods

Two 2-year-old children who underwent radical nephrectomy due to left renal mass were presented. The characteristic of imaging, histopathological features, differential diagnosis, and treatment alternatives were discussed.

Results

CT scan revealed a well-defined circumscribed exophytic mass consisting of cystic elements and contrast holding septations, arising from the outer border of the left kidney. A radical nephrectomy has been finally performed. On microscopic examination, the cysts are lined by cuboidal epithelial cells arranged in a hobnail pattern, and they were separated by cellular spindle cell stroma. No adjunct therapy was administered. In our follow-up, the patients were completely asymptomatic and free of recurrence and metastasis.

Conclusions

Most MLCNs have been managed by radical nephrectomy due to the suspicion of renal cell carcinoma, such as in our case. But nephron-sparing surgery should be kept in mind if the mass is solitary, localized, unilateral, and smaller than 4 cm. Also, nephron-sparing surgery becomes more important for the patients who have solitary kidney or contralateral renal pathology.

EP-550

Renal Tumours

WILMS TUMOUR: A SINGLE CENTRE STUDY IN SINGAPORE

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Objectives

Wilms tumour is the most common malignant renal tumour in childhood. We retrospectively reviewed clinical profile and outcome of Wilms tumour cases in KK women's and Children's hospital (KKH), Singapore.

Methods

The study was approved by Singhealth Centralized Institutional Review Board. We included all patients with malignant renal tumours seen at KKH from 1997 to 2012 (16 years).

Results

There were 21 patients with Wilms tumour in the study period. There were eight males and 13 females; male:female ratio was 1:1.6. The median age at diagnosis was 3.3 years (range 0.25 to 10.8 years). Abdominal mass was the most common presentation (n=16, 76%), either isolated or together with other symptoms such as abdominal pain, fever, poor feeding, vomiting, hypertension and haematuria. One patient had hypospadias and bilateral cryptorchidism. Two presented with gross painless haematuria only. Two patients had tumour diagnosed on screening – one had underlying aniridia; the other had hemihypertrophy with umbilical hernia. Another child was diagnosed incidentally during workup for diabetic ketoacidosis and fever. All had unilateral disease. One patient had nephroblastomatosis on contralateral kidney. The staging according to NWTS was: seven (33%) stage I, five (24%) stage II, seven (33%) stage III and two (10%) stage IV (with lung metastasis). All were treated by NWTS protocol except one with SIOP. One patient had unfavourable histology (diffuse anaplasia). Median follow up time was 4.7 years. All were alive with no disease recurrence.

Conclusions

Abdominal mass was the most common presentation seen in spectrum of presentation. The survival outcome was excellent even in stage IV disease. Multidisciplinary treatment with standardization of protocol is vital for optimal care.

EP-551

Renal Tumours

MALIGNANT RHABDOID TUMORS IN CHILDHOOD: REPORT OF 15 CASES TREATED AT A SINGLE INSTITUTION

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Objectives

Malignant rhabdoid tumors (MRTs) are rare high-grade malignancies in the renal or extrarenal organs. MRTs of the extrarenal organs mostly affect the liver, central nervous system, pelvis, soft tissue, and intra-abdominal cavity. The treatment of patients with non-Wilms renal tumors remains challenging.

Methods

Between 2006 and 2014, 15 children with MRTs, aged 9 month to 8 years, were diagnosed at a single institution.

Results

10 patients were diagnosed as renal MRTs. 5 patient were diagnosed as extrarenal MRTs, including 1 patient of central nervous system MRT, 3 patients of intra-abdominal cavity MRT and 1 patient of soft tissue MRT. The follow-up time was 1 month to 3.5 years, and the median follow-up time was 6 month. Seven of these patients subsequently received radiotherapy. During follow-up, 9 patients had recurrence of the tumor within 4month to 3.5 years, 6 patients died of progressive disease and one died of operative mortality. The median survival time of all patients was 11 months. One 1 year old boy with recurrent soft tissue MRT received aggressive chemotherapy and radiotherapy, and his disease remained stable for 14 month.

Conclusions

Malignant rhabdoid tumors (MRTs) are rare malignant tumors with very worse prognosis. Surgical operation treatment combined with radiotherapy and aggressive chemotherapy may help alleviating the disease.

EP-552

Renal Tumours

CLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES OF UNILATERAL WILMS' TUMOR IN EGYPT, REPORT FROM A PROSPECTIVE COHORT ANALYSIS

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Objectives

A huge progress has been made in treatment of Wilms' tumor (WT) resulting in an outcome exceeding 85% in the modern era. Our study aimed at evaluating the demographics, disease characteristics and treatment outcome for unilateral WT patients treated at National Cancer Institute, Cairo University and Children Cancer Hospital, Egypt (57357)

Methods

This prospective cohort study included 98 eligible patients with newly diagnosed nephroblastoma during the period from January 2010 to December 2011. Patients were treated according to Unilateral Renal Tumors Protocol "CCHE_RenTUL#7" based on COG Protocols. Patients were followed till December 2013.

Results

Among the 98 patients, 52 were males (53%); mean age at diagnosis was 3.5±2.6 years. 25 patients (25.5%) were metastatic at presentation. Post surgery, 36 patients (36.7%) had a stage III tumor, 29 patients (29.6%) had stage I, and 8 patients (8.1%) had a stage II disease. Anaplasia was seen in 11 patients (11.2%) while all other patients (n=87) had favorable histology WT (FHWT). The median follow up period was 29.3 months (range 0.3 to 46.6 months). The 3-year overall (OS) and event-free survival (EFS) rates in FHWT patients were 83.4% and 64.2% respectively. Patients with anaplastic WT had 3-year OS and EFS rates of 88.9% and 79% respectively. Early tumor stages (I/II) were associated with significantly improved EFS compared to stage III and stage IV (3-Y EFS 83.3% versus 63.8% versus 18.2 % respectively, P < 0.001). Regarding OS, no statistically significant difference was found between stages (I/II) and stage III, however, it was significantly better compared to stage IV disease (3-Y OS: 95.7% versus 94.7% versus 66% respectively, P < 0.001).

Conclusions

In our study, outcome for early stages WT was comparable to results from other western groups, while metastatic WT had a significantly worse outcome compared to other groups.

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WILMS TUMOR OUTCOME IN ADOLESCENT AND YOUNG ADULT PATIENTS AT ANN & ROBERT H. LURIE CHILDREN'S HOSPITAL OF CHICAGO

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Objectives

Historically, adults with Wilms tumor have inferior outcomes compared with pediatric patients. Recent studies suggest that adult Wilms tumor patients when treated on a pediatric protocol fare better than patients who were not treated on a pediatric protocol (5 year event-free survival (EFS): 77% and 24%, respectively). The purpose of this study was to determine outcome of adolescent and young adult (AYA) Wilms tumor patients treated at Lurie Children's and to identify factors, which may affect outcome.

Methods

We performed a retrospective chart review of patients ≥ 10 years old who were diagnosed with and completed therapy for Wilms tumor at Lurie Children's from 1994-2011.

Results

Nine patients aged 10-26 years were identified. Stage distribution was: 1 stage I, 3 stage II, 1 stage III and 4 stage IV. Only 1 patient had unfavorable histology. EFS was 11%, and overall survival was 44% (median follow-up of 40 months). Median time to relapse was 16 months. Second complete response rate was 43%. The median time from presentation to treatment was 13 days with 3 of the 5 deceased patients having 26 or more days from presentation to treatment. All patients who relapsed > 16 months from diagnosis are alive (n=3) while those patients who relapsed prior to 16 months are deceased (n=4). Only one patient had significant delay in treatment due to toxicity. Available tumors were tested for loss of heterozygosity (1p loss (n=0), 16 loss (n=1), and 1q gain (n=2)). The patient with 16 loss and 1q gain is alive without relapse (67 month follow up). The patient with 1q gain died from disease progression.

Conclusions

The outcome for our cohort of AYA patients with Wilms tumor is worse than expected for patients treated with pediatric protocols. Tumor biology does not appear to explain the poorer outcome. Delay in initial referral and start of treatment may contribute to the inferior outcome.

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Renal Tumours

RESULTS OF TREATMENT OF CHILDREN WITH BILATERAL NEPHROBLASTOMA

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Objectives

To improve the results of treatment of children with bilateral nephroblastoma

Methods

During the period from 1980 to 2011 at the Institute of Oncology and Hematology were examined and treated 75 children with bilateral nephroblastoma. In all patients, the diagnosis was confirmed morphologically. The main peak of incidence of bilateral nephroblastoma accounts for the period from age 3 to 5 years - 41 (54.7%). Surgical treatment was 71 of 75 children. The other four children have not received surgical treatment due to progression of the disease on the background of the treatment. 54 children (76.1%), surgical treatment was carried out in two stages, first at the least affected kidney tumor, then - on the contralateral organ. 17 patients (23.9%), surgery was performed in one step.

Results

Median follow-up of all patients was 28 months, median progression-free survival - 26 months. (10-60 months). In the group of patients who received surgical treatment in two stages (54 patients), the figures were 29 and 28 months respectively. In the group of patients who received surgical treatment in one stage (17 patients), 26 and 25 months respectively. Overall two-year survival of patients with bilateral nephroblastoma was 86.5%. Two-year disease-free survival - 83.6%.

Overall and disease-free two-year survival of children with bilateral nephroblastoma who underwent surgical treatment in two stages, was 91.2% and 88.5%, respectively. In the group of patients in whom surgery was performed simultaneously, the total two-year survival rate was 92%, disease-free - 88.2%.

Conclusions

The correct diagnostic and modern strategy therapy can improve overall survival in children with bilateral nephroblastoma.

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Renal Tumours

MANAGEMENT AND TREATMENT OF CHILDHOOD WILMS TUMOR DURING THREE YEARS OF FOLLOW-UP AT A HOSPITAL BASED STUDY

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Objectives

Wilms tumor is a curable childhood malignancy that can develop in healthy child too. Since 1980, the five-year survival rate of this tumor has been above 90%. The purpose of this topic is to evaluate the Pediatric Cancer Treatment epidemiology, treatment and follow-up of children with Wilms tumor who referred to MAHAK's and Research Center.

Methods

This cohort study complied children less than 15 years old with favorable Wilms tumor pathology report, who referred to MAHAK's Pediatric Cancer Treatment and Research Center since Jan 2007 to Jan 2010. The standard checklist contained additional information filled for each individual.

Results

The enrolled patients were 33 cases (18 female, 54.5%) with the mean age of 5 ± 4.4 years old. at the time of diagnosis, the stages of patients were as III (11, 31.3%), IV (8, 25%), I (7, 21.9%), II (6, 18.8%), V (1, 4%) respectively. Tumor involvement were 18 (54.5%) in right and 15 (45.5%) in left kidney. The most common symptoms were as 22 (66.7%) patients with mass of abdomen and 3 (9.1%) with hematuria. All of the patients had nephrectomy surgery at the early diagnosis. Twelve cases (36.4%) had relapsed during or after their treatment that the mean of relapse time was 21 ± 36.5 months. Out of enrolled patients, there were 24 (72.7%) off treatment, six (18.2%) dead and 3 (9.1%) lost to follow-up. The five years survival was the same as three years survival rate in this study ($94\%\pm 0.04$).

Conclusions

Literature and reviews determine that most children with Wilms tumor are cured and very few of them will have long-term renal problems. Multimodality therapy with surgery and radiotherapy can result in excellent tumor control rate. For achieving the highest survival rate all children with Wilms tumor should be monitor in long-term surveillance programs for the early detection and management of therapy related toxicities.

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Renal Tumours

MALIGNANT RENAL TUMOURS IN CHILDREN STUDY AT HOSPICE AFRICA UGANDA

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Objectives

To review the frequency, mode of presentation and histological pattern of children with malignant renal tumours

Methods

A 7 year retrospective review of all our renal tumour folders in the institution

Results

19 children qualified for the study with a male/ female ratio of 1:2.8 and a mean age of 52.6 +/- 15.8 years. The peak age was in fifth birth day. Most patients present late (78.9%). Renal cell cancer was the commonest tumour type with the commonest mode of presentation being abdominal mass and pain

Conclusions

Malignant renal tumours present very late in our environment and patients hesitate in accepting available treatment option which is surgery. There is a need for increased patient awareness and high index of suspicion by the clinician, particularly during imaging procedures, as this would significantly enhance the early detection of these patients

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Renal Tumours

WILMS TUMOR: EXPERIENCE OF 56 CASES TREATED IN A SINGLE CENTRE

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Objectives

To illustrate our clinical experience in the long-term follow-up of children with Wilms tumor.

Methods

Medical records of 56 children with Wilms tumor diagnosed in the Department of Pediatric Oncology, Gazi University Medical School during 1991-2014 were reviewed. Clinical, radiological, pathological and survival data were collected. The analysis was performed using SPSS version 15.0.

Results

The female/male ratio was 1.3:1. The mean age at diagnosis was 50.7±40.3 (8-204) months. Clinical manifestations included abdominal mass (58.9%), abdominal pain (32.1%) and hematuria (8.9%). One of our patients had Beckwith Wiedemann syndrome and another patient had hemihypertrophy. Thirty-five patients were stage 3 or more at diagnosis. Four cases were bilateral (7.1%) and two patients had extrarenal Wilms tumor. All patients received chemotherapy; 35 patients also received radiation therapy. Blastemal predominant histology was elicited in 31 (55.4%) of our cases, focal or diffuse anaplasia were found in 13 (23.2%) of the cases. Late complications were observed in 12 patients; including proteinuria (5 patients), bronchiectasis (3 patients), secondary malignancy (2 patients), pulmonary alveolar proteinosis (1 patient) and chronic renal failure (1 patient). Mean follow-up time was 100.5±84.9 (1-274) months. Thirty-one patients were alive in remission without disease. Fifteen patients experienced recurrence or progressive disease; nine of these patients died under treatment. Five-year event free survival and overall survival was 78%, 82%, respectively. Ten-year event free survival and overall survival was 66%, 73%, respectively. One patient had chronic kidney disease and the patient died due to electrolyte disturbance. Two patients had secondary malignancy: one of these had rhabdomyosarcoma, and the other patient had acute myeloid leukemia.

Conclusions

Wilms tumor is a well treatable disease. However significant number of our patients presented in advanced staged. Advance stage at presentation and presence anaplasia require more aggressive management resulting in more complications and higher mortality rate.

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Renal Tumours

A TEN YEAR RETROSPECTIVE AUDIT OF THE CLINIC-PATHOLOGICAL MANAGEMENT AND TREATMENT OUTCOMES OF CHILDREN WITH WILMS TUMOR AT A TERTIARY CENTER

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Objectives

The objectives of this study were to review the clinical presentation and management of children with Wilms tumor and the factors influencing the outcome at Kenyatta National Referral and Teaching Hospital (KNH). The findings of the study will form a basis for revision of treatment design for patients diagnosed with Nephroblastoma at KNH.

Methods

The records of 140 WT patients, aged less than 16 years, who were treated in Kenyatta National Hospital, Kenya, during the period from January 1997 to December 2008 were reviewed. The management protocol followed the scheme of the US National Wilms Tumor Study Group (NSWTG).

Results

Thirteen cases (38.2%) were diagnosed as stage I, 4 (11.8%) as stage II, 13 (38.2%) as stage III and 2 (5.9%) as stage IV. Two cases with bilateral disease (stage V) had stage I tumors in both kidneys. Four-year overall survival (OS) and event free survival (EFS) rates were 65.2% and 52.7%, respectively. Univariate analysis by Log-rank test revealed statistically significant associations between OS and nodal status (p -value < 0.01), manifestation of gross hematuria (p -value 0.02), and tumor size of 10 centimeters or more (p -value 0.02). Multivariate analysis found only the nodal status to be independently associated with OS at a Hazard Ratio of 16.6 (p -value < 0.01). Eight of 13 stage I cases and 6/13 stage III cases had relapsed, with two-year post-relapse survival of 42.8%. Significantly poorer outcome was found in cases with early relapse within 200 days after enrollment (p -value 0.02).

Conclusions

Childhood Wilms' tumor presents late in our setting with its consequent management challenges. The need to educate the populace and the primary healthcare providers on the benefits of early diagnosis and treatment of this condition cannot be overemphasized. Large tumor size and gross hematuria were associated with risk of a poorer outcome.

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Renal Tumours

MANAGEMENT OF BILATERAL WILMS' TUMOR: OUR EXPERIENCE

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Objectives

Management of bilateral Wilms' tumor is particularly challenging, considering the chances of recurrence and long term renal function for affected patients. Aggressive surgical resection to prevent recurrence must be balanced with the desire to preserve renal function. We evaluated our experience in the management of bilateral Wilms' tumor stressing the challenges encountered in decision making and the role of Nephron sparing surgery(NSS) in a limited resource setting.

Methods

Four children presenting with bilateral Wilms' tumor were evaluated. All of them were appropriately staged and given standard chemotherapy as per NWTS 5 guidelines. Tumors were considered to have 'good' response to chemotherapy if sufficient tumor shrinkage was observed so that renal hilum was seen free of tumor and vice-versa. NSS was considered in all and was performed when feasible; followed by completion adjuvant chemotherapy. All patients were followed up with serial ultrasound scans (3-6 monthly) and CECT abdomen (yearly once). Blood urea and serum creatinine, hypertension and proteinuria were assessed during follow up visits.

Results

All 4 children received neo-adjuvant chemotherapy as per NWTS-5 guidelines. The results are summarized in the following table

	Treatment planned based on Pre-operative imaging	Treatment executed on table
I child	Left radical and right partial nephrectomy	No treatment offered as the parents refused treatment.
2 nd child	Left partial and right radical nephrectomy	Bilateral partial nephrectomy
3 rd child	Bilateral nephrectomy with subsequent transplantation	Right partial and left radical nephrectomy
4 th child	Right partial and left radical nephrectomy	Left radical nephrectomy with right tumor biopsy

The 4th child is presently awaiting right partial nephrectomy following 2nd line chemotherapy. The second child is on follow up for 1.5 yrs, doing well.

Conclusions

Management of bilateral Wilm's tumor is challenging and NSS should be considered in all patients having bilateral Wilm's tumor with favourable histology, even if preoperative imaging studies suggest that the lesions are unresectable.

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TREATMENT-RELATED PULMONARY HYPERTENSION IN A PATIENT WITH WILMS TUMOR

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Objectives

Patients with metastatic Wilms tumor (WT) require multimodality treatment with surgery, chemotherapy and radiation to achieve optimal outcome. Such therapy may result in toxicities; a recent clinical trial of high risk renal tumors encountered lung toxicity including pulmonary arterial hypertension (PH). We describe the development and successful treatment of PH in a patient with stage IV WT.

Methods

A 5 year-old female presented with stage IV, favourable histology WT involving the left kidney with extension into the proximal inferior vena cava, and liver and lung metastases. Treatment included surgical resection of the primary tumor, chemotherapy (doxorubicin, dactinomycin and vincristine) and irradiation to the lung and liver with boost to a poorly responding lesion in the upper left lung field. Four months into treatment, she developed persistent tachycardia, respiratory distress and subsequently decreased cardiac function without evidence of hypoxia. Spiral CT revealed no evidence of pulmonary embolism. Although her initial presentation was thought to be cardiac or pulmonary in nature, echocardiogram and subsequent cardiac catheterization were consistent with PH. A lung biopsy showed preserved lung parenchyma with patchy eccentric and mostly non-laminar concentric fibrointimal hyperplasia and medial hypertrophy noted in the small pulmonary arteries, while the pulmonary veins were unremarkable; again findings consistent with PH.

Results

She was treated with supplemental oxygen therapy, pulse intravenous doses of steroid and oral sildenafil for 10 months to maximize pulmonary vascular dilation. With normalization of ECHO and cardiac function she underwent a gradual withdrawal of PH directed therapy; she remains asymptomatic at 5 months off PH therapy.

Conclusions

Cardiac and pulmonary toxicities have been described in metastatic WT patients attributed to radiation and anthracycline administration. Our patient presented with isolated PH that was reversed with treatment. PH must be considered early in symptomatic WT patients in order to implement appropriate therapy.

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WILMS TUMOR TREATMENT RESULTS IN PEDIATRIC POPULATION

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Objectives

Introduction: Wilms tumor (WT) is the most common form of malignant kidney tumor in childhood. According to PINDA protocols, its treatment includes, depending on stage and presentation, early surgery, radiotherapy (RT) and chemotherapy (CT). The objective of this work is to review the results of all patients of the National Cancer Institute (NCI) with this condition.

Methods

Patients and Method: A retrospective review of all patients diagnosed with WT at the NCI was conducted. Patient population, RT treatment received and overall survival results were described and prognostic factors were searched.

Results

From September 1993 to December 2010, 110 children were treated with RT. The median age at diagnosis was 3.6 years old. Median follow-up was 148 months after RT. In March 2014, out of a total of 107 patients with follow up, 24 had died, 21 due to disease progression. All deaths occurred within three years of treatment. Overall survival at 2, 4 and 12 years old was 83 %, 78 %, 78 % respectively. A multivariate analysis showed that each day after surgery and without starting RT, the chances of survival decreased ($p = .04$).

Conclusions

WT treatment has an excellent prognosis. Survival after 3 years stabilizes without presenting complications, regardless of the group to which the patient belongs. Among the prognostic factors for patients with RT prescription, this radiation should be started early, as close to the surgery as possible.

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URETERAL THROMBUS IN WILMS TUMOUR-THE PGIMER CHANDIGARH EXPERIENCE

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Objectives

Ureteral thrombus in Wilms' tumour is a rare occurrence, about 2% of all Wilms' tumour. We present our experience of these patients, being managed with a modified SIOP protocol.

Methods

Records of children with ureteral extension of tumor were reviewed over a period of two years. Presenting symptoms, diagnostic and Histopathological studies, operation performed and outcomes were recorded.

Results

Of the 67 patients operated for Wilms' tumor over a period of two years (2012-2103). There were 4 patients (~5.9%) with ureteral thrombus. All patients had received standard preoperative chemotherapy. There were 2 females and 2 males. Mean age was 3.2 years. Left sided tumour was commoner with L:R ratio 3:1. One patient presented with hematuria and the rest with asymptomatic abdominal mass. One patient was a follow up of WAGR syndrome. Preoperative ultrasound and CT scan showed ureteral involvement in 2 patients. All patients showed some degree of hydronephrosis. All patients successfully underwent nephroureterectomy. In 3 cases we could get below the tumor thrombus and divide the ureter more than a centimetre below the thickened ureter. In the last patient the entire ureter was thickened, right down to the uretrovesical junction. All patients received adjuvant chemotherapy and are event free at mean 21.2 months post operatively.

Conclusions

The incidence of ureteral thrombus is commoner than previously reported. There should be preoperative suspicion in patients with gross hematuria and hydronephrosis. Accurate imaging will help in preoperative planning.

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Renal Tumours

THE CLINICAL EFFECTS OF COMPREHENSIVE TREATMENT FOR WILMS TUMOR IN CHILDREN

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Objectives

To investigate the therapeutic effects of individualized comprehensive treatment for Wilms tumor in children.

Methods

The clinical data of patients with Wilms tumor confirmed by clinical features, radiology and pathology from January 2006 to December 2012 were collected. Diagnosis and treatment were decided and conducted by applying therapeutic regimens stratified by stage and histology in accordance With National Wilms Tumor Study criteria of USA. The patients of favorable histology (FH) stage I and II and anaplastic stage III were only received chemotherapy, and the patients who cannot removed completely received two cycles neoadjuvant chemotherapy. The period of following-up was 4 months to 6 years and 7 months.

Results

There are 25 boys and 17 girls in this group, According to the tumor stage criteria after operation, 9 cases were at stage I, 18 cases at stage II, 9 cases at stage III, 5 case at stage IV and 1 case at stage V. Pathologic analysis showed that 35 cases were at favorable-histology, 7 case at unfavorable-histology. At present 36 patients were alive without tumor except 6 patients died of disease.

Conclusions

Multidisciplinary therapy protocol for childhood Wilms tumor can achieve good effects.

EP-564

Retinoblastoma

CHALLENGES IN TREATING ADVANCED STAGE RETINOBLASTOMA AND ROLE OF NEOADJUVANT CHEMOTHERAPY IN DEVELOPING COUNTRIES: CHILDREN'S HOSPITAL LAHORE EXPERIENCE

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Objectives

The Children's Hospital Lahore is a tertiary government centre receiving over 500 new cancer patients per year from all over the country. The purpose of this study was to analyze management and outcome of children with retinoblastoma and to discuss the role of neoadjuvant chemotherapy in developing countries.

Methods

Retrospective review of 56 patients enrolled between January 2011 – January 2014 was done. Data regarding their age, stage, histopathology, treatment, outcome and impact of neoadjuvant chemotherapy was analyzed. Patients were treated according to UKCCSG RB 2005 11 protocol.

Results

Total 56 patients with age ranging from < 1 to 7 years (89%

Conclusions

Mortality of 18% can be reduced by early diagnosis and early treatment strategies. Majority of patients have advanced extra ocular disease at presentation and a high rate of abandoning treatment. In developing countries late referrals are strongly associated with orbital and metastatic disease. The prognosis can significantly be improved by public awareness to seek early treatment and establishing multidisciplinary team approach, strong social support, utilising neoadjuvant chemotherapy, and intense psychosocial counselling for timely enucleation.

EP-565

Retinoblastoma

PROFILE AND OUTCOME OF RETINOBLASTOMA PATIENTS AT A PHILIPPINE NATIONAL REFERRAL CENTER

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Objectives

Retinoblastoma (RB) has a high incidence in the Philippines (17.4 per million children 0-4 years) and the expected number of new cases each year is 180. Many of these children are referred to the national referral center, Philippine General Hospital. We reviewed the cases seen at the ophthalmology and pediatric oncology charity service.

Methods

Records of newly-diagnosed retinoblastoma patients from January 2008 to December 2012 were reviewed.

Results

There were 112 cases (88 unilateral; 24 bilateral) from Jan 2008 to Dec 2012. Mean ages were 32.5 months for unilateral RB and 19 months bilateral. Initial presentation were leukocoria in 70 % (n=79), mass 21 % (n=24), strabismus 4 % (n=4), eye redness in 3 % (n=3), blindness 1 % (n=1) and dilated pupil 1 % (n=1). Staging was based on pathology report: Intra-ocular 44 % (n=49), extra-ocular 52 % (n=59) and missing data 4 % (n=4). Records of metastatic work-up were lacking. 109 (97 %) patients were treated with upfront enucleation. Two refused treatment; one transferred care. Adjuvant chemotherapy included Vincristine, Carboplatin and Etoposide. Only two patients received radiation. For outcome, 29 patients (26 %) were alive; with 19 children treated with enucleation alone. Fifty-six (50 %) abandoned therapy, 17 died (15 %) and 8 (7 %) were lost to follow up. Of those who abandoned therapy, 52 % (n=29) stopped before adjuvant chemotherapy; 30 % (n=17) during chemotherapy; 14 % (n=8) before radiation; and 4 % (n=2) during radiation. The cause of death was intracranial extension in 65% (n=11) and not recorded in 35% (n=6).

Conclusions

Advanced disease and abandonment are major causes of poor outcome. Early detection campaigns and establishment of a referral system will facilitate timely diagnosis and treatment. Prospective studies are needed to identify specific barriers to care and monitor impact of interventions.

EP-566

Retinoblastoma

IMPACT OF IMPLEMENTING A RETINOBLASTOMA PROGRAM IN A PUBLIC TERTIARY HOSPITAL IN A RESOURCE LIMITED SETTING

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Objectives

Retinoblastoma has a high incidence in the Philippines (17.8 per million children 0-4 years), and majority of the patients present late with extra-ocular extension. Reasons for delayed diagnosis include financial constraints, inaccessibility to care and misdiagnosis. For Mindanao, Philippines, 35-40 new cases are expected yearly, yet fewer than 10 were seen in the government referral center. To address this, a multifaceted program was established in May 2011 at Southern Philippines Medical Center, involving education of healthcare providers from local health centers and government hospitals on early warning signs of retinoblastoma; establishment of a referral system; development of stage-based treatment regimens; and multi-disciplinary team formation. Capacity building included a dedicated retinoblastoma patient coordinator, specialist clinic, and interdisciplinary case discussions.

Methods

Data on all retinoblastoma patients were prospectively collected as part of routine clinical care from May 2011, and compared with retrospective data prior to program implementation. Treatment included enucleation, radiation and chemotherapy with Vincristine, Carboplatin and Etoposide.

Results

From May 2011 to February 2014, 40 newly-diagnosed patients were seen (33 unilateral, 7 bilateral). Mean age was 2.6 years. Lag time to diagnosis was 16 months (median 11, range 0.5– 96) IRSS staging were: Stage 0 (n=3); Stage 1 (n=9); Stage 2 (n=1); Stage 3 (n=10); and Stage 4 (n=13). Four patients refused staging work-up. Overall and event-free survival rates were 40% and 27% at 1 year and 30% and 25 % at 2 years, respectively. Nine patients (23 %) abandoned treatment. Compared to baseline estimates (2005-2010), the mean annual referrals increased from 7 to 14, and extra-ocular presentation dropped by 19%.

Conclusions

The development of effective public health education and referral system for retinoblastoma and the establishment of centers of excellence through local and international collaborations increased patient referrals and decreased extra-ocular presentation rates. The sustainability of this model is needed to impact outcomes.

EP-567

Retinoblastoma

ONCOGENIC HUMAN PAPILLOMA VIRUS 16 ISOLATED IN ONE-FOURTH EYES WITH NON-FAMILIAL RETINOBLASTOMA: A PROSPECTIVE CASE-CONTROL STUDY IN NORTH INDIAN CHILDREN

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Objectives

The risk factors for non-familial retinoblastoma are poorly understood. The incidence of retinoblastoma is higher in developing countries. A few reports have described human papilloma virus (HPV) in retinoblastoma tumor tissue. The aim was to investigate the prevalence of HPV in retinoblastoma tumor tissue and compare with controls.

Methods

The study was prospective. The cases included eyes enucleated for retinoblastoma. Controls were donor eyes obtained from the eye-bank. DNA was isolated from normal retinal tissue from donor-eyes and tumor tissue from eyes with retinoblastoma. PCR for HPV was performed by HPV Genotyping Array kit (HybriBio Ltd., Hong Kong). **It utilizes L1 consensus primers to simultaneously amplify 21-HPV genotypes followed by hybridization with respective probes embedded on membrane fibers.** High-risk HPV types: 16,18,31,33,35,39,45,51,52,56,58,59 and 68; probable high-risk types: 53 and 66; low-risk types: 6,11,42,43,44 and 81. Funding: research-grant from parent institution.

Results

The study enrolled 42 retinoblastoma and 42 normal retinal tissues. Disease was bilateral in 14 (33%). Three (7%) patients had a family history of retinoblastoma. 10 (23.8%) tumor tissues were infected with HPV. HPV-16 was the only subtype isolated. None of the control eyes or familial cases were HPV positive.

	HPV positive n=10	HPV negative n=32	P-value
Mean age (months)	36.3	44.5	0.40
Males	7 (70%)	15 (47%)	0.56
Low socio-economic status	8 (80%)	12 (37.5%)	0.24
Rural background	6 (60%)	14 (44%)	0.76
Extra-ocular disease	3 (30%)	5 (15.6%)	0.41
Vaginal delivery	10 (100%)	24 (75%)	0.18

Conclusions

HPV-16 was isolated from 10 (25.6%) of the 39 eyes with non-familial retinoblastoma. None of the control or familial cases were HPV positive. A greater number (though not significant) of HPV positive cases, had a vaginal delivery and belonged to a low socio-economic background. The link of HPV with retinoblastoma can be explored for preventive strategies in developing countries.

EP-568

Retinoblastoma

THE IMPACT OF OPTIC NERVE RESECTION LENGTH ON SURVIVAL IN RETINOBLASTOMA

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Objectives

Enucleation cures most patients with unocular retinoblastoma, however, some patients present with extraocular relapse after enucleation. There are many high risk factors such as scleral involvement, choroidal invasion, post laminar optic nerve involvement and disease free optic nerve length which impact survival. However due to overall good survival rate impact of tumor free optic nerve length on survival has not been studied exhaustively. This study was done to determine if the resection length of the optic nerve had an impact on the survival so as to guide surgeons to do optimum surgery and thereby improve outcomes.

Methods

This was a retrospective analysis of prospectively maintained data at our database. All patients who had undergone surgery for Retinoblastoma between September 2004 and September 2013, were included. Data was analysed using SPSS to assess the impact of optic nerve tumor free resection margin on survival and to delineate other various prognostic factors that affect survival in Retinoblastoma-

Results

A total of 115 cases were included in the study. The median length of optic nerve obtained was 1cm (range 0.2-2.5 cm). Of the 18 cases wherein there was involvement of the optic nerve, (post-laminar: n=11, pre-laminar: n=3 and laminar involvement: n=4) the cut margin was found to be positive in only one case. Histological factors were unfavorable in 44 patients, no residual tumor in two and favorable rest. The event free survival was better in patients with optic nerve length >1cm than in patients with optic nerve length <1cm (p<0.03).

Conclusions

Better event free survival is seen with 1cm or more of resected optic nerve length. Thus optimal surgery should include at least 1 cm of tumor free length of optic nerve to improve outcomes.

EP-569

Retinoblastoma

DIENCEPHALIC TUMOR IN RETINOBLASTOMA PATIENTS: A RARE COINCIDENCE?

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Objectives

Retinoblastoma (RB) patients present an high risk to develop second malignant neoplasm (SMN), especially children with an hereditary RB. Diencephalic tumors are rare in paediatric age. We report on three cases of diencephalic tumors occurring in RB patients

Methods

Clinical and imaging finding of the three patients were reviewed. The RB database was checked in order to identify patients with similar diencephalic lesions diagnosed from January 1999 since December 2012.

Results

107 RB patients were diagnosed over 14 years. Three patients (2,8%) presented a diencephalic tumour during the follow-up period: none of them presented a family RB history while a RB1 alteration was identified in two patients with bilateral RB. The diencephalic lesion occurred 15, 43, and 53 months from RB diagnosis without any symptoms. Biopsy was performed in one patient and histology showed a low grade glioma. After a period of stable disease, the lesions progressed in the first two patients; the first patient received radiotherapy (54 Gy) while the later one chemotherapy based on bevacizumab plus irinotecan. Three patients are alive at 20 months, 10 months and 8 years from CNS tumour diagnosis.

Conclusions

Diencephalic tumour in previously treated RB patients seems a peculiar SMNs. Considering the site, the short time interval between tumours and the absence of risk factors clearly associated with SMNs, an alternative pathogenetic mechanism should be supposed. Further analyses of large series are needed to clarify this entity.

EP-570

Retinoblastoma

ANGIOGENESIS IN RETINOBLATOMA: REVISED ASSESSMENT AND THERAPEUTIC SUGGESTION

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Objectives

Retinoblastoma (RTB) is a well-known vascularized tumor. We assessed the expression of angiogenic markers in RTB patients to explore possible associations with clinical and pathological parameters. Therapeutic considerations were addressed according to our results.

Methods

Seventy-four primary RTB paraffin-embedded samples were analyzed by immunohistochemistry. Cell proliferation potential was determined by Ki67 staining. The expression of CD31, CD105, Smooth Muscle Actin, VEGF and VEGFR2 was evaluated as indicative of the angiogenic tumor features. The tumour necrosis was also measured. The clinical and histological data such as age, laterality, clinical stage according to International Retinoblastoma Staging System (IRSS) and Classification System Intraocular Retinoblastoma were reviewed. Coroid, scleral and nerve involvement evaluated according to IRSS and anterior chamber involvement were correlated with markers expression.

Results

CD31, CD105 and Smooth Muscle Actin were expressed at different levels in all RTB specimens while VEGF and VEGFR2 in 70% and 58%, respectively. Ki67 was positive in 90% and tumor necrosis > 50% present in 35% of samples. CD31, CD105 and Smooth Muscle Actin were more expressed in bilateral cases and in samples from patients with anterior chamber involvement. VEGFR2 was expressed in 50% of samples from RTB patients with primary enucleation and in 71% after chemotherapy treatment ($P < 0.02$), whereas no difference was seen for the expression of VEGF.

Conclusions

Our data show that VEGFR2 is expressed in the majority of resistant RTBs. This result suggests that an anti VEGFR2 treatment could be proposed and theoretically effective. Probably, bilateral cases and patients resistant to standard antiproliferative drugs could benefit of an anti-angiogenesis approach.

EP-571

Retinoblastoma

DEVELOPING CLINICAL CANCER GENETICS SERVICES IN RESOURCE LIMITED COUNTRIES: THE CASE OF RETINOBLASTOMA IN KENYA

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Objectives

Clinical cancer genetics is an integral part of cancer control and management, yet its development as an essential medical service has been hindered in many Low-and-Middle-Income Countries. We report our experiences in developing a clinical cancer genetics service for retinoblastoma in Kenya.

Methods

A genetics task force was created within the membership of the existing Kenyan National Retinoblastoma Strategy group. The task force engaged in multiple in-person and telephone discussions, offering experiences, opinions and suggestions for an evidence-based, culturally-sensitive retinoblastoma genetic service. Discussions were recorded and thematically categorized to develop a strategy for design and implementation of a national retinoblastoma clinical genetic service.

Results

Discussion among the retinoblastoma genetics task force supported the development of a comprehensive genetic service that rests on three pillars: 1) Patient and Family Counseling, 2) Community Involvement, and 3) Medical Education.

Conclusions

A coordinated national retinoblastoma genetics task force led to the creation of a unique and relevant approach to delivering comprehensive and accurate genetic care to Kenyan retinoblastoma patients. The task force aims to stimulate innovative approaches in cancer genetics research, education and knowledge translation, taking advantage of unique opportunities offered in the African context.

EP-572

Retinoblastoma

IDENTICAL TRIPLETS WITH RETINOBLASTOMA ILLUSTRATE THE SPECTRUM OF THERAPY FOR OPTIMAL OUTCOMES

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Objectives

To describe treatment choices to optimize outcomes for identical triplets affected by retinoblastoma.

Methods

A digital image of the tear-drop shaped pupil in one eye of 2 month-old triplet boys revealed leukocoria. Examination under anaesthesia revealed that five of the six eyes had retinoblastoma tumors. All eyes had varying degrees of minor iris coloboma.

Results

Treatment for each child and eye depended on size and location of tumors, and degree of involvement of the other eye. Triplet 1 had on eye International Intraocular Retinoblastoma Classification Group 0 (no tumor on visual and RetCam imaging). The other eye was Group C (macular tumor with adjacent vitreous seeds, one peripheral tumor), treated with 532 nm laser (peripheral tumor) and subtenon's Topotecan and intravitreal melphalan. Triplet 2 had Group A and B eyes, with no threat to vision. Five of ten tumors were invisible, detected by optical coherence tomography (OCT). Eight tumors were treated with laser, confirmed correct by OCT for the invisible tumors; peripheral tumors were treated with cryotherapy. Triplet 3 had Group A and D eyes. The Group D eye had macular large tumor overhanging the optic nerve, inferior retinal detachment and subretinal seeding. Extensive discussion with parents and family evaluated the child's interests: salvage of the right eye would require invasive treatments, repeated and monitored for at least 3 years under anaesthetic, with ongoing risks; simple enucleation of the Group D eye would avoid invasive extended interventions. Enucleation was performed with immediate placement of a temporary prosthetic eye.

Conclusions

All three children avoided initial systemic therapy. All children have excellent visual prognosis. Until one year of age OCT will be regularly used to detect and treat early, tiny visually threatening tumors.

EP-573

Retinoblastoma

PATHOLOGIC RISK FACTORS AND ESTIMATE OF RISK OF RELAPSE IN RETINOBLASTOMA AT INSTITUTO NACIONAL DE CÂNCER- BRAZIL

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Objectives

Unilateral retinoblastoma accounts for 60% of cases with advanced intraocular disease at diagnosis requiring enucleation. Adjuvant chemotherapy to avoid the risk of relapse should be based on pathologic evaluation. We describe histopathological study of intraocular unilateral RB (RE group V/IRCE) primarily enucleated with or without adjuvant therapy according to pathologic risk factors and its correlation to outcome.

Methods

Retrospective study of primarily enucleated advanced RB between 2006 and 2013: 103 patients with RB were admitted, 65 unilateral (63%); 45/65 enucleated (69%); 16/45 received previous treatment and one enucleated before admission at hospital were excluded from analysis. All eyes were reviewed by experienced pathologists to assess choroidal and/or optic nerve involvement according to pathology guidelines from the International Retinoblastoma Staging Working Group. They were classified as low-risk group (minimal or no choroid invasion and/or prelaminar or absence of optic nerve involvement), intermediate-risk (massive choroidal invasion and/or intraor retrolaminar involvement) and high-risk groups (scleral invasion and/or tumor at the cut end of optic nerve). Outcome was assessed in all cases.

Results

Twenty out of 28 (71,4%) had low-risk pathologic findings: in 13/28, no choroidal invasion, optic nerve involvement or optic nerve involvement up to the lamina cribrosa were observed and no further treatment was given. They are alive without evidence of disease; Seven isolated choroid invasion: focal (n= 3) and massive (n= 4) and received no adjuvant chemotherapy. Of these, 6/7 alive without evidence of disease and one with massive invasion, developed bone and bone marrow relapse, treated with intensive chemotherapy and is alive with evidence of disease; Eight (28.6%) had intermediate-risk and high-risk features: In 3/28 cases with invasion of the optic nerve beyond the lamina cribrosa and received chemotherapy. Two of them are alive disease-free and one developed CNS relapse dying from progressive disease (PD); Two or more risk factors observed in 5 cases received chemotherapy: 2 alive/disease-free and 3 relapsed. In our series, 90% (n=25) are alive.

Conclusions

An accurate histopathologic assessment after enucleation is crucial to indicate adjuvant therapy and graduation intensity approach. Survival was excellent and low-risk group. Intermediate- and high-risk groups indicate the need of chemotherapy intensification

EP-574

Retinoblastoma

BILATERAL RETINOBLASTOMA , CONSERVATION MODALITIES CASE REPORT

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Objectives

To report a case of a one year old bilateral retinoblastoma who was treated successfully with preoperative chemotherapy and locoregional treatment .

Methods

case report of a one year old bilateral retinoblastoma

Results

A one year old girl - with no family past history - presented a right leukocoria. Clinical examination and MRI concluded to retinoblastoma Reise V right and Reise III left with no cerebral or other second location .

She received 3 courses of chemotherapy CEV (Carboplatin , Etoposide , Vincristin) well tolerated , which reduced much more the left tumor volume than the right one .

A collaboration with Curie Institute was considered to offer the chance to preserve the right eye . To avoid the tumor spread during the delay , the child received 3 other CEV courses .

A favorable response were noticed with only persistant calcified formations of 5-6 mm in both eyes (3 in the right eye and one in the left eye) .

The patient had 3 laser sessions and cryotherapy on the right eye and laser combined to plaque radiotherapy on the left eye .

After 6 months , no relapse neither sequelae are noticed .

Conclusions

Combination modalities of first line chemotherapy , eye laser , cryotherapy and plaque radiotherapy are a good strategy to avoid enucleation especially in bilateral retinoblastoma.

EP-575

Retinoblastoma

THE CLINICAL ANALYSIS OF 42 CASES WITH BILATERAL INTRAOCULAR RETINOBLASTOMA

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Objectives

Retinoblastoma(RB) is the most common primary malignant intraocular tumor in children. This study was to analyze the clinical characteristics of diagnosis and treatments for patients with bilateral intraocular retinoblastoma.

Methods

The clinical document of 42 cases with bilateral intraocular retinoblastoma confirmed in our hospital from December 2009 to February 2011 were retrospectively analyzed.

Results

The median age of primary diagnosis was 13 months, that was younger than unilateral Rb patients at same time. In all patients, leucocoria was the most common manifestation with the primary diagnosis rate 69% based on this symptom (29 cases). Of 84 intraocular retinoblastomas, 3(3.6%) in Group A;9(10.7%) in Group B; 10(11.9%)in Group C; 40(47.6%)in Group D;22(26.2%)in Group E. 21 patients had enucleation. In Group D and E, Enucleation rate before chemoreduction or not had significant difference (P=0.016). Among 42 patients 5 were dead(12%), only 1 patient for complication caused by chemoreducton. Only 3 patients occurred transient hearing losses, hear losses recovered during fellow up. In sum, 67.8 percent of the sick eyes are preserved. The preserving eyes percentage of group E was 50%, that of group D was 62.5%; that of group C was 90%; Group C and group B and group A have no enucleation case.

Conclusions

Chemoreduction combined with local ophthalmic therapy is effective for treatment of intraocular retinoblastoma. Systemic chemotherapy can reduce enucleation without significant systemic toxicity.

EP-576

Retinoblastoma

RB1 MUTATIONS IN SOUTH AFRICAN CHILDREN WITH RETINOBLASTOMA

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Objectives

Retinoblastoma, the most common intraocular tumour in children, is caused by mutations in the *RB1* tumour suppressor gene. The aim of this study was to screen children with retinoblastoma, treated at two treatment centers in South Africa for *RB1* mutations.

Methods

A total of 99 blood samples and 75 FFPE tumour samples from 106 RB families; (8 familial with 17 affected individuals; 53 sporadic bilateral; 45 sporadic unilateral cases) were screened for large re-arrangements of the *RB1*-gene by MLPA analysis and for small sequence changes by SSCP and direct sequencing.

Results

A total of 94 mutations, consisting of 8 large genomic deletions/insertions, 22 frame-shift, 43 nonsense, 14 splice-site, 5 missense, one in-frame deletion and one promotor mutation, were detected. The small mutations were the most frequent (91%), and large deletions/insertions less common. Two of the large genomic deletions were somatic mutations (2 sporadic unilateral cases), whereas the other six were all germ-line changes in one familial (duplication of exon 3) and five bilateral sporadic cases (deletions of varying sizes). Frame-shift and nonsense mutations were the most frequent small mutations (75%). The R320X mutation in exon 10 was the most common recurrent (n=8) nonsense mutation. Heritable cases (47/53 sporadic bilateral and 8/8 familial cases) had a germ-line mutation detection rate of ~ 87% (55/61) and ~ 18% (8/45) of the sporadic unilateral cases also had a germ-line mutation. Somatic mutations were detected in 64% (29/45) of the sporadic unilateral cases. Unidentified mutations in the bilateral probands may be due to the presence of low-level mosaicism, not detected with our screening methods. Eight unilateral sporadic cases that did not appear to have *RB1* mutations may be due to epigenetic changes.

Conclusions

This is the first report of *RB1* mutations in South African children which is important for genetic counseling.

EP-577

Retinoblastoma

LIFE STYLE PARAMETERS AND PATERNAL SPERM DNA HEALTH - ROLE IN SPORADIC RETINOBLASTOMA

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Objectives

As compared to somatic cells and oocyte sperms are most vulnerable to oxidative stress due to minimal cytosolic anti-oxidants. Oxidative stress damage both sperm's nuclear and mitochondrial DNA. Therefore we planned to analyze sperm DNA integrity, free radical level, oxidized DNA bases in father of children with sporadic Retinoblastoma and correlated these parameters with life style habits of the father.

Methods

A total of 115 cases of sporadic retinoblastoma and 50 control men were recruited at a tertiary referral centre in India. Semen samples were collected from the father of Rb patients and analyzed for semen parameters as per WHO (1999) guideline. Biological markers for sperm DNA damage such as DNA Fragmentation Assay (DFI) by SCSA, 8-Oxo-2'-deoxyguanosine (8-OHdG) by ELISA and Reactive Oxygen Species (ROS) levels by Chemiluminescence assay were measured. By mutation analysis (qPCR sequencing) of Rb gene, inheritance was ruled out in blood DNA of parents. Logistic binary regression was used to compute the odds ratios (OR) for Rb.

Results

Among the cases and controls, significant difference in all experimental parameters such as ROS ($p < 0.001$), DFI ($P = 0.01$) and 8-OHdG ($p < 0.001$) were observed. ORs for smokers [10.0 (2.9-34.45; $p < 0.001$); 95%CI] while for pesticides exposed and alcoholics the [95% CI] was [3.5 (95%CI; 1.01-12.16); $p = 0.037$] and [7.292 (95%CI; 2.13-24.92); $p < 0.001$] respectively.

Conclusions

Majority of sperm DNA damage is repaired by oocyte but there is a threshold beyond which sperm DNA damage may not be repaired, and accumulation of ethenonucleosides (type of DNA lesion) in sperm may inhibit nucleotide excision repair mechanism. The mutational load thus carried by the embryo after fertilization has a high level of DNA damage and is influenced by DNA repair capacity of oocyte. Thus accumulation of sperm DNA damage may result in sporadic Rb. Smoking, pesticides exposure and alcohol intake adversely affects DNA quality and thus life style interventions can significantly improve DNA health.

EP-578

Retinoblastoma

PLASMA MIR-320, MIR-LET-7E AND MIR-21 AS NOVEL POTENTIAL BIOMARKER FOR RETINOBLASTOMA DETECTION

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Objectives

Our study aimed to investigate whether the expression of candidate miRNAs(miR-373,miR-503, miR-320, miR-let-7e, miR-492, miR-498 and miR-21) show some differences between the plasma of RB patients and healthy controls by real-time quantitative polymerase chain reaction (qRT-PCR). We also discuss the relationship of plasma miRNAs and the clinical characteristics of RB patients, and evaluate the value of plasma miRNAs to distinguish RB patients from healthy controls.

Methods

In our study, we collected 65 plasma samples from RB patients and another 65 samples from healthy people as control. MicroRNA levels were measured via real-time quantitative polymerase chain reaction (qRT-PCR) and its relativity to retinoblastoma was tested through statistic data analysis and receiver operating characteristic (ROC) curve.

Results

Plasma miR-320, miR-let-7e and miR-21 were down-regulated in patient samples, AUCs ranged from 0.548 to 0.660 and those of combined classifiers were no less than 0.990.

Conclusions

Plasma miRNA level shows some importance in RB diagnose and can be regarded as novel diagnose biomarker especially for miR-320.

EP-579

Retinoblastoma

PRESENTATION AND OUTCOME OF RETINOBLASTOMA (RB) IN A DEVELOPING COUNTRY: EXPERIENCE AT A SINGLE INSTITUTION

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Objectives

In Pakistan, the incidence of RB is 4/100,000 children but there is limited information about their outcomes. Objective of this study is to review the presenting features and outcome for RB at a tertiary care cancer center in Pakistan.

Methods

We conducted a retrospective review of all the patients treated at SKMCH &RC for RB between January 2007-2012. Demographics, presenting features, treatment details and outcomes were collected and analyzed using SPSS 19.

Results

Out of 139 patients studied 67% (n=87) had unilateral disease. Median age at presentation was 3 years with male to female ratio of 1.6:1. Median time to presentation was 5 months. Most common presenting symptom was leukocoria in 83%. Forty percent (n=55) reported loss of vision at the time of presentation. Almost half of the patient underwent upfront enucleation, 48% had extraocular disease and 15% presented with distant metastases. Cut end of optic nerve was involved in 37% of patients while 16% had scleral involvement, 33% showed choroidal involvement, 32% anterior chamber involvement and 35% lamina cribrosa invasion. Twelve percent (n=17) abandoned before initiation of therapy. Only 13% did not require chemotherapy whereas others were treated with 4-6 cycles of chemotherapy (Carboplatin/Vincristine/Etoposide). Half of the patients had intraocular disease and eye salvage was possible in only 10% of them. Overall survival was 44% at 5 years. Event free survival was significantly better ($p < 0.01$) for patients without cut end involvement (70% vs. 20%). In terms of global survival, 88% of patients with unilateral disease underwent enucleation while in case of bilateral disease, 56% lost one eye whereas 19% underwent bilateral enucleation.

Conclusions

Global and overall survival in our patient is much lower than that reported in the literature. This may be related to advanced stage and adverse histologic features due to delay in presentation.

EP-580

Retinoblastoma

RETINOBLASTOMA IN INDIAN CHILDREN: CLINICAL PROFILE AND PREDICTORS FOR METASTASIS

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Objectives

Retinoblastoma is the most common primary intraocular malignancy in children. The tumor is highly curable when it is intraocular. In developing countries rate of ocular salvage and patient survival are low since diagnosis is delayed .

Objective: To determine the burden and clinical profile of retinoblastoma in a tertiary center in India and to ascertain the risk factors for metastasis

Retinoblastoma is the most common primary intraocular malignancy in children. The tumor is highly curable when it is intraocular. In developing countries rate of ocular salvage and patient survival are low since diagnosis is delayed .

Objective: To determine the burden and clinical profile of retinoblastoma in a tertiary center in India and to ascertain the risk factors for metastasis.

Methods

Retrospective analysis of case records of newly diagnosed patients of retinoblastoma over a period of 18 months was done. Clinical profile was ascertained .Reasons for delayed presentation and risk factors for metastasis were identified.

Results

201 patients of retinoblastoma were diagnosed in the study period. 35 patients (51 eyes) had extraocular retinoblastoma(non metastatic).Majority of children with EORB were below 4 years of age. Bilateral involvement was seen in about 46% cases. M;F ratio was 1.5:1.Majority belonged to low socio economic strata. Family history was seen in only 4 cases;these cases had a bilateral involvement. leukocoria was the commonest presentation followed by squint and proptosis.

Conclusions

Extraocular involvement was seen in 35 cases.All children were below 4 years of age and majority presented with proptosis /exophytic mass .All 4 children with EORB and bilateral disease developed metastatic disease. Delayed diagnosis was a risk factor for metastasis. Ignorance on behalf of parents, delay in referral on behalf of general practitioner/pediatrician and refusal of medical advice lead to delayed diagnosis and poor treatment outcomes

EP-581

Retinoblastoma

CORRELATION OF HIGH MOBILITY GROUP PROTEIN (HMGB1) WITH HISTOPATHOLOGICAL HIGH RISK FACTORS IN RETINOBLASTOMA

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Objectives

Retinoblastoma is a malignant tumor composed of embryonic tumor cells from retinoblasts of neuroepithelial origin. HMGB1 is the most important chromatin proteins. This protein organizes the DNA and regulates transcription. HMGB1 are associated with cell proliferation, differentiation and neoplastic transformation. However, the role of HMGB1 is still unclear in retinoblastoma.

Methods

Prospective analyses of 69 primary enucleated retinoblastoma cases over a period of one year were included. Expression of HMGB1 was performed by immunohistochemistry (IHC) in formalin fixed retinoblastoma specimens. mRNA expression was performed by semi-quantitative Reverse Transcriptase PCR (RT-PCR).

Results

A total of 69 eyes were taken of which 12(17.39%) eyes had bilateral involvement. Ages ranged from 7months to 8years. 53 (76.81%) cases were reported as poorly differentiated tumors whereas 38(55.07%) and 20(28.98%) cases had necrosis and calcification respectively. Histopathologically, 16(23.18%) had massive choroid invasion, 16(23.18%) had optic nerve invasion, 6 cases each had sclera and ciliary body invasion. Strong expression of HMGB1 were seen in 38/69(55.07%) cases. RT-PCR was performed on 31 cases in which 24 cases show mRNA expression (24/31) (77.41%). Expression of HMGB1 was statistically significant with poor differentiation ($p=0.0440$), optic nerve invasion ($p=0.0128$) and with HRF ($p=0.0166$).

Conclusions

Expression of HMGB1 is more frequently found in poorly differentiated tumors and those with, histopathological high risk factors. HMGB1 could serve as a poor prognostic marker in retinoblastoma. Further understanding of the molecular mechanisms underlying HMGB1 function could yield novel therapeutic approaches to anti-cancer strategies.

EP-582

Retinoblastoma

EVALUATION OF THE CEREBROSPINAL FLUID IN RETINOBLASTOMA: USE OF CYTOLOGY, IMMUNOCYTOLOGY AND MOLECULAR MARKERS

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Objectives

To evaluate the role of immunocytology for the ganglioside GD2 and RT-PCR for GD2 synthase and the cone transcription factor CRX for confirmation of malignancy and minimal dissemination (MD).

Methods

From 2007 to 2012, CSF evaluation was done at diagnosis in children IRSS stages II-IV, trilateral disease, high risk stage I and in all cases where an extraocular relapse was clinically suspected. Morphological evaluation of the CSF was done and immunocytology for GD2 was done for confirmation in cases with pleocytosis or abnormal cells in the morphologic examination

Results

No positive CSF was detected in 68 children with high risk stage I (1 had MD). One CNS relapse occurred in a child that had negative MD. Nineteen children had stage II-IVa (CNS relapse occurred in 7, 2/5 of those with MD). There were 4 patients with stage IVb or trilateral disease (2 relapsed, 1/1 with minimal disease). One patient with stage 0 had a CNS relapse after delayed enucleation because of problems in compliance. Overall, 11 positive diagnostic CSF examinations were obtained at the moment of CSF relapse in symptomatic patients. Nine had a positive cytology confirmed by immunocytology, 2 had inconclusive cytology with positive immunocytology or evaluation of CRX. In 2 children, molecular detection of MD preceded CNS relapse.

Conclusions

In cases with positive or inconclusive CSF examinations, the use of immunocytology for GD2 or PCR for CRX may improve diagnostic accuracy. MD may be detected in children with advanced disease correlating with increased risk of CSF relapse.

EP-583

Retinoblastoma

THE PREDICTIVE VALUE OF TNM CLASSIFICATION, THE INTERNATIONAL CLASSIFICATION, AND REESE-ELSTHWORTH STAGING OF RETINOBLASTOMA FOR THE LIKELIHOOD OF HIGH RISK PATHOLOGIC FEATURES

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Objectives

To evaluate the predictive value of the 7th edition American Joint Committee on Cancer/the Union for International Cancer Control (AJCC/UICC) TNM classification, the International Classification (ICRB), and Reese-Elsthworth (RE) Staging for Retinoblastoma (RB) for the likelihood of High risk pathologic features (HRF) in eyes treated by primary enucleation.

Methods

A retrospective, observational case series of 50 eyes of 49 patients who had pathologically confirmed RB after enucleation as primary therapy by reviewing medical records, pathology reports and Ret-Cam images. The main outcome measures included: demographics, laterality, TNM stage, ICRB group, RE stage, choroid invasion, optic nerve invasion, anterior chamber invasion, and scleral invasion.

Results

The median age at enucleation was 30 months. Twenty-seven (55%) patients were males, and 19(39%) patients had bilateral RB. HRF mandating adjuvant chemotherapy were seen in 5 (22%) of T2 eyes, and in 15 (56%) of T3 eyes ($p= 0.021$), and in 1(13%) of ICRB group C eyes, 8 (33%) of group D eyes, and 11 (61%) of group E eyes ($p=0.035$). Stage RE-Va tumors had higher incidence of HRF than the upstaged RE-Vb eyes. Twenty (40%) patients received adjuvant chemotherapy for HRF, and at median follow up of 40 months, no single case had metastasis or was dead.

Conclusions

The higher AJCC/UICC T stage of the disease and the more advanced IIRC group at presentation are associated with a higher incidence of HRF, while that was not the case for RE staging system. Very large tumors (occupying >50% globe) should be considered ICRB group E rather than group B since they have a higher incidence of HRF.

EP-584

Soft Tissue Sarcomas

PACLITAXEL IN RELAPSED OR REFRACTORY PEDIATRIC BONE AND SOFT TISSUE SARCOMAS

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Objectives

Given the poor outcomes of relapsed/refractory soft tissue and bone sarcomas we retrospectively review our results with paclitaxel, cyclophosphamide and carboplatin (PCC) regimen to evaluate the effectiveness and outcome.

Methods

The files of 12 children diagnosed as rhabdomyosarcoma (n=9), Ewing sarcoma (n=2) and malignant mesenchymal tumor (n=1) treated with PCC regimen on relapsed/refractory disease were retrospectively.

Results

The median age of 7 boys and 5 girls was 11,6 years (ranged 0,7-17). Median EFS until the first event was 7,2 months (3,4-63,5). PCC regimen was used as 2nd-line in 2 patients, 3rd-line in 9 patients and 4th-line regimen in 1 patient. Patients received median 4 courses (1-10) either as the only PCC 4-weekly in 6 patients or alternated with reduced dose VAC regimen (vincristine, dactinomycin and cyclophosphamide) in 6 patients. Objective response rate was %58 (2 CR + 3 VGPR + 2 SD). Five patients had progressive disease. Median EFS and OS after PCC were 7,8 months (1-68 months) and 13,5 months (2,5-82 months). Two-year EFS and OS rates were %33 and %81 for 12 patients. Median EFS of PCC and alternated PCC-VAC regimens were 12 and 19 months (p=0,5).

Conclusions

Relapsed or refractory soft tissue and bone sarcomas have dismal prognosis. Paclitaxel might be an alternative for these patients. Although patient numbers are low to conclude PCC alternated with reduced dose VAC might have better response rate. Further studies should be warranted.

EP-585

Soft Tissue Sarcomas

TREATMENT OUTCOME OF GENITOURINARY RHABDOMYOSARCOMA -10 YEARS EXPERIENCE

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Objectives

Genitourinary rhabdomyosarcoma is a special entity that needs complex treatment algorithm with chemotherapy, surgery and radiotherapy, which impacts the disease control and long term outcome. We aim to retrospectively review genitourinary rhabdomyosarcoma outcome in our limited resources country

Methods

A retrospective review was made of the clinical records of all patients younger than the age of 18 years diagnosed with Genitourinary RMS and treated at Alexandria University Hospital, over a period of 10 years (2002 – 2012).The primary outcome examined was Overall survival. A secondary outcome, local recurrence, and progression free survival rates were calculated. Toxicities and adverse effects following treatment were evaluated by the National Cancer Institute–Common Toxicity Criteria version 4.0.

Results

20 patients histologically confirmed GU – RMS. The age at presentation varied between 9 months to 18 years with a median of 9 years. There were 11 males (55%) and 9 females (45%). Median follow up for the entire group was approximately 2.6 years (range 0.8 to 8.3) from initiation of therapy. The most common primary tumor site was the Bladder / Prostate 9 patients (45 %) , paratesticular in 4 (20%), retroperitoneum in 2 (10%) , uterus in 3 (15%) , cervix in 1 (5%) and vagina in 1 (5%). All patients presented with IRS group III disease. 16 patients were treated according to SIOP MMT protocol, while the remaining 4 patients were treated according to IRSG protocol IV. At the end of our study, 15 patients (75%) showed no evidence of disease. 4 cases showed recurrence (22%). Grade 3/4 toxicities were 20% diarrhea and 19% febrile neutropenia .2 cases died, one case died due to severe febrile neutropenia, the other died from advanced disease.

Conclusions

Our results in a limited resource country, is close to published data, when multimodal treatment was applied.

EP-586

Soft Tissue Sarcomas

SURVIVAL AND FACTORS AFFECTING THE OUTCOME OF SYNOVIAL SARCOMA IN CHILDREN AND ADOLESCENTS

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Objectives

To evaluate the impact of the clinicopathologic features at diagnosis and treatment given, on the outcome of synovial sarcoma in children and adolescents.

Methods

Retrospective analysis of patients below 19 years old diagnosed by synovial sarcoma and treated at Children Cancer Hospital Egypt 57357 (CCHE) between July 2007 and May 2013. Clinical characteristics, pathological information, treatment modalities and survival data were reviewed.

Results

Seventeen patients were included with median age at diagnosis was 14.8 years, the most common affected primary site were the extremities (n= 8, 47.1%), tumor size was less than or equal 5 cm in only 4 cases (23.5%). Initial surgical excision was feasible in 10 patients (58.8%) while 5(29.4%) patients underwent surgical excision after response to preoperative chemotherapy. Two patients had unresectable tumor, showed no response to chemotherapy and received radiotherapy as the only local control therapy. Adjuvant radiotherapy only was given in 2 patients and 5 patients received chemotherapy without local radiotherapy and 8 patients received both modalities. The estimated 3 –year overall survival and failure free survival rates for the entire group were $86.5 \pm 8.9\%$ and $48.8 \pm 14.8\%$ respectively, the 3-year FFS was better in patients who underwent complete surgical excision either initial or post chemotherapy as it was 66.7% versus 55.6% for those with gross or microscopic residual(p-value=0.38). Also, the 3-year failure free survival was 75% versus 56.3% for those smaller than or equal 5 cm and those larger than 5 cm respectively(p-value=0.3).

Conclusions

Tumor size and complete surgical excision are important prognostic factors though they were statistically insignificant. Preoperative chemotherapy can help for delayed excision in patients presented initially with unresectable tumors.

EP-587

Soft Tissue Sarcomas

LOCALIZED RHABDOMYOSARCOMA OF HEAD AND NECK: A RETROSPECTIVE ANALYSIS OF 80 PATIENTS TREATED AT A TERTIARY CARE CENTRE IN INDIA

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Objectives

Rhabdomyosarcoma (RMS) is the most common soft-tissue sarcoma in children, however, it is rare in adults. The head and neck site accounts for 35% of all RMS. The study aim was to retrospectively review the clinic-pathologic factors, treatment outcome and prognostic factors in patients of localized RMS of head and neck treated at our centre.

Methods

Data pertaining to 80 patients reported in the database as having localized RMS of head and neck, diagnosed from May 2003- Dec 2012 , was retrieved. Factors evaluated were age, histology, site, tumor size, stage, risk and Intergroup Rhabdomyosarcoma study (IRS) group. Survival estimate were determined using survival time with the end point being event or death from any cause.

Results

Median age was 10.8 years and median symptom duration was 3 months. Males constituted 68.7% and females 31.2% with a male:female ratio of 2.2:1. The primary site of tumor was orbit in 23.7% , parameningeal in 56% and non-orbit non-parameningeal in 20%. Median tumor size was 6cm (range 2-12cm). The most common histology was embryonal in 76% cases. Forty-four percent patients were stage III, 51% were intermediate risk and 75% were IRS group III. Seventy-three percent (73%) patients received chemo-radiotherapy. Five-years EFS and OS were 36.4% and 57% respectively. Univariate survival analysis found that intermediate risk group patients had worse EFS as compared to low-risk (27.3% vs 44.6%, $p=0.02$). Stage III tumors and tumor size >5cm had a trend towards poor EFS with a p value of 0.06 and 0.06 respectively. None of the factors affected overall survival.

Conclusions

This is a single center experience of unselected patients. The survival in our cohort is less as compared to published data from West. Intermediate risk was significantly associated with poor EFS. Perhaps relatively large tumors contributed to higher failure rates.

EP-588

Soft Tissue Sarcomas

MALIGNANT RHABDOID TUMORS OF SOFT TISSUE. SINGLE CENTER EXPERIENCE IN RUSSIA

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Objectives

The aim of the study was to analyze clinical data and therapy results in a cohort of patients with malignant rhabdoid tumor of the soft tissue (MRT) treated in federal cancer center in Russian Federation.

Methods

8 patients included in this analysis were treated in Federal Research Center of Pediatric Hematology, Oncology and Immunology during the period of 01.2012 - 01.2014. We analyzed age at diagnosis, primary tumor location, stage of the disease (according to Intergroup Rhabdomyosarcoma Study criteria). All diagnosis were established by histopathologic examination and confirmed by lack of nuclear expression of INI1. Patients were treated according to European Rhabdoid Tumor Registry recommendations.

Results

Median age at diagnosis was 8.3 months (0.3-126 months). Diagnosis was verified on the 1st year of life in 5 (62.5%) patients (in 1 case on the 8 day of life). M:F ratio was 1:1. Topography of primary tumor included liver - 3 (37.5%) cases, deep soft tissues of a neck – 2 (25%) cases, abdominal cavity – 2 (25%) cases, orbit – 1 (12.5%) case. In 1 (14.3%) tested case germ-line mutation in INI1 gene (c.362G – T) was identified. 4 (50%) patients had localized disease, 4 (50%) patients had distant metastases. Clinical group distribution according to IRS: III – 2 (25%) patients, IV – 6 (75%, in 1 case - because of initial tumor rupture, in 2nd case - because of intraoperative tumor rupture) patients. Outcomes: 3 (37.5%) patients alive (2 - completed therapy, 1 – is undergoing therapy). 5 (62.5%) patients died (4 - due to early progression, 1 - due to refractory disease).

Conclusions

Our data confirmed presentation of disease in most cases on the first year of life and demonstrate unfavorable prognosis due to advanced stage of the disease and poor response to therapy.

EP-589

Soft Tissue Sarcomas

CLINICAL ANALYSIS OF THREE CASES OF RHABDOMYOSARCOMA WITH BONE MARROW METASTASIS

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Objectives

To investigate violations of children rhabdomyosarcoma with bone marrow metastasis, clinical characteristics , treatment and outcomes.

Methods

Retrospectively analyzed three cases of children rhabdomyosarcoma with bone marrow metastasis from January 2008 to December 2012.

Results

Three patients were boys, mean age 5 years (1 year 8 months to 11 years old in November). According to U.S. Rhabdomyosarcoma Study Group (IRS) staging criteria , 3 patients were stage IV stages , clinical grouped is high-risk group . Primary in the head and neck, the other two cases were primary in the pelvic cavity , retroperitoneal area, buttock mass, partially occupying oppression cause oliguria , anuria, all patients were confirmed by biopsy and immunohistochemical staining confirmed , histological type, including 2 cases of alveolar type , one case of embryonal . The clinical manifestations , mainly for tumor tissue mass, oppression caused by the invasion. Carried out strictly in accordance with the treatment of children with IRS installment. U.S. Oncology Research Center using the group (COG) rhabdomyosarcoma chemotherapy. one case's tumor progression in the treatment after 4 months, one case in the treatment of more than one year , through chemotherapy, surgery, radiotherapy and autologous stem cell transplantation relapse , and the other one case in accepting chemotherapy and surgery, 1 year later recurrence. Currently, survived only one case .

Conclusions

Children with bone marrow involvement rhabdomyosarcoma, early diagnosis is difficult, generally poor, no specific clinical features, often misdiagnosed as other hematologic malignancies , complications and more often associated with renal failure, various serious infections , poor long-term prognosis , survival rate is low, chemotherapy combined with surgery, radiotherapy, stem cell transplantation combined therapy is an effective treatment to control the disease, but the treatment scheme requires further discussion.

EP-590

Soft Tissue Sarcomas

SUCCESSFUL TREATMENT OF SCLEROSING RHABDOMYOSARCOMA IN A PATIENT WITH DUCHENNE MUSCULAR DYSTROPHY

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Objectives

A 22 year old male with Duchenne Muscular Dystrophy (DMD) and Clinical Stage III sclerosing Rhabdomyosarcoma (sRMS) was successfully treated with surgery, chemotherapy and radiation.

Methods

The patient presented with a one month history of a painful thigh mass; staging studies showed a heterogeneous mass (8x8 cms) within the left rectus femoris muscle with localized and regional node involvement. Tumor biopsy and sentinel node dissection showed sclerosing rhabdomyosarcoma. Treatment consisted of 12 weeks of Vincristine, Cyclophosphamide and Actinomycin (with cardiac monitoring in the PICU), then tumor resection, followed by radiation to the tumor bed and nodal sites and additional chemotherapy (for a total of 39 weeks). Anthracyclines were avoided due to underlying cardiac dysfunction.

Results

After 12 weeks of chemotherapy, the tumor mass showed no metabolic activity on PET scan compared to an SUV of 11 at presentation. The resected tumor (6x6 cms) showed an excellent pathological response to chemotherapy with less than 5% viable tumor cells. The patient tolerated therapy well but did have episodes of fever and neutropenia and needed parenteral nutrition and blood product support. He did not experience any significant deterioration in his neuromuscular or cardiac function during treatment.

Conclusions

There have been only a few patients with DMD who have developed RMS. Successful treatment can be accomplished by a coordinated treatment plan between the oncologist, oncology surgeon, PICU, and radiation therapy.

EP-591

Soft Tissue Sarcomas

OCCIDENT OF MEXICO RHABDOMYOSARCOMA (RMS) EXPERIENCE: SLIGHT IMPROVEMENT WITH A LOT OF WORK TO DO

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Objectives

Identify the clinical characteristics, event free survival and global survival of the patients of the Occident of Mexico with RMS from 1998 to 2012

Methods

This study reviewed 60 children's electronic charts with RMS from 1998 to 2012 from the institution. They were treated with Intergroup Rhabdomyosarcoma Study Group (IRSG) III or IV regimens.

Results

Median age of diagnosis was 5.3 years range (0.2 to 14 years); geographical characteristic of the patients 47% where from Jalisco, Mexico. According to IRSG classification, 4 (7%) were staged as low-risk (LR); 29 (48%) Intermediate-Risk (IR), 15 (25%) were high-risk (HR), and it was unknown in 12 patients (20%). The primary sites of tumor were: trunk and retroperitoneum (n=16); head and neck (n=11), parameningeal (n=9), orbit (n=9), genitourinary (n=7), paratesticular (n=2), extremity (n=6), Histopathology (n=41) embryonal, alveolar (n=8), botryoid (n=3), anaplastic (n=4), unknown (n=4). IRSG group I Localized disease 3%, microscopic residual disease group II 12%, group III incomplete resection or biopsy with macroscopic residual 60%, group IV distant metastases 25%, received radiotherapy (n=36), no radiotherapy (n=24), at the time of the study 3% was alive with activity, alive without activity 43%, 25% died of the disease, 10% died from a different cause, abandonment 13%, transferred to another unit 3%. By disease risk group the 5 and 10 year event free survival (EFS) for LR group disease was survival 75% at 17 months, 64% for IR, 46% HR. global survival (GS) for LR 75% at 79 months, 62% IR, HR 51%.

Conclusions

In the comparison between EFS that we had in 2007 and 2012 with slight improvement. The outcome of patients with RMS in the Occident of Mexico can be further improved by coming together as a cooperative group to provide the best of care. Improved communication, multidisciplinary team collaboration.

EP-592

Soft Tissue Sarcomas

WILMS TUMOR TREATMENT AND OUTCOME AT A MULTIDISCIPLINARY PEDIATRIC CANCER CENTER IN LEBANON

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Objective: The approach to treatment of Wilms Tumor (WT) differs between the European school, which advocates for neoadjuvant chemotherapy, and the North Americans school, which favors upfront tumor resection. At the Children's Cancer Institute in Lebanon, the approach to WT has followed the North American protocols since 2002, using a multidisciplinary approach to diagnosis and treatment planning. We here review the clinical outcomes of patients with WT and identify prognostic determinants of outcome.

Methods: After IRB approval, we retrospectively reviewed the clinical records of patients with WT treated at our hospital between April 2002 and June 2013.

Results: Our study included 35 children. Male: female ratio was 1:2.5, with a mean age of 3.9 years. Eight patients (23%) had stage I disease, 4 (11%) stage II disease, 9 (26%) stage III disease, 9 (26%) stage IV disease and 4 (11%) stage V tumors. Treatment was as per the North American NWTS protocols. Upfront resection was done in 24 cases; while biopsies were performed for Stage V tumors (n=5), tumors associated with IVC thrombus (n=3), locally extensive tumors that were deemed unresectable (n=1), and patients that had been subtotally resected prior to referral (n=2). At the time of the analysis, 30 (88.1%) of patients were free of disease, at a median follow-up of 57 months from diagnosis (range 5-124 months). Four patients had relapse, at a median time of 8.75 months (range 7- 12 months); all four had initial metastatic disease. One patient developed chronic renal failure during treatment.

Conclusion: NWTS protocols resulted in favorable outcome in children with non-metastatic Wilms tumor, in the setting of multidisciplinary approach to therapy. We observed a relatively high incidence of patients with bilateral tumors- a finding which suggests the need for further studies at genetic and molecular levels in this group of patients.

EP-593

Soft Tissue Sarcomas

LYMPHOCYTE RECONSTITUTION AS A PROGNOSTIC FACTOR IN SARCOMAS

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Objectives

The lymphocyte reconstitution has been identified as a prognostic factor in malignancies. We try to determine if early lymphocyte recovery is a predictor of survival in our cohort of paediatric patients with any type of sarcoma receiving chemotherapy.

Methods

All children diagnosed of a sarcoma and treated with chemotherapy in our institution from 2000 to 2012 were retrospectively evaluated. Chemotherapy was applied according to international protocols then current. Demographic, hematologic and related to treatment data were collected.

Results

Data of 33 pediatric sarcoma patients were analyzed (median age 12.2 [0.5-16.8]; male:female 18:15). Diagnosis were: 9 Ewing sarcoma/PNET, 6 Osteosarcoma, 10 rhabdomyosarcoma and 8 non rhabdo-soft tissue sarcomas. Six (18.2 %) were metastatic at diagnosis and 27 (81.8 %) non-metastatic. Twenty-six (78,8%) had a surgery done and 21 (63.6%) received any type of radiotherapy (including intraoperative radiotherapy). Five year overall survival [OS-5] was 63.3% (19 alive and 11 deceased). Good histological response at time of resection (>90%) was founded in 6/14 patients with an OS-5 of 100% and poor histological response in 8/14 patients with an OS-5 of 23%. Classifying patients into two groups according to a threshold absolute lymphocyte count 15 days after starting chemotherapy [ALC+15]. OS-5 in patients with ALC+15 ≥ 800 cells/ μ L was 86% while OS-5 with ALC+15 < 800 cells/ μ L was 58% although difference was not statistically significant ($p=0.136$). Analyzing it separately in each tumor, data of 7 rhabdomyosarcomas: 3 with ALC+15 ≥ 800 cells/ μ L are alive more than 10 years after diagnosis while 4/7 with ALC+15 < 800 cells/ μ L died of disease ($p=0.007$).

Conclusions

Despite the limitations of such a small study, it supports the role of lymphocyte recovery in paediatric sarcomas and its potential usefulness on risk stratification after initiation of therapy in addition to the need of immune reconstitution as a treatment strategy.

EP-594

Soft Tissue Sarcomas

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMAS (NRSTS): A SINGLE-CENTRE STUDY IN SINGAPORE

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Objectives

Non-rhabdomyosarcoma soft tissue sarcomas (NRSTS) represent 4% of childhood cancers. Though useful, adult data cannot be directly translated to children, as paediatric entities have been shown to be different in biology, treatment response and outcomes. We report our experience with NRSTS in the largest public paediatric hospital in Singapore.

Methods

Retrospective analysis of 22 children with NRSTS diagnosed between 1997 to 2011 was conducted. Data on patient demographics, tumour characteristics, treatment and survival status was obtained from Singapore Children's Cancer Registry and reviews of case records. The study was approved by the Institutional Review Board.

Results

Median age of diagnosis was 10.8 years (range: 0.2 – 17.8 years). Male: female ratio was 1:2.7. The different types of tumours seen were: infantile fibrosarcomas (n=4), malignant peripheral nerve sheath tumours (MPNST) (n=4), fibrous histiocytomas (n=2), leiomyosarcomas (n=2), alveolar soft part sarcoma (ASPS) (n=1), hemangioblastomas (n=2), spindle cell sarcomas (n=2), myofibroblastic sarcoma (n=1), rhabdoid tumours (n=2), embryonal sarcoma (n=1), angiosarcoma (n=1). Staging was done according to IRSG in all except one where it was not described – seven (32%) were stage 1, four (18%) were stage 2, seven (32%) were stage 3, three (14%) were stage 4. All patients underwent tumour resection, nine had chemotherapy (out of which three patients received neoadjuvant chemotherapy) and five received radiotherapy. Median follow-up was 2.3 years. Three patients relapsed, all within the first year. At time of analysis, sixteen patients survived – seven had stage 1, four had stage 2, three had stage 3 and two had stage 4 disease. The six non-survivors were patients with MPNST, myofibroblastic sarcoma, malignant rhabdoid tumour, hemangioblastoma and spindle cell sarcoma.

Conclusions

The spectrum of NRSTS seen showed great heterogeneity in histology. Survival outcome was good. Multidisciplinary treatment with uniformity of approach is vital in treating this heterogeneous group of tumours.

EP-595

Soft Tissue Sarcomas

EPITHELIOID ANGIOSARCOMA OF COLON: A RARE CASE REPORT IN AN INFANT

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Objectives

Epithelioid angiosarcoma (EA) is a rare tumor affecting children and usually occurs in liver and extremities. Mesenteric angiosarcoma that occurs in infants has only rarely been reported. We report a case of colon EA affecting a female child, emphasizing the clinical features, its difficult management and a brief review of literature.

Methods

A four-month-old girl presented with three-week history of intestinal bleeding associated with paleness, inadequate weight gain and perineal dermatitis. Initially dairy allergy was considered, however, as the intestinal bleeding persisted, the infant was hospitalized for investigation.

Results

The imaging findings on US and CT showed a heterogeneous-vascularized mass in the cecum extending into the mesentery. Small liver and lung nodules were also found. Surgery was performed with complete resection of the tumor. Anatomopathological result showed a 4.5 x 3.5 x 2.0 cm hemorrhagic tumor involving the colon with 60% necrosis and classified as a high grade sarcoma. Surgical margin was tumor-free. EA was confirmed by immunohistochemistry, with strong reactivity for endothelium markers (CD31, CD34) with negative markers for other tumors. The infant has undergone four chemotherapy cycles with Ifosfamide and Adriamycin, with disappearance of the pulmonary nodes. No signs of tumor were found on second-look surgery and also in the liver node biopsy. She did two more equal chemotherapy cycles and now is 4 months off therapy with an excellent recovery and normal CT images without any signs of relapse.

Conclusions

Angiosarcomas are rare tumors of vascular endothelium cell origin that may occur anywhere in the body. The occurrence in the gastrointestinal tract is quite uncommon with a few cases reported in the medical literature and with unfavorable outcomes. To our best knowledge, this is the first reported case in a child below one year of age and with a very good response.

EP-596

Soft Tissue Sarcomas

NATIONAL TREATMENT PROTOCOL FOR PEDIATRIC PATIENTS WITH NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMAS: THE NATIONAL INSTITUTE OF PEDIATRICS (MEXICO) EXPERIENCE

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Objectives

Non-Rhabdomyosarcoma soft tissue sarcomas (NRMSSTS) are infrequent malignant tumors in children. Treatment depends on histology, biologic behaviour and staging. Mexico implemented a national treatment protocol for this entity seven years ago. We present herein the results obtained at the National Institute of Pediatrics.

Methods

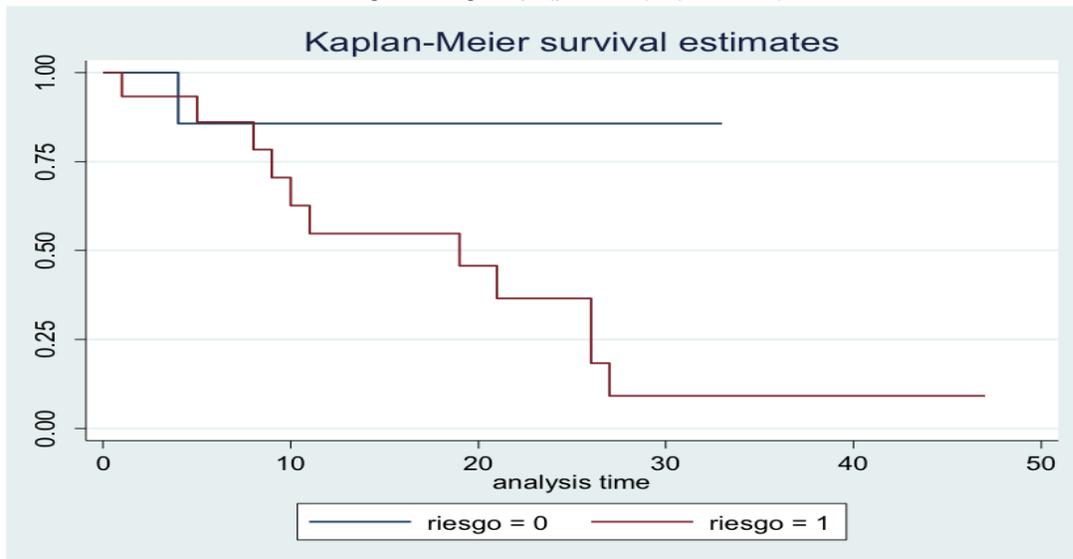
We studied a cohort of patients with NRMSSTS between January 2007 and January 2014. Patients were categorized as high or low risk according to clinical and histological features. Depending on risk stratification, treatment included surgery and radiotherapy, with or without 6 cycles of ifosfamide and doxorubicine.

Results

There were 22 patients with a median age of 9 years. 55% were males with a ratio of 1.2:1. Median time between first symptoms and arrival to our department was 3.3 months. Most frequent histologic types were peripheral nerve sheath tumor (PNST) and sinovial sarcoma (SS).

Every patient underwent surgical resection of the primary tumor. 95% received radiotherapy. Sixteen patients were categorized as high-risk, thus receiving chemotherapy.

Overall survival was 50%. However, for the low-risk group, survival was 85%, compared with a 45% survival rate for the high-risk group (p=0.05). (Table 1)



Conclusions

NRMSSTS are an heterogenous group of neoplasms. Prognosis depends on histology and staging. In low-risk patients, surgery and radiotherapy alone offer a good chance for survival. However, in high-risk patients, prognosis remains dismall in spite of multimodal therapy. New treatment strategies are required for this group of patients.

EP-597

Soft Tissue Sarcomas

MALIGNANT RHABDOID TUMOR OF THE POSTERIOR BLADDER WITH SEVERAL LOCAL RELAPSES

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Objectives

Malignant rhabdoid tumors are generally characterised aggressively and overall survival is approximately %20-25 if not surgically resected. One of the suppressor genes, INI-1 exone mutation or deletion could be found in these kind of tumoral tissue. Central nervous and urinary systems are frequently involved. Extra-renal and extra-cranial involvements could be seen in thorax, liver, cervical region and axilla. Multimodal therapies combined with surgical resection are the best treatment option.

Methods

Here we present a case firstly diagnosed malignant rhabdoid tumor of the posterior bladder represented with renal failure when 12 years old. He is now 18 years old and had local relapses for five times and experienced several surgical interventions.

Results

Rhabdomyosarcoma protocol firstly initiated but after that vincristine, adriamycin, topotecan protocol; after that vinorelbine, cytarabine protocol; than oral etoposide protocols have been used until the last relapse and surgery. Total 5600 cGy dosage radiotherapy was applied following the end of firstly used rhabdomyosarcoma protocol. Pathological immunohistochemical examination of tumoral tissue from the resection material revealed INI-1 mutation.

Conclusions

Our case is now in remission with repeating eight cures of gemcitabin combined with docetaxel therapy after surgery.

EP-598

Soft Tissue Sarcomas

COMPARATIVE STUDY ON 184 PEDIATRIC AND ADULT PATIENTS WITH RHABDOMYOSARCOMA

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Objectives

To compare the prognostic factors and clinical differences between pediatric and adult rhabdomyosarcoma.

Methods

We reviewed the clinical data of 184 patients who were diagnosed to have RMS by pathology and had complete follow-up data between January 1993 and June 2009 in our Hospital . There were 93 pediatric patients and 91 adult patients.

Results

The 1,3 and 5-year survival rates in the pediatric group were 90.3%, 62.0%, 43.1%, respectively, while these were 86.8%, 35.1%, 20.0%, Significant statistical differences were showed between the pediatric group and adult group in the factors of histological subtypes, primary site and distant metastasis by Chi-square Test.

Conclusions

The prognosis of adult with rhabdomyosarcoma is significantly worse than pediatric tumor, and the differences of the histological subtypes, primary site and distant metastases between the two groups should be responsible for it.

Document not received

EP-599

Supportive Care/Palliative Care

OUTCOME OF PATIENTS WITH SOLID TUMORS AFTER FIRST EVENT

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Objectives

Limited publications are available regarding the outcome of pediatric patients with solid tumors after first event. Recognizing the outcome of this group of patients can help in selecting patients who may benefit from further treatment and improve utilization of palliative care.

Methods

A retrospective chart review of patients registered in POND database in King Hussein Cancer Center from Jun2006 till Dec2013. Events were defined as relapse, progression or refractory disease. Patients who had death as their first event were excluded.

Results

Among 615 patients with solid tumors, 131 (46% females) experienced an event after a median of 9.6 months (range, 0 to 47) after diagnosis. Median age at relapse was 7.2 years (range 0.1 to 19.4). The most common disease categories were bone tumors (31%), neuroblastoma (26%), soft tissue sarcomas (13%) and renal tumors (11%). The 4-year overall survival of the whole group was 12% ± 3.8%. The 4-year overall survival for different disease categories were as follows: bone tumors (4±4%), neuroblastoma (11±7%), soft tissue sarcomas (8.3±7.9%) and renal tumors (16±13%). We did not find significant differences between patients who received and did not receive multiagent chemotherapy in terms of survival and the last reported pain score. Patients who did not receive chemotherapy were more likely to spend less time in hospital and to have earlier placement of DNR orders.

Conclusions

The findings of our study are important in highlighting the importance of early palliative care for this group of patients. The burden of treatment on the family and the unit are not justified in most cases where open clinical trials are not available.

EP-600

Supportive Care/Palliative Care

PEDIATRIC PALLIATIVE PROGRAM IMPLEMENTING HOME CARE IN JORDAN

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Objectives

Pediatric palliative care decreases pain and suffering of children with cancer and their families. It also decreases the burden on busy units allowing them to treat more patients. Home care is an essential extension of this important service.

Methods

We started a home care service attached to our pediatric palliative care program. A driver, 2 nurses and a social worker made daily visits to a prepared list of patients. Visits vary in duration from 0.5 to 3 hours based on patients' needs. The frequency to individual patient varied according to specific needs. After 6 months of starting home care visits, data was collected by visiting nurses using a data collection sheet. Data collected included demographics, disease-related data, home care issues, and family social issues.

Results

There were 30 patients included in this analysis (10 females). Patients with CNS tumors (14) and solid tumors (12) were the majority of referred patients. After referral, the majority of patients had pain well controlled (N=27, 90%) using one or more medications. Emergency room visits (median=2 per patient) and hospital admission days (median=3) were minimal and reflected satisfaction with home care. Six patients (20%) needed enteral feeding by nasogastric or PEG tubes. Two patients needed intensive wound care for deep ulceration. Three patients were referred back to the center for palliative procedures (Tracheostomy, VP shunt placement). Of note, families represented typical social status in Jordan with a median income of 300 JD (420 US\$ per month) and a median family size of 5.

Conclusions

Home care is essential even in low-income countries to enhance the services of palliative care. With limited resources, we were able to demonstrate the successful implementation of the service and had impact on the quality of life of patients at home with minimal utilization of services at the center.

EP-601

Supportive Care/Palliative Care

COMPOSITE ADVERSE EVENT OUTCOME IN PROLONGED FEBRILE NEUTROPENIC PEDIATRIC CANCER PATIENTS

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Objectives

Pediatric cancer patients (PCP) with prolonged neutropenia have increased risk for severe, recurrent or new bacterial and fungal infection and adverse outcome. The aim of this study was to identify the risk factors associated with adverse outcomes in this group.

Methods

This study was a retrospective analysis of clinical data on PCP with prolonged febrile neutropenia (PFN) from a tertiary health care center of Pakistan.

Results

We analyzed 135 hospitalizations of PCP with PFN. The mean age was 7.3±4.1 years. There was 98 (72.6%) male. The mean duration was 10.3±5.2 days (range:1–25 days). Acute leukemia 88 (65.2%) were the most common diagnosis followed by lymphomas 19 (14.1%) and solid tumors. Cause of neutropenia were identified in only 58 (43%) patients, out of BSI 22 (16.3%), pneumonia 15 (11.1%), fungal infection 13 (9.6%), infectious diarrheas 5 (3.7%) and UTI 3 (2.2%). More than 50% of the patients had severe myelosuppression. The composite adverse event outcome were observed in 28 (20.7%) of patients, with in-hospital mortality occurring in 7 (5.2%), PICU admission occurring in 12 (8.9%) and inotropic support was required in 9 (6.7%). On logistic regression analysis cancer type AML (AOR, 7.63 [95% confidence interval, 1.12-91.35]; $P < 0.001$), Platelets count $< 50,000/cm^3$ (AOR, 5.17 [95% CI, 1.17-23.78]; $p < 0.001$), BSI (AOR, 2.33 [95% CI, 0.84-15.79]; $p < 0.05$) and fungal infection (AOR, 4.26 [95% CI, 1.34-86.57]; $p < 0.001$) were found as independent risk factors associated with development of composite AE outcome in PCP with PFN.

Conclusions

AML, severe myelosuppression, blood stream infection and fungal infection were identifiable risk factors associated with development of adverse event outcome in PCP with PFN.

Prospective studies in large cooperative trials may be beneficial in evaluating these risk factors further.

EP-602

Supportive Care/Palliative Care

FEBRILE NEUTROPENIA IN PEDIATRIC CANCER PATIENTS: EXPERIENCE FROM A TERTIARY HEALTH CARE FACILITY OF PAKISTAN

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Objectives

Febrile neutropenia (FN) is a common complication of therapy among children with cancer. The aim of this study was to describe the demographic, clinical feature, laboratory data and management outcomes of FN in pediatric cancer patients.

Methods

This study was a retrospective analysis of clinical data on pediatric cancer patients with febrile neutropenia from a tertiary health care facility of Pakistan.

Results

We analyzed 872 hospitalizations of pediatric cancer patients with FN. The mean age of the study population was 5.32 ±4.07 years. There was 559 (64.1%) male and 313 (35.9%) female. ALL (n=590; 67.7%) was the most common diagnosis followed by AML (n=105; 12.2%), lymphoma (n=86; 9.9%) and sarcomas (n=51; 5.8%). Cause of neutropenia were identified in only 58 (43%) patients, out of URTI (n=192; 22%), BSI (n=58; 6.6%), pneumonia (n=31; 3.5%), infectious diarrheas (n=16; 1.8%) and UTI (n=11; 1.3%). Age less than 5 year (OR=1.5; p= 0.043), AML (OR=1.8; p=0.019), patients who received chemotherapy within 2 week of FN (OR=1.9; p=0.007), severe neutropenia ANC < 50/cm (OR=1.5; p < 0.041), platelets count < 50,000/cm (OR= 1.5; p < 0.027), Fungal infection (OR=15.6 ; p 5 days) in pediatric cancer patients. A total of 25 (2.9%) patients were required PICU admission and overall 12 (1.4%) patients were expired. Both outcome variables were statistically significant regarding PICU admission (9% Vs 2%; OR= 5.4; p < 0.001) and mortality rate (5.2% Vs 0.8%; OR=8.1; p < 0.001) in patients with prolonged FN versus FN respectively.

Conclusions

Younger age, AML, severe myelosuppression, fungal infection and pneumonia were identifiable risk factors associated with prolonged FN. Outcomes regarding PICU admission and mortality was worse in patients who had prolonged FN.

EP-603

Supportive Care/Palliative Care

PROLONGED FEBRILE NEUTROPENIA: RISK FACTORS AND OUTCOME IN PEDIATRIC ONCOLOGY PATIENTS

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Objectives

Pediatric cancer patients with febrile neutropenia (FN) have increased risk for severe, recurrent or new bacterial and fungal infection. Although prompt initiation of empirical antibacterial antibiotics has leads to substantial improvement in morbidity and mortality, infectious complications still persist. The aim of this study was to describe the demographic, clinical feature, laboratory data, risk factors and outcomes of FN in pediatric cancer patients.

Methods

This study was a retrospective analysis of clinical data on pediatric cancer patients with FN from a tertiary health care center of Pakistan.

Results

We analyzed 872 hospitalizations of pediatric cancer patients with FN. The mean age of the study population was 5.32 ± 4.07 years. There was 559 (64.1%) male and 313 (35.9%) female. ALL (67.7%) was the most common diagnosis followed by AML (12.2%), lymphoma (9.9%) and sarcomas (5.8%). Cause of neutropenia was identified in only 58 (43%) patients, out of URTI (22%), BSI (6.6%), pneumonia (3.5%), infectious diarrheas (1.8%) and UTI (1.3%). Additionally, the median neutrophil count and platelet count revealed profound myelosuppression in more than 50% cases. Age less than 5 year ($p= 0.043$), AML ($p=0.019$), patients who received chemotherapy within 2 week of FN ($p=0.007$), severe neutropenia $ANC < 50/cm$ ($p < 0.041$), platelets count $< 50,000/cm$ ($p < 0.027$), Fungal infection ($p < 0.05$) in pediatric cancer patients. A total of 25 (2.9%) patients were required PICU admission and overall 12 (1.4%) patients were expired. Both outcome variables were statistically significant regarding PICU admission and mortality rate in patients with prolonged FN versus FN respectively.

Conclusions

Younger age, AML, severe myelosuppression, fungal infection and pneumonia were identifiable risk factors associated with development prolonged FN. Outcomes regarding PICU admission and mortality were worse in patients who had prolonged FN.

EP-604

Supportive Care/Palliative Care

ADRENAL INSUFFICIENCY IN CHILDREN WITH CANCER PRESENTING WITH FEVER IN NEUTROPENIA

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Objectives

To detect whether children with cancer have a sufficient adrenal function at presentation with fever in neutropenia (FN).

Methods

In the setting of a prospective observational single-center study, serum was sampled in pediatric patients with cancer presenting with FN, and stored at -20°C. Cortisol concentration was measured by a commercially available ELISA. It was correlated to different clinical characteristics, including cumulative doses of past corticosteroid therapy. Cortisol concentrations < 500 nMol/L were considered insufficient in the stressful FN situation.

This study was approved by the Institutional Review Board. Patients, if able to judge, and their legal guardians gave written informed consent prior to study entry.

Results

Serum samples were available in 21 (49%) of 43 FN episodes, from 14 patients aged 1.2 to 16.5 years. Patient characteristics and outcome were comparable in patients with and without serum samples. Freezing time was not significantly associated with cortisol. Median cortisol was 435 nMol/L (IQR, 262 to 653; range, <28 to 1301), with 11 concentrations <500 nMol/L (52%; exact 95% CI, 30% to 72%). Cumulative doses of corticosteroid therapy within one month preceding FN were tendentially associated with cortisol (Spearman's rho, -0.39; 95% CI, -0.85 to 0.07, p=0.080), while earlier doses were not. Cortisol was not significantly associated with patient characteristics, temperature at presentation, or outcomes (adverse events, duration of hospitalization and of intravenous antimicrobial therapy).

Conclusions

At presentation with FN, about one half of pediatric patients with cancer had an insufficient adrenal stress response, which was associated with past corticosteroid therapy. Larger prospective studies of adrenal response in FN are warranted.

EP-605

Supportive Care/Palliative Care

THE INFLUENCE OF DIFFERENT FEVER DEFINITIONS ON THE RATE OF FEVER IN NEUTROPENIA DIAGNOSED IN CHILDREN WITH CANCER

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Objectives

The temperature limit defining fever (TLDF) is based on scarce evidence. This study aimed to determine the rate of fever in neutropenia (FN) episodes additionally diagnosed by lower versus standard TLDF.

Methods

In a single center using a high TLDF (39.0°C tympanic temperature, Limit_{Standard}), pediatric patients treated with chemotherapy for cancer were observed prospectively. Results of all temperature measurements and CBCs were recorded. The application of lower TLDFs (Limit_{Low}; range, 37.5°C to 38.9°C) versus Limit_{Standard} was simulated *in silicon*.

This study was approved by the Institutional Review Board. Patients, if able to judge, and their legal guardians gave written informed consent prior to study entry.

Results

In 39 patients, 8896 temperature measurements and 1873 CBCs were recorded during 289 months of chemotherapy. Virtually applying Limit_{Standard} resulted in 34 FN diagnoses. At Limit_{Low} 38.4°C 10 additional FN were recorded (Poisson rate ratio_{Additional/Standard}, 0.29; 95% lower confidence bound, 0.16). Further lowering Limit_{Low} to 37.5°C led to earlier diagnosis in the majority of FN (median, 4.5 hours; 95% CI, 1.0 to 20.8), and to 53 additional FN diagnosed. In 51 (96%) of them, spontaneous defervescence without specific therapy was observed in reality.

Conclusions

Lower TLDFs led to many additional FN diagnoses, implying overtreatment because spontaneous defervescence was observed in their vast majority. The question if the high TLDF is not only efficacious but as well safe remains open.

EP-606

Supportive Care/Palliative Care

POSACONAZOLE SALVAGE THERAPY IN IMMUNOCOMPROMISED CHILDREN WITH MALIGNANCIES OR IMMUNE DEFICIENCIES : A PRELIMINARY REPORT

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Objectives

Posaconazole is an extended spectrum triazole with invivo and invitro activity against Aspergillus and mainly used for prophylaxis in immunocompromised children with malignancies. We present five cases with refractory and/or relapsing invasive pulmonary Aspergillosis (IPA) treated with Posaconazole as salvage therapy.

Methods

All five patients with either relapsed leukemia (n:3) or chronic granulomatous disease (CGD) (n:2), of age ≥ 13 years (median : 14, range : 13-17) were treated with Posaconazole (200mg tid, po) for IPA resistant to Voriconazole or combination therapies for 15 days to 4 months till radiologic regression and/or resolving Galactomannan. Their initial diagnosis was based on clinical symptoms, weekly Galactomannan survey and/or radiologic findings while they were severely immunocompromised due to their diseases and or aggressive treatments including BMT.

Results

Two of the three relapsed leukemia patients expired in 15 days to 3 months after the initiation of Posaconazole mainly because of the progression of their underlying disease. One patient was responsive and currently under treatment for IPA since 4 months. Two patients with CGD were responsive and still under treatment for 3 and 4 months. The drug is well tolerated without any major side-effects.

Conclusions

An azole-based, mould-active antifungal, Posaconazole might be an efficient alternative salvage therapy for pediatric patients with resistant IPAs. Although it is a safe drug in children, its effectiveness is dependant on factors like the state of underlying disease, drug absorption and metabolism, but iv formulation might solve this problem in the near future.

EP-607

Supportive Care/Palliative Care

SUPPORTIVE CARE AFTER CHEMOTHERAPY AND RADIATION WITH A SWISH & SWALLOW GLUTAMINE + DISACCHARIDE NUTRITIONAL SUPPLEMENT TO REDUCE MUCOSITIS AND IMPROVE ENTERAL NUTRITION

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Objectives

Two of the of the most common supportive care questions parents and patients ask are: 1) What foods and diet can help fight cancer, and 2) do you recommend nutrition supplements? Prior evidence has shown that glutamine + disaccharide suspensions can reduce mucosal toxicity; glutamine supplementation of diet may also be associated with less cancer growth by facilitating improved lymphocyte proliferation and immune function. However, because of time to write prescriptions for glutamine + disaccharide suspensions, pharmacy to compound, taste of sucrose vehicle, and caking during refrigeration, a more convenient product was needed. Therefore, a powder that contains glutamine, sucrose + trehalose, suspending agents, and orange or grape flavoring (Healios) was developed.

Methods

Glutamine powder (from Healiosproducts.com) as 1 scoop containing 4 gm glutamine + disaccharides is added to 50mL water, swished 10 seconds, and swallowed twice/day during and after chemotherapy or radiation involving mouth, throat or esophagus.

Results

Rapid facilitated uptake of glutamine by disaccharide reached peak uptake within 10 seconds. Glutamine suspended in water had poor cellular uptake. Glutamine+ disaccharide suspensions were successful in in reducing mucosal toxicity of cancer therapy in 1 pilot and 4 different randomized, placebo double-blind trials, 3 of which included children. Glutamine suspensions were needed not only during, but also after completion of radiation for at least an additional 7 days - probably to facilitate healing of residual damage.

Conclusions

A glutamine + disaccharide supplement has been developed that has high patient acceptance; it is useful when chemotherapy and/or radiation have high likelihood of causing stomatitis, pharyngitis, and/or esophagitis. If there are enteral nutritional concerns, care providers can consider recommending this safe and inexpensive nutritional supplement as a rational supportive care measure to reduce and ameliorate mucosal toxicity of cancer therapy and to promote better enteral nutrition during chemotherapy and/or radiation.

EP-608

Supportive Care/Palliative Care

**ESTABLISHING A PAEDIATRIC PALLIATIVE CARE UNIT WHERE
NON/INADEQUATE FACILITIES EXIST – CHALLENGES AND OPPORTUNITIES**

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Objectives

Can kids support children and their families from the time of diagnosis of cancer through treatment and on to survival, reintegration or into bereavement in 34 centres across India. Few children have access to palliative care within cancer centres in India and in order to address this need Cankids has set up a dedicated palliative care service for children in Delhi with the vision to develop a model of cost effective paediatric palliative care support pan India.

Methods

An inpatient facility was opened in New Delhi in August 2012 close to the major cancer centres , with easy access to public transport which can accommodate and care for up to 14 children plus attending parents. Creating a child friendly, hygienic environment was essential in order to nurse children undergoing chemotherapy with increased risk of infection. Educational support and an activities programme, together with counselling, psychological support and physical therapy were considered core components of the service which are provided free of charge.

Results

In the first year of operation there were 197 admissions and a bed occupancy ranging from 50 to 130%. Around 75% of admissions were for less than 14 days with only 9% of children needing to stay longer than 2 months. More boys (71%) than girls (29%) were admitted supporting the sad reality that females are neglected even at the end of life.

Conclusions

The Cankids palliative care centre fills gaps at cancer centers with no or inadequate palliative care facilities. The need to provide 24 hour access to suitably trained medical and nursing staff to comply with nursing home regulations and palliative care standards proved a major challenge and is likely to limit the development of inpatient services in favour of a nurse led, doctor supported outpatient /day care model to disseminate pan India.

EP-609

Supportive Care/Palliative Care

A SURVEY OF IMMUNISATION PRACTICES IN CHILDREN WITH CANCER IN INDIA

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Objectives

Children with cancer, when on treatment and immunosuppressed, are at risk of infection from live vaccines and do not mount an adequate protective response to inactivated vaccines. Hence, immunizing them during and after treatment requires special considerations. We wanted to identify the immunization practices for these children in India.

Methods

Clinicians attending the Indian Pediatric Oncology Initiative meeting, the Indian Pediatric Oncology Group meeting, and the Pediatric section of the Indian Cancer Congress in 2013 were invited to complete a questionnaire.

Results

Respondents were from 37 institutions in 21 cities (49% public sector; 46% annual caseload >100 new patients). 46% advised inactivated but not live vaccines and 40% advised no vaccine during cancer treatment to the child. 67 % recommend Hepatitis B vaccine (83% public hospitals, 53% private hospitals, p=0.08) and 34% annual Influenza vaccine (25% public hospitals, 42% private hospitals, p=0.48) to the child undergoing treatment. 76 % recommenced vaccination 6 months after completion of treatment. Revaccination was in the form of booster + continue normal schedule 32%, continue normal schedule 30%, repeat entire immunization schedule 16% and measure antibody levels and then decide 11%.

Conclusions

There is heterogeneity in the immunization practices of children with cancer. Development and dissemination of immunisation guidelines specific to India in children who are undergoing or have completed cancer treatment would be useful in standardizing practice.

EP-610

Supportive Care/Palliative Care

QUALITY OF LIFE OF CHILDREN WITH CANCER TREATED WITH PALLIATIVE CARE: A QUALITATIVE STUDY ON PROFESSIONALS' PERCEPTIONS

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Objectives

The Steering Committee of the Canadian Cancer Society (2011) estimated that in 2011, 1,310 people aged between 0 and 19-year-old have been diagnosed with cancer. Close to 1 in 7 will die from it. Partly due to the deteriorated health status of these children, clinical and ethical literature has raised the question of the valid definition of quality of life (QoL) of children in palliative care. The ability of professionals to define and evaluate QoL is key to make appropriate decisions in the trajectory of children and end-of-life issues. Although the concept behind adult QoL in palliative care has been clarified and is now subjected to measure, this is not the case in pediatric palliative care. Our objective is to describe the main dimensions of QoL in the context of pediatric palliative care in hematology-oncology, based on professionals' views.

Methods

Semi-structured interviews were conducted with 20 medical and non-medical professionals of CHU Sainte-Justine Hematology-Oncology department. The interview guide was inspired by questions used by Hinds & al. (2004) in their qualitative study to assess how children with cancer perceived their QoL. During interviews, professionals were asked about their representations of QoL of children with cancer receiving palliative care, based on their past experiences. Interview data were analyzed using thematic analysis and coded using QDAMineur.

Results

The analysis identified dimensions of QoL in this context with the following elements being prominent aspects: social relationships, physical and psychological health status, autonomy, unmet needs and pain. Verbal descriptions of professionals insisted on preserved abilities and positive behaviors and emotions such as smiling, playing, etc.

Conclusions

The representation of professionals on QoL in this context is marked by maintained abilities including social ones likely to be changing over time. It makes it possible to develop appropriate measures to evaluate QoL in very ill children.

EP-611

Supportive Care/Palliative Care

ONE-THIRD PATIENTS WITH FEBRILE NEUTROPENIA AND UPPER RESPIRATORY TRACT INFECTION HAVE AN IDENTIFIABLE VIRAL ISOLATE IN NASOPHARYNGEAL ASPIRATE: A PROSPECTIVE OBSERVATIONAL STUDY FROM NORTH INDIA

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Objectives

The aim was to identify viruses in nasopharyngeal aspirate in children with hematological malignancy with febrile neutropenia and upper respiratory tract infection.

Methods

Hospitalized children, on treatment for hematological malignancies, with febrile neutropenia and clinical evidence of upper respiratory tract infection (rhinorrhea and/or cough) were enrolled. Patients with lower respiratory tract infection were excluded. Nasopharyngeal aspirate was obtained in each patient for qualitative polymerase chain reaction for 5 viruses: Respiratory syncytial virus, Influenza A, B, Human parainfluenza virus-3 and Human Metapneumovirus.

Results

The study included 57 children; all were receiving broad-spectrum antibiotics. The mean age was 6 years (range: 0.5-14). The majority (89.5%) had ALL. At admission, the duration of fever ranged from 1-10 days (mean: 2.3±1.3). The absolute-neutrophil-count was <200/mm³ in 51 (89.5%), and 200-500/mm³ in 6 (10.5%). Platelet count was <20 x 10⁹/L in 23 (41%) patients. The mean duration of hospitalization was 5.7 days (range: 3-16). Viruses were isolated in 19 (33%) patients. The most common identified virus was Influenza (A and B) (62% of positive cases), followed by RSV and HPIV-3 (14% each), and hMPV (10%). Two had coinfection. Age (p=0.35), ANC (p=0.68), phase of chemotherapy (p=0.36) or duration of hospitalization (p=0.73), did not influence viral positivity. Patients with a positive viral isolate were more in winter/spring (57%), as compared to the rest of year (15%) (p=0.036). None of the Influenza viruses were isolated in summer/autumn. The procedure of nasopharyngeal aspirate was well tolerated with transient epistaxis in 44%. No bacterial organism was isolated from blood culture in any patient. There were no complications/deaths.

Conclusions

One-third children with febrile neutropenia and upper respiratory tract infection had an identifiable viral isolate in nasopharyngeal aspirate along with a sterile blood culture. Trials need to be conducted which would explore the option of early cessation of antibiotics in this select group.

EP-612

Supportive Care/Palliative Care

PATIENT REPORTED OUTCOMES IN CLINICAL TRIALS AND RANDOMISED CLINICAL TRIALS IN CHILDREN RECEIVING PALLIATIVE OR END OF LIFE CARE

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Objectives

The purpose of this study was to identify published research describing the use of patient reported outcomes (PRO) in clinical and randomised clinical trials in children receiving end-of-life/palliative care, and explore the medical conditions, health care domains and clinical trends that they describe.

Methods

A literature search was conducted using the NHS-Evidence (MEDLINE, CINAHL, EMBASE, PsychINFO). All search terms were cross referenced to the thesaurus of each database. Results were limited to < 18 years-of-age, English language and clinical-trials/randomised clinical-trials.

Results

A total of 18 articles were identified (PsychINFO 4, EMBASE 4, CINAHL 10, MEDLINE 0) Defining a PRO as any report of the status of the child's health condition that came directly from the patient, without interpretation by a clinician or other, no articles were included as none described a PRO, or relevant measure or tool. A manual literature and internet search further identified no relevant articles. No database included PRO as a search term within their Thesaurus. Further to this, there was low consistency between the definition (i.e. scope) and indexing of basic search terms (e.g. end of life) as referenced in the Thesaurus of each database.

Conclusions

Despite increasing interest in the use and development of patient reported outcomes in the development of health care services, their use as primary and even secondary outcomes in clinical trials within paediatric palliative care research remains limited at best. Perhaps the greatest barrier is the lack of developed, fit for purpose and validated outcome measures. A significant amount of research needs to be done before PRO can be used to measure and evaluate the benefit of potential treatments at the end of life in children.

EP-613

Supportive Care/Palliative Care

PREVALENCE AND OUTCOME OF MULTIDRUG RESISTANT BACTERIAL SEPSIS IN CHILDREN ON CHEMOTHERAPY

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Objectives

Multidrug resistance (MDR) gram negative sepsis is associated with high mortality in children undergoing chemotherapy. We report on the prevalence and outcome of MDR bacterial sepsis in children at a tertiary cancer centre in India.

Methods

Positive blood cultures obtained from all in-patients from Jan 2012 -Dec 2013 were reviewed. MDR in gram negative bacteria were defined as those producing carbapenemase, extended spectrum beta lactamase (ESBL) or those resistant to multiple broad spectrum antibiotics. All patients admitted with febrile neutropenia initially received Cefepime empirically and changed to Meropenem if ESBL organisms were isolated. Patients with carbapenemase producing organisms received Colistin in addition.

Results

Of the 335 blood cultures sent during the study period, 105 positive blood cultures were obtained in 65 patients with a mean age of 6.6 years (range 0.9-16.1 years). Forty seven patients (72%) had hematological malignancies and 18 (28%) had solid tumors. 28/105 (26.6%) blood cultures were identified as probable non-significant isolates. Of the remaining 77, MDR gram-negative organisms were identified in 24 (31%) [ESBL 8, carbapenemase producer 15, other MDR 1], and obtained from 20 patients. Thus 17/47 (36%) and 3/18 (17%) of patients with hematological and non-hematological malignancies respectively had MDR organisms isolated from blood cultures. Three (15%) patients, all with hematological malignancies and carbapenemase producing organisms, succumbed to their infections; while prolonged intravenous antibiotic successfully cleared the MDR in the others.

Conclusions

In our experience, MDR organisms are isolated in a third of positive blood cultures obtained from children with cancer undergoing therapy. Over half of these were carbapenemase producing MDR's. MDR's were also more likely to be isolated from patients with hematological malignancies. Early identification and prompt intervention can decrease mortality associated with MDR organisms. Nevertheless, more effective antibiotics against carbapenemase resistant organisms are required especially with the emergence of Colistin resistance.

EP-614

Supportive Care/Palliative Care

ASSESSMENT OF NUTRITIONAL STATUS IN NEWLY DIAGNOSED PEDIATRIC PATIENTS: MAYO CLINIC EXPERIENCE

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Objectives

Children newly diagnosed with cancer are at high risk for developing weight loss. Causes include treatment related adverse effects and disease related reasons. Despite the high prevalence of malnutrition, there is a paucity of data on appropriate management. We reviewed the nutritional status of pediatric cancer patients receiving chemotherapy and/or radiation who were diagnosed and treated at our institution from 2011 to 2012.

Methods

Retrospective chart analysis. Patients older than 21 years or younger than 2 years were excluded.

Results

Our cohort included 55 patients (31 male, 24 female) with mean age at diagnosis of 11.1 +/- 5.6 years. All patients received chemotherapy and thirty received radiation therapy. Diagnoses included leukemia (n=11), lymphoma (n=13), central nervous system tumors (n=10), sarcomas (n=12), wilms tumor (n=5) and other tumors (n=4). 29% of patients had 5-10% weight loss (n=16), 29% had between 10 to 20% weight loss (n=16), and 11% had >20% weight loss (n=6). Median time to nadir weight loss was 2.1 (0.9 to 3.7) months. Patients with metastases (n=9) had a higher median percent weight loss (12.5%, range of 4.4 to 20.8%) than other patients (8.2%, range of 3.3 to 13.6%). Patients with osteosarcoma had the greatest median weight loss after eight weeks (7.9%, range of 1.8 to 10.9%). Eighteen patients received either nasogastric (n=15, 27%) or gastrostomy tube feeds (n=3, 5%). Patients receiving nasogastric or gastrostomy feeds had a median percent weight loss of 9.5% (6 to 15%) at the time feeds were started. Median time to tube insertion was 2.8 months (1.2 to 4.9).

Conclusions

Our cohort had a high prevalence of weight loss especially in patients with osteosarcoma and metastatic disease. Patients tended to have the most weight loss within about eight weeks from initiation of therapy. Our results highlight the need for early nutrition intervention in newly diagnosed cancer patients.

EP-615

Supportive Care/Palliative Care

SYMPTOMS AND SUFFERING PERCEPTION AT THE END OF LIFE OF CANCER CHILDREN AND THE IMPACTS ON THE CAREGIVERS

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Objectives

Little is known about the symptoms and suffering at the end of life in children with cancer. Facing this, we assessed the perception that parents have of the symptoms and suffering that the children underwent at the end of life, and the presence of mood disorders and grief reactions in the parents and their correlations.

Methods

The casuistics comprised parents whose children were admitted to Barretos Cancer Hospital with a cancer diagnosis and died between 2000 and 2010. The patients were all under 21 years old. Self- Administered questionnaires were sent by mail. A Brazil Economic Classification Criteria, a symptom scale, the Hospital Anxiety Depression Scale (HADS) and the Texas Revised Inventory of Grief (TRIG) were used.

Results

The caregivers reported an average of 10 symptoms for leukemia/lymphoma and central nervous system tumour patients and an average of 12 symptoms for solid tumour patients. There was considerable disagreement when the questionnaires were compared to the doctors' reports, even regarding the presence of pain (Kappa 0,236).

With regard to caregivers, 73.7% presented symptoms of anxiety and 81.0% presented symptoms of depression. Regarding their grief, 8 of them (16,0%) presented accute grief, 19 (38,0%) presented moderate grief, 6 (12,0%) presented delayed grief, and 17 (34,0%) presented prolonged grief.

There was statistical significance among education (p 0,052), economic status (p 0,021) and delayed/ prolonged grief, as well as association with HADS anxiety (p 0,001) and depression (p <0,001) with delayed/ prolonged grief. **Conclusions**

The presence of a symptom during the last week of life of the child showed no association with complicated grief (TRIG). There was statistical significance among education (p 0,052), economic status (p 0,021) and delayed/ prolonged grief, as well as association with HADS anxiety (p 0,001) and depression (p <0,001).

EP-616

Supportive Care/Palliative Care

BIOELECTRICAL IMPEDANCE VECTOR ANALYSIS (BIVA) IN CHILDREN AND ADOLESCENTS WITH CANCER UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION IN SAO PAULO, BRAZIL

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Objectives

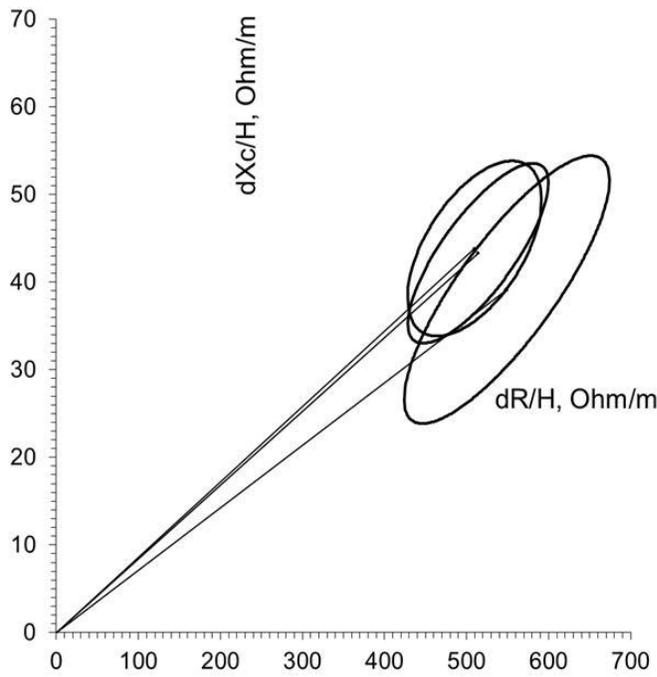
The Hematopoietic Stem Cell Transplantation (HSCT) represents increased nutritional risk to pediatric oncology patients. Considering that nutritional status is a prognostic factor in HSCT, the nutritional assessment during this procedure is essential. Bioelectrical Impedance Vector Analysis (BIVA) is used for screening and monitoring of nutrition and hydration status, and the Phase Angle (PA) has been considered a prognostic and nutritional status indicator as it estimates body cell mass. The aim of this study is to investigate whether the confidence ellipses of mean vectors and PA, assessed through Bioimpedance Analysis (BIA) techniques, differed from a group of children and adolescents with cancer in three different moments of HSCT.

Methods

A prospective study was carried out with pediatric oncology patients undergoing HSCT. Resistance, reactance and PA were assessed before, 15 and 30 days after HSCT. BIVA Software 2002 was used to construct confidence ellipses of mean vectors and SPSS 22.0 to conduct the related samples Wilcoxon signed rank test with PAs.

Results

At the beginning of this study there were 12 patients (n=12) aged from 4 to 14 years old, 50% were female. Due to clinical conditions, 2 patients were excluded in the second analysis (n=10) and 2 more in the third analysis (n=8). The confidence ellipses of mean vectors graph showed similarity between the three HSCT moments, as did the phase angle statistical analysis, with p=0.513, p=0.235 and p=0.204 at before and 15 days, before and 30 days and 15 and 30 days after HSCT, respectively.



Conclusions

Although no statistical difference between BIVA and PA in the three analyzed moments was found in this study, a trend of decrease in both parameters was observed. However, further studies with larger samples should take place in order to better understand the behavior of those variables during HSCT.

EP-617

Supportive Care/Palliative Care

AN EVALUATION OF PHYSICIAN KNOWLEDGE AND ATTITUDES TO PAEDIATRIC PALLIATIVE CARE (PPC)

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Objectives

Many children with life-limiting illnesses are referred late to PPC or not at all, particularly those with non-oncological illnesses. Paediatricians' knowledge and attitudes are important because they are the primary gatekeepers. We aim to evaluate physician knowledge and attitudes to PPC, specifically when to refer and barriers faced.

Methods

This is a multi-centre, cross-sectional anonymised self-administered questionnaire study.

Results

Seventy paediatricians were recruited, majority from KK Women's and Children's Hospital or National University Hospital, with equal proportion of generalists and subspecialists and even spread of seniority. Although > 90% is aware of PPC availability, majority (63%) feel they have inadequate knowledge and skills. The roles of PPC are clear but there is no consensus on when or who to refer. Most (65%) believe that parents should decide whether to involve the sick child in decision-making. The barriers to referral identified include difficulty in matching appropriate services to patient's needs, lack of resources and parental factors, like denial, communication difficulties and fear of 'giving up'. Physician factors (like lack of knowledge, 'prognostic paralysis') are rarely a barrier. Interestingly 58% feel that burnout is common and that grieving of health care professionals remains hidden while 54% feel there is inadequate grief support. Most (61%) agree that PPC needs to be integrated into mainstream practice and that all paediatricians equipped with basic palliative skills.

Conclusions

The identified barriers can be used to set direction in PPC education and service provision so that integration into mainstream practice is possible; and all children are given the option of palliative care, regardless of stage of disease.

EP-618

Supportive Care/Palliative Care

EFFECTS OF STRONG OPIOIDS ON INFLAMMATORY COMPLICATIONS IN HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN

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Objectives

Use of the strong opioids is increasing in the pediatric field through education about supportive care. Preconditioning for hematopoietic stem cell transplantation (HSCT) often brings patients severe mucositis, resulting in need of strong opioids. However, strong opioids can raise the risk of intestinal bacterial translocation and systemic inflammation, because of the suppression of intestinal motility, especially in strongly immunocompromised patients. Furthermore, systemic inflammation sometimes induce other complications. The purpose of this research is to estimate the association between use of strong opioids and inflammatory complications with HSCT in children.

Methods

Consecutive HSCTs for patients younger than 20 years old from October, 2003 were analyzed retrospectively. Strong opioids were used within the periods from the starting of preconditioning to the engraftment. Sedative use was excluded. The analytical factors included HSCT modality, opioid and dosage, stool frequency, fever duration, CRP, and blood culture.

Results

One hundred and nineteen HSCTs for 105 pediatric patients were done for these 10 years. Strong opioids were used in 26 HSCTs (10 autologous PBSCT, 4 related allogeneic BMT, 1 related allogeneic PBSCT, 4 unrelated allogeneic BMT, 7 unrelated allogeneic CBSCT) for severe pains that were not controlled by NSAIDs and weak opioid. Continuous intravenous Fentanyl (5.32~42.61mcg/kg/day, 7~24days) was given in 16 cases and Morphine (0.28~1.27mg/kg/day, 5~58days) in 10. Both opioids provided enough pain-killing effects. A decrease in stool frequency was observed after starting of strong opioids in most of patients. However, there was not statistical significance between use of strong opioids, kinds of opioids and duration of fever, maximum CRP.

Conclusions

These data suggest that strong opioids can be used safely in pain control during HSCT in children.

EP-619

Supportive Care/Palliative Care

THE EFFECTS OF USING GLUTAMINE AND HYDROXYMETHYL BUTYRATE ON THE GASTROINTESTINAL MUCOSITIS DUE TO THE USE OF METHOTREXATE IN RATS

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Objectives

In this study, glutamine (Gln) and β -hydroxy β -methylbutyrate (HMB) were used combined or one by one, for the prevention of intestinal mucositis, and there was made the comparison of the efficacy of either methods.

Methods

Fifty Wistar albino rats were divided to 5 groups. All of the study groups got 20 mg/kg MTX intraperitoneally at the third day. At the third day of the experiment, 6 ml/kg distilled water was given by nasogastric route for 5 days to the first 2 groups as placebo. The third group was "MTX and Gln" group and they were given 1 g/kg Gln for 5 days. "MTX and HMB" group was 4th group and was given 200 mg/kg HMB for 5 days. "MTX, Gln ve HMB" combination was used to the fifth group and they had been given 1g/kg Gln with 200 mg/kg HMB for 5 days. On the fifth day of the experiment, blood and intestinal tissue samples were obtained from all of the groups.

Results

When compared, the degree of the intestinal cripts were deepest in the MTX group ($p < 0.05$), despite that MTX-Gln and MTX-HMB groups were shown better scores ($p < 0.05$). When park scoring system and "erythrocyte reproduction index" were applied, the MTX-Gln-HMB group had higher scores among five study groups. When the tissue was inspected by caspase-3 coating, apopitosis was highest in MTX group. The percentage of apopitosis was lowest in MTX-Gln-HMB group. Expression of caspase-3, -8, and -9 genes were highest in the MTX group ($p < 0.05$) where lowest in the MTX-Gln-HMB group but there was no significant difference ($p > 0.05$).

Conclusions

To our knowledge, there is not any study investigating Gln and HMB use in the prevention of MTX induced intestinal mucositis. This research showed that the combination Gln and HMB use is more effective then the seperate use of both chemicals.

EP-620

Supportive Care/Palliative Care

HOW TO EVALUATE ANTI-EMETIC PROPHYLAXIS IN CHEMOTHERAPY-INDUCED VOMITING IN CHILDREN?

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Objectives

Lack of specific schemes for chemotherapy-induced nausea and vomit in children may lead to inadequate management of emesis. In our unit we chose to adapt to our pediatric population the same guidelines designed for adult patients, including combinations of ondansetron, dexamethasone and aprepitant. These schemes were applied to all patients according to administered chemotherapy and to age and weight of the child, and their effectiveness was assessed through medical record data and the opinions of parents and patients.

Methods

Data collection was performed on patients aged between 3-17 years, who received chemotherapy for malignancy through October-December 2013. We considered data of nausea and vomiting reported in the nursing records and carried out, after informed consent, a structured interview to the parents, asking their opinion on the effectiveness of antiemetics. Finally, it was requested the child's opinion by a visual-analog method (BRAFF scale).

Results

We evaluated 186 courses of chemotherapy with different degree of emetic risk: high, 23%, moderate, 34%, low, 33%, and very low 10%. Medical records showed a total control of nausea and vomiting in 72% of cases and absence of vomiting, with occasional episodes of nausea in 21%. Among parents, 87.6% rated the treatment as effective, while 11.8% considered it as not effective. Data collection concerning the BRAFF scale showed that 80% of children selected the cartoons equivalent to a state of little or no nausea, without vomit.

Conclusions

Our data indicate that nurses, parents and children expressed a concordant evaluation of effectiveness of the anti-emetic prophylaxis and, therefore, our method of assessment appears sufficiently reliable. The schedule used was efficacious for 80% of patients; therefore efforts need to be pursued in order to improve stratification of patients according to emetic risk and subsequent selective intensification of anti emetic strategy.

EP-621

Supportive Care/Palliative Care

PEDIATRIC PALLIATIVE CARE AT A TERTIARY ONCOLOGY DEPARTMENT IN BANGLADESH

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Objectives

Pediatric palliative care services are unavailable for the majority of children in Bangladesh. The Pediatric Hematology/Oncology Department at Bangabangu Sheikh Mujib Medical University is the only cancer treatment facility which provides pediatric palliative care consultations for children with cancer. Our objective was to describe the palliative care services provided to children at this tertiary care hospital in Dhaka, Bangladesh.

Methods

A retrospective chart review of pediatric palliative care records for children treated in our department from January to March 2014 was performed. All palliative care encounters are documented electronically in our online patient database using a standardized data collection tool.

Results

There were 163 patient palliative care encounters with 70 unique patients during the specified time period. The median number of encounters per patient was 2. Twenty patients were treated for physical symptoms, 80% of these children had pain and 20% had gastrointestinal symptoms. In children with physical symptoms, medications prescribed included paracetamol (56%), morphine (50%), laxatives (50%), and other medications (19%). Emotional interventions, including play therapy, art therapy and supportive counseling, were provided on 155 occasions. On eight occasions the palliative care team was asked to assist in discussing the child's incurable disease status with family members. In all of these meetings, families were also taught how to provide basic end of life care at home.

Conclusions

The majority of children with cancer in Bangladesh have significant palliative care needs. A previous study in our department found that 43% of families will refuse or discontinue treatment after their child's diagnosis. Training of oncology care providers (physicians and nurses) to address the physical, psychological, social and emotional needs of children with cancer will improve palliative care for children in Bangladesh.

EP-622

Supportive Care/Palliative Care

INDICATORS FOR ASSESSING THE QUALITY OF PALLIATIVE AND END-OF-LIFE CARE FOR CHILDREN WITH CANCER

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Objectives

The purpose of our systematic literature review was to 1) identify potential structure, process, and outcome indicators of quality palliative and end-of-life care (PEOLC) for children with cancer and their families and 2) identify reliable and valid methods of measurement for these indicators.

Methods

We conducted our search using 3 electronic databases (CINAHL, MEDLINE, EMBASE) and a combination of the following key terms: neoplasms, palliative care, terminal/hospice care, advance care planning, outcome assessment, and quality of life. Results were limited to studies in children, published in English since 2003. Book chapters and theses were excluded. An iterative process was used to screen article titles and abstracts for relevance and then review the selected full articles. Two reviewers were involved at each level of review.

Results

After removal of duplicates, 5191 titles and abstracts were screened for relevance and 626 full articles obtained for further review. Many articles were excluded as children (0-18 years) constituted less than 5% of the sample. More than 100 articles were retained in the final review. The most common indicator identified was health-related quality of life for the child, siblings, or parents, with a number of potential tools for measurement available. Other indicators included a reduction in pain, fatigue, or other symptoms. Nevertheless, the majority of indicators identified were related to structures and processes of care, rather than outcomes.

Conclusions

There are a number of indicators and associated measures for assessing the quality of PEOLC in children with cancer; however, further work is required to identify additional outcomes indicative of high-quality PEOLC. A comprehensive summary of key quality indicators and associated measures will provide a basis for assessing the impact of interventions designed to improve the quality of PEOLC for children with cancer.

EP-623

Supportive Care/Palliative Care

BLOOD TRANSFUSION IN PAEDIATRIC ONCOLOGY PATIENTS: A REPORT OF THE AUDIT IN A TERTIARY CARE HOSPITAL FROM INDIA

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Objectives

Transfusion therapy is key to successful management of children with cancer or hematologic diseases and recipients of HSCT. We observed the pattern of blood product requirement in patients diagnosed at our center.

Methods

All paediatric oncology patients who received blood products during the period from 2010 to 2013 were analysed for age, gender, primary diagnosis, treatment protocol, phase of therapy and blood products received. Patients were given blood transfusion as per BCSH guidelines.

Results

A total of 210 patients received 655 episodes of transfusion during the study period. Among which majority were males (n=143) and mean age was 5.4 years (6 months to 15 years). Mean hemoglobin of 7 gm/dl (4.2gm/dl to 8.6gm/dl) and platelet of 27,000/ul (2000/micL to 60,000/micL) was observed. Patients with Acute lymphoblastic leukemia (ALL) received transfusion most often (504 episodes, 76.9%) among which majority had B-cell ALL (404, 61.6%), followed by neuroblastoma stage IV(53, 8%). Among patients of ALL, Patients on UKALL-XI protocol received maximum number of transfusion (262, 40%) followed by patients on BFM-95 protocol (227, 34.6%). Majority of patients required transfusion during reconsolidation phase (190, 29%). Platelets transfusion (514, 78.4%) were required more often than PRBC (371, 56.6%) and 230 episodes required both. 124 episodes required prophylactic PRBC transfusion and 243 prophylactic Platelet transfusions.

Conclusions

Red cells and platelet concentrates are frequently used in Paediatric oncology patients during chemotherapy. Patients with acute lymphoblastic leukemia during reconsolidation phase require more episodes of transfusion.

EP-624

Supportive Care/Palliative Care

ONCOLOGIC EMERGENCIES THAT NEED INTENSIVE CARE AT DIAGNOSIS IN CHILDREN WITH CANCER

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Objectives

The onset of some oncologic processes is a life-threatening condition that needs to be managed at Intensive Care Units (ICU). The aim of this study is to analyse our experience in the management of severe complications observed before confirming the malignancy diagnosis.

Methods

Retrospective study of children who need critical care at diagnosis, from January 2004 to December 2013. Epidemiological data, tumour characteristics, site, type of complication, treatment and mortality, were reviewed. The statistical analysis was performed by SPSS 22.0.

Results

Emergencies as presenting symptoms were observed in 60 out of 391 new cancer patients and 47 required admissions in ICU at diagnosis. 63% were boys and the median age at diagnoses was 6 year-old (range 0.25-14). These complications were intracranial hypertension-67%, haemorrhage-13%, airway obstruction-6% and 2% each (hyperleukocytosis, tumor lysis syndrome, arterial hypertension, cardiac tamponade, hypercalcemia, superior vena cava syndrome and urinary obstruction). Most frequent diagnoses were brain tumours-72%, lymphoma-6%, acute leukemia-6%, rhabdomyosarcoma-4% and rhabdoid tumour-4%. Most malignancies were located in brain-78%, bone marrow-6%, mediastinum-6% and abdomen-4%. Therapy included ventriculoperitoneal shunt 55%, surgery 10%, ventilatory support 10%, external ventricular drainage 6%, ventriculostomy 2%. The death rate was 8%, before reaching cancer diagnosis.

Conclusions

Early identification of symptoms before life-threatening situations at onset in suspected malignancies and the admission at ICU are crucial for improving the prognosis of severe cases. Innovative ways to educate the communities and health professionals in recognising the warning signs and symptoms for cancer are essential to improve early detection and ensure prompt referral to specialist medical care. Collaboration among physicians of ICU and Oncology Units is very important for the management of children with cancer and it supports the need of therapy in specialized tertiary hospitals.

EP-625

Supportive Care/Palliative Care

TUMOUR LYSIS SYNDROME IN CHILDHOOD MALIGNANCIES IN A TERTIARY HOSPITAL IN NIGERIA: A CALL FOR INCREASED VISIBILITY OF SUPPORTIVE / PALLIATIVE CARE

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Introduction:

Tumour lysis syndrome is a life-threatening emergency due to metabolic derangements secondary to tumour cell necrosis. Early detection of the metabolic disturbances is imperative to avert this complication, promptly initiate treatment and thus improve management outcome of the primary disease.

Objectives:

To determine the prevalence of tumour lysis syndrome among children treated for malignancy at the University of Port Harcourt Teaching Hospital (UPTH), evaluate its impact on the primary disease management.

Materials and Methods:

This retrospective study reviewed all cases of childhood malignancies admitted into the Paediatric Oncology unit of the UPTH over a two year period, January 2011 to December 2012. Clinical profile of patients, uric acid levels, serum calcium, phosphate, potassium and bicarbonate, and outcome of treatment were reviewed. Also retrieved were the duration of disease before presentation, diagnosis and mode of therapy. Data was analysed using SPSS version 20.0 and p value was significant if less than 0.05.

Results:

Out of 58 children treated for malignancy, 16 (27.5%) had laboratory parameters suggestive of TLS. Half of them (8 children) were identified prior to chemotherapy whilst the other half had commenced chemotherapy before developing TLS.

Five (31.25%) of those who had TLS presented within 4 weeks of onset of illness and 11 (68.75%) of them presented with metastatic disease. ALL and neuroblastoma topped the list in terms of diagnosis with 5 cases each, followed by hepatoblastoma (2). They all had hyperuricaemia, 8 (50%) had hyperkalemia while 5 had low serum calcium. Mortality was recorded in 10 (62.5%) of these cases. Performance status was also correlated with outcome.

Conclusion:

Prevalence of TLS in more than 25 % of the patients is quite high. Since the presence of TLS can delay specific therapy of the primary disease creating opportunity for further spread worsening outcome, there is need to advocate for intensification of supportive management and palliative care as many care givers may give up too early on their patients because of the poor clinical picture that patients with TLS may present with.

Acknowledgements:

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Document not received

EP-626

Supportive Care/Palliative Care

INCIDENCE AND OUTCOME OF INFECTIOUS COMPLICATIONS AMONG PEDIATRIC CANCER PATIENTS RELATED TO PERMANENT CENTRAL VENOUS CATHETERS

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Objectives

To assess the incidence of permanent catheter –related morbidities including blood stream infections and catheter related septicemia, systemic infection as toxic endocarditis, toxic myocarditis among immunocompromised pediatric patients, finally outcome of portcath infection (regarding salvagibility of the line and mortality related to central line infection)

Methods

A study done on 78 out of 151 pediatric cancer patient below age of 18 years who inserted portcath with microbiological documented permanent central line infection in the period between 1st of October 2010 till the end of March 2012. Each episode was analyzed regarding causative organism, morbidities related as septicemia, toxic myocarditis and endocarditis, cause of removal of central line and mortality related to central line infection

Results

There is total number of 107 episodes of portcath infection, gram + ve organisms 60/107(56%), gram – ve organisms 45/107(42%) and finally candida 2/107(2%). The most common organisms was coagulase – ve staph (28.03%). Among patients with gram + ve organisms (40 patients) 34 patients (34/40) (85%) had normal echo, four patients 4/40 (10 %) had septic myocarditis, two patients 2/40 (5%) with impaired contractility & valvular affection with vegetations & valvular regurg. Regarding patients with gram – ve organisms episodes (38 patients (33/38) (86.8%) had normal echo, three patients (7.89%) had septic myocarditis and finally two patients (5.2%) with impaired contractility & valvular affection with vegetations. Porta- cath were removed in 53 patients (67.9%) due to failure of sterilization (45.3%) and sepsis (54.7%) while in 25 patients (32.1%) portcath were salvaged. 7 patient died from central line infection (9%) , gram + ve were isolated in 5 patients who died while gram – ve were isolated in 2 patients

Conclusions

gram + ve pathogens are most common cause of permanent central line (portacath) infection which required better infection control, high mortality rate related to portcath systemic infection enforce us to select patients who are in urgent need for portcath insertion

EP-627

Supportive Care/Palliative Care

**DELAYED PRESENTATION AND EARLY DEATHS IN A PEDIATRIC ONCOLOGY UNIT:
A SINGLE CENTER EXPERIENCE IN A DEVELOPING COUNTRY**

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Objectives

To evaluate patients who died early after first admission to a Pediatric oncology unit, in a center located in a developing country.

Methods

The following data were collected by a retrospective review of reports of all newly admitted patients in the pediatric oncology unit, South Egypt Cancer Institute (SECI), Assiut University, Egypt, between 2006 and 2010 who died very early after admission and before reaching a final diagnosis: sex, symptoms, time interval between initial symptoms and first time admission to the pediatric oncology department and after admission until death, and cause of death.

Results

For all available data of 712 patients who were admitted in SECI, 21 patients (3%) (13 males and 8 females) died early after presentation to the unit with a mean of 1.2 day after admission, and a mean duration since initial symptoms till first visit to the pediatric oncology unit of 64.5 days. Initial symptoms were: abdominal swelling (n=7, 33.3%), fever (n=6, 28.6%), head and neck swellings (n=3, 14.3%), hemorrhage (n=3, 14.3%), pallor (n=2, 9.5%). Main causes of death were due to a pulmonary complication (n=8, 38.1%), tumor lysis syndrome and acute renal failure (n=5, 23.8%), septicemia (n=3, 14.3%), mediastinal syndrome (n=2, 9.5%), anemic heart failure (n=2, 9.5%), and hemorrhage (n=1, 4.8%).

Conclusions

There are special problems of childhood tumor management in developing countries; one of them is the initial very late presentation of these patients with advanced disease which leads to early death before appropriate management.

EP-628

Supportive Care/Palliative Care

CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING IN CHILDREN RECEIVING HIGH DOSE METHOTREXATE WITH OR WITHOUT VINCRIStINE

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Objectives

Chemotherapy-induced nausea and vomiting (CINV) negatively influences the quality of life of children receiving chemotherapy. Little is known about the severity of CINV experienced by children receiving IV methotrexate $\geq 1\text{g/m}^2/\text{dose}$ (HD-MTX). The purpose of this study was to describe the prevalence of acute and delayed phase CINV in children receiving HD-MTX \pm vincristine.

Methods

Children aged 4-18 years about to receive HD-MTX participated in this prospective, observational study. Nausea severity, time of emetic episodes, and administration of antiemetics were recorded in a diary beginning immediately before HD-MTX administration, for 24 hours after achievement of the protocol-specific threshold MTX concentration (acute phase), and for an additional 7 days (delayed phase). Nausea severity was assessed by children using a validated tool (PeNAT). Children received antiemetics as ordered by their primary care team. Complete CINV control was defined as no vomiting, no retching and a maximum nausea assessment score of 1 (out of 4).

Results

Thirty children (mean age \pm SD: 11.8 ± 4.0 years; 19 boys) who received HD-MTX plus vincristine (19) or HD-MTX alone (11) participated. Antiemetic prophylaxis consisted of ondansetron (21) or granisetron (9) with (13) or without (17) dexamethasone. Eleven patients received CINV prophylaxis consistent with institution-specific antiemetic guidelines. Two (7%) and 10 (33%) patients experienced complete CINV control during the acute and delayed phases, respectively. More patients experienced complete vomiting control during the acute (57%) and delayed (60%) phases than experienced complete nausea control (7% vs 33%). Of the 11 children who received guideline-consistent acute CINV prophylaxis, none experienced complete and six experienced partial acute CINV control.

Conclusions

Acute and delayed phase CINV control following HD-MTX administration is sub-optimal. The emetogenicity ranking of HD-MTX should be reconsidered in light of these findings. Attention should also be focused on provision of guideline-consistent CINV prophylaxis.

EP-629

Supportive Care/Palliative Care

OPTIMIZING MUCOSITIS PREVENTION PROTOCOL DECREASES LOCAL INFECTION IN CHILDREN AND ADOLESCENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Objectives

Mucositis is a frequent adverse event of conditioning regimens in HSCT in children. It is a painful complication that predisposes to local and systemic infections due to the disruption of the mucosal barrier. In our BMT unit, we have established a specific protocol for the prevention of this complication. Our aim was to compare the frequency of local infections among groups with good and poor adherence.

Methods

The mucositis prevention protocol was as follows; 1. Panorax radiography, 2. Oodontogram (to identify deteriorated amalgams), 3. Bacterial plaque index, 4. Soft tissue status, 5. Use of antibacterial disinfectants (Clorhexidine), 6. Family education, and 7. Frequent use of sugar free gum. The BMT unit dentist had daily active surveillance in the application and adherence to the protocol, and also, in the classification of mucositis severity. We estimated the OR of local infection by adherence group. We used multivariate logistic regression to adjust the OR by age, type of conditioning regimen, and graft source.

Results

We included in the protocol 46 patients from March/2011 to January/2014. Mean age was 9 years old; 63% boys and 59% showed an optimal adherence to the protocol. The overall frequency of mucositis and local infection was 28%, and in patients with mucositis GII to III was 11%. Adjusted OR for local infection by adherence group was 5.2 (95% CI: 1.4, 23.0).

Conclusions

We found that achieving optimal oral hygiene, before and during HSCT, strongly reduces the risk of local mucosal infections. This is relevant, not only to decrease the risk of systemic infections but also to improve the quality of life during pre-engraftment phase of the transplant. Moreover, this could have an effect in decreasing the occurrence of acute GvHD, an issue that merits further studies.

EP-630

Supportive Care/Palliative Care

PALLIATIVE CARE IN PEDIATRIC ONCOLOGY: MATERNAL PERSPECTIVES

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Objectives

The overall goal of this research was to understand the concepts and experiences about palliative care from mothers whose children had been hospitalized in a national cancer hospital, located in the state of São Paulo.

Methods

This is a qualitative study, descriptive in nature. For data analysis, the method of content analysis of Bardin was used, thematic approach.

Results

The maternal testimonies collected were organized into five themes: Conceptions about palliative care; Maternal care after the announcement of impossibility of healing; Professional care after the announcement of impossibility of healing; Maternal feelings about the stage of palliative care; Maternal perspectives on children's feelings when under palliative care.

Maternal conceptions about palliative care proved to be vague, distorted or even nonexistent, showing a need for institutional investments to change this situation. . As to the experiences reported by these women, those were permeated by feelings of different types and intensities, especially those of helplessness and nonconformity. The religious conviction proved to be an important resource for the acceptance and the overcoming of problems. The perceptions about maternal and professional care during the palliative phase pointed to the importance of comprehensive care to children and their families, the team's qualification for such care and inclusion, guidance and active participation of family in decisions to be taken to get the best quality of life for these children during this same phase.

Conclusions

By the end of this study, in addition to what was proposed, it could be confirmed the necessity of establishing a line for comprehensive care to children with cancer, from its municipalities, as well as the importance of continuity of care for the service, to families who have lost their children.

EP-631

Supportive Care/Palliative Care

**CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY IN NON-CNS CANCERS:
COMPARISON BETWEEN DIAGNOSTIC GROUPS**

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Objectives

Chemotherapy-induced peripheral neuropathy (CIPN) is a common side-effect of cancer treatment in children that can have lasting, negative consequences. CIPN is commonly recognized in patients with acute lymphoblastic leukemia (ALL), but is not well documented in other populations. The purpose of the study was to identify severity and clinical characteristics of CIPN that occurs in children/adolescents treated across a variety of cancers.

Methods

The pediatric modified Total Neuropathy Score (ped-mTNS) as well as standardized measures of balance and manual dexterity were administered to all subjects (n=85). Patients treated for ALL (n=31) were tested near the end of delayed intensification (approximately 6 months into treatment) whereas subjects treated for lymphoma (n=32) or other non-CNS solid tumors (n=22) were tested approximately 3 months into treatment. Treatment information was extracted from the medical record. Total and item ped-mTNS scores, as well as balance and manual dexterity scores, were compared between diagnostic groups using ANOVA.

Results

Although subjects treated for ALL received longer duration of treatment and were exposed to higher cumulative doses of vincristine (22.1 mg/m² ALL, 8.86 lymphoma, 11.34 other solid tumors), they had lower overall ped-mTNS scores (7.7 ± 3.1) than patients with lymphoma (10.8 ± 5.5, p=0.003) and other solid tumors (10.4 ± 4.5, p=0.035). Subjects with lymphoma had increased sensory symptoms, vibratory impairment, and deep tendon reflex decrements while subjects with ALL had worse strength deficits. All groups had mean balance and manual dexterity scores that were not significantly different from one another but were below normative values with the exception of manual dexterity in subjects with ALL which was in the normal range.

Conclusions

Patients with lymphoma and other solid tumors experience on-treatment CIPN that may be more significant than in patients with ALL. Increased attention to CIPN needs to occur in these groups.

EP-632

Supportive Care/Palliative Care

PALLIATIVE CARE AND END-OF-LIFE ISSUES IN PEDIATRIC ONCOLOGY: REPORT FROM A MOROCCAN PEDIATRIC ONCOLOGY UNIT

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Objectives

The care of children at the end of life may be particularly complex and high-quality palliative care is now an expected standard at the end of life. To better understand the needs of the Moroccan children and their families the parents of terminally ill children were asked to answer to a questionnaire.

Methods

The study was conducted in the Pediatric Hematology and Oncology Institute of Rabat during 2013. We interviewed the parents of children who were in palliative care about physical symptom, psycho-social needs and whether or not they talk about death with their child. The questionnaire was administered in Arabic by a psychologist. Medical records were reviewed for additional informations.

Results

Among the 20 parents who participated to the study, 19 refused that announcement of the palliative phase to their children. The most frequent parent reaction was death anticipation and resignation. Most of the parents avoid discussing with the child about his imminent death or talk about indirectly discussing the death of "the others"

Concerning the preferred place for the end of life 55% chose the patient's house and 40% the hospital. The main symptoms reported were pain (75%) and fatigue (75%).

Finally Over 20 relatives interviewed 19 of them expressed physical needs such as a better symptoms management and more contact with the caregivers, 15 expressed a need of social support (transport fees, support for medication fees..), and all the parents reported the need of psychological support.

Conclusions

In pediatric oncology, palliative cares are the most difficult phase for the parent, the children and also for the caregiver especially in low income countries where palliative care are poorly structured. One of the most important steps to improve its management is to understand the needs of each person involved.

EP-633

Supportive Care/Palliative Care

NUTRITIONAL STATUS OF CHILDREN WITH MALIGNANCY

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Objectives

Nutritional assessment is an essential component of the initial assessment of children with cancer, and malnutrition is associated with an increased risk of morbidity and mortality. This study evaluated the nutritional status of children with cancer during initial diagnosis, in a tertiary health care center in Bangladesh

Methods

A cross sectional observational study was done in the Paediatric Haematology & Oncology Department of Bangabandhu Sheikh Mujib Medical University (BSMMU) between May and October 2010. Nutritional status of one hundred children, under 15 years of age, with newly diagnosed malignancy was evaluated. Weight, height/length, and mid upper arm circumference (MUAC) were recorded at the time of diagnosis, before beginning treatment, using standard techniques. Z-scores for weight for height/length, height/length for age, and weight for age were derived using National Center for Health Statistics (NCHS) growth curves. Body mass index (BMI) was calculated using standard formula.

Results

A total of one hundred patients were included. The mean age was 6 years (range 2 months to 14 years). Sixty-four percent of patients were male and thirty-six percent were female. Hematological malignancies accounted for 87% of diagnoses, with solid tumors comprising 13% of diagnoses. The overall proportion of under nutrition, wasting & stunting were 61%, 59% and 20% respectively. The proportion of malnutrition by body mass index & mid upper arm circumference were 69% and 63% respectively.

Conclusions

In this study the proportion of malnutrition among children with cancer was high. Fifty-nine percent of Bangladeshi children are wasted at the time of presentation and sixty-one percent are underweight. Children with solid tumors are more frequently severely wasted (50% vs. 33%) and severely underweight (40% vs. 24%) than children with hematological malignancies. These results suggest that interventions to improve the nutritional status of children with cancer are needed for the majority of children presenting with cancer in Bangladesh.

EP-634

Supportive Care/Palliative Care

IMPACT OF CANCER FINANCIAL SUPPORT GROUPS ON CHILDHOOD CANCER TREATMENT AND ABANDONMENT IN A PRIVATE PEDIATRIC ONCOLOGY CENTRE IN A DEVELOPING COUNTRY

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Objectives

Globally, an estimated 2,50,000 children develop cancer each year, and 80% of them live in developing countries.. In India, approximately 45,000 children are diagnosed with cancer every year.

Treatment abandonment is a significant barrier to cancer care in the developing world.

Though the reasons for abandonment are complex and multifactorial, economic issue appears to be the main factor in abandonment. We analysed the impact of financial support of two cancer support groups on the treatment and abandonment in pediatric oncology.

Methods

Aims: To analyze the impact of two cancer support groups in the treatment and abandonment of childhood cancer.

Methods and Material: This is a retrospective review of children with cancer funded and non funded who were treated at Kanchi Kamakoti CHILDS Trust Hospital from 2010 to 2013

Results

A total of 100 patients funded, 57 by Ray of Light Foundation and 43 by Pediatric Lymphoma Project and 70 non-funded. The total current survival of 80%, including those who have completed treatment and those currently undergoing treatment is comparable in both the groups. Abandonment of treatment after initiating therapy was not seen in the financially supported group whereas abandonment of treatment after initiation was seen in one child in the non funded group.

Conclusions

Besides intensive treatment with good supportive care, financial support also has an important impact on compliance and abandonment in all the socioeconomic strata of society. Financial supports from private cancer support groups also has its impact beyond the patient and family in reducing the burden on government institutions by non-governmental funding in private sector. Improvement in the delivery of pediatric oncology care in developing countries could be improved by financial support from the private sector.

EP-635

Supportive Care/Palliative Care

VITAMIN D DEFICIENCY IN CHILDREN WITH CANCER

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Objectives

INTRODUCTION: Very few studies only have measured vitamin D levels in pediatric patients with malignancy. We undertook a study to assess vitamin D status in pediatric cancer patients in a developing country in our pediatric oncology centre.

AIM: This study aims to compare the vitamin D levels between a population group of childhood cancer patients and a control group in a tertiary care pediatric oncology unit in a developing country.

Methods

This is a prospective case control study conducted in Sri Ramachandra Medical College, pediatric oncology tertiary care centre. A total of 51 children were included in this study from the age group of one month to 18 years of age who has been diagnosed with cancer and on treatment for atleast six months. Controls were age and sex matched who are without cancer. The duration of sampling was from March 2012 to July 2013. 25 OH Vitamin D levels were assessed by chemiluminescence. Comparison of the two groups was done using t tests, ANOVA and Mann Whitney test as appropriate. Statistical analysis was done with the use of SPSSv17.

Results

Mean vitamin D levels among cases were found to be 22.6 ng/dl, while mean vitamin D levels among the controls were found to be 33 ng/dl. 78.43% of children with cancer were found to have insufficient levels of vitamin D as opposed to 50.98% of controls.

Other factors compared included age, sex, type of malignancy and nutrition status. Mild variables were seen in each factor but were deemed to be not statistically significant.

Conclusions

Children with cancer have a lower vitamin D level than children of a control population. Since cancer survivors are at a higher risk for low bone mineral density, interventions to improve 25-OH D status in this vulnerable population are needed.

EP-636

Supportive Care/Palliative Care

INFECTION ASSOCIATED MORBIDITY AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANT IN CHILDREN AND ADOLESCENTS: WHAT IS THE OPTIMAL PROPHYLAXIS STRATEGY?

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Objectives

Invasive infections are a major cause of morbidity and mortality following hematopoietic stem cell transplantation (HSCT). Standardised strategies to prevent infections are established in allogeneic HSCT; however, evidence to recommend prophylactic antimicrobial drugs in autologous HSCT is limited. In addition these drugs have potentially significant side effects. Our aim was to review the practice and experience in this Regional Children's Cancer Centre over a ten year period; to undertake a review of the literature, and produce guidance to standardise the approach to infection prophylaxis and management in this patient group.

Methods

We retrospectively analysed data relating to children and adolescents undergoing autologous HSCT at our institution between January 2004 and December 2013. Additional information included source of stem cells, diagnosis, and age at transplant, diagnosis, source of stem cells, infection prophylaxis, complications and outcome.

Results

27 children underwent autologous HSCT, totalling 30 HSCT procedures. Neuroblastoma was the most common diagnosis (11/27). 13 patients underwent autologous bone marrow transplants, 14 peripheral blood stem cell transplants. Fungal, viral or a combination antimicrobial prophylaxis was used in 18 patients. Bacterial infections occurred in 8 patients including bacteraemia in 3 patients and lower respiratory tract infection in 2. Viral infections affected 5 patients including 2 episodes of VZV reactivation and 1 HSV reactivation. Fungal infection was uncommon; only 1 case of pulmonary aspergillosis was strongly suspected clinically and on imaging but unproven on BAL. Relapse of disease accounted for all 6 deaths following HSCT.

Conclusions

To date there is no standard practice for infection prophylaxis although our review of practice did not reveal a high incidence of invasive infection. Production of an evidence based guideline will lead to patient focussed infection prophylaxis and minimise morbidity associated with infection and its management.

EP-637

Supportive Care/Palliative Care

**ABANDONMENT OF TREATMENT AS A BANE FOR CARE GIVERS IN THE
PEADIATRIC ONCOLOGY UNIT AT UNIVERSITY OF PORT HARCOURT TEACHING
HOSPITAL, RIVERS STATE NIGERIA**

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Objectives

The Paediatric Oncology unit at University of Port Harcourt Teaching Hospital over the years has experienced a high incidence of abandonment of treatment by parents/guardians of children who have been admitted and undergoing chemotherapy.

This is attributable to a number of reasons such as cost implications, ignorance, denial syndromes and granting patronage to traditional healers. Most often than not, the latter reason accounts for the late presentation of the patients in the hospital. There are few treatment centres across the state.

Methods

The study was carried out using cohorts from the patients in the ward and those coming from time to time for chemotherapy spanning a period of one year (2013 - 2014)

Results

About 55% the patients presented four weeks after the onset of (symptoms) of the illness. In the course of their therapy, 40% defaulted for several reasons. Mortality recorded is 45%. Statistical evaluation using ANOVA was also carried out.

Conclusions

Late presentation due to the various reasons and high default rates are contributory factors to poor outcome in the treatment of patients even for those who have good prognosis.

EP-638

Supportive Care/Palliative Care

ONCE A DAY CEFTRIAXONE-AMIKACIN COMBINATION AS INITIAL EMPIRIC THERAPY FOR FEBRILE NEUTROPENIA IN CHILDREN

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Objectives

We present our experience regarding the use of once daily(OD) ceftriaxone(CFT) plus amikacin(AMK) as initial therapy for febrile neutropenia(FN).

Methods

Retrospective Study; Study period January2002--December2011; Inclusion Criteria: age<18 years, treatment for cancer, fever >100.4°F with ANC<500/cmm. Exclusion criteria: FN at time of diagnosis of malignancy; patients undergoing BMT. Empiric therapy for FN was IV CFT 100mg/kg and AMK 15mg/kg OD. Patients having respiratory distress, hypotension or altered sensorium were treated with Piperacillin-tazobactam(PTZ) and AMK as initial therapy. Antibiotics were upgraded if no response within 48-72 hours, or earlier if clinical deterioration. Vancomycin was added in case of skin/soft tissue infections, line-related sepsis or documented infections on culture. Amphoterecin was added if persistent fever > 4-5 days. Age<1year, AML chemotherapy, poor performance status, need for blood products, insurance, patient convenience were indications for admission. High-risk FN was defined as duration of neutropenia>7days, malignancy not in remission and poor performance status.

Results

464 episodes of FN were documented, of which 418 episodes were initially treated with CFT-AMK. (hemato-lymphoid malignancies in 82%). There was no focus of infection in 49% episodes. 224/418 episodes were considered high risk as per our definition. 148/418 episodes were treated initially on OPD basis, of which 19 required admission for persistent fever. There were no deaths in this group. In 270/418 episodes, patients were initially admitted for treatment, of which 66 could be discharged within 3-4 days. There were 6 deaths in the admission group. Overall, 214/418(52%) episodes could be managed wholly/partially on OPD basis. 327/418(78%) episodes responded to CFT-AMK, while 91/418 required switch to other antibiotics. Additionally, in 25 episodes, breakthrough fever occurred after initial response and required change in antibiotics.

Conclusions

Use of CFT-AMK combination as initial empiric therapy for FN may permit OPD management of a significant number of patients, considerably reducing the burden on indoor services.

EP-639

Supportive Care/Palliative Care

PAEDIATRIC PALLIATIVE CARE: A SYSTEMATIC REVIEW AND RECOMMENDATIONS FOR TREATMENT OF SYMPTOMS

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Objectives

Children dying of a life threatening disease suffer a great deal at the end of life. Symptom control in children dying of cancer is often unsatisfactory at this stage of disease, partly because many caregivers are simply not familiar with paediatric palliative care. Symptom control and relieve of suffering are the cornerstones of paediatric palliative care, but evidence based recommendations in paediatric palliative care are not available. The aim of this study is to improve palliative care for children by making high quality care recommendations to recognize and relieve symptoms in paediatric palliative care.

Methods

An extensive search was performed for guidelines and systematic reviews on paediatric palliative care. An expert panel combined the evidence that resulted from this search with consensus to form recommendations on the treatment of symptoms in paediatric palliative care.

Results

We appraised 21 guidelines and identified 693 potentially eligible articles of which only four met our inclusion criteria. None gave recommendations on recognizing and treating symptoms in paediatric palliative care. Two textbooks and an adult palliative care website were eventually our main sources of evidence on recognizing and treating symptoms in paediatric palliative care.

Conclusions

Hardly any evidence is available for the treatment of symptoms in paediatric palliative care. By combining evidence for adult palliative care and the sparse evidence for paediatric palliative care with paediatric expert opinion we were able to define a unique set of high quality care recommendations to relieve symptoms and lessen the suffering of children in palliative care. The results of this study are an important tool to educate caregivers on how to relieve symptoms in children with life threatening conditions and improve quality of paediatric palliative care.

EP-640

Supportive Care/Palliative Care

DEVELOPMENT OF AN EDUCATIONAL BOOKLET FOR FAMILIES OF CHILDREN WITH LEUKEMIA

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Objectives

Although the survival rate of childhood leukemia in Japan has exceeded 80%, being diagnosed with leukemia, a life-threatening illness, still causes great anxiety for patients and their families (i.e., parents and siblings). Families face unpredictability and uncertainty both in their present situation and future lives. Providing education to patients and families about the prospect of recovery, quality of life (QoL), and management of family life would help families to deal with hardship more easily. The purpose of this study was therefore to develop an educational booklet promoting parental involvement and providing instructions about parental management of the child's and family's life, both during and after treatment.

Methods

To compile information and select the contents of the educational tool, the members of the Committee of QoL in the Japan Association of Childhood Leukemia Study Group (JACLS) reviewed previous studies regarding the family life and QoL of families of children with leukemia. In addition to literature reviews, we referred to the results of previous longitudinal studies that had been conducted by the JACLS to clarify family life trajectory and the QoL of children with leukemia and their families.

Results

Based on the results of this research, the educational booklet contains three themes: 1) the QoL of children with leukemia and their family members, 2) family life challenges by treatment phase, and 3) support resources and hints for overcoming family life challenges. The cardinal messages of the booklet are to provide hopeful prospects to patients and their families and to encourage family management.

Conclusions

The acceptability, utility, and helpfulness of the educational booklet should be examined in future research.

EP-641

Supportive Care/Palliative Care

EARLY PALLIATIVE CARE CONSULTATION FOR HIGH RISK PEDIATRIC ONCOLOGY PATIENTS: A FEASIBILITY STUDY

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Objectives

As part of a larger study evaluating the impact of early palliative care in children with high risk malignancies, we assessed the feasibility of obtaining palliative care consultations within one month of diagnosis.

To assess the feasibility of obtaining early (at diagnosis) palliative care consultations for children with high risk malignancies

Methods

Children were eligible for early palliative care consultation if they had a high risk malignancy, defined as: 1) relapsed disease, 2) need for stem cell transplantation (SCT), or 3) newly diagnosed with an estimated overall survival of < 50%. The pediatric hematology/oncology division identified eligible patients at a weekly patient-care conference. Medical charts were reviewed every two weeks to assess the status of the consultation and number of follow-up visits after initial consultation.

Results

Since implementation in March 2013, 20 of 25 eligible patients received an early palliative care consultation. No children or families declined the consult. Four patients did not participate in the study: two were children from an outside hospital referred to our institution for autologous SCT, two were children with recurrent disease treated primarily as outpatient, and one patient had a long post-operative course and was discharged prior to receiving a consult. The median time from diagnosis to consult was 12 days (2 - 180). . Seventeen of 20 (85%) patients received consultation within 30 days of diagnosis. Eight of 20 (40%) were newly diagnosed, and 12/20 (60%) had relapsed/recurrent disease. Fifteen of 20 (75%) had follow up palliative care visits after initial consultation; 2/20 had only one follow visit. The median number of follow up visits for the group was 4 visits (1-24).

Conclusions

An early palliative care consultation program for children with high risk malignancies is feasible and is well-accepted by pediatric hematologist/oncologists, children and families.

EP-642

Supportive Care/Palliative Care

ATYPICAL PELLAGRA IN PEDIATRIC ONCOLOGY PATIENTS: THE MYSTERIOUS RASH

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Objectives

Pellagra is a severe state of niacin deficiency. Pellagra in pediatric cancer patients is unknown in developed world. We describe two pediatric oncology patients who developed pellagra.

Methods

Case records of pediatric cancer patients managed at the Stollery Children Hospital were reviewed.

Results

Case 1: A 5 year old boy diagnosed with Burkitt's lymphoma was treated using protocol ANHL01P1 (Group C). On day +29 of consolidation I chemotherapy, he developed a hyperpigmented, symmetrical rash on the neck and dorsum of his hands and wrists. This patient also had a 4 week history of diarrhea. Supplemental niacin 100 mg daily was given for 14 days, then a multivitamin with 10 mg niacin was given daily. His rash resolved within 8 days of supplementation. Preceding the rash, the patient's niacin intake was ≥ 8.8 mg daily (Dietary Reference Intake is 8 mg daily).

Case 2: A 13 year old boy with acute myeloid leukemia was treated as per protocol AAML0531. On day +10 of induction-II, the patient developed a dark brown hyperpigmented rash on the dorsum of wrists, elbows and face without diarrhea but with fatigue 3 weeks prior to presentation. On day +22, the Dermatology service suggested pellagra. Niacin supplementation of 100 mg daily was initiated for 10 days, then a multivitamin with 15 mg niacin was provided daily. The rash resolved within 20 days of supplementation. Enteral and parenteral niacin intake prior to pellagra diagnosis was ≥ 17 mg daily (Dietary Reference Intake is 12 mg daily).

Conclusions

Pellagra is extremely unusual in pediatric oncology patients. These cases illustrate the potential for development of relative niacin deficiency following chemotherapy, possibly related to high-dose cytarabine. Clinical evidence of pellagra existed despite assessed adequate niacin intake, suggesting higher requirement during certain phases of treatment.

EP-643

Supportive Care/Palliative Care

A CROSS-SECTIONAL SURVEY EXPLORING BEHAVIORS AND PSYCHOSOCIAL DETERMINANTS OF PHYSICAL ACTIVITY AND DIET DURING AND AFTER TREATMENT FOR A PEDIATRIC MALIGNANCY

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Objectives

Unhealthy lifestyle behaviors can promote the development of cancer-related morbidities among children and adolescents with cancer across all phases of treatment. Lifestyle interventions may reduce this risk during and after treatment. We performed a cross-sectional survey to learn about current practices and barriers to healthy lifestyle behaviors.

Methods

Information on fruits and vegetable (FV) and dietary fat intake, physical activity (PA), and their associated psychosocial variables were measured using the Patient-Centered Assessment & Counseling for Exercise survey during a routine clinical visit. Frequencies of demographics and survey responses were analyzed with SPSS (v21).

Results

Data from 61 patients (31F/30M; Mean age: 18.2y (range: 12-25y); 19% Hispanic, 11% Asian, 10% Black) were available. Only 13% of patients reported meeting PA recommendations, though 55% intended to meet guidelines within 6 months. Eighty seven percent reported eating < 5 servings of FV per day, but 71% of them intended to increase FV consumption within 6 months. 43% reported consistently avoiding high fat foods; yet dietary analysis revealed fat intake (55g/d) in excess of guidelines (20 – 35g/day). Only 40% of subjects had consistent friend or family support for eating low fat foods, only 46% had support for PA, and only 55% had support for FV consumption.

Conclusions

Pediatric oncology patients are not following healthy lifestyle behaviors, despite the majority intending to do so. The gap between intentions and reported behavior may be partly explained by data indicating a lack of support for these behaviors. Improving support for and access to healthy lifestyle resources may facilitate the adoption of healthy behaviors and improve the health outcomes and quality of life for these patients.

EP-644

Supportive Care/Palliative Care

PALLIATIVE RADIOTHERAPY FOR CHILDHOOD CANCERS

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Objectives

Despite accepted and widespread application of palliative RT for children with advanced malignancies, few reports have been published on its use. The goal of this study was to describe clinical characteristics, treatment response, and survival of children receiving palliative RT.

Methods

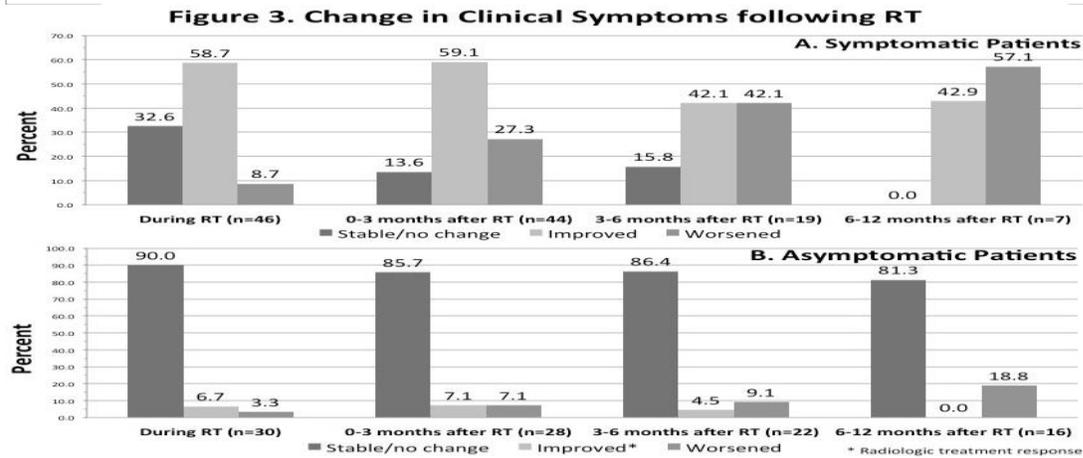
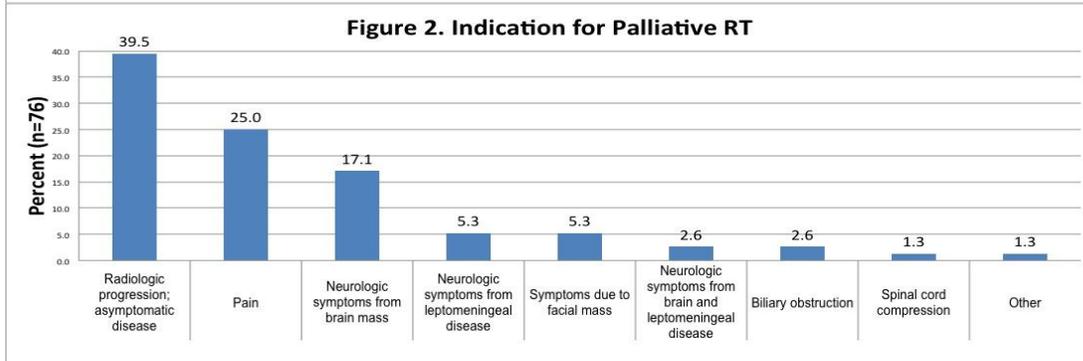
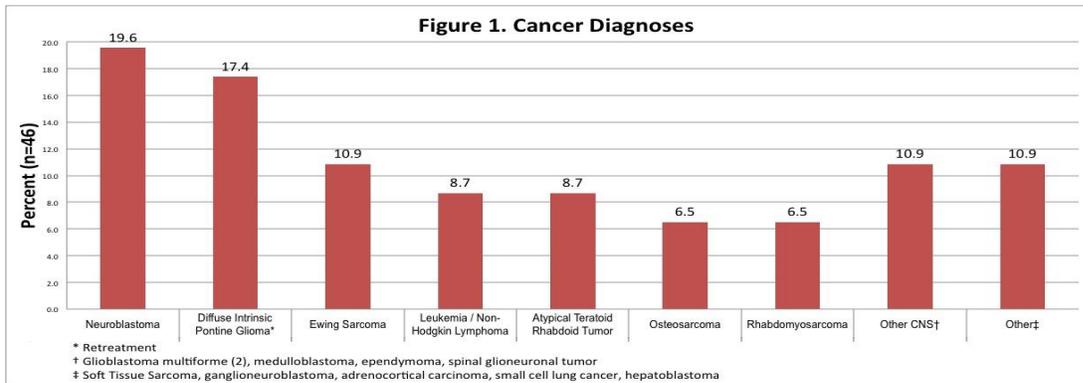
Pediatric patients (age ≤18 years) treated with palliative RT for advanced incurable cancer from 01/01/08-02/26/14 were included. Diagnosis, indication and details of palliative RT, treatment response, toxicity, and survival were retrospectively reviewed.

Results

Forty-six patients were treated in 76 palliative treatment courses. Fifteen patients (33%) had ≥2 palliative RT courses (maximum: 6 courses). Median age at time of palliative RT was 10.3 years (range: 1.5-18.9); 54% were male. The most common diagnoses (Figure 1) were neuroblastoma (20%) and diffuse intrinsic pontine glioma (retreatment; 17%).

The most common indications for RT were radiologic progression in asymptomatic patients (39%) and pain (25%; Figure 2). The most common treatment sites were brain (32%) and bone (29%). Six treatment courses were not completed (8%). Median RT dose was 30 Gy (range: 2.5-54). Median duration of RT was 16 days (range: 1-48). Sixty-five treatment courses (86%) were delivered with fraction sizes ≥250 cGy. Twenty-seven treatment courses (36%) were given under general anesthesia.

Median follow-up was 3.9 months. RT-related toxicity was 24% during treatment and 8%, 5%, and 4% at 0-3, 3-6, and 6-12 months after RT, respectively. Over 80% of asymptomatic patients, and 91%, 73%, 58%, and 43% of symptomatic patients had improved or stable symptoms during RT and 0-3, 4-6, and 6-12 months afterwards, respectively (Figure 3). Median survival after palliative RT was 4.2 months. Of 21 surviving patients (46%), four (19%) were in hospice care at last follow-up.



Conclusions

Palliative RT was well-tolerated in children with incurable malignancies, and was associated with improved or stable symptoms in the majority of cases.

EP-645

Supportive Care/Palliative Care

THE PROFILE OF INFECTIONS IN THE RECIPIENTS OF HEMATOPOIETIC STEM CELL TRANSPLANT- A SINGLE CENTRE EXPERIENCE FROM INDIA

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Objectives

Infections are an important cause of morbidity and mortality in hematopoietic stem cell transplant (HSCT) patients. Knowledge about the infections patterns at a centre would facilitate early initiation of treatment. This review was done to analyze the pattern of infections in the first 100 days following HSCT.

Methods

A retrospective review of data of pediatric patients who underwent HSCT between January 2007 and December 2013 was done to find out the number and types of infection upto day +100.

Results

Of 56 HSCT patients, 28 (50%) had at least one episode of proven sepsis. Of 56 transplants, 38 (67.85%) were allogeneic and 18 (32.14%) autologous. The M:F ratio was 3.33:1 and the mean age was 6.7yr (range: 8m-18.3yrs). According to HSCT source, 27 Peripheral blood stem cell transplants (PBSCT), 11-Cord Blood Transplants (CBT) , 16 Bone Marrow (BM) and 2 BM+CBT. Among allogeneic transplants 25(65.7%) were Matched Sibling Donor (MSD), 10(26.3%) were CBT, 1(2.6%) was a MSD+CBT, and 2(5.2%) were haplotransplants (donors were parents- 1 BM and 1 PBSCT).

There were a total 56 episodes of infections, of which 31 (55.3%) were culture proven bacterial infections (*Klebsella sp*-4, *Staphylococcus aureus*-2, *staphylococcus hominis*-2, *Acinetobacter sp*-1, *Enterococcus fecalis*-3 *psuedomonas*-2 others-17), 10(17.8%) were CMV. There were 15(26.7%) fungal infections of which probable were 8(14.2%) and proven infections 7(12.5%) (*Aspergillus sp*-8, *Candida sp*-6, *Trichosporon sp*-1)

There were 30 (53.5%) episodes of infection in allogeneic transplant and 26 (46.4%) in auto transplant. Total episodes of infection in the PBSCT were 23 (41%), 10 (17.8%) in CBT, 18 (32.1%) in BM and 5 (8%) in BM+CBT group. There were total of 19 (33.9%) transplant related mortalities of which 6 (31.5%) were attributable to infections.

Conclusions

Infections are very common post HSCT. *Klebsella sp*, CMV and *Aspergillus sp* were the most common infections in their respective categories.

EP-646

Supportive Care/Palliative Care

EFFORTS TO CONTROL INVASIVE FUNGAL INFECTION IN A DEVELOPING COUNTRY

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Objectives

A single institution retrospective study to analyze the outcome of pediatric cancer patients who are at risk of developing invasive fungal infection (IFI). Patients with IFI were treated with antifungal drugs according to availability and financial support. Diagnosis of IFI was only done by CT chest .

Methods

The study included 126 pediatric cancer patients (80 females, 46 males) at risk of developing IFI, with hematological malignancies and solid tumors (85 and 41 respectively) from 2012 till 2014. Patients were divided into 3 groups. Group A (58 patients): 48 patients received prophylactic Itraconazole, 10 patients received prophylactic Voriconazole. Group B (55 patients) who developed fever and neutropenia during treatment. Group C: 13 patients who presented with IFI.

Results

In group A, 48/58 (82.7%) patients received prophylactic Itraconazole, while 10/58 (17.3%) received prophylactic Voriconazole. 27/48 (56.2%) receiving Itraconazole were controlled and did not develop IFI, while 31/48 (64.5%) developed IFI and received AmphotericinB: 7/31 (22.5%) died, 11/31 (35.5%) were shifted to Caspofungin and 13/31 (42%) shifted to Voriconazole. Those receiving Voriconazole, 5 /10 (50%) were controlled while 5 /10 (50%) developed IFI. Group B: 8/55 (14.5%) were controlled on antibiotics, 47/55 (85.5%) were given empiric AmphotericinB, where 14/47 (30%) were controlled while 33/47 (70%) had IFI, 12/33 (36.4%) were controlled on AmphotericinB, while 21/33 (63.6%) had progressive IFI. Group C: 10/13 (77%) received Voriconazole. 8/10 (80%) were controlled, while 2/10 (20%) had progressive IFI. 3/13 (23%) received AmphotericinB with a complete response in 2/3 (66.6%) and 1/3 (33.4%) were shifted to Voriconazole. Caspofungin was better than Voriconazole as salvage ($p=0.632$). Voriconazole was significantly superior than Itraconazole as prophylaxis ($p=0.002$).

Conclusions

Prophylactic Itraconazole and empirical AmphotericinB seem suitable in developing countries. Caspofungin is preferred as second line.

EP-647

Supportive Care/Palliative Care

THE TRANSITION FROM ACTIVE TO PALLIATIVE CARE IN CHILDREN WITH CANCER: EXPERIENCES OF PARENTS AND STAFF

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Objectives

Exploration of personal and professional challenges associated with the period of transition between active and palliative care for paediatric oncology. This uncertain, little researched, turning point of treatment will be described and, aspects of effective and less effective practice in managing such situations will be highlighted.

Methods

Qualitative interviews with 2 groups took place. Firstly, 10 staff members working within the Oncology/Haematology ward at a single Primary Treatment Centre, (PTC) were interviewed and a staff focus group followed to discuss the common themes arising within the interviews. Secondly, 7 sets of parents who had lost a child to cancer within the last 1-10 years. All parents had children who were treated for cancer at the same 'PTC'. Each parent was offered a second interview which explored themes arising from the first interview using the technique of emotional touch point stories.

Results

Established transition theories were supported although complex interplay between the transition for each group was present. Requirements for transition were described clearly by both groups, awareness & acknowledgement of the move from active to palliative care was particularly evident in the parent group. The importance of support systems and strong connections with others was a strong focus for both groups, particularly staff. Use of the Emotional Touchpoint Tool aided families in finding the right words.

Conclusions

The process of the transition differs between families as different circumstances undeniably lead to individual experiences; however arising themes have met required aims allowing effective description of transition.

Interviews naturally alluded to the greater transition following the death of the child and the move into bereavement.

Importance of continuing support mechanisms were identified and will lead to recommendations for local practice, especially relating to introduction to the ward environment and continuity of care through palliation and beyond into bereavement care.

EP-648

Supportive Care/Palliative Care

KETAMINE HALVES OPIATE REQUIREMENTS AND SIMULTANEOUSLY REDUCES PAIN SCORES TO ZERO IN HIGH RISK NEUROBLASTOMA PATIENTS RECEIVING IMMUNOTHERAPY

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Objectives

Assessment of ketamine efficacy and tolerability in patients receiving immunotherapy for Neuroblastoma.

Methods

Retrospective case note and pain database review of patients on the HR-NBL-1/SIOPEN protocol .

Results

9 patients, 4 male, median age 36months (IQR: 25-70months) received a total of 42 cycles of immunotherapy between 2009 and 2013. 2 of the 6 patients who received CH14.18/CHO antibody with aldesleukin (IL2) completed all 5 cycles of treatment. 20 of a possible 30 antibody cycles were delivered in total. 1 patient relapsed and died following cycle 2. All 4 patients receiving ketamine as second line analgesia were in the combined antibody/IL2 group. These patients had high pain scores despite multiple Nurse Controlled Analgesia boluses or clinician overrides. Pain scores fell to 0 soon after ketamine infusions were commenced despite greater than 50% decreases in opiate requirements. Ketamine was administered prophylactically in all subsequent cycles and significant pain was not experienced thereafter.

Conclusions

Ketamine is a safe and effective adjunct to morphine when administered to High Risk Neuroblastoma patients receiving immunotherapy.

Ketamine facilitates a decrease in morphine dosage and toxicity. Following ketamine commencement the median morphine dose was reduced by 50-75% when compared to the peak morphine dose prior to its introduction. The use of ketamine improves tolerability of immunotherapy allowing maximal delivery which may positively impact on High Risk Neuroblastoma survival.

EP-649

Supportive Care/Palliative Care

THE BENEFIT OF COMMUNITY ENGAGEMENT IN PUBLIC HEALTH AND PALLIATIVE CARE SERVICES FOR CHILDREN WITH CANCER IN LOW RESOURCE SETTINGS.

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Objectives

To facilitate early referral of identified at risk sick children to the local district hospital for clinical referral to Ocean Road cancer hospital in Tanzania for further diagnosis and treatment.

Methods

The Global Fund supported St. Lucia Nursing Home to identify 35,000 children and their families for community health fund, which included a payment scheme for vulnerable children to attend hospital services with special card named TIKA, TREATMENT PER CARD. The local government authorities identified children, as well as individuals in need of training to assist with identification, engaging participatory services of government hospitals for treatment. The training module offered was "Introduction to Palliative care", using tool such as HELPFUL to identify early signs of cancer in children and to create awareness in the general public of the importance of urgent referrals and early attendance to the hospitals. The HELPFUL tool was adapted from Muhimbili Cancer institute describing early diagnosis of Cancer which was translated in the local vernacular language. Between 2009 to 2013, 13,867 children were enrolled in 8 district hospitals for various medical conditions and recorded in each hospital registry.

Results

After a mean of 5yrs, 13,867 children were followed, 9740 were males 4127 females aged 1-19 yrs. Out of 13, 867 cases , 735 children needed palliative care as 3 children had hydrocephalus, 3 cerebral palsy, 9 ,mental retardation , 717, HIV/AIDS, 1 Albino. 8 children with cancer were referred to Ocean Road Cancer hospital for management of cancer 4 male were diagnosed with Burkitts lymphoma, 1 male with Acute lymphoblastic leukemia while 1 female had Burkitts lymphoma, 1 female had brain tumor.

Conclusions

The trained community members enhanced quality of care through early referrals, creating community awareness regarding cancer care, and eradication of stigma in settings where resource and infrastructures are limited.

EP-650

Supportive Care/Palliative Care

A REVIEW OF TREATMENT OUTCOMES OF KAPOSI'S SARCOMA IN CHILDREN ATTENDING HOSPICE AFRICA UGANDA AND ITS IMPLICATIONS FOR THE PROVISION OF PALLIATIVE CARE

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Objectives

To associate between the prevalence of antibodies against sarcoma-associated HIV/AIDS
To find out the response of treatments once given to patients

Methods

A chart review of 10 children with HIV/AIDS and KS at Hospice Africa Uganda was carried out. All the children had been on programme for at least a month prior to review.

Results

Of the children reviewed, 6 (60%) were male and 4 (40%) female, the age of the children ranged from 3 to 15 years with the mean age being 9.4 years. In reviewing their histology, the most common presentation was lymphadenopathic KS. 5 of the children were receiving treatment in terms of both chemotherapy and ARVs whereas 5 of the children were unable to start either treatment. Three out of the 5 children receiving chemotherapy had earlier shown signs of clinical improvement but following treatment default, they had presented with rapidly progressing symptomatology. These three children fared poorly on retreatment courses of chemotherapy with one fatality.

Conclusions

Children commonly get lymphadenopathic KS and this is more common in the older children although this review is small in scale, it does seem to suggest that combination of therapy with chemotherapy and ARVs is beneficial. On the other side, treatment default can lead to rapidly progressing symptomatology, poor response to retreatment regimens and possibilities of high fatality rates. Within the provision of palliative care, this has implications for both management of KS but also for the palliation of symptoms associated with both treatments for the disease as it progresses. Bigger studies are recommended in the pediatric population to study this in more depth

EP-651

Supportive Care/Palliative Care

PALLIATIVE CARE SERVICES IN CHILDHOOD CANCER IN BANGLADESH – CURRENT SITUATION AND CHALLENGES

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Objectives

Palliative care is a major priority in childhood cancer care strategy as it provides compassionate support both for the children and their families. The aim of the present study was to observe the current situation of palliative care services in childhood cancer in Bangladesh and its challenges.

Methods

A survey was done between July and December of 2013 in some specialized pediatric oncology units of different public and private hospitals in Dhaka city of Bangladesh, based on a semi-structured questionnaire. A total of 300 respondents including physicians, nurses, caregivers, hospital managers who deal with childhood cancer, and parents of children suffering from cancer took part in this survey. Queries addressed are access to treatment, availability of drugs, palliative care, pain management, cost of treatment, quality of care and perceived challenges.

Results

Difficulty in access to treatment (86%), out-of-pocket payment for oncology therapies (88%), palliative care (91%) were evident. 93% reported that availability of specialized palliative care services, pain management and psychological plus decision-making support were inversely related to income level. Overall, 96% of respondents indicated that palliative care is important for their patients and 79% indicated that they were competent to provide this care; however, only 64% indicated that they had enough time to deliver quality palliative care. Challenges include less availability of facility, high cost, limited and inefficient manpower, low quality of care, less communication between health professionals and parents/family members of the patient.

Conclusions

In Bangladesh, pediatric oncology is usually practiced in resource-strained oncology units of pediatric divisions in different public hospitals along with few private hospitals. However, this survey confirmed that many of the children lack access to quality palliative care. Effective palliative care requires establishment of more facilities with cancer registry, availability of drugs for therapies and pain management, manpower development, communication with patients and families in decision-making.

EP-652

Supportive Care/Palliative Care

BODY MASS INDEX FOR SCREENING BACTEREMIA AMONG PEDIATRIC CANCER PATIENTS WITH FEBRILE NEUTROPENIA

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Objectives

Currently available clinical prediction models are suboptimal for screening bacteremia among pediatric cancer patients with febrile neutropenia. The addition of better markers of bacteremia may improve screening. Given evidence supporting an association between body mass index (BMI) and infection, we explored whether BMI could improve screening of bacteremia among pediatric cancer patients with febrile neutropenia in Mexico.

Methods

We prospectively collected data for febrile neutropenia episodes among pediatric cancer patients admitted to Hospital Infantil de Mexico Federico Gomez (Mexico City) between November 2009 and September 2010 ($n=115$; 147 episodes of febrile neutropenia). Generalized estimating equation logistic regression was used to predict bacteremia for one model with 2 markers commonly used in previous studies (C-reactive protein [CRP] and hypotension), and a second model with CRP, hypotension, and BMI. We subsequently estimated the area under the receiver operating characteristic curve (AUC) and corresponding 95% confidence limits (CL) for each model, and used decision curve analysis to assess the clinical net benefit of adding BMI.

Results

Bacteremia was microbiologically confirmed in 14% (21/147) of febrile neutropenia episodes. The addition of BMI improved clinical discrimination of bacteremia (with BMI: AUC=0.77, 95% CL: 0.68, 0.85; without BMI: AUC=0.74, 95% CL: 0.64, 0.84). The model with BMI also yielded a greater clinical net benefit compared with the model without BMI between risk thresholds of 7% and 17%.

Conclusions

Our results suggest that BMI may be a promising complementary marker for screening bacteremia among pediatric cancer patients with febrile neutropenia, particularly for individuals with predicted bacteremia risks in an otherwise clinically ambiguous range. The added value of BMI for screening bacteremia should be explored in other geographic areas, and could be particularly useful in low- and middle-income countries given the feasibility of measuring BMI.

EP-653

Supportive Care/Palliative Care

DEVELOPING AN INTEGRAL PEDIATRIC PALLIATIVE CARE PROGRAM: THE ROLE OF PARENTS, VOLUNTEERS AND PERIPHERAL CLINICS IN NICARAGUA.

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Objectives

Background/Purpose: Manuel de Jesus Rivera, La Mascota, Children's Hospital is the only pediatric cancer unit in Nicaragua. Since the early 90's the pediatric oncology staff have implemented palliative care. The National Ministry of Health introduced Palliative care in 2010 as a Health strategy by recommendation of the World Health Organization (WHO). Although a National Palliative Care Protocol exists, most of the medical staff remains unaware of its presence. As in most low income country patients arrived with advance disease, for this reason this program was developed aiming to provide integral palliative care since diagnosis to alleviate suffering, and to improve the quality of life of children in the hospital setting and at home.

Methods

Methods: A survey assessing symptom control and physician report with families in the palliative care setting was performed on 45 progressive disease, oncology patients out of the 181 newly diagnosed from January-December 2010. Findings of the survey were used to establish the work plan of the multidisciplinary palliative care team.

Results

Results: In 50% of patients, disturbing symptoms were moderately controlled; half of families interviewed referred to be satisfied with the communication of bad news that prepared them for the terminal phase. Multidisciplinary meetings including parents' association, volunteers and members of the hemato-oncology staff were conducted to train in communication skills, and to review family needs assessed by home visits from members of MAPANICA. Medical, nursing staff, psychologists and social workers from five peripheral clinics were trained in palliative care. Three out of the five clinics are providing palliative care follow up to children near their homes.

Conclusions

Conclusion: Integrating efforts of medical personnel, parents and volunteers can contribute to provide good palliative care practices in countries with limited resources. Assessment of the needs of the children and their families contribute to improve the quality of care.

EP-654

Supportive Care/Palliative Care

A FEASIBLE COMPUTER-BASED EXERCISE PROGRAM FOR DAILY CLINICAL PRACTICE IN PAEDIATRIC ONCOLOGY INCREASES MOTIVATIONAL BENEFITS

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Objectives

The benefits of physical activity in cancer therapy in adults are well documented. In addition to an increase of physical performance there can be positive effects on quality of life and reduction in fatigue syndrome. However, in paediatric oncology this approach has not been sufficiently explored, well controlled exercise programmes are still missing. The purpose of our PAPO-Study (Physical Activity in the Paediatric Oncology) was to investigate the integration of a child-friendly computer-based exercise program in paediatric oncology and furthermore to research effects of the intervention on motivational benefits. Results could underline the need for exercise therapy as an useful supportive care in paediatric oncology.

Methods

Ten subjects with malignant neoplasm (ICD10 C00-C97) between 9-14 years were included. The intervention included a weekly computerized exercise program over three months. Intensity and duration were dependent on individual day´s form and contained different sport games. A brief emotional questionnaire (MoodMeter®) was answered before and after a sport unit every month. Integrability of the intervention was determined by dropout and analysis of the number of interventions.

Results

Subjects performed on average approximately 10 sport units with about 45 minutes, no dropouts. During the sport units mean heart rate was approximately 136 beats per minute. Pre-post comparison showed a significant increase in the overall motivational states (including self-confidence, social acceptance, readiness to strain and willingness to seek contact) ($p < 0.05$).

Conclusions

The PAPO-Study shows that physical activity can be well integrated into paediatric oncology clinical practice and furthermore the exercise intervention produces verifiable motivational benefits. The results indicate the importance of physical activity for the quality of survival in paediatric oncology. Exercise could restore a piece of normality to children´s lives and help in handling with psychological side effects of chemotherapy. More studies exploring this approach and supporting natural need for movement will be needed.

EP-655

Supportive Care/Palliative Care

EFFECTS OF MALNUTRITION ON TREATMENT RELATED MORBIDITY (TRM) AND SURVIVAL IN CHILDREN WITH CANCER IN NICARAGUA

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Objectives

Most children with cancer live in low- and middle-income countries where rates of malnutrition are often high. This study aimed to identify the relationship between malnutrition and treatment related morbidity (TRM), abandonment of therapy, relapse, and death of children with cancer in Nicaragua to better inform targeted nutritional interventions.

Methods

A retrospective study of patients ages 6 months-18 years newly diagnosed with ALL, AML, Wilms tumor, Hodgkin disease, or Burkitt lymphoma between January 1st 2004 and December 31st 2009 and treated at Children's Hospital Manuel de Jesus Rivera in Managua, Nicaragua. Children were included only if nutritional evaluation was recorded at diagnosis. Statistical analysis examined the relationship between nutritional status and cancer type, risk category, TRM and event-free survival (EFS) using de-identified data from the POND database.

Results

Of the 282 patients included in the study, 67% were malnourished at diagnosis. Malnutrition was highest among Wilms tumor (85.7%), Burkitt lymphoma (75%), and AML (74.3%), and lowest in Hodgkin disease (58.3%). Malnourished patients had inferior EFS (2.25 vs. 5.58 years) with significance across the distribution ($p=0.049$), and malnutrition was associated with abandonment at 2 years ($p=0.015$). Of the 244 patients included in the TRM analysis, almost all (92.2%) experienced morbidity during the first 90 days of treatment, and 84% experienced severe (grade ≥ 3) morbidity. Malnutrition was significantly associated with severe infection ($p=0.033$) but not other specific morbidity types. Malnourished patients had severe morbidity on a higher proportion of days ($p=0.023$); and were more likely to experience severe morbidity during $>50\%$ of days ($p=0.032$, OR 3.27 [95% CI 1.05-10.16]).

Conclusions

Pediatric oncology patients from Nicaragua with malnutrition at diagnosis experience increased TRM, particularly severe infection, and have inferior EFS. Standardized nutritional evaluation of all newly diagnosed patients with targeted provision of nutritional support is essential to decrease TRM and improve outcomes.

EP-656

Supportive Care/Palliative Care

IDENTIFICATION OF ISSUES INVOLVED IN THE ROAD TO DIAGNOSIS OF CHILDHOOD CANCER IN A DEVELOPING COUNTRY

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Objectives

Cure rates for children with childhood malignancies are 80–85% in high-income countries (HICs). However, cure rates are much lower in many low income countries (LICs). Globally, an estimated 250,000 children develop cancer each year, and 80% of them live in developing countries. Unfortunately, late presentation and delayed diagnosis of childhood cancers remains a problem in developing countries.

The principle objectives of this study is to assess the referral pattern and identification of issues related with road to diagnosis of childhood cancer in India

Methods

70 families with children undergoing treatment participated in the study. The parents/guardians were interviewed in a prepared questionnaire session. Study Period - Aug 2012 -Aug 2013.

Results

Of the 70 patients with hematological malignancies, with 69% boys and 31% girls, the mean age was 7.8 ± 2.2 years. The diagnostic delay, in most patients, was attributed to healthcare system delay with a median delay of 18 days (Mean – 26 days) (Range 5-39). Parental delay was significantly higher with patients from rural areas and whose parents had lower levels of education (highest being 44 days). Diagnosis and physician delay was relatively shorter for patients who visited a pediatrician than for patients whose first health contact was a general physician or other specialties. Number of different contacts and hospital admissions in the health system is significant factor causing delay in diagnosis. The median number of healthcare visits by parents is 4 and average number of days of admission is 9 days, before they were evaluated by a specialist. Geographical distance from access to tertiary healthcare is also positively associated with diagnostic delay.

Conclusions

Prompt and early diagnosis of cancer is considered the corner stone of a healthy prognosis for the patient.

EP-657

Supportive Care/Palliative Care

OUTCOME OF SURGICAL INSERTIONS OF TOTALLY IMPLANTABLE VENOUS ACCESS DEVICES: AN INSTITUTIONAL EXPERIENCE FROM PAKISTAN

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Objectives

To determine outcomes of surgical insertions of totally implantable venous access devices (TIVAD) in children in a cancer hospital in developing world.

Methods

This is retrospective study of patients with TIVAD in children requiring chemotherapy for cancer. All these procedures were performed in a specialized cancer hospital in Pakistan. Period of study was from June 2005 to June 2013. Data was retrieved from hospital information system using identified parameters and analysed using SPSS.

Results

A total of 370 patients underwent TIVAD insertion during the study period. Indication of insertion of device was chemotherapy for cancer in all patients. There were 62% males. One hundred seventeen patients were lost to follow up with TIVAD in place. All other lines were either removed at completion of treatment (42.4%) or due to infection or blockage of line. A total of 94 (25%) devices were removed prior to completion of therapy. Out of these 29 (7.8%) TIVADs were removed due to infection proven by microbiology cultures from of the line tip. Mean life of device in our patient was 278 days. In our study we could not find a correlation between neutropenia and line infection (P= 0.88). We have studied factors responsible for early removal of line and a large number of patients being lost to follow up. Role of nursing care, long distances from hospital and advanced stage of cancer in device care is also highlighted.

Conclusions

Benefits of central venous device for chemotherapy can not be denied. However it is challenging to care for these devices in a charity cancer hospital in a developing country setting. In our study we have proven that TIVADs can be safely inserted and managed for chemotherapy in children in a low resource setting with extra vigilant care while devices are in place.

EP-658

Supportive Care/Palliative Care

VANCOMYCIN RESISTANT ENTEROCOCCI COLONIZATION AND INFECTION IN CHILDREN WITH CANCER

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Objectives

Vancomycin-resistant enterococci (VRE) were previously reported to be responsible for a serious hospital-acquired infection. This study aimed to identify risk factors and resistance profile associated with VRE intestinal colonization and infection in a cohort of children with cancer.

Methods

Seventy five children were included in this case-control study. They were divided into 3 groups; group (1) includes 25 cancer outpatient having no symptoms and signs suggestive of infection and having a neutrophil count more than 500/uL, group (2) includes 25 cancer inpatient who were admitted for febrile neutropenia, group (3) includes 25 healthy, age and sex matched children as a control. Stool analysis, rectal swab and blood culture were performed for inpatient on admission, at 3 and 7 days later. Outpatients and controls were studied by rectal swab and stool analysis. The analysis of samples includes culture, isolation, identification and detection of susceptibility of isolates to antibiotics.

Results

The median duration of admission was 15 days (9-60); 20% of blood culture showed VRE isolates. VRE were detected in one inpatient on admission, compared to 5 patients after one week ($p=0.01$). Infected inpatients had significant lower neutrophil count compared to non-infected ones ($p<0.001$), meanwhile there was no significant difference in age, sex, duration of neutropenia and duration of admission between infected and non-infected inpatients ($p>0.05$), The use of vancomycin, metronidazole and imipinem antibiotics were significantly higher in those infected with VRE compared to non-infected ones ($p<0.05$). Twenty eight percent of inpatients had a positive stool culture after one week, enterococci were found in 4% of inpatient 3 days post admission, compared to 28% one week post admission.

Conclusions

We conclude that children with cancer are at high risk for VRE colonization and infections. Severity of neutropenia and excess use of vancomycin are important risk factors.

EP-659

Supportive Care/Palliative Care

INVASIVE POSITIVE PRESSURE VENTILATION IN CHILDREN WITH FEBRILE NEUTROPENIA: FIVE YEARS OF EXPERIENCE IN A PAEDIATRIC ONCOLOGY INTENSIVE CARE UNIT

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Objectives

To evaluate the feasibility and outcome of -invasive positive pressure ventilation (IPPV) in children with febrile neutropenia due to haematological malignancy.

Methods

Design: Observational retrospective cohort study.

Setting: Pediatric intensive care unit in a university hospital.

Patients: children with hematological cancer with febrile neutropenia treated by IPPV, regardless of the indication, during five consecutive 5 years (2008-2013).

Results

A total of 101 patients were included, and 61 of the 101 patients (60%) were successfully treated by IPPV. The success rate of IPPV was significantly lower (22%) in the patients with acute respiratory distress syndrome ($p < .05$) than in the other patients

Conclusions

This study demonstrates the feasibility and efficacy of IPPV in the daily practice of a pediatric oncology intensive care unit, but. This ventilatory support could not be proposed as a first-line treatment in children with acute respiratory distress.

EP-660

Supportive Care/Palliative Care

THE ROLE OF PROCALCITONIN IN DIAGNOSIS OF SEVER SEPSIS AND CLINICAL OUTCOME IN CRITICALLY ILL FEBRILE NEUTROPENIC CHILDREN WITH CANCER

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Objectives

Evaluate the significance of early diagnostic serum procalcitonin (PCT) in febrile neutropenic children and its value for ICU admission and outcome.

Methods

The study was conducted on 200 episodes of febrile neutropenic children with hematological malignancies who presented to the South Egypt Cancer Institute (SECI) diagnosed with fever and neutropenia with no prior treatment with antimicrobial therapy for the present episode. The patients were divided to two equal groups, group A and group B. Both groups were further classified into high risk group (HR) and low risk group (LR) 50 patients in each group. complete blood count, serum procalcitonin (PCT) in the first day of admission, blood culture and other cultures (sputum, urine, wounds), liver function, kidney function, random blood sugar, serum electrolytes, and chest radiograph were done.

Results

The number of unimproved patients in our study were 35. 21 patients had gram -ve isolates (60%), 9 patients had gram +ve isolates (25.7%) (5 died and 4 alive) and 5 had no growth (14.3%). From the 35 unimproved patients, 23 patients had sepsis level of PCT, 7 patients had systemic infection and 5 patient had local infection level of PCT, the difference was statistically significant, ($P < 0.001$). From 50 high risk patients treated inside ICU, 11 patients not improved, and those treated outside ICU, 17 patients not improved, the difference was statistically not significant. In the studied groups, 15 cases put on mechanical ventilation (7.5%), 13 patients had profound neutropenia (86.6%) and 10 patients had sepsis level of serum PCT level (75%), and only 9 patients improved (60%).

Conclusions

Sepsis level of serum PCT is a useful marker for suggesting severe sepsis and estimation of serum PCT support the decision to start antibiotics therapy and ICU admission.

EP-661

Supportive Care/Palliative Care

INFECTION PATTERN OF NEUTROPENIC CHILDREN IN POST-CHEMOTHERAPY PHASE OF HEMATOLOGICAL MALIGNANCIES TREATMENT

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Objectives

Neutropenia following chemotherapy regimens in hematological malignancies children is of major concern since it makes these patients vulnerable to infections.

In this study, we tried to identify the pattern of infections and their antibiotic resistance.

Methods

This retrospective multi-center study took place in 2012 and included patients with hematological malignancies who had been febrile for at least 12 hours. In order to assess the type of infection, This study took place in 3 places in Egypt.

Results

From all our positive cultures, it was seen that 80.4% of them had gram-negative bacteria with a dominance of E. coli of 22.8% over the other colonies. Also, antibiograms revealed the sensitivity of almost all the gram-negatives to amino glycosides. In contrast with most of the literature.

Conclusions

in our patients, gram-negatives are the most common cause of infection and, therefore, administering amino glycosides would be the safest antibiotic therapy to prescribe before culture results are available.

EP-662

Supportive Care/Palliative Care

THE IMPACTS OF ESTIMATION OF SERUM PCT LEVEL AS EARLY DIAGNOSTIC MARKER OF BACTEREMIA IN FEBRILE NEUTROPENIC CHILDREN

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Objectives

Many studies have succeeded in identifying a subset of children with febrile neutropenia (FN) who are at lower and higher risks of infectious complications and eventual death. but small of them that discuss the impacts of estimation of a diagnostic marker of bacteremia which is the procalcitonin (PCT).

Methods

Between January 2010 and July 2012, 200 episodes of FN in 143 children were included in a prospective study in South Egypt Cancer Institute Assiut University, Assiut, Egypt to evaluate the outcome of febrile neutropenia in children with hematological malignancies and to determine the impacts of estimation of a diagnostic marker of bacteremia which is the procalcitonin (PCT).

Results

In the present study profound neutropenia (ANC less than 100 cell/m³) was significantly observed in high risk febrile neutropenic patients and observed also in patients with high PCT level (sepsis level i.e more than 10 ng/ml and systemic infection level more than 0.5 ng/ml,) and with patients with positive blood cultures in comparison to patients with mild to moderate neutropenia (ANC more than 100 cell/m³). Profound neutropenia also was significantly observed to be associated with monocytopenia (96%) in comparison to mild and moderate neutropenia (3%). Patients with profound neutropenia were also significantly observed to be more liable to develop shock (86.6%) more than of that of higher ANC (5%). Bacteriologically documented infection were detected in 162 neutropenic episodes (81%), of them gram positive infection were detected in 111 patients (55.5%) and gram negative were detected in 52 (25.5%) and 38 (19%) patients had no growth. Gram negative infection were significantly observed in high risk febrile neutropenia episodes and associated with poor prognosis.

Conclusions

-It was concluded that sepsis level of serum PCT is a useful marker strongly suggestive of severe sepsis and bacteriologically documented infection.

-High serum level of PCT may help in stratification of patients with febrile neutropenia in high risk and low risk group.

EP-663

Supportive Care/Palliative Care

VENOUS CATHETERIZATION AS A MIRROR OF RUSSIAN PEDIATRIC ONCOLOGY

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Objectives

The treatment of any oncologic disease is impossible without a venous access. What kind of properties should it possess? It has to be safe, easy to use, implanted only once during the treatment course and have minimal risks associated with implantation and use.

Methods

From 2010 to 2013 we were monitoring the treatment of 228 children (aged 3 months to 17 years) with oncologic diseases. 110 patients underwent 605 subclavian vein catheterization, 118 patients – 118 venous port implantation.

Results

Complications and technical difficulties during catheter insertion were observed in 98.3% of cases, during venous port implantation – in 23% of cases. Complications of subclavian catheter and venous port use were observed in 97.3% and in only 11% of cases, respectively. Subclavian catheters compromised cancer treatment in 45.9% of patients, implantable venous ports – in 1.7% of patients. Each patient with a subclavian catheter underwent central venous catheterization 4 to 19 times (mean 6 times) during treatment. Catheter dwell time exceeded the recommended limit in all patients except for cases of catheter removal by patients. On multiple occasions all patients were discharged with a subclavian catheter in place.

Conclusions

Venous ports obviously match the criteria mentioned in the introduction. Subclavian catheter use resulted in cancer treatment protocol deviation in almost 50% of cases, thus leading to a poorer prognosis and significantly increasing the number of invasive procedures and instances where general anesthesia was needed.

EP-664

Supportive Care/Palliative Care

APPLICATION OF EPIDURAL IMPLANTABLE ACCESS SYSTEMS FOR PAIN MANAGEMENT IN INCURABLE PATIENTS

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Objectives

Domiciliary chronic pain syndrome management in incurable patients with disseminated cancer is of paramount importance in improving their quality of life.

Methods

In the period of 2012-2013, 5 incurable patients with various types of cancer (aged 10 to 15 years; mean age 12.7 years) underwent epidural access system implantation. Epidural space catheterization at the L₃ – L₄ interspace was performed followed by x-ray to ensure the catheter proper placement. A 1 cm skin incision and blunt dissection of the subcutaneous tissue was made at the catheter exit site. A clip for catheter fixation was then inserted into the created subcutaneous space and sewn to the adjacent tissues. The port was implanted into the soft tissues above right ribs 10-12. The catheter was threaded through the subcutaneous tunnel up to the port. The incision above the clip and port was closed in layers. Only Huber needles were used to access the port. The choice of type and dosage of the analgesic was based on the pain syndrome severity, as well as cancer localization and stage.

Results

The patients noted the improvement in quality of life, improved emotional state, and almost complete pain relief. 1 patient (20%) is currently alive, 4 (80%) died due to cancer progression. The epidural implantable access system was used for up to 5 months. No infection or occlusion of the system was observed. One patient (20%) experienced blood pressure drop due to an opioid analgesic overdose.

Conclusions

Epidural access systems facilitate pain syndrome management, improve the quality of life, and reduce the opioid dose. Besides, these routes of opioid administration are commonly associated with adverse effects. However the introduction of epidural access systems in the Russian medical setting is stalled due to the absence of qualified medical staff in hospices as well as in outpatient departments which provide in-home care for incurable patients.

EP-665

Supportive Care/Palliative Care

RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN IS SAFELY AND EFFICIENTLY USED FOR DISSEMINATED INTRAVASCULAR COAGULATION (DIC) IN CHILDHOOD ACUTE PROMYELOCYTIC LEUKEMIA (APL)

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Objectives

Patients with APL are usually complicated with DIC at onset, which occasionally lead to life-threatening hemorrhage. Efficacy of heparin, other anticoagulants, or antifibrinolytic therapy remains questionable for the management of DIC complicated with APL. In 2008, a new anticoagulant, recombinant human soluble thrombomodulin (rTM) was approved for the treatment of malignancy- or infection-associated DIC in Japan. So we retrospectively evaluated the safety and efficacy of rTM for the treatment of DIC in childhood APL.

Methods

We reviewed three patients with DIC associating underlying untreated APL, who were treated with rTM from October 2010 to February 2014. rTM were used at the recommended dosage in adults, 380 U/kg/day. Toxicity profiles were graded based on CTCAE ver.4.0. Diagnosis of DIC was based on the criteria released from Japanese Ministry of Health, Labor and Welfare. Concurrent treatment with fresh frozen plasma and platelet transfusion are administered, but no other anticoagulant therapies were performed. Endpoint for efficacy was complete resolution of bleeding disorders, such as petechiae, purpura, gingival hemorrhage and intramuscular bleeding.

Results

Three patients with APL presented bleeding disorders at the onset of APL. Median age at diagnosis was 6 years (range 5-6). Duration of rTM treatment was 13 days (range 7-19). DIC status were resolved with the median of 8 days (range 6-14) and bleeding disorders were recovered with the median of 6 days (range 5-7) after initiation of rTM. No patient experienced severe hemorrhagic complication as well as grade 3-4 non-hematologic toxicities related with rTM. Neither of dose-escalation nor dose-reduction was clinically needed.

Conclusions

Administration of rTM for the treatment of DIC related with childhood APL appears safe and probably effective to control hemorrhagic complication of DIC. A large prospective trial is necessary to confirm efficacy and safety of rTM treatment for DIC of childhood APL.

EP-666

Supportive Care/Palliative Care

PROPHYLACTIC USE OF OCTREOTIDE FOR ASPARAGINASE-INDUCED ACUTE PANCREATITIS

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Objectives

Acute pancreatitis develops in up to 18% of patients with acute lymphoblastic leukemia who are treated with asparaginase. Re-administration of asparaginase is often avoided because of the risk of pancreatitis recurrence. Octreotide is a synthetic somatostatin analogue that has been suggested for use in the treatment of acute pancreatitis, although its ability to prevent asparaginase-induced pancreatitis has not been fully evaluated. The purpose of this study is to evaluate the prophylactic use of octreotide for asparaginase-induced acute pancreatitis.

Methods

We performed a retrospective chart review in two institutions to evaluate pediatric patients who had experienced asparaginase-induced pancreatitis and underwent prophylactic octreotide treatment with re-administration of asparaginase. We also performed a literature review using PubMed with the following search terms: octreotide, pancreatitis, and asparaginase.

Results

We identified seven patients who received prophylactic octreotide in the two institutions between 2008 and 2013. Of these patients, four experienced recurrence of pancreatitis after asparaginase re-administration, and three completed treatment without recurrence. Our literature review yielded three additional cases with no recurrence. Among the six patients without recurrence, the severity of the first episode of pancreatitis was grade 2 for four patients and grade 3 for two patients. Among the four patients with recurrence, pancreatitis severity was grade 3 for three patients and grade 4 for one patient. No adverse events associated with octreotide were reported for any patient.

Conclusions

Our results suggest that the prophylactic use of octreotide prevents asparaginase-induced pancreatitis. Therefore, re-administration of asparaginase with octreotide may be warranted for patients with mild to moderate asparaginase-induced pancreatitis. For patients with severe pancreatitis, however, the re-administration of asparaginase requires caution.

EP-667

Supportive Care/Palliative Care

CATATONIA IN COURSE OF HSCT IN A 17 YEAR-OLD PATIENT WITH AML

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Objectives

Catatonic disorders in a form of inertness, negativism and mutism or hyperactivity, echolalia, echopraxia, occur rarely during treatment serious somatic diseases. Sometimes catatonia may develop as a result of psychic trauma.

Aim of the study

Presentation of catatonia case study in 17 year-old girl with AML treated with HSCT.

Methods

Analysis of medical history, available lab tests as well as interdisciplinary consultations, on basis of which catatonic disorder was diagnosed among the patient hospitalized due to several post transplant complications.

Results

The patient with AML derivative to MDS was treated according to AML BFM Interimphase protocol, and required two MUD PBSCT. During treatment complications occurred (kidney and multiorgan failure requiring hemodialysis). From 36th day after 1st MUD PBSCT on, paroxysmal disorders were observed in form of head and arm shaking, anxiety, without losing conscience, without sleepiness after the seizure as well as an episode of sight perception disorder. From 60th day after 2nd MUD PBSCT progressive loss of verbal contact, with periods of agitation, active resistance in attempt to move and feed, catalepsy. Due to this, the patient was multiple times consulted. In EEG, MRI and CT examinations organic basis of disorders was excluded. Patient's state was impossible to explain also because of balanced metabolic state. After secondary psychiatric opinion the patient was classified to pharmacological treatment and electroshock therapy was in question. Due to deteriorating somatic state of the patient and progressive symptoms of muscle flaccidity, the psychiatric treatment was canceled 3 weeks after its start.

Conclusions

1. Catatonic disorders during treatment of an aggravating somatic disease are rarely diagnosed.
2. Due to diagnostic difficulties, especially among patients with various complications, there is a risk of not diagnosing this disorder.
3. The diagnosis of catatonia among adolescents during cancer treatment requires multidimensional diagnostics prior to difficult therapeutic decisions.
4. Not undertaking the proper catatonia treatment is a threat to a patient's life.

EP-668

Supportive Care/Palliative Care

FREQUENCY OF OCCURENCE OF MENTAL DISORDERS AMONG ADOLESCENTS TREATED FOR CANCER

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Objectives

Pediatric cancer is an intense emotional and physical experience for patients and their families. Comprehensive psychiatric assessment of these children is complicated by symptoms of medical comorbidities that overlap mental health conditions.

Aim of the study. The analysis of frequency of symptoms of mental disorders among adolescents treated for cancer.

Methods

Between Jan 2010 to Feb 2014, 101 consecutive adolescents diagnosed with cancer were hospitalized at single pediatric oncology centre in Lublin, Poland. Following patients were excluded from the study: patients hospitalized once due to neutropenia, stem cells separation, and with mental retardation. 80 patients entered the study (45% girls), with average age at the diagnosis 14.9. The List of Psychiatric Symptoms (LPS) was used to assess mental functioning.

Results

26.3% of patients showed symptoms of mental disorders and were consulted with psychiatrist. Among 21 children psychiatric treatment was used. Average time of occurring symptoms from the moment of diagnosis was 6.05 months. Among girls following symptoms were more frequent: Talking about death, Frequent cry, Low self-esteem, Refusal to eat, Decrease of concentration, Mutism ($p<0.05$). Moreover, among patients with treatment complications aggravation of psychiatric symptoms was observed: Talking about death (72,4%), Irritability (74,2%), Affective instability (51,7%), Sadness, Low mood (89,7%), Anxiety (62,1%), Social withdrawal (69%), Lack of interest in environment (62,1%), Anhedonia (44,8%) – $p<0.5$. Talking about death and Anhedonia were most frequently observed in patients with osteosarcoma ($p<0.5$). The most alarming symptoms were observed in patients with leukemia. Among 20,7% of them conscience and orientation disorders occurred, which was not observed in patients with lymphoma and solid tumors.

Conclusions

1. More than one fourth of adolescents with cancer revealed different psychiatric symptoms.
2. All patients consulted with psychiatrist was treated with antidepressants.
3. LPS questionnaire is a useful clinical tool but we need further research on methods with better psychometric features.

EP-669

Supportive Care/Palliative Care

PREVALENCE OF SYMPTOMATIC AND ASYMPTOMATIC THROMBOSIS IN PEDIATRIC ONCOLOGY PATIENTS WITH TUNNELED CENTRAL VENOUS CATHETERS

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Objectives

Pediatric oncology patients are at increased risk to develop venous thrombo-embolic events (VTE); up to 500 times higher than in the general pediatric population. The incidence of VTE in pediatric cancer patients with CVCs varies widely among studies between 2.1 and 50%. Objective in this study; To determine the prevalence of (a)symptomatic venous thrombo-embolic events (VTE) in pediatric oncology patients with tunneled central venous catheters (CVC).

Methods

We systematically screened for (a)symptomatic VTE in patients included in the Aristocaths study: a randomized controlled trial investigating the prophylactic effect of 70% ethanol locks on CVC-associated bloodstream infections (CABSI). Patients were monitored clinically for symptomatic VTE and with ultrasound (US) at the end of the study. Follow-up was six months, unless patients developed one of the following events: symptomatic VTE, CABSI, CVC removal, or death.

Results

We included 305 patients (hematologic malignancy, N=148; solid tumor, N=157) for symptomatic VTE and 182/305 patients were evaluated for asymptomatic CVC-related VTE. Twenty patients developed VTE: 8/305 (2.6%) patients developed symptomatic VTE (CVC-related, N=3), 11/185 (6.0%) patients evaluated with US had asymptomatic CVC-related VTE and one patient was diagnosed with asymptomatic non CVC-related VTE. There was no significant difference in symptomatic and asymptomatic CVC-related VTE between the ethanol and heparin treatment group (p=0.25 and p=0.17 respectively).

Conclusions

This was the first systematic assessment of (a)symptomatic VTE in a large cohort pediatric oncology patients. Prevalence of symptomatic VTE was 2.6% and of asymptomatic CVC-related VTE (6.0%). These rates were lower than the prevalence reported in literature. This may in part be explained by the inclusion of patients with solid tumors, but also the reduction of CABSI by ethanol locks may have influenced the development of asymptomatic CVC-related VTE.

EP-670

Supportive Care/Palliative Care

CLINICAL EVALUATION OF ORAL MUCOSITIS IN CHILDREN WITH LYMPHOMA AND SOLID TUMORS

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Objectives

The aim of this study is to compare the demographic and clinical characteristics of children with and without oral mucositis receiving chemotherapy for cancer.

Methods

This study is conducted prospectively in a total of 106 children receiving chemotherapy for lymphomas and solid tumors, between May 2012 and May 2013. Age, sex, diagnosis, the chemotherapy regimen, the presence of daily oral care, the time between the beginning of chemotherapy and oral mucositis, duration of oral mucositis were recorded. Severity of oral mucositis assessed by WHO oral toxicity scale.

Results

The mean age of patients is 80 ± 64 months (median 64 m, range: 1 m-17 yrs) Of all patients 34% are lymphomas, 19% are CNS tumors, 10.5% are bone tumors, 36.5% are other solid tumors. 43.3% of the cases developed chemotherapy-induced oral mucositis. More than 80% of them were severe. When compared according to tumor subgroups there was significant difference between patients with and without oral mucositis. Mucositis observed in 91% of patients with non-Hodgkin lymphomas, 72% of the patients with bone sarcomas. Mucositis ratio was only 8% for Hodgkin's lymphoma cases ($p:0.02$). Of patients without oral mucositis 92.7%, applied daily oral care. This rate was 67% in patients with mucositis ($p:0.004$). The mean time between the onset of chemotherapy and development of oral mucositis is found 11.3 ± 8.1 days, and the mean duration of oral mucositis is found as 6.14 ± 8.15 days respectively. Recurrent oral mucositis is observed in 56.5% of patients.

Conclusions

Patients with non-Hodgkin lymphomas and bone tumors are major risk groups for developing oral mucositis. Daily oral care is another factor which lowers mucositis ratio in this study.

EP-671

Supportive Care/Palliative Care

EXPERIENCES AND OPINIONS ON BREAKING BAD NEWS; A SURVEY ON CHILDHOOD CANCER SURVIVORS AND THEIR PARENTS

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Objectives

The purpose of this study is that childhood cancer survivors and their parents who had diagnosed cancer in relation to awareness of how to know about the cancer diagnosis, and the preference for cancer diagnosis disclosure is intended to identify.

Methods

A survey was conducted of patients and their family members who were diagnosed with childhood cancer by pathologic diagnosis at 10 cancer institutes from July of 2011 to January of 2012. Patients with multiple original carcinogenesis of tumor and a history of psychiatric illness were excluded. All patients experienced one or more treatments of chemotherapy, radiation therapy, or surgery.

Results

We survey 283 dyads of pediatric cancer survivors aged 10 to 24 years and their parents answered multiple choice questions, respectively. Two hundred five parents (76%) knew about their child's diagnosis, cancer survivors were 99 survivors (35%) knew about their diagnosis. One hundred thirty-four parents (45.7%) wanted physicians to explain the treatment plan and prognosis, and also to inform the survivors. In contrast, 106 parents (36.2%) wanted to hear the diagnosis first and to explain their children by themselves. Fifty parents (17.1%) wanted physicians to explain directly to their children, and the other 3 parents (0.01%) didn't want to inform about the diagnosis to the children. Among the 193 survivors, 112 survivors (39.5%) was informed the cancer diagnosis by the parents, and 35 survivors (12.4%) was informed by the physician, respectively.

Conclusions

Health care providers should effectively convey information that is tailored to the emotional needs of patients and their families who have experienced a never before experience of being diagnosed with cancer. The role of being able to motivate their active participation for treatment is important.

EP-672

Supportive Care/Palliative Care

IN-HOSPITAL SUPERVISED EXERCISE TRAINING PROGRAM TO ENCOURAGE CHILDREN AND ADOLESCENTS WITH CANCER TO PRACTICE SPORTS

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Objectives

Evidence for the positive effects of physical activity in children and adolescents with cancer is growing. In the past, the dogma that cancer diagnosis precludes participation in exercise training prevailed. Primary objective of our hospital & outdoor exercise interventions was to explore an effective strategy in promoting physical activity in cancer patients during and soon after treatment.

Methods

Characteristics of the exercise training program developed at our Institution: 1) 30 m² gym installed on the floor (treadmill, exercise bike, other training equipment); 2) supervision by the treating clinical care team and three sports professionals, providing individual training programs (phases: cardiovascular training, toning exercises; cool-down/relaxation exercises; muscle stretching); 4) connection with the institutional physiotherapy service; 5) joint with structured outdoor adventure activities (sailing).

Results

During pilot 10-month period, 100 (in- and out-)patients participated. Giving the high demand, we moved from once to twice weekly 3-hour attendance. The delicate relation between individual wishes and capabilities (possibly altered by cancer) sometimes called for parallel psychosocial intervention, or for adaptive sports to meet needs of patients with disabilities. Reported benefits of active sport engagement included a recovered self-estimation of a lively and working body, new opportunities to relate comfortably and without frustration with peers. Limitation stays in difficulties to measure physical and mental conditioning through exercise-oncology studies.

Conclusions

Hospital exercise training demonstrated to be feasible during treatment and improved accessibility to play and exercise spaces for our patients. Despite physical activity was linked to physical and psychosocial integrity, on a patient-by-patient base, harmonized recommendations that guide participation to sport activities of patients during and after treatments might help. Treating oncologists (who have an in-depth knowledge of the individual's medical history) can provide exercise guidance to move safely, which nearly every patient can do.

Aknowledgments: Associazione Bianca Garavaglia.

EP-673

Supportive Care/Palliative Care

ANALYSIS OF RISK FACTORS BACTERAEMIA AMONG CHILDREN WITH CANCER AND EARLY DIAGNOSTIC

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Objectives

The most common complication during cancer therapy occurs bacterial infection. The key factor in risk prediction for bacterial infection is to consistently and reliably identify patients "at risk." Of the several risk prediction models proposed, few apply to pediatric patients.

Methods

This study was retrospective analytic study. There were enrolled according to the criteria patients with cancer who received treatment during January 2009 and February 2014 in Clinic of Children Hematology and Oncology in Bratislava, Slovakia. We evaluated patients with hematological and non-hematological malignancies as well. In the study group were 342 patients with positive hemoculture.

Results

Patients with coagulase-negative staphylococci (CoNS) were responsible for 61% of positive hemocultures with 33% of clinical presentation. Median of the patients was 7.0 years. The non-CoNS were 132 bacteraemias. 73% of the patients with non-CoNS developed Hospital-acquired Infection (HAI) and 27% developed infection up to 48 hrs after admission to the hospital and were enrolled in group of community-acquired infection (CAI). CRP and procalcitonin were not statistically significant predictors of bacterial inflammation and markers for differential diagnosis. More than 38% of those who had central venose catheter from group of HAI, have confirmed multidrug resistant strain in hemoculture. 73% of the patients received during prior admission an antimicrobial therapy. The most frequent isolates were coagulase-positive staphylococci (18%); *Corynebacterium* spp. (14%); *Ps. aeruginosa* (12%); *Enterobacter* spp. (12%); *Klebsiella* spp. (9%), *E. coli* (6%), *Enterococci* (7%). In our study only 2 patients with laboratory confirmed bloodstream infection died.

Conclusions

In our study was observed that the frequent use of antimicrobial drugs prior blood culture may have crucial impact on detection of the micro-organism, antibiotic testing and susceptibility to commonly used antibiotics.

EP-674

Supportive Care/Palliative Care

LACK OF TREATMENT-RELATED MORTALITY DEFINITIONS IN STUDIES OF CHILDREN, ADOLESCENTS AND YOUNG ADULTS WITH LYMPHOMAS, SOLID TUMORS AND BRAIN TUMORS: A SYSTEMATIC REVIEW

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Objectives

There is a lack of standardized definition for treatment-related mortality (TRM), which represents an important endpoint in cancer. Our objectives were (1) to determine the frequency with which TRM has been defined; and (2) to describe the utilized TRM definitions among studies of lymphomas, solid tumors and brain tumors.

Methods

We conducted a systematic review of studies enrolling children, adolescents and young adults with lymphomas, solid tumors and brain tumors in which an anti-cancer intervention was randomized, or all study designs in which TRM was a primary or secondary outcome. We searched Ovid MEDLINE, EMBASE and Evidence-Based Medicine Reviews from 1980 to June 2013. Two reviewers evaluated study eligibility and abstracted data.

Results

A total of 19,129 titles and abstracts were reviewed; 131 full articles were retrieved for detailed evaluation; 62 randomized therapeutic studies and 5 studies in which TRM was a primary or secondary outcome (TRM studies) satisfied eligibility criteria to be included in the systematic review. None of the studies (0/67) provided a definition for TRM.

12 therapeutic and 3 TRM studies reported their TRM rate. Among therapeutic studies, TRM rates ranged from 0.2% to 7.0% (mean 2.7%) in these patient populations that consisted of neuroblastoma (n=996), rhabdomyosarcoma (n=2,073), medulloblastoma (n=364), soft tissue sarcomas (n=1,115), Hodgkin lymphoma (n=1,572), and non-Hodgkin lymphoma (n=280). Hodgkin lymphoma patients had the lowest TRM rate while the highest TRM rate was reported among neuroblastoma patients. For TRM studies, reported TRM rates were much higher, ranging from 8.0% to 27.1% (mean 15.6%).

Conclusions

We were unable to identify any TRM definitions used in studies of children, adolescents and young adults with lymphomas, solid tumors and brain tumors. Given that a proportion of this patient population may receive intensive treatment, there is an urgent need for consensus-based definitions of TRM for use across clinical trials.

EP-675

Supportive Care/Palliative Care

A PROSPECTIVE PILOT STUDY TO DESCRIBE THE OUT-OF-POCKET EXPENSES INCURRED BY FAMILIES OF CHILDREN NEWLY DIAGNOSED WITH CANCER IN GUATEMALA

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Objectives

In resource poor countries, parents may abandon their child's cancer treatment to ensure the financial sustainability of the family; however, the precise magnitude of their out-of-pocket (i.e. direct) costs remains unknown in Guatemala. The study objectives were to identify the costs incurred by families of children diagnosed with cancer during (a) the period prior to the diagnosis and (b) the three-month period following the diagnosis.

Methods

After ethical approval, a prospective cost of illness design with 13 repeated assessments over a 3-month time frame was piloted from a family household perspective. Parents met 13 times with a member of the research team to record their costs and resource utilization with a validated cost diary. Descriptive statistics were used to express costs in 2013 Guatemalan quetzal (GTQ; 1USD = 7.8GTQ). Costs were analyzed according to a uniformly determined set of 17 cost categories. Total cost was computed as the sum of all cost categories.

Results

Eleven families with a mean monthly income QTQ3,333 (SD 3,245) reported utilizing 9 cost categories and 28 cost items/resources. Ten families were eligible for a hospital subsidy following the child's cancer diagnosis. Collectively, families incurred a total sum of GTQ11,808 in direct costs. Nearly 90% of costs were attributed to food, travel, and communication. Families received over GTQ14,214 in donations from the cancer community and their support network. Over 75% of donations were payments for the child's treatment (e.g. use of health services prior to diagnosis, medications, and complementary medicine). Nearly 25% of donations were monetary given by the families' support networks.

Conclusions

The reliance on family's scarce resources and philanthropy subsidies/ donations are essential for the diagnosis and treatment of children with cancer in Guatemala. A subsequent grant submission will ensue for a larger study to correlate family costs with abandonment and therapy outcomes.

EP-676

Supportive Care/Palliative Care

DEVELOPMENT OF CLINICAL PRACTICE GUIDELINES REGARDING SUPPORTIVE CARE IN CHILDHOOD CANCER IN THE NETHERLANDS - PRIORITIZATION OF TOPICS USING A DELPHI QUESTIONNAIRE

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Objectives

Currently, nationwide Dutch guidelines for supportive care for children with cancer are over 10 years old and not evidence based. There is growing support and need for clinical practice guidelines (CPGs), which bridge the gap between research and clinical practice. However development of CPGs is time consuming, therefore it is important to prioritise subjects for which the clinical importance is the greatest. Thus, our objective is to prioritise childhood cancer supportive care topics for development of CPGs.

Methods

A core research group formed a list of relevant topics regarding supportive care in childhood cancer. These topics were incorporated in a modified two-round Delphi questionnaire to determine the order of development of CPGs for all topics in supportive care in childhood cancer (see figure 1). The Delphi method is a well-recognized process to achieve consensus among a group of experts (pediatric oncologists, pediatric oncology nurses and pediatricians involved in care for childhood cancer patients), based on anonymity, iteration, controlled feedback and statistical group response.

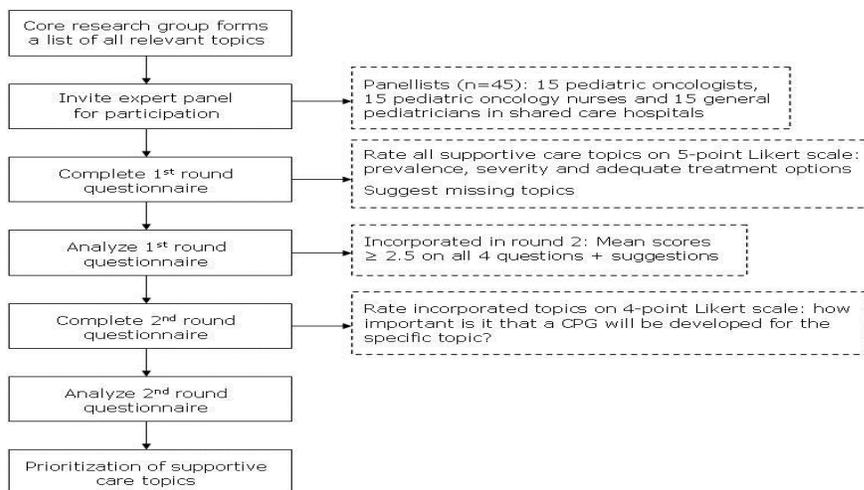


Figure 1. Outline of the Delphi method used in the questionnaire

Results

In both rounds, 36 panellists (80%) responded. The five topics with the highest score in round 2 were infection, sepsis, febrile neutropenia, pain and nausea/vomiting.

Conclusions

We successfully used a Delphi questionnaire to prioritize childhood cancer supportive care topics for the development of clinical practice guidelines. This is a first step towards uniform and evidence based Dutch guidelines in supportive care in childhood cancer.

EP-677

Supportive Care/Palliative Care

WHY DO PARENTS NOT TALK WITH THEIR TERMINALLY ILL CHILD WITH CANCER ABOUT DEATH?

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Objectives

Limited data is available about parents' reasons for not talking with their terminally ill child about death. This study explores parents' reasons for not having a conversation with their terminally ill child with cancer.

Methods

Parents were asked whether they had talked with their terminally ill child with cancer about death, and how they felt about this decision. Parents who did not talk were subsequently asked to indicate their reasons for not talking and parents who had talked were asked to indicate how the conversation took place. Descriptive and qualitative analyses were performed identifying emerging themes.

Results

Fifty-five parents (67%) did not talk with their child about death. The following themes were identified for not talking about death: parent-related reasons (e.g. unable to cope, not feeling confident, fearing consequences, preventing painful moments), child-related reasons (e.g. child does not want to talk, never started conversation, avoided conversation) and parental perception of child (e.g. already aware, too young). Parents who talked about death used stories or indicated simply telling the child that they would not be cured. Although the majority of parents felt good about their decision, ten parents did not, predominantly based on the subsequent negative emotional response of their child.

Conclusions

The majority of parents did not talk with their terminally ill child about death. Parental confidence and uncertainty about consequences played an important part in reasons for not talking to the child. In addition, children may avoid or not want to talk, or already be aware of their impending death. Our findings highlight the complexity of engaging in these conversations and the role for clinicians in supporting parents who will find these conversations difficult.

EP-678

Supportive Care/Palliative Care

EUTHANASIA IN MINORS: A PROBLEM OF THE PATIENT, THE PEDIATRICIAN OR THE COMMUNITY?

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Objectives

The discussion on euthanasia in minors flared up in Belgium by the call of 16 pediatricians ("Euthanasia for children. Now!) to develop a legal framework for practicing euthanasia in minors. We posed the question to what extent in neighboring countries a need is perceived by pediatric oncologists.

Methods

Three questions with four pre-defined answers were sent to 253 colleagues from pre-existing email lists. We asked only about the situation in adolescents. We asked not to express a personal opinion but only afterwards.

Results

Fifty-four colleagues from 19 countries answered. A legal framework for euthanasia in minors exists only in the Netherlands. There is no legal framework in Australia, Austria, Czech Republic, Denmark, France, Hungary, Ireland, Israel, Italy, Norway, Portugal, Slovenia, Spain, Sweden and the UK. Euthanasia is regulated by State in the US. For Germany, one pediatrician believed that discussions were started to develop a legal framework. The other German colleagues replied that there was no legal framework, and no initiative to develop one. In Austria, Czech Republic, Denmark, Hungary, Ireland, Israel, Italy, Norway, Portugal, Slovenia and Sweden pediatricians estimated that there is no question to develop a legal framework in the general population or in their own professional category. Only a minority of the general population and of the pediatricians was estimated for asking for a legal framework in Australia, France, Germany, Spain, UK and US. No conclusive answers came from Canada. Forty two pediatricians took the chance to write a personal comment.

Conclusions

In most countries there is no legal framework for euthanasia in minors, and there is no need for it felt in the general population and the pediatric community. Nevertheless, a debate in SIOOP might be needed. We will sum up some objective arguments that can be of help in discussions on this issue.

EP-679

Supportive Care/Palliative Care

TIME-TREND, OVER 10 YEARS, OF INCREASING MULTI-DRUG RESISTANT SUPERBUGS IN PEDIATRIC ONCOLOGY UNIT OF A TERTIARY CANCER CENTRE: CORRELATION WITH ANTIBIOTIC UTILIZATION AND COMMUNITY COLONIZATION

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Objectives

Multi drug resistant organisms (MDRO) colonization and infections are of serious concern due to the associated high morbidity and mortality. This study was undertaken to determine the temporal trends in prevalence of MDRO in pediatric oncology unit at a tertiary cancer centre, over last decade and correlate these with antibiotic utilization and community colonization.

Methods

We analyzed the prevalence of extended spectrum beta-lactamase positive (ESBL), carbapenem resistant (CRE) and Vancomycin resistant enterococci (VRE) in blood cultures from 2005 to 2013 by audit of microbiology records of alternate years.

Results

In 2005, 1587 blood cultures were sent, of which 199 (12.54%) were positive and incidence of ESBL and VRE was 32 (16.08%) and 2 (0.50%) respectively. CRE were 27 (13.57%). In 2007, 2011 blood cultures were sent, of which 179 (8.9%) were positive and prevalence of ESBL and CRE was 29 (16.76%) and 12 (6.7%) respectively. In 2009, 154 (7.38%) out of 2087 cultures were positive, 17 (11.04%) and 27 (17.53%) were CRE and ESBL respectively. In 2011, of 1600 blood cultures, 112 (7%) were positive. Of these, 21 (18.75%) were ESBL, 32 (28.57%) were CRE, and 50 (44.64%) were pan sensitive bacteria. In 2013, a total of 1597 blood cultures were sent, of these total 107 (6.7%) showed positivity. Of these, 20 (18.69%) were ESBLs, 31 (28.97%) were CRE, and 56 (52.73%) were pan sensitive organisms. Correlation with antibiotic utilization revealed increasing use of carbapenems as well as colistin. 923 patients on admission in pediatric oncology unit were assessed for stool culture by rectal swabs. 644 (69.77%) showed bacterial growth, of which 265 (41.15%) were ESBL, 202 (31.37%) MDRO and 72 (11.18%) were VRE. Rectal swabs from newly registered outpatients (62) showed 8 (12.9%) MDRO and 30 (53.22%) ESBL positivity.

Conclusions

This study shows the increasing trend of multidrug resistance in a tertiary cancer care centre in a developing country. Colonization of MDRO in the community is a dangerous trend and would require stringent policy decisions to curb this epidemic.

EP-680

Supportive Care/Palliative Care

A RETROSPECTIVE CLINICAL ANALYSIS OF NEUTROPENIC ENTEROCOLITIS IN CHILDHOOD ACUTE LEUKEMIA

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Objectives

To summarize the clinical characteristics of neutropenic enterocolitis(NE) secondary to childhood acute leukemia(AL)

Methods

10 pediatric AL patients diagnosed with NE from January 2007 to December 2013 were retrospectively analyzed the clinical features,management experience and outcome.

Results

Among the 10 patients, 8 were diagnosed as acute lymphoblastic leukemia (ALL) and 2 with acute myeloid leukemia(AML). The average age at diagnosed was 3.4 years old. All 10 patients presented enterocolitical symptoms as fever,abdominal distension with rigidity and neutropenia. Abdominal imaging revealed different severity of intestinal cavity expansion or bowel wall thickening. Treatment procedures were including fasting and total peripheral nutrition maintained till the recovery of neutrophil count and intestinal peristalsis function; given powerful broad-spectrum antibiotics (G+/G-, anti fungal when necessary); transfusion of blood component(IVIg, concentrated red cells, apheresis platelets, and apheresis granulocyte). The average recovery time was 13.2 days. 3 patients had been suffered again from NE immediately after neutrophil count recovery and liquid diet restored as abdominal distension with pain and digestive tract hemorrhage. Among them, 1 patient received surgical operation for intestinal necrosis. *Enterococcus faecium* infection had been confirmed on the culture of this patient's blood and fecal samples. NE symptoms repeated in 4 patients were identified in the follow-up chemotherapy, and 3 patients died from pulmonary fungal infection,sepsis, or septic shock, another one patient had been reduced 1/3 formal chemotherapy dosage. A total of seven patients survived.

Conclusions

NE is a rare but life-threatening complication of chemotherapy in childhood AL patients. Clinical symptoms and abdominal imaging would be helpful to the early diagnosis. Immediate powerful support treatment is necessary when NE diagnosed. Subsequent chemotherapy could be interfered negatively by NE, which might be recurrent and need be taken a high premium by clinics.

EP-681

Supportive Care/Palliative Care

AGGRESSIVENESS OF END OF LIFE CARE FOR NEUROBLASTOMA PATIENTS

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Objectives

Patterns of end of life care are poorly understood in pediatric cancer population. This study aimed to elucidate aggressiveness of end of life care for children with neuroblastoma that is the most common life-threatening solid tumor in Japan.

Methods

Patients who were diagnosed as neuroblastoma in our institute and died between September 1, 1995 and December 31, 2013 were enrolled. Medical records were retrospectively reviewed. Chemotherapy, life-sustaining treatment such as mechanical ventilations or CPR in the last month of life, the period between the last chemotherapy and death and place of death were investigated as indicators for aggressiveness of end of life care.

Results

Fifteen patients (6 boys and 9 girls) were identified. The median age at death was 3.5 years (range, 3 months-12.2 years). Thirteen patients (87%) died of neuroblastoma, and 2 (13%) died of treatment-related toxicity. Chemotherapy was performed for 10 patients (67%) in the last month of life and 5 patients (33%) continued to receive chemotherapy in the last week of life. Our hospital was the sole place of death. Three patients (20%) received life-sustaining treatments due to treatment-related toxicity and died in ICU. Fourteen patients (93%) did not receive cardiac or cardiopulmonary resuscitation. The median period between the last chemotherapy and death was 14 days (range, 0-498).

Conclusions

The proportion of terminally ill cancer patients who received chemotherapy was higher than the previous reports. Meanwhile, cardiac or cardiopulmonary resuscitation was not performed in the majority. Further large research is required to determine aggressiveness of end of life care for pediatric cancer patients in Japan.

EP-682

Supportive Care/Palliative Care

PROSPECTIVE AND RANDOMIZED STUDY OF FIXED VS FLEXIBLE SCHEDULE OF POST CHEMOTHERAPY ADMINISTRATION OF GRANULOCYTE COLONY-STIMULATING FACTOR (G-CSF): PRELIMINARY DATA.

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Objectives

G-CSF is commonly used after chemotherapy to shorten neutropenic periods. Administration of G-CSF contributes to the cost of treatment and may cause some side effects. Based on our studies of kinetics of post chemotherapy bone marrow recovery we hypothesized that doses of G-CSF given during the first few days after chemotherapy do not significantly contribute to the final neutrophil recovery due to the absence of myeloid progenitors in the bone marrow.

Methods

To evaluate this in the clinical setting, we have initiated a prospective randomized clinical study of two different prophylactic G-CSF schedules in children with solid tumors: a "fixed" schedule where G-CSF is started 24 hours after the completion of chemotherapy and a "flexible" schedule where G-CSF is not started until the absolute neutrophil count (ANC) falls below 1,000/mm³. We used a crossover study design with each patient receiving 2 cycles of the same chemotherapy followed by the fixed or the flexible schedule of G-CSF chosen in random order.

Results

To date, 6 patients have been enrolled since October 2013 and the study continues to enroll patients. There was no significant difference in the time to neutrophil recovery (number of days from the start of chemotherapy to ANC > 1,000/mm³ post nadir) between the two schedules of G-CSF: 14.6 ± 1.1 days with the fixed vs. 14.6 ± 0.6 days using the flexible schedule. The patients received 4.7 less G-CSF injections (5.3 ± 2.1 vs. 10.0 ± 2.0 daily injections) after cycles followed by the flexible schedule which would translate into an average of \$1,700 direct savings from reduced injections of G-CSF per chemotherapy cycle.

Conclusions

Our preliminary data show that the flexible schedule of post chemotherapy G-CSF administration resulted in a significant reduction in the treatment cost without compromising of G-CSF effects on neutrophil recovery after myelotoxic chemotherapy in children with solid tumors.

EP-683

Supportive Care/Palliative Care

THE NEED FOR PEDIATRIC PALLIATIVE CARE IMPLEMENTATION IN MEXICO: A CASE REPORT

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Objectives

To analyze the missed opportunities of a case report in which Pediatric Palliative Care (PPC) could have been integrated in order to create a framework for Mexican pediatric oncologists to recognize the need for implementing palliative care in their patients.

Methods

A case of high-risk medulloblastoma of the cerebellum occurring in a 14-year-old patient is presented. He was first diagnosed and treated at 13 years of age with partial surgical resection of the tumor and ventriculoperitoneal shunt placement. During the next 6 months he concluded 6 cycles of chemotherapy. He developed worsening brain edema and in his last hospitalization he was admitted with progressive intracranial hypertension. The patient himself asked to continue with chemotherapy and begged the team to not give up on him. He received chemotherapy until the last day of his life with few or almost none palliative care for him or his family.

Results

Within the patient's evolution (from diagnosis until his death) 5 opportunities were identified in which PPC could have been initiated.

Conclusions

More than 85% pediatric cancer cases occur in developing countries. In low resource settings mortality is approximately 80%, or even 90% in the world's poorest countries. In Mexico, being a developing country, it is estimated that childhood cancer has an incidence of more than 3,800 per year, and a mortality rate of approximately 90,000 per year, meaning every 4 hours a Mexican child dies because of cancer. PPC reduces the morbidity and improves the quality of life at any stage of the disease. Clearly all this patients could benefit from PPC, however, this situation will not improve until we get Mexican pediatric oncologists to recognize this need and integrate PPC into their medical practice.

Acknowledgments: Sebastian Rodríguez Llamazares for his invaluable help.

EP-684

Surgery (IPSO)

GANGLIONEUROMA : BECOMING SYMPTOMATIC TUMOR?

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Objectives

Ganglioneuromas are commonly defined as a benign silent tumor more frequent in adults than children. Very often misdiagnosed before surgery because radiological appearance could be non-specific. However surgical approach still the mean treatment when becoming symptomatic. But is really a silent tumor or is becoming symptomatic?

Methods

We review all the pathologic reports about neuroblastic tumors in two pediatric departments. We focus on ganglioneuroma diagnosis after complete surgery in the last 10 years. Also reviewing the literature in adults to compare with children.

Results

We describe 4 cases of ganglioneuroma in this institutions: 1 neck and thorax and 3 abdominal (1 retroperitoneal, 1 adrenal and 1 liver hilum). This cases were hormonally silents. Ultrasound was taken because of persistent abdominal pain in 3. A neck mass was the iceberg of the bilateral thoracic tumor. The one located in the liver hilum has spontaneous eye movements although had been operated for optokinetic nistagmus as a child. Misdiagnosis before surgery in 3 (ganglioneuroblastoma, suprarrenal adenoma, and cyst duplication). No complications after open surgery in those cases.

Conclusions

A few cases reported about symptomatic ganglioneuroma in children if we compare with adults, where pain is the main indication for surgery in the early 40s.

Difficult to obtain the diagnosis previously at surgery because the imaging characteristics are very similar to other tumors.

Maybe we have to became more active doing surgery in this 'benign tumor' before the symptoms appear in adults . Long follow up and a common registrar also for benign lesions might be considered.

EP-685

Surgery (IPSO)

COMBINED APPROACH FOR THE MANAGEMENT OF REFRACTORY CHYLOUS ASCITES IN PEDIATRIC ONCOLOGY PATIENTS

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Introduction: Postoperative chylous leak is a rare result of lymphatic channels disruption or obstruction following surgical resection of retroperitoneal tumors that represent a difficult management problem due to the serious mechanical, nutritional and immunological consequences of the constant loss of protein and lymphocytes. The management of chylous leak is either conservative or interventional (surgical and/or radiological).

Methods: We are reporting two pediatric patients with refractory chylous ascites following retroperitoneal tumor resection (neuroblastoma and nephroblastoma). They were managed successfully using the combined approach (Intra operative lymph-angiogram and laparoscopy) . The intervention was dictated by the failure of conservative treatment (Total parental nutrition, Octerotide, and low fat diet), and/or timing of scheduled chemotherapy cycle. Our combined approach was utilized to identify and treat the source of lymphatic leak simultaneously. The Modalities of intervention included diagnostic laparoscopy, Intraoperative ultrasound localization of the inguinal lymph nodes followed by lymph angiogram under fluoroscopic guidance. The identified sites of the lymphatic leak were handled by Mini-laparotomy, suture ligation, omental patch and hemostatic agents. The Patients continued their chemotherapy regimen within one week of the intervention.

Results: No Recurrences were observed on six months of follow up.

Conclusion: The usual conservative management of lymphatic leak for long time should be discouraged from being an option in oncologic patients, as it may delay the completion of the chemotherapeutic regimen, which might theoretically increase the risk of recurrence. With the Available advanced resources, an early intervention for the lymphatic leak is recommended in these patients.

EP-686

Surgery (IPSO)

CONGENITAL JUVENILE GRANULOSA CELL TUMOR OF THE TESTIS: CASE REPORT AND REVIEW OF THE LITERATURE

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Objectives

Even though represents the most common stromal cord tumor of the infant testis, juvenile granulosa cell tumor (JGCT) is a very rarely diagnosed benign tumor, accounting for 1.2% of all prepubertal testicular tumors.

Methods

We retrospectively reviewed the data of one patient diagnosed in the first day of life.

Results

Case report: A full-term healthy neonate was diagnosed with a painless left escrotal mass. During evaluation it was identified to have about two times the volume of the contralateral testis, presenting a firm consistency, not so hard as the consistency of a prenatal testicular torsion. Doppler ultrasound detected a multicystic left testicular mass, with normal blood flow, but failed in detecting normal-appearing testis. Human chorionic gonadotropin (b-HCG) and serum alpha-fetoprotein (AFP) were normal. Inguinal approach was performed, exposing the testis and spermatic cord. After cord clamping, a section of the lesion was sent to frozen biopsy and excluded yolk sac tumor, however the impossibility of detecting normal testis tissue indicated orchiectomy with high ligation of the spermatic cord. Histological evaluation demonstrated gray testicular parenchima with multicystic aspect fullfilled with yellow fluid. Postoperative evolution was uneventfull. Six months after surgery the patient is asymptomatic and being followed by pediatric oncology.

Conclusions

Discussion: The usual clinical presentation of JGCT is a painless scrotal mass, detected during clinical routine examination or perceived by the parents. Prenatal diagnosis has been described. Radiological imaging demonstrates a multicystic circumscribed tumor. Tumoral markers levels are normal and the standart treatment is the inguinal orchiectomy. As the tumor presents as a benign tumor, testicular sparing surgery can be performed in cases normal parenchima is identified. Adjuvant therapy is not indicated.

EP-687

Surgery (IPSO)

URETEROSIGMOIDOSTOMY IN A CASE OF BLADDER RHABDOMYOSARCOMA WITH TOTAL CYSTECTOMY

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Objectives

Urinary diversion with Mitrafanoff and neo-bladder formation is the most utilized option for bladder rhabdomyosarcoma in a child who has undergone total cystectomy. Presenting here a child who underwent Ureterosigmoidostomy - a continent urinary diversion 5 years following total cystectomy and subtotal urethrectomy.

Methods

Retrospective case study wherein all details of the patient were retrieved from the records

Results

2 day old male neonate presented with poor stream of urine and palpable bladder, was suspected to have posterior urethral valves, underwent cystoscopy and fulguration of valves. 2 months later, child was brought in severe urosepsis with a fungating mass from the hypocondrium, which was found to originate from the urinary bladder. Total cystectomy with bilateral end ureterostomies were performed, and post-operative chemotherapy was given after confirmation of diagnosis of rhabdomyosarcoma. Tumor recurred in the bladder neck/prostatic urethra and later in distal urethra for which subtotal urethrectomy was done. 5 years later with no evidence of recurrence, the child underwent ureterosigmoidostomy as a continent urinary diversion. The child is able to pass urine every 2-3 hours per rectally and is also continent for stools. No evidence of renal upper tract damage has been found.

Conclusions

With the myriad complications of bladder augmentation/neo-bladder creation from ileal or sigmoid loop and life-long catheterization of the neo-bladder via the Mittraffanoff, ureterosigmoidostomy seems to be better option wherein the child can voluntarily void urine per rectally and remains dry without the need to repeatedly catheterize. In the event of late recurrence of the tumor, redo-ureterostomies would be much more easily carried out till loco-regional control of the tumor is done.

EP-688

Surgery (IPSO)

IMPORTANCE OF SURGICAL TREATMENT AND PROGNOSTIC FACTORS IN NEUROBLASTOMA STAGE 4S, ACCORDING TO OUR CASE

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Objectives

Stage 4S neuroblastoma is said to have very favourable outcome than other patients with metastatic neuroblastoma, often demonstrating spontaneous maturation and regression, and hardly requires any treatment. Is it true really? Stage 4S neuroblastoma is a benign, or a deadly disease? How to treat this „benign" entity? Do we need to do any surgical treatment or to administer chemotherapy? Is there any prognostic factor?

Methods

Case report: A 2 days old, mature newborn has been admitted to our clinic with bilateral advanced tumor in the adrenal regions. She had multiplex liver metastases, extreme hepatomegaly, substantially distended abdomen, and dyspnoea. After the investigation and biopsy, the laesion was proved to be a neuroblastoma, and it was staged to 4S. According to our case we reviewed the literature.

Results

Under 1 month of age, neuroblastoma stage 4S has very bad prognosis, many cases end with death. Most of the deaths are caused by the rapidly worsening abdominal status. Infants must be administered chemotherapy and operated urgently at the first signs of abdominal compartment syndrome.

Conclusions

Stage 4S neuroblastoma's estimated survival rates of 75% to 90% have been reported. These tumors are usually associated with favourable biologic features, but infants under 1 month of age have very bad prognosis, many cases end with death. It seems that under 1 month of age, the more intense, and earlier the treatment is, the better the results. Studies may identify markers to more accurately predict the clinical outcome of various subtypes of neuroblastoma stage 4S. Moreover, surgeons have an important role to prevent abdominal compartment syndrome, and raise survival rates.

EP-689

Surgery (IPSO)

CONSERVATIVE SURGERY WITH COMBINED HIGH DOSE RATE BRACHYTHERAPY FOR PATIENTS WITH BLADDER-PROSTATE RHABDOMYOSARCOMA: TECHNICAL ISSUES, CHALLENGES AND INITIAL EXPERIENCE

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Objectives

Although treatment of patients suffering from bladder-prostate-rhabdomyosarcoma (BPRMS) has been improved in the past regarding the outcome, the bladder preservation rates in the large multi center trials are still too low. In the past, conservative surgery with combined low dose rate brachytherapy has been advocated as a novel treatment option. Nevertheless, low dose rate brachytherapy is not available in many centers. Therefore, the aim of the study was to establish a new treatment modality combining high dose rate brachytherapy and conservative surgery.

Methods

The principle of the study was to perform an organ preserving microscopical complete (R_0) or incomplete (R_1) tumor resection with intraoperative placement of 4 to 6 brachytherapy tubes around the urethra. Only patients with tumor extension below the bladder neck were treated. After surgery, high dose rate brachytherapy (3 Gy / fraction) was carried out for 6 days (2 fraction / d). After that, brachytherapy tubes were removed. A total number of 4 patients were treated up to now.

Results

In all patients bladder preservation was feasible. Conservative surgery and brachytherapy was well tolerated without significant side effects. All patients are in the first complete remission. One patient developed a neurogenic bladder and required creation of a Mitrofanoff stoma.

Conclusions

Combined conservative surgery and high dose rate brachytherapy is a treatment option for selected patients with BPRMS. The paper highlights the essential technical challenges and clearly shows limitations of this treatment approach.

EP-690

Surgery (IPSO)

MANAGEMENT OF WILMS' TUMOUR WITH INFERIOR VENA CAVA EXTENSION: A SINGLE-INSTITUTION EXPERIENCE

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Objectives

Current treatment strategies for Wilms' tumour with inferior vena cava(IVC) extension include pre-operative chemotherapy, followed by radical nephrectomy and tumour thrombectomy. Literatures report regression of tumour thrombus with pre-operative chemotherapy facilitating surgery. However there were also reports regarding dense adherence of a tumour thrombus to vessel wall resulting from pre-operative chemotherapy. This study aims to examine management of Wilms' tumour with IVC extension in our institution.

Methods

Patients diagnosed with Wilms' tumour with IVC extension between 1997-2013 were included. Data were collected from patient notes regarding presentation, operative details, and outcome.

Results

Twenty-three cases of Wilms' tumour were treated in our institution during the study period. Two patients(8.6%) had tumour extension into infrahepatic vena cava. One patient(4.3%) had thrombus extending from iliac veins to right atrium, and extending into the left renal and right hepatic vein leading to Budd-Chiari syndrome. All 3 patients received pre-operative chemotherapy based on NWTS-5 regime(Duration: 4-9 weeks) followed by radical nephrectomy and tumour thrombectomy. Pre-operative chemotherapy had reduced thrombus extent in 2 cases with infrahepatic vena cava extension and complete thrombectomy achieved. However, for the patient with intra-trial extension the tumor thrombus was only cleared from the atrium with pre-operative chemotherapy. The thrombus in intrahepatic and infrarenal IVC were densely adhered to vessel wall and could not be completely excised. All 3 tumours had favourable histology and the excised thrombus showed no viable tumour. Two patients received post-op radiotherapy. All the 3 children are alive and tumor free.

Conclusions

Management of Wilms' tumour with IVC and intra-atrial extension is technically challenging. Pre-operative chemotherapy may cause dense adherence of thrombus to vessel wall, but it may be effective as all thrombus excised reported no viable tumour cells. More careful studies are needed to make recommendations on staging and treatment of Wilms' tumour with extensive IVC thrombus.

EP-691

Surgery (IPSO)

UNUSUAL PRIMARY PAEDIATRIC TESTICULAR TUMOURS

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Objectives

To describe the unique clinical presentation, diagnostic difficulties and uncommon histology in 2 cases of primary paediatric testicular tumour(TT).

Methods

A retrospective clinical chart review of 2 boys with rare primary TT.

Results

A 2-year old boy presented with a painless left scrotal swelling a year after bilateral inguinal orchidopexies for bilateral undescended testicles. Ultrasound demonstrated an enlarged heterogeneous left testis measuring 5.0x 3.5x 2.5cm with increased vascularity. Serum Alpha-fetoprotein and Beta-hCG were normal. A left testicular biopsy was performed via an inguinal approach. Intra-operative frozen section was inconclusive but the diagnosis of embryonal rhabdomyosarcoma was made on paraffin sections. Radical inguinal orchidectomy and hemi-scrotectomy was performed. Tumour margins were clear except for focal microscopic involvement at the spermatic cord margin. He received adjuvant chemotherapy as per ARM A protocol and has remained disease-free for 3.5years. Another child, 4.5years old, presented with a 3-month duration of painless right scrotal swelling. Ultrasound scan revealed a heterogeneous enlarged right testis measuring 1.9x 2.8x 1.6cm with increased vascularity, raising the possibility of a germ cell tumour(GCT). Tumour markers were normal. Intra-operatively, the right testis measured 4.0x 2.5x 2.5cm with no normal testicular tissue evident. A radical orchidectomy was performed. Histopathology diagnosed primary paediatric follicular lymphoma of the testis grade IIIa. He received standard-risk chemotherapy for lymphoma and has remained disease-free for 10.5years.

Conclusions

Traditionally, elevated serum Alpha-fetoprotein and Beta-hCG play a significant role in pre-operative counselling for primary paediatric TT. Our experience with these 2 patients illustrates the limitations of these tumour markers, and that of intra-operative frozen section to direct the need for radical orchidectomy. While GCT are the commonest primary TT in children, other rare malignancies should be considered when tumour markers are normal. While testis-sparing surgery for primary TT may be possible, these patients should be carefully selected and pre-operative imaging thoroughly evaluated.

EP-692

Surgery (IPSO)

MULTIMODALITY THERAPY FOR WILMS' TUMOR WITH INFERIOR VENA CAVA AND ATRIAL TUMOR THROMBUS

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Objectives

We introduce one case of Wilms' tumor with inferior vena cava and right atrial tumor thrombus successfully treated with multimodality therapy.

Methods

A 18 months old girl was admitted with history of abdominal distension and hematuria for 5 days. Abdominal ultrasound, CT and MRI showed a right renal mass measured 12.8 cm×10.6 cm×10.2 cm with tumor thrombus extending into inferior vena cava and right atrium. Echocardiogram confirmed a mass (3.3cm×3.2cm×2.0cm) in the right atrium. The histological diagnosis of Wilms' tumor was confirmed by core-needle biopsy. Combined-modality neoadjuvant therapy with transcatheter arterial chemoembolization (TACE) and systemic chemotherapy was taken. The patient subjected to transcatheter arterial chemoembolization by Seldinger method. Chemoembolization emulsion was injected into the involved renal artery. The chemoembolization emulsion consisted of cisplatin (80 mg/m²), pirarubicin (40 mg/m²), vindesine (3mg/m²), and iodized oil (5 ml). Two sessions of intravenous chemotherapy administered 3 weeks after TACE. That was alternating using ifosfamide(1200mg/m²), etoposide(100 mg/m²), vindesine(3mg/m²) and carboplatin(300mg/m²), pirarubicin(40mg/m²), vindesine(3mg/m²), one each treatment interval of 3 weeks. The tumor decreased in size to 10.8cm×8.5cm×8.2cm on CT images. The tumor thrombus within the IVC and RA also shrunk but has not disappeared.

Results

The patient was operated after twelve weeks Combined-modality neoadjuvant therapy. Complete resection of tumor kidney first, then the right atrium opened and the tumor thrombus completely removed under cardiopulmonary bypass with deep hypothermia and circulatory arrest. Recovery was uneventful. Pathological examination of the resected tumor showed necrosis more than 95%. The child was given radiotherapy to the right flank followed by postoperative chemotherapy. The patient was free of recurrence with a follow-up of 15 months.>

Conclusions

Multimodality Therapy is effective for the treatment of Wilms' tumor with inferior vena cava and right atrial tumor thrombus.

EP-693

Surgery (IPSO)

SURGICAL INTERVENTION FOR RESIDUAL LUNG NODULES AFTER CHEMOTHERAPY FOR PEDIATRIC MALIGNANCIES

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Objectives

we retrospectively reviewed the surgical managements for residual lung nodules after chemotherapy for pediatric malignancies.

Methods

Eleven pediatric oncology patients who had undergone a resection of pulmonary nodules between 2001 and 2013 were included in the study. They included five hepatoblastomas, three Wilms tumors, two osteosarcomas and one neuroblastoma. All lung nodules were identified on preoperative CT imaging for routine surveillance, and were resected by either thoracotomy or thoracoscopic surgery. Patient demographics, initial diagnosis, location of the lung nodule, procedure performed, and pathology of the lesion were recorded.

Results

Six patients had lung nodules at diagnosis, remaining five developed lung nodules during or after the treatments. Biopsy of the multiple nodules was performed in 3 cases by thoracoscopic surgery. In eight cases, complete resections of the lung nodules were performed. In the bilateral case, each side was resected by separate operation. Five cases were resected by thoracotomy and remaining three were resected by thoracoscopic surgery. In three cases with the small nodules less than 5mm, CT guided marking were successfully performed before surgery. Pathological examination revealed that the nodules were viable metastasis in five cases, complete necrotic metastasis in 3 cases and benign lesions in two cases. Two patients died of recurrence, however remaining nine are alive without disease for 1 to 13 years.

Conclusions

Complete resection of the lung nodules contributed to the achievement of complete remission. Pathological findings of the nodules were useful to decide the further management of these patients and, ultimately, to improve their overall survival. CT guided marking were useful to resect the small nodules less than 5 mm.

EP-694

Surgery (IPSO)

SURGICAL RESECTION AND BUCCAL MUCOSA VAGINOPLASTY FOR LOCAL CONTROL IN VAGINAL BOTRYOID RHABDOMYOSARCOMA

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Objectives

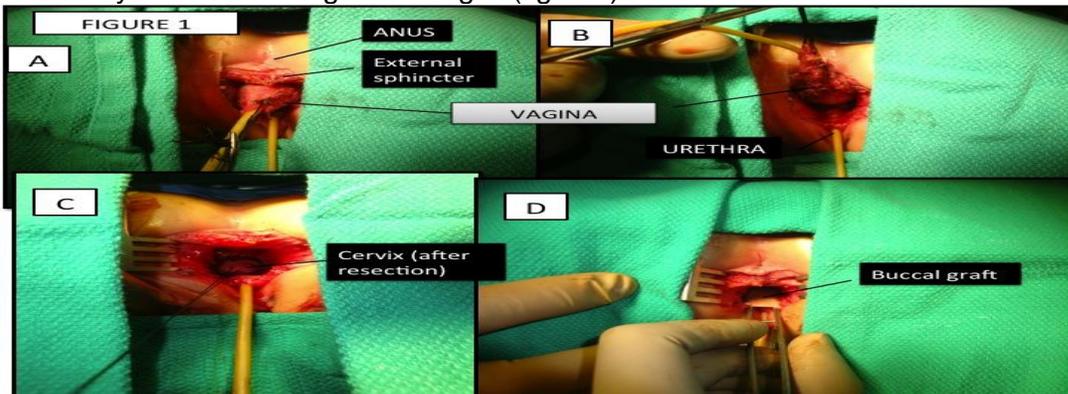
Standard treatment for vaginal botryoid rhabdomyosarcoma (RMS) in children encompasses systemic chemotherapy and radiation therapy (RT) for local control with good results. RT to the young pelvis leads to significant long-term complications. Herein, we report a surgical alternative for local control with the goal of sparing RT to the pelvis.

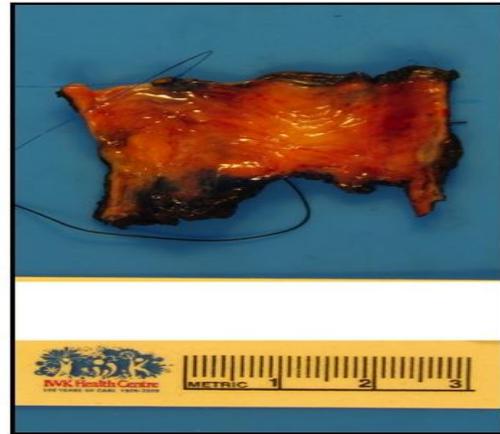
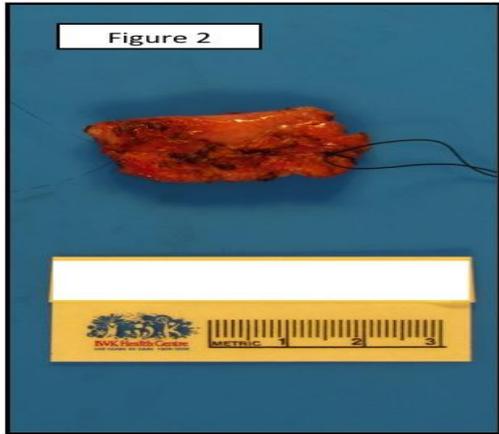
Methods

Case report (after informed consent) of a new surgical technique used for local control in the treatment of vaginal botryoid RMS in a 30-month old girl.

Results

The child has been treated on Children's Oncology Group D9803 protocol (VAC chemotherapy) for group III, stage II biopsy-proven vaginal botryoid RMS. At 12 weeks, vaginoscopy depicted very good response with small residual lesions containing rhabdomyoblasts identified in the anterior and posterior vaginal walls. At 24 weeks, instead of standard RT as per protocol, we performed a subtotal vaginectomy using an anterior sagittal approach and buccal mucosa vaginoplasty, with bilateral grafts harvested from the patient's cheeks (figure1). A 20 fr. chest tube was left in situ as a vaginal mold. The cervix and other internal reproductive organs were left intact and the grafts were anastomosed to the forniceal mucosa. The patient was discharged on postoperative day (POD) 3. Vaginal stent was removed on POD9. Fifteen days after surgery, the patient presented with a superficial dehiscence of the perineal body. Examination under anesthesia revealed well-healed grafts with a patent vagina and no evidence of perineal infection. The wound healed by secondary intention without any further complications. Pathology revealed focal residual rhabdomyoblasts with negative margins (figure2).





Conclusions

Subtotal vaginectomy and buccal mucosa vaginoplasty using an anterior sagittal approach offers an alternative for local control in children with botryoid RMS that may spare these patients from receiving RT to the pelvis. Long-term follow-up to assess function of the neovagina and oncological outcomes is mandatory.

EP-695

Surgery (IPSO)

SURGICAL PROBLEMS IN CHILDREN WITH GENITO-URINARY TRACT'S RHABDOMYOSARCOMA

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Objectives

The prognosis of children with rhabdomyosarcomas (RMS) has improved over the last 30 years. Their survival rate gets to 80-85% because the modern algorithm based on chemotherapy and radiotherapy. Surgery comes to the second plan in local therapy but there are a lot of surgical problems based on specific urogenital localization of tumor.

Methods

19 children (11 boys and 8 girls) in the age from 9 month to 12 years. Tumors localization was in 4 – paratesticular, in 12- bladder with/without prostate, uterus or/and vulva – 3. Follow up from 1 till 22 years after the treatment.

Results

In all patients there were “surgical” reasons of primary treatment: abdominal pain (8), acute retention of urine or disuria (7), palpable or visual tumor mass (4). Primary laparotomy or laparoscopy were done in all children with abdominal pain by common surgeons, but the biopsy wasn't perform in all cases and in 4 of them the primary resection of tumor was done. Complications of primary surgery were urinous infiltration in 3 patients and large vascular disruption in 1 of them. Primary urine diversion has been done in 3 patients by bladder catheterization and by nephrostomy in 2. All patients undergone XR therapy.

Secondary radical resection was done in 7 children after radiotherapy: total cystectomy (4) and/or total prostatectomy (2), uterus- and vaginaectomy in 2. Later reconstruction in 3.

Urinary tract obstruction as side effect in long term follows up after radiotherapy was shown in 8 patients. Urethral reimplantation was done in 3 of them, vesicostomy in 1, internal urethral stents were placed in 2

Conclusions

Surgical intervention in the first step of treatment in patients with RMS of genitourinary tract must be more safety and be limited by biopsy and urinary diversion. Delayed reconstructive surgery is necessary for most patients after the both methods of local treatment.

EP-696

Surgery (IPSO)

RECURRENT MONOPHASIC WILMS' TUMOR IN PELVIC KIDNEY - A THERAPEUTIC CHALLENGE

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Objectives

To report an unusual case of repeated loco-regional recurrences in a patient with stage I intermediate-risk monophasic (epithelial variant) Wilms' tumor (WT) of pelvic kidney requiring aggressive therapy over a decade.

Methods

Retrospective case study

Results

One-year-old boy presented with lower abdominal lump. Investigations showed WT in left ectopic kidney. Left nephroureterectomy was done; HPE confirmed WT with predominant tubule formation, minimal atypia and mitosis (stage I). Repeat CECT a month later showed thrombus in infra-hepatic inferior vena cava (IVC) and right common iliac vein with para-aortic and iliac lymphadenopathy. This was followed by early abandonment of therapy; the patient received only 2 cycles of chemotherapy (VAC regimen). He returned with local relapse in retroperitoneal lymph nodes after 7 years. After 6 cycles of ICE chemotherapy, RPLND was done but HPE showed no tumor. Fourteen months later, he developed second recurrence in mesocolic lymph nodes that was completely excised followed by 6 cycles of IE chemotherapy and 20 Gy whole abdominal irradiation. Histopathology was again epithelial variant of WT. Four months later, he presented with 3rd recurrence - a large pelvic mass (15x8x7cm); trucut biopsy again showed epithelial predominant WT. He received 6 cycles of Paclitaxel based salvage chemotherapy followed by excision of the retro-vesical tumor and boost radiotherapy of 10.8 Gy to the pelvis. We had planned to excise the persistent calcified thrombus in subhepatic IVC that could be harboring a nidus of tumor cells but he suffered acute renal failure from radiation nephritis 4 months later. He had repeated dialysis over next 10 months before he succumbed to chronic renal failure.

Conclusions

Inert tumor cells in the calcified IVC thrombus has possibly caused the repeated loco-regional recurrences of a low-risk localized monophasic WT. The importance of initial completion of therapy and need for long term follow-up cannot be overemphasized.

EP-697

Surgery (IPSO)

SYNCHRONOUS IPSILATERAL WILMS' TUMOR AND NEUROBLASTOMA IN AN INFANT

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Objectives

To report synchronous co-existence of ipsilateral adrenal neuroblastoma and Wilms' tumor

Methods

Retrospective case study

Results

A 10-month-old girl was admitted with complaints of abdominal distension since 1½ months, cough and fever since 3 weeks and weight loss. Examination revealed a large right retroperitoneal mass; clinical diagnosis was right Wilms' tumor (WT). Ultrasonography revealed 2 heterogeneous, echogenic masses- a well defined, 4.8X4.3 cm mass in right suprarenal region and another 8.9X7 cm mass with multiple internal anechoic areas along anterolateral aspect of kidney. CT scan revealed 13 X 9 X 9cm well defined heterogeneous mass abutting the right kidney with loss of fat planes. Superiorly, the lesion had a well-defined round component, which was seen abutting the undersurface of liver. Inferiorly, it extended till the pelvic brim and medially it crossed the midline causing effacement and displacement of Inferior vena cava, however no encasement of major vessels was noted. WT was confirmed on trucut biopsy. Metastatic workup was negative.

She was administered pre-operative chemotherapy (Vincristine+ Adriamycin) over 4 weeks. At surgery, 13 X 8 X 8cm right renal mass was noted. There was a separate mass of 5 X 5 X 3cm in the area of the right suprarenal gland with a clear plane of separation between the two masses. Local lymph nodes were enlarged. Complete excision of both masses and lymph node sampling was done.

Histopathology revealed co-existing intermediate-risk stage I WT and stage I neuroblastoma (NB). Bone survey, bone scan, bone marrow aspiration and MIBG scan were negative. The child has been started on OPEC regimen, as NB was positive for N-myc amplification.

Conclusions

The co-existence of 2 embryonal tumors in the same patient may merely be a coincidence. However accumulation of data on similar cases may help to clarify if there is an association between these 2 tumors.

EP-698

Surgery (IPSO)

CHEMOTHERAPY INDUCED CHANGES IN WILMS' TUMOR – OUR EXPERIENCE

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Objectives

Preoperative chemotherapy propagated by SIOP renal tumour trials reduces tumor rupture and increases favourable stage distribution of Wilms' tumor (WT). It is known that chemotherapy induced changes (CIC) alter the tumor's histological features and distribution of subtypes, making staging more difficult. We studied CIC in our patients.

Methods

Histopathology slides of 10 children with WT treated in our institute as per SIOP WT 2001 protocol, were reviewed in the light of current knowledge by an experienced senior pathologist. Since a mandatory pre-chemotherapy tru-cut needle biopsy was done in all patients (UKCCG protocol), the tumor morphology was compared before and after chemotherapy.

Results

6 pre-chemotherapy tru-cut biopsies could be subtyped: mixed (n=5), epithelial (n=1). Mean tumor volume decreased from 919 to 564cc after chemotherapy (mean response 38.6%); only 2 patients had a good response ($\geq 40\%$ reduction). The most common histological subtype after chemotherapy was mixed [akin to traditional terminology of triphasic WT] (n=4); followed by stromal (n=3), epithelial (n=1), regressive (n=1) and cystic partially differentiated nephroblastoma (CPDN) (n=1). All except 1 were intermediate risk. CPDN was low risk and did not show any CIC. In the remaining 9 cases, CIC was demonstrated involving 25 – 70 % (mean 38.8 %) of the tumor area. The nephrectomy specimen correlated histologically in epithelial subtype. However, only 2/5 nephrectomy specimens had subtype concurrence in mixed type. The other 3 were subtyped subsequently as stromal (n=1), regressive (n=1) and CPDN (n=1). Fibrous pseudocapsule was seen in 1 epithelial subtype and rhabdomyoblastic differentiation was seen in all 3 stromal subtypes, 1 of which also had focal anaplasia.

Conclusions

It is possible to subtype WT on trucut biopsy preoperatively in majority of specimens. The incidence of regressive subtype was much lower in our series as compared to SIOP study results (10% Vs 37.6%).

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Surgery (IPSO)

VASCULAR TUMORS AND MALFORMATIONS-MULTIDISCIPLINARY APPROACH AND OUTCOME IN NORTH INDIAN CHILDREN

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Objectives

To evaluate the presentation, treatment and outcome of vascular tumors and malformations in North Indian children.

Methods

Retrospective analysis of consecutive cases of vascular tumors and malformations presenting at VMMC and Safdarjung Hospital, New Delhi from 2008 through 2013 was carried out. The age at presentation, type of vascular tumors and malformations {International Society for the Study of Vascular Anomalies(ISSVA) Classification}, associated abnormalities, treatment options and outcome were reviewed. Protocol based radiological examinations were colour Doppler and CT angiography. Treatment options were conservative, oral propranolol and steroids, intralesional therapy with Bleomycin & Sodium tetradecyl sulphate, laser therapy, compression therapy and surgical excision.

Results

Two hundred six patients (125 female, 81male) were identified. **Vascular tumors 118 pt (57%)** were Infantile hemangioma 84pt (40%, 52female, 27male, mean age of presentation 4 week, 70% over head and neck, good response to propranolol and 8 required excision), hepatic hemangioma 4 pt (2%, large, responded well to prednisolone), congenital hemangioma 18 pt {8%, 8RICH, 10NICH(trunk & extremities, required excision, good cosmesis)}, pyogenic granuloma 12 pt (6%, excision). **Vascular malformations 88pt (43%)** were venous malformation 52 pt(25%, over trunk, extremities and face, age ranges 1month to 12 years, major role of colour Doppler and CT angio for flow pattern and vascular anatomy, responded well to inj sclerotherapy, rarely excision), capillary malformation 6pt (3%), lymphatic malformation 20 pt {10%, 15 cystic hygroma(cervical, responded well to bleomycin, excision in 2 pt), 5 macrocystic lymphangioma, responded well to bleomycin}. Complex vascular malformation was Klippel-Trenaunay syndrome in 10pt (5%, lower extremities & perineum with bony overgrowth, satisfactory response to compression bandage and local sclerotherapy).

Conclusions

Multidisciplinary approach and treatment, with appropriate clinical and radiological assessment provide satisfactory outcome and accepted morbidity in vascular tumors and malformations cases.