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EESTI VÄHIHAIGETE LASTE VANEMATE LIIT

A case of meningitis by Pseudomonas aeruginosa in a patient with Acute Lymphoblastic Leukemia

by Grazina Kleinotiene | Vilma Rutkauskaite | Ramunas Raugalas | Dainius Rinkevicius | Egle Stoncaityte | Goda Elizabeta Vaitkeviciene | Jelena Rascon | Center for Pediatric Oncology and Hematology, Vilnius University Hospital Santaros Clinics, Lithuania | Center for Pediatric Oncology and Hematology, Vilnius University Hospital Santaros Clinics, Lithuania | Center of Neurosurgery, Vilnius University Hospital Santaros Clinics, Lithuania | Center of Neurosurgery, Vilnius University Hospital Santaros Clinics, Lithuania | Center for Pediatric Oncology and Hematology, Vilnius University Hospital Santaros Clinics, Lithuania | Center for Pediatric Oncology and Hematology, Vilnius University Hospital Santaros Clinics, Lithuania | Center for Pediatric Oncology and Hematology, Vilnius University Hospital Santaros Clinics, Lithuania

Abstract ID: 106
Themes: Infections
Presenter Name: Grazina Kleinotiene
Keywords: Pseudomonas aeruginosa, external ventricular drain., meningitidis, ventriculoperitoneal shunt

Acute lymphoblastic leukemia is one of the most common childhood malignancies with cure rates surpassing 90%. During treatment, different complications often arise: neuropathy, pancreatitis, thromboembolism, infections and other. One of them infectious meningitis is very rare, however, life threatening complication.

We present a clinical case of a 2-year-old girl, treated for acute pre-B lymphoblastic leukemia (ETV6-RUNX1 pos), CNS1 who developed Pseudomonas aeruginosa meningitis (PAM) at the beginning of Consolidation1 followed after InductionA according to ALLTogether protocol. Minimal residual disease on day 29 was (PCR) – negative, FCM – 0.0036% stratifying to IR-low risk group.

On day 33 the patient was readmitted to our department for febrile fever without neutropenia. General condition was unremarkable, no CNS symptoms. Treatment with piperacillin-tazobactam, ambisome was initiated. Due to the worsening condition: fever, haedaches, the antibiotic regimen was changed to meropenem. A lumbar puncture was performed, cerebrospinal fluid (CSF) microscopy revealed bacterial meningitis caused by VIM-expressing P. aeruginosa resistant to carbapenems, which was yielded from CSF culture. Meropenem was switched to intravenous colistin and cefiderocol with no improvement: brain MRI revealed progressing internal hydrocephalus with signs of periventricular edema. Consequently, an external ventricular drain was implanted.

Intraventricular colistin treatment was added. This resulted in significantly clinical improvement and stop of growth of P.aeruginosa in CSF. A ventriculoperitoneal shunt was formed.

Management of P. aeruginosa meningitis resulted in 2 months interruption of chemotherapy. To spare the patient from potential further chemotherapy-related toxicity,

the two consolidation blocks were replaced with two Blinatumomab courses with further plans to continue with Delayed Intensification with Doxorubicin and Maintenance therapy with Vincristin/Dexamethason pulses.

Conclusion: PAM is a rare and severe complication requiring considerable ALL treatment modification. Intraventricular antibacterial therapy can salvage the patient.

Biallelic hexokinase 1 (HK1) variants causative of non-spherocytic haemolytic anaemia: a case series with emphasis on the HK1 promoter variant and literature review

by Elli-Maija Ukonmaanaho | MD/Oulu University Hospital, Finland

Abstract ID: 90
Themes: Benign Hematology
Presenter Name: Elli-Maija Ukonmaanaho
Keywords: HK1, anaemia, haemolysis, hexokinase deficiency, promoter variant

The hexokinase enzyme (HK) plays a key role in red blood cell energy production. Hereditary non-spherocytic haemolytic anaemia (HNSHA) caused by HK deficiency is a rare disorder with only 12 different mutations identified. Here, we describe the clinical features and genotypes of four previously unreported patients with hexokinase 1 (HK1*)*-related HNSHA yielding two novel truncating *HK1* variants. The patients' phenotypes varied from mild chronic haemolytic anaemia to severe infantile-onset transfusion-dependent anaemia. Three of the patients had mild haemolytic disease caused by the common *HK1* promoter c.-193A>G variant combined with an intragenic *HK1* variant, emphasizing the importance of including this promoter variant in the haemolytic disease gene panels. HK activity was normal in a severely affected patient with a homozygous *HK1* p. c.2599C>T, p.(His867Tyr) variant, but the affinity for ATP was reduced hampering the HK function. In cases of HNSHA, kinetic studies should be considered in the functional studies of HK. We reviewed the literature of previously published patients to provide better insight into this rare disease and add to the understanding of genotype–phenotype correlation.

BRINGING THE ESMART PLATFORM TRIAL FOR CHILDREN AND ADOLESCENTS WITH RELAPSED OR REFRACTORY CANCERS TO THE NORDIC COUNTRIES

by Karsten Nysom | Mimi Kjærsgaard | Ruta Tuckuviene | Jonathan Rubino | Pablo Berlanga | Birgit Geoerger | Department of Paediatrics & Adolescent Medicine, Copenhagen University Hospital – Rigshospitalet, Denmark | Department of Paediatrics & Adolescent Medicine, Copenhagen University Hospital – Rigshospitalet, Denmark | Department of Paediatrics & Adolescent Medicine, Copenhagen University Hospital – Rigshospitalet, Denmark | Gustave Roussy Cancer Campus, Clinical Research Direction, Université Paris-Saclay, Villejuif, France | Gustave Roussy Cancer Campus, Department of Paediatric and Adolescent Oncology, Université Paris-Saclay, Villejuif, France | Gustave Roussy Cancer Campus, Department of Paediatric and Adolescent Oncology & INSERM U1015, Université Paris-Saclay, Villejuif, France

Abstract ID: 132
Themes: Novel Methods and Therapies
Presenter Name: Karsten Nysom
Keywords: Clinical phase 1/2 platform trial, Experimental therapy, Proof-of-concept precision cancer medicine trial, Relapse, Targeted combination therapies

The ‘Accès sécurisé - European proof-of-concept therapeutic stratification trial of molecular anomalies in relapsed or refractory tumors’ (AcSé-ESMART, NCT02813135) was developed in 2016 to explore new biology-driven targeted treatment strategies in a molecularly enriched study population. ESMART is a platform trial with multiple arms, mostly with combination therapies, where new treatment arms are added through amendments. Our aim was to open ESMART in Copenhagen, thereby giving Nordic and Baltic children with relapsed or refractory cancers better access to new experimental therapies.

ESMART in Copenhagen was funded by NordForsk in December 2018 as part of the NOPHOmatch project (grant 91387). Initially, none of the oral drugs in ESMART were labelled in Danish, excluding the opening. The application (174 documents) was finally submitted to the Danish authorities in December 2022 and approved by the Danish Medicinal Ethics Committee (January 2023) and the Danish Medicines Agency (November 2023). By then, of the total of 16 arms opened since 2016, three arms of protocol version 5.1 had completed enrolment (arm D, PARPi olaparib + irinotecan) or discontinuation of the targeted drug formulation (arms K; CDK2/5/9i fadraciclib + temozolomide and L; fadraciclib + cytarabine).

In December 2023, ESMART was finally opened in Copenhagen with the following five arms: I (IDH2i enasidenib); M (CDK4/6i ribociclib + mTORi everolimus ±dexamethasone), N (ATRi ceralasertib + olaparib), O (FGFRi futibatinib. and P (METi capmatinib + everolimus). Arm Q (DNA-PKi peposertib + PD1i avelumab + temozolomide) will be submitted during 2024 through the new EU procedure. By February 2024, two patients have been transferred from the site in Paris (one from Copenhagen, one from Bergen), and one patient from Stockholm has been approved for screening.

We will present an update on ESMART and our experience of giving Nordic and Baltic children with relapsed or refractory cancer regional access to ESMART.

CARDIORESPIRATORY FITNESS, PHYSICAL PERFORMANCE, AND METABOLIC SYNDROME IN ADULT SURVIVORS OF PAEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

by Anne Nissen | Tina Gerbek | Kathrine Fogelstrøm | Peter Schmidt-Andersen | Kaspar Sørensen | Abigail L. Mackey | Martin Kaj Fridh | Klaus Müller | Department of Paediatrics and Adolescent Medicine, Copenhagen University Hospital - Rigshospitalet, Copenhagen, Denmark | Department of Paediatrics and Adolescent Medicine, Copenhagen University Hospital - Rigshospitalet, Copenhagen, Denmark | Department of Paediatrics and Adolescent Medicine, Copenhagen University Hospital - Rigshospitalet, Copenhagen, Denmark | Department of Paediatrics and Adolescent Medicine, Copenhagen University Hospital - Rigshospitalet, Copenhagen, Denmark | Department of Paediatrics and Adolescent Medicine, Copenhagen University Hospital - Rigshospitalet, Copenhagen, Denmark | Institute of Sports Medicine Copenhagen, Department of Orthopaedic Surgery, Copenhagen University Hospital - Bispebjerg & Frederiksberg, Copenhagen, Denmark | Department of Paediatrics and Adolescent Medicine, Copenhagen University Hospital - Rigshospitalet, Copenhagen, Denmark | Department of Paediatrics and Adolescent Medicine, Copenhagen University Hospital - Rigshospitalet, Copenhagen, Denmark

Abstract ID: 140
Themes: Late Effects
Presenter Name: Anne Nissen
Keywords: Cardiorespiratory fitness, Hematopoietic Stem Cell Transplantation, Late effects, Metabolic Syndrome, Survivors

Aim:

Long-term survivors of paediatric allogeneic hematopoietic stem cell transplantation (HSCT) are at high risk of developing treatment-related late effects, including impaired cardiorespiratory fitness, reduced physical performance, and metabolic syndrome (MetS). However, it remains unknown to what extent, reduced cardiorespiratory fitness and physical performance may account for the high risk of MetS among the survivors.

Methods:

This cross-sectional study included 90 survivors of paediatric HSCT (median age 30.3 years; 46 males) with a median time from HSCT to follow-up examination of 20.2 years (range: 5.9;37.0 years), and 32 healthy, age- and sex-matched controls. Cardiorespiratory fitness was evaluated by a cardiopulmonary exercise test, and physical performance through sit-to-stand test, handgrip strength, timed-up-and-go, walking pace, and 6-minute walk tests. We measured blood pressure and waist circumference. Fasting plasma samples were analysed for HDL-cholesterol, triglycerides, and glucose.

Multiple regression analyses corrected for age and sex were applied for categorial covariates and the physical outcomes, and multiple regression analysis corrected for sex was applied for continuous covariates. *P*-values below 0.05 were considered significant.

Results:

HSCT survivors demonstrated lower cardiorespiratory fitness (mean±SD VO_2 peak: survivors 29.3±7.0 ml/kg/min vs. age-matched controls 44.3±6.8 ml/kg/min, $p<0.0001$), and impairments in all physical performance outcomes compared with controls.

Twenty-eight percent of survivors had MetS. The presence of MetS negatively associated with VO_2 peak, the 6-minute walk test, walking pace and the timed-up-and-go test.

Conclusions:

Long-term survivors of paediatric HSCT are at risk of having markedly reduced cardiorespiratory fitness and physical performance as compared with healthy controls. The high incidence of MetS in these survivors may be partially ascribed to reduced physical capacity.

These data underline the importance of monitoring physical performance status in the follow-up care of survivors of paediatric HSCT. The potential of reducing the risk of MetS in HSCT survivors by physical training should be further investigated.

CHEK2 GERMLINE VARIANTS AND ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT OUTCOMES

by Maarja Karu | Atte K. Lahtinen | Jessica Koski | Jarmo Ritari | Kati Hyvärinen | Satu Koskela | Jukka Partanen | Kim Vettenranta | Minna Koskenvuo | Riitta Niittyvuopio | Urpu Salmenniemi | Maija Itälä-Remes | Kirsi Jahnukainen | Outi Kilpivaara | Ulla Wartiovaara-Kautto | Department of Hematology and Oncology, Tallinn Children's Hospital, Tallinn, Estonia; New Children's Hospital, Pediatric Research Center, University of Helsinki and Helsinki University Hospital, Helsinki, Finland | Applied Tumor Genomics Research Program, Faculty of Medicine, University of Helsinki, Helsinki, Finland; Department of Medical and Clinical Genetics, Medicum, Faculty of Medicine, University of Helsinki, Helsinki, Finland | Applied Tumor Genomics Research Program, Faculty of Medicine, University of Helsinki, Helsinki, Finland; Department of Medical and Clinical Genetics, Medicum, Faculty of Medicine, University of Helsinki, Helsinki, Finland | Research and Development, Finnish Red Cross Blood Service, Helsinki, Finland | Research and Development, Finnish Red Cross Blood Service, Helsinki, Finland | Research and Development, Finnish Red Cross Blood Service, Helsinki, Finland | Research and Development, Finnish Red Cross Blood Service, Helsinki, Finland | New Children's Hospital, Pediatric Research Center, University of Helsinki and Helsinki University Hospital, Helsinki, Finland | New Children's Hospital, Pediatric Research Center, University of Helsinki and Helsinki University Hospital, Helsinki, Finland | Helsinki University Hospital, Comprehensive Cancer Center, Department of Hematology, and University of Helsinki, Helsinki, Finland | Helsinki University Hospital, Comprehensive Cancer Center, Department of Hematology, and University of Helsinki, Helsinki, Finland | Turku University Hospital, Department of Clinical Hematology and Stem Cell Transplant Unit, and University of Turku, Turku, Finland | New Children's Hospital, Pediatric Research Center, University of Helsinki and Helsinki University Hospital, Helsinki, Finland; NORDFERTIL Research Lab Stockholm, Department of Women's and Children's Health, Karolinska Institutet and University Hospital, Stockholm, Sweden | Applied Tumor Genomics Research Program, Faculty of Medicine, University of Helsinki, Helsinki, Finland; Department of Medical and Clinical Genetics, Medicum, Faculty of Medicine, University of Helsinki, Helsinki, Finland; HUSLAB Laboratory of Genetics, HUS Diagnostic Center, Helsinki University Hospital, Helsinki, Finland | Applied Tumor Genomics Research Program, Faculty of Medicine, University of Helsinki, Helsinki, Finland; Helsinki University Hospital, Comprehensive Cancer Center, Department of Hematology, and University of Helsinki, Helsinki, Finland

Abstract ID: 128
Themes: Other
Presenter Name: Maarja Karu
Keywords: germline variants, hematopoietic stem cell transplantation, toxicity

Background and aims: Germline alterations in genes functioning in DNA damage repair, like *CHEK2* variants regulating *CHEK2* protein synthesis, are frequently identified in individuals tested for hereditary cancer predisposition. Their effect on success of high intensity therapies is not known. Our aim was to assess the correlation between germline *CHEK2* variants and allogeneic hematopoietic stem cell transplantation (HSCT) outcomes.

Methods: We analyzed the whole exome sequencing and clinical data of 432 patients transplanted between 1999-2020. The patient series comprised of Helsinki University Hospital cohort and the Finnish Bone Marrow Transplantation Registry cohort (adult patients) and a national pediatric cohort. We focused on recipients carrying founder

mutations or pathogenic (P) or likely pathogenic (LP) variants in *CHEK2*. We compared HSCT recipients without variant to recipients with a *CHEK2* variant, recipients with gene variants clinically relevant to hereditary hematological malignancies, bone marrow failure syndromes or inborn errors of immunity (Hematology gene variants) and those with gene variants others than *CHEK2* clinically associated with predisposition to solid tumors (Cancer gene variants). Patients carrying multiple gene variants (N=8) were excluded.

Results: We identified a germline *CHEK2* P/LP alteration in 10.6% of the HSCT recipients. We found no correlation in the overall survival (*P*=.339), non-relapse mortality (*P*=.185) or risk of relapse (*P*=.723) between HSCT recipients with *CHEK2* variants vs no variant. No difference was observed in frequency of graft failure, acute or chronic graft versus host disease (GVHD) (0%, 42.2% and 44.4% vs 2.7%, 50.3% and 44.4%, respectively). Recipients with Hematology gene variants showed higher frequency of acute liver GVHD (23.1% vs 5.5%, *P*= <.001), tendency to higher frequency of graft failure (9.5% vs 2.7%, *P*= 0.097) and early non-relapse mortality (19.2% vs 11.3%, *P*=0.158).

Conclusions: Germline variants in *CHEK2* do not affect HSCT outcome supporting standard HSCT care for recipients with a germline *CHEK2* variant.

DENTAL ANOMALIES AFTER ACUTE LYMPHOBLASTIC LEUKEMIA - PRELIMINARY REPORT

by Dorota Malgorzata Wojcik | Britt Nygard Tvilde | Tine Birkeland Sivertsen | Torgils Lægreid | Sigbjørn Suk Løes | Haukeland University Hospital, Bergen, Norway | University of Bergen, Bergen, Norway | Haukeland University Hospital, Bergen, Norway | University of Bergen, Bergen, Norway | Haukeland University Hospital, Bergen, Norway

Abstract ID: 116
Themes: Late Effects
Presenter Name: Britt Nygard Tvilde
Keywords: , ALL, cancer treatment, children, dental anomalies

Late effects following cancer treatment in growing individuals include permanent changes resulting from the disease itself and/or its treatment. High risk of long-term dental anomalies varying on age at diagnosis and type of treatment are reported as disturbances in teeth formation, eruption, morphology, mineralization, caries, etc. The aim is to examine the relation between childhood cancer and its treatment and late effects in the oral cavity.

Material and methods

Children who finished cancer treatment between years 2017-2021 at Haukeland University Hospital in Western Norway, were invited to a case-control study n=113. Age and gender matched controls were randomly selected. The oral cavity and surrounding structures were clinically examined and documented by photos- and radiographs (bitewing and orthopantomogram).

Findings are presented here in a cohort of n=28 children with ALL treated according to the NOPHO ALL 2008 protocol consisting of standard risk (SR) n=20 and intermediate risk (IR) n=8 individuals. Treatment started before age of 5 in 19 patients. One child age <5 years was excluded due to dental problems not related to the disease itself or its treatment.

Results

Mean age at cancer diagnosis was 4.8 years (range: 1.1-13.25 years). The gender distribution was approximately equal with 56% females. Dental agenesis was found in one patient, and short roots of molars and premolars in 11% (3/27). Microdontia was observed in 59% (16/27). Among patients treated before age 5, 66% (12/18) had microdontia. Mean age of those with microdontia was 2.4 years compared to 4 years for those without. The number of affected teeth varied from 2-8. Hypomineralization and/or hypoplasia of permanent teeth varied from 1-24 affected teeth and was seen in 59% (16/27) patients.

Conclusion

Children diagnosed and treated for ALL according to the NOPHO - ALL 2008 protocol are at

high risk for developing long term dental anomalies.

DIAGNOSIS AND MANIFESTATION OF HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS: A SINGLE CENTRE EXPERIENCE

by Venckutė Greta | Už a Tautvydas | Rutkauskienė Giedrė | Kiudelienė Rosita | Lithuanian University of Health Sciences Kaunas Clinics, Lithuania | Lithuanian University of Health Sciences Kaunas Clinics, Lithuania | Lithuanian University of Health Sciences Kaunas Clinics, Lithuania | Lithuanian University of Health Sciences Kaunas Clinics, Lithuania

Abstract ID: 114
Themes: Other
Presenter Name: Greta Venckutė
Keywords: HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS, MAS, PRIMARY HLH

Hemophagocytic lymphohistiocytosis (HLH) is an inflammatory hyperactivity disorder that can potentially endanger one's life. We revised all HLH cases diagnosed at Kaunas Clinics paediatric onco-haematology centre in 2010-2023 based on HLH-2004 criteria, analysed clinical manifestations, laboratory tests, aetiology, and outcomes. We found 12 cases, (3 boys and 9 girls) with a median age of 9,08 years. All the patients had fever, splenomegaly was diagnosed in 8 (66,7%). Laboratory findings included anaemia (61,5%), neutropenia (91,6 %), thrombocytopenia (75%), hypertriglyceridemia (45.5 %), hypofibrinogenemia (63,6 %). Hemophagocytosis was discovered in 7 (58.3%): bone marrow (41,6 %), liver (33,3%), skin (8.3%), three patients had hemophagocytosis in more than one site. Serum ferritin concentration varied from 102 to 20000 µg/L; with ≥500 µg/L occurring in 8 (66.7 %) cases. Soluble CD25 and natural killer activity were performed in 7 and 4 patients respectively, and all of them were abnormal. Other manifestations that were not included in HLH criteria were hepatitis in 8, rash and/or arthralgia in 4 and neurological damage in 2 cases.

Primary HLH was diagnosed in 2 cases, while secondary HLH occurred in the setting of macrophage activation syndrome (4), Langerhans cell histiocytosis (1), Ebstein-Barr viral infection (1), unknown (4). Altogether, 5 deaths were registered, the last one in 2015.

We conclude that the diagnosis of HLH is always problematic because of the diversity of presentation and variability of laboratory tests. Tests such as NK-cell activity, and soluble CD25 levels are not always possible to perform and receive in time for diagnosis confirmation. Hepatitis and neurological damage, although not included in the criteria, can help to suspect this syndrome and start treatment in time. Acknowledgment of HLH is essential for diagnosis and immediate treatment leading to improved prognosis.

EDUCATIONAL OUTCOMES IN CHILDREN TREATED FOR ACUTE LYMPHOBLASTIC LEUKEMIA: A POPULATION-BASED REGISTRY STUDY FROM SWEDEN

by Otto Zhou | Arja Harila | Emma Hovén | Malin Lönnerblad | Uppsala University, Sweden | Uppsala University, Sweden | Uppsala University, Sweden | Uppsala University, Sweden

Abstract ID: 99
Themes: Late Effects
Presenter Name: Otto Zhou
Keywords: ALL, late effects, leukemia, pediatric

Background: Acute lymphoblastic leukemia (ALL) makes up approximately 25% of pediatric cancers, and nowadays has a 5-year survival rate of approximately 90%. Despite improved survival, long-term consequences of treatment, including neurocognitive impairments, raise concerns. This registry study aims to explore the impact of ALL treatment on educational outcomes in Swedish children.

Methods: A population-based cohort of 503 children diagnosed with ALL born between 1988-1996 was identified from the Swedish Childhood Cancer Registry and each was matched with five controls without history of cancer. Assessed variables were grades from school year nine, the last year of compulsory school as well as high school eligibility, total merit value and delayed graduation. Both grades and rate of absence were studied in national exams. Analyses were performed between cases and controls and in subgroups by gender, age group and risk group and adjusted for maternal education. Analyses were performed with logistic regression for categorical variables, and linear regression for continuous variables using SPSS.

Results: Preliminary results showed that the cases final grades from school year nine were significantly worse in the school subject of Physical Education ($p=0.024$ for failing), as well as for some subgroups in English but not in Swedish or mathematics. Children diagnosed at ages 6-9 exhibited lower odds of eligibility for high school ($p=0.006$). Delayed graduation was more prevalent among cases ($p=0.003$). High-risk treatment correlated with lower grades. Higher rates of absence were found in many subtests of the national exams, but no significant differences in grades.

Conclusion: Swedish children treated for ALL mostly exhibited comparable educational outcomes to controls, with notable exceptions in Physical Education and, to a lesser extent, English. Findings highlight subgroups requiring additional educational support. This study

contributes insights applicable for designing targeted interventions and serves as a baseline for future comparisons.

EPIDEMIOLOGICAL ANALYSIS OF CENTRAL NERVOUS SYSTEM TUMORS IN LATVIAN PEDIATRIC POPULATION: 2012-2021

by Raita Anna | Cebura Elizabete | Children's Clinical University Hospital, Department of Pediatric Hematology - Oncology, Latvia | Children's Clinical University Hospital, Department of Pediatric Hematology - Oncology, Latvia

Abstract ID: 121
Themes: CNS
Presenter Name: Raita Anna
Keywords: CNS tumors, oncology, pediatric

Objectives. Central nervous system (CNS) tumors account for about a quarter of all childhood malignancies, making them the most common solid tumor type and the second most common childhood malignancy overall. Despite advancements in treating pediatric tumors, malignant brain tumors remain a major cause of mortality and morbidity. The aim of the study was to summarize data about the Latvian pediatric population with CNS tumors – demography, CNS tumor morphology and survival rate.

Materials and methods. This retrospective study involved accessing patient records through the Children's Clinical University Hospital clinical system, "Andromeda". Statistical analysis was conducted using SPSS. The Shapiro-Wilk test and Q-Q plots were used to determine the normality of quantitative data. Descriptive statistics and Kaplan-Meier survival estimator were applied for further data analysis.

Results: The study gathered data on 137 patients with a total of 139 primary tumor cases – 40.9% were female (N=56) and 59.1% were male (N=81). Age categorization was as follows: 0-4 years (32.1%; N=44), 5-9 years (27.7%; N=38), 10-14 years (26.3%; N=36), and 15-17 years (13.9%; N=19). Gliomas were the predominant histological type in all age groups, accounting for 69.1% (N=96) of cases, with pilocytic astrocytoma (23.0%; N=32) being the most frequent glioma subtype. Embryonal tumors were the second most common tumor type (23.0%; N=32).

The overall five-year survival rate for pediatric brain tumors was 73.1% (N=138). Low-grade malignant tumors, including pilocytic astrocytomas (N=32), diffuse astrocytomas (N=13), and other less common tumor subtypes (N=33), showed a 100% five-year survival rate. High-grade malignant tumors had significantly lower survival rates, with the five-year survival being at 38.7%.

Conclusions: CNS tumors were more commonly diagnosed in male rather than female patients. This study's findings on the prevalent types of CNS tumors and survival rates align with data from existing literature.

EVALUATION OF INTRAVENOUS IRON THERAPY EFFECTIVENESS IN PAEDIATRIC FEMALE PATIENTS WITH MENORRHAGIA

by Morkūnaitė Agnė1 | Vaišnorė Ramunė2 | Šaulytė Trakymienė Sonata3 | 1Faculty of Medicine, Vilnius University, Lithuania | 2Institute of Data Science and Digital Technologies, Faculty of Mathematics and Informatics, Vilnius University, Lithuania | 3Clinic of Children's Diseases, Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, Vilnius University Hospital Santaros Clinics, Vilnius, Lithuania

Abstract ID: 139
Themes: Novel Methods and Therapies
Presenter Name: Morkūnaitė Agnė
Keywords: Menorrhagia, intravenous iron, iron deficiency (anaemia), iron isomaltoside, low molecular weight dextran

Introduction. Menorrhagia, characterised by excessive or prolonged menstrual bleeding, poses a significant risk of iron deficiency with or without anaemia among paediatric female patients, often necessitating therapeutic interventions such as intravenous (IV) iron supplementation.

Aim. To assess the efficacy of IV iron therapy in managing hemostatic consequences of menorrhagia among paediatric female patients.

Methods. Data from paediatric females with menorrhagia treated with IV iron at Vilnius University Hospital Santaros Clinics (Oct 2021-Dec 2023) were retrospectively analysed. Statistical tests included Shapiro-Wilk (normality), Pearson's Chi-squared (frequency differences), t-test, and Wilcoxon test (before-after comparisons). Significance was set at $p<0.05$.

Results. A total of 23 IV infusions with low molecular weight dextran (LMWD) (36%) and iron isomaltoside (ISS) were administered (64%) to 14 patients with iron deficiency with or without anaemia of menorrhagic origin. 36% patients had moderate to severe anaemia. The median age was 14.4 (SD 1.9). The median dose was 800 mg [IQR 500-1000]. 57% received 1 dose, and 43% 2-3 doses. Compared with baseline mean pre-infusion haemoglobin content of reticulocytes of 21.4 pg (SD 7.3), a significant rise was seen at 3-7 days post-infusion (29.8 pg (SD 1.9), $p < 0.001$). Significant increase in haemoglobin and serum ferritin at 4-6 weeks post-infusion was observed (99.2 (SD 26.8) vs 128.9 (SD 19.4) g/L, $p<0.001$) and (7.6 [IQR 3.3-16] vs 135.6 [IQR 75-157.1] µg/L, $p<0.001$) respectively (Table 1). Hematologic responses to the two intravenous products were equivalent. Thirteen patients (93%) did not experience any adverse effects; one (7%) had mild effects. No severe hypersensitivity reactions were recorded.

Conclusion. IV iron therapy with LMWD and ISS effectively and safely treats menorrhagia-induced iron deficiency in paediatric females, significantly improving haemoglobin and iron

levels with minimal adverse effects. It may reduce transfusion needs in moderate-to-severe anaemia. Further research is needed to confirm these results and evaluate long-term safety and efficacy.

Evolution of osteonecrosis lesions in children and adolescents with Hodgkin lymphoma

by Henri Aarnivala | Mia Giertz | Sascha Wilk Michelsen | Caroline Björklund | Annika Englund | Marika Grönroos | Lisa Lyngsie Hjalgrim | Pasi Huttunen | Tuukka Niinimäki | Eva Penno | Tytti Pokka | Tuuli Pöyhönen | Päivi Raittinen | Susanna Ranta | Johan E Svahn | Lisa Törnudd | Arja Harila | Riitta Niinimäki | Department of Pediatrics, Oulu University Hospital, and Research Unit of Clinical Medicine, University of Oulu, Finland. | Department of Pediatric Oncology and Hematology, Uppsala University Hospital, and Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden. | Department of Pediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen, Denmark. | Department of Pediatric Hematology and Oncology, Umeå University Hospital, Umeå, Sweden. | Department of Pediatric Oncology and Hematology, Uppsala University Hospital, and Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden. | Department of Pediatrics, Turku University Hospital, Turku, Finland. | Department of Pediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen, Denmark. | Department of Pediatric Hematology, Oncology and Stem Cell Transplantation, New Children's Hospital, Helsinki University Hospital, Helsinki, Finland. | Department of Surgery, Oulu University Hospital, and Research Unit of Clinical Medicine, University of Oulu, Finland. | Department of Diagnostic Radiology, Uppsala University Hospital, Uppsala, Sweden. | Research Service Unit, Oulu University Hospital, Finland. | Department of Pediatrics, Kuopio University Hospital, Kuopio, Finland. | Centre for Child Health Research, Tampere University and University Hospital, Tampere, Finland. | Astrid Lindgren Children's Hospital, Karolinska University Hospital, and Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden. | Department of Pediatric Oncology, Skåne University Hospital, Lund University, Lund, Sweden. | Department of Pediatrics, Linköping University Hospital, Linköping, Sweden | Department of Pediatric Oncology and Hematology, Uppsala University Hospital, and Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden. | Department of Pediatrics, Oulu University Hospital, and Research Unit of Clinical Medicine, University of Oulu, Finland.

Abstract ID: 110
Themes: Late Effects
Presenter Name: Riitta Niinimäki
Keywords: Hodgkin, glucocorticoids, late effects, lymphoma, osteonecrosis

Introduction: The natural evolution of osteonecrosis (ON) lesions remains poorly understood and, despite its high incidence in Hodgkin lymphoma (HL), the prognosis of ON lesions has not yet been explored in children with HL.

Aim: This study investigated the radiological evolution of ON lesions in a Nordic population-based cohort of 489 consecutively treated pediatric HL patients as well as risk factors for adverse outcomes of ON.

Subjects & Methods: We identified 46 HL patients with ON and found a total of 202 ON lesions, out of which 77 were in the joints. We reviewed the magnetic resonance imaging (MRI) scans of these lesions to both confirm the diagnosis and grade the ON lesions using the Niinimäki classification.

Results: A median of six (range 1-16, interquartile range [IQR] 4-9) sites per patient were

affected with ON. Follow-up images were available for 146/202 lesions, with a median of three (range 1–13, IQR 3–7) follow-up MRI scans available. The median follow-up time was 13 (range 0–96, IQR 0–35) months from ON diagnosis. Among the lesions with follow-up images, 71% remained stable, 18% resolved completely, 8% improved, and 3% progressed. Hip ON required surgery in 29% of cases, yielding a 13-fold risk ($p < 0.001$) compared to other joint lesions. The higher the Niinimäki grade was at ON diagnosis, the lower was the likelihood for ON resolving. The chance for resolution halved for each year of increasing patient age, adjusted for sex and symptoms due to ON ($p < 0.01$).

Conclusion: Hip ON has an inferior prognosis compared to other joint sites in HL patients, and older patients have a worse outcome. As joint ON has the potential to both improve and progress, grade 3-4 ON lesions warrant close follow-up and possible interventions should be directed at such lesions.

EXPANDING INTRAVENOUS IRON OPTIONS IN PAEDIATRIC PATIENTS: SAFETY AND EFFICACY ASSESSMENT AT VILNIUS UNIVERSITY HOSPITAL SANTAROS CLINICS

by Bernatonytė Ernesta1 | Vaišnorė Ramunė2 | Šaulytė-Trakymienė Sonata3 | 1Faculty of Medicine, Vilnius University, Lithuania | 2 Institute of Data Science and Digital Technologies, Faculty of Mathematics and Informatics, Vilnius University, Lithuania | 3Clinic of Children's Diseases, Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, Vilnius University Hospital Santaros Clinics, Vilnius, Lithuania

Abstract ID: 108
Themes: Other
Presenter Name: Bernatonytė Ernesta
Keywords: anemia, intravenous iron, iron deficiency, iron isomaltoside, low molecular weight dextran

Introduction: In paediatric population, the use of intravenous iron (IV), particularly low molecular weight dextran (LMWD), remains limited, especially in younger children. There are no paediatric data on the use of iron isomaltoside (IIS).

Aim of the study: To assess the safety and efficacy of IV iron in pediatric patients with iron deficiency (ID) or iron deficiency anemia (IDA).

Methods: Retrospective data were collected from pediatric patients who received IV iron at Vilnius University Hospital Santaros Clinics between Jan 2021 and Dec 2023. Demographics, hematologic response, and adverse effects were analyzed using statistical tests. A t-test for repeated measures was applied to compare the means of measurements before and after treatment. The medians of repeated measurements were compared with the Wilcoxon signed rank exact test. P-values<0.05 were considered statistically significant.

Results: A total of 135 IV infusions were administered to 72 patients with ID (19.4%) and IDA (69.4%). The median age 13.5 years (IQR 6-15), with two patients below 12 months. LMWD was used in 30.2% of patients, while IIS was used in 69.4%. The mean pre-infusion and post-infusion hemoglobin content of reticulocytes was 18.1 (4.8) pg and 26.3 (5.2) pg, respectively, at 3-7 days after the initial infusion. Mean pre-infusion and post-infusion hemoglobin values were 89.5 (20.0) g/L and 122.8 (14.0) g/L, respectively (at 4-6 weeks after the initial infusion). Median serum ferritin increase was 113 µg/L post-infusion. The hematologic response did not differ between the two IV products. Sixty-eight patients (94.0%) experienced no adverse effects. One patient (4.5%) in the LMWD group and three (6.0%) in the IIS group experienced mild adverse effects. There were no severe hypersensitivity reactions.

Conclusion: Both LMWD and IIS demonstrated safety and efficacy, supporting their expanded use treating ID and IDA in the pediatric group.

FAMILIAL HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS SECONDARY TO UNC13D MUTATION (FHL3) IN A 37-DAY-OLD GIRL WITH CMV INFECTION: A CASE REPORT

by Smane, Liene | Kovaļova, Žanna | Grinēviča, Agnese | Mašinska, Madara | Kursīte, Santa | Valaine, Anna | Rascon, Jelena | 1.Department of Pediatrics, Children's Clinical University Hospital, Riga Stradins University, Riga, Latvia | 1. Department of Pediatrics, Children's Clinical University Hospital, Riga Stradins University, Riga, Latvia | 2. Children's Clinical University Hospital, Riga, Latvia | 2. Children's Clinical University Hospital, Riga, Latvia | 2. Children's Clinical University Hospital, Riga, Latvia | 2. Children's Clinical University Hospital, Riga, Latvia | Center for Pediatric Oncology and Hematology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

Abstract ID: 135
Themes: Other
Presenter Name: Smane, Liene
Keywords: Cytomegalovirus infection (CMV), Familial Hemophagocytic Lymphohistiocytosis (FHL), UNC13D

Introduction. Familial Hemophagocytic Lymphohistiocytosis (FHL3) is a rare genetic disorder, characterized by primary innate immunodeficiency, resulting in heightened T-lymphocyte and macrophage activity leading to aberrant cell proliferation. This condition causes multiorgan damage and dysfunction, including the spleen, liver, bone marrow, and brain. We report the first confirmed case of FHL3 in Latvia.

Case Description. We present the case of a 37-day-old girl admitted to the Children's Clinical University Hospital with persistent fever, hoarseness, skin rash, and an enlarged spleen. Laboratory results revealed cytopenia involving more than two cell lines, hypertriglyceridemia, hypofibrinogenemia, hyperferritinemia, elevated CRP, IL-6, LDH, ALT, AST, and increased D-dimers. Ultrasound revealed splenomegaly, gallbladder wall thickening unrelated to cholecystitis, and ascites. CMV DNA was detected in urine and blood. Following the diagnosis on September 21st, she underwent HLH-2004 protocol-based treatment, received intravenous Ganciclovir (when the CMV DNA copy number in the blood was above 1000), broad-spectrum antibiotics, and antifungal therapy for severe neutropenia and fever. On October 26th, cerebrospinal fluid changes were observed. This analysis utilized DNA isolated from blood leukocytes via the WES NGS technique. The identified pathogenic germline variants in the UNC13D gene were: 1.NM_199242.2:c.2346_2349del p.(Arg782SerfsTer12); 2. NM_199242.2:C.2625+2T>C r.splp. The patient underwent a bone marrow transplant on December 15th, utilizing stem cells from a matched unrelated donor. The latest post-transplant chimerism is 99%. The patient is currently in recovery.

Conclusions. Early diagnosis, adherence to the HLH-2004 protocol, and subsequent hematopoietic stem-cell transplantation are crucial in managing FHL. This emphasizes the importance of prompt complex treatment initiation to improve outcomes.

FOLLOW-UP ON THE MANAGEMENT OF METASTATIC EWING SARCOMA WITH 3-YEAR SURVIVAL

by Trakymas Gaudas Benediktas1 | Diglys Domantas3 | 1Faculty of Medicine, Vilnius University, Lithuania | 3Hematology, Oncology and Transfusion Medicine Center, Vilnius University Hospital Santaros Clinics, Vilnius, Lithuania

Abstract ID: 142
Themes: Solid Tumours
Presenter Name: Trakymas Gaudas Benediktas
Keywords: Cabozantinib, Ewing sarcoma, chemotherapy, electrochemotherapy, survival analysis.

Introduction. Our patient was diagnosed with Ewing sarcoma with ganglioneuroblastoma-like differentiation. Disease stabilisation was documented following first and second line chemotherapies.

Aim. To detail our long-term management strategies for a unique case of Ewing sarcoma.

Methods. Our patient is a 19-year-old male, diagnosed with EWSR1-ERG Ewing sarcoma 3 years ago with the primary tumour in the right iliac bone, as well as metastases in the lungs, liver and tenth thoracic vertebra. As first and second line treatments the patient was administered 8 alternating cycles of vincristine, doxorubicin, cyclophosphamide / ifosfamide, etoposide at 14-day intervals, followed by 12 irinotecan/temozolomide cycles. During the course of the last year, the patient was administered 6 cycles of Cyclophosphamide and Topotecan. The patient also underwent liver metastases electrochemotherapy and started receiving Cabozantinib as fourth-line chemotherapy.

Results. 4 months after the first and second line treatments and subsequent disease stabilisation in 2023, a follow-up full-body CT scan revealed new bilateral lesions in the lungs and a significant increase in one of the liver lesions (20cm->44 mm), with indolence of the primary lesion. Considering the relapse, 6 cycles of third-line chemotherapy were administered as well as an electrochemotherapy procedure, interrupted by ventricular fibrillation and successful cardiopulmonary resuscitation. The latest CT showed minor progression of the lung lesions, a new lung lesion, and a 25% reduction in liver metastasis size. The lung metastases were deemed highly mitotic upon post-resection histological evaluation. Given the progression, fourth-line chemotherapy with Cabozantinib was initiated. A PET/CT is scheduled to evaluate treatment effectiveness and determine future management.

Conclusions: Despite initial stabilisation, the patient has undergone extensive treatment, including third and fourth-line chemotherapies, due to metastatic Ewing sarcoma progression. Pending the outcome of current treatments, high-dose chemotherapy with autologous stem-cell transplantation remains a consideration for this unique case of Ewing sarcoma with long-term survival.

GENETIC PROFILING OF ESTONIAN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS AT DIAGNOSIS

by Keernik, Maria | Tammur, Pille | Lepik, Kristi | Saks, Kadri | Kõrgvee, Lenne-Triin | Mikkel, Sirje | Pohlak, Triin | Ilisson, Piret | Šamarin, Ustina | Kahre, Tiina | Tartu University Hospital, Genetics and Personalized Medicine Clinic, Estonia | Tartu University Hospital, Genetics and Personalized Medicine Clinic, Estonia | Tallinn Children´s Hospital, Department of Hematology and Oncology, Estonia | Tallinn Children´s Hospital, Department of Hematology and Oncology, Estonia | Tartu University Hospital, Hematology and Oncology Clinic, Estonia | Tartu University Hospital, Hematology and Oncology Clinic, Estonia | Tartu University Hospital, Hematology and Oncology Clinic, Estonia | Tartu University Hospital, Genetics and Personalized Medicine Clinic, Estonia | Tartu University Hospital, Genetics and Personalized Medicine Clinic, Estonia | Tartu University Hospital, Genetics and Personalized Medicine Clinic, Estonia

Abstract ID: 100
Themes: Leukemia
Presenter Name: Maria Keernik
Keywords: Genetics, Leukemia

Introduction

Acute lymphoblastic leukemia (ALL) is an aggressive malignancy of immature B or T lymphoid cells with the peak incidence in children aged 1 to 4 years. Molecular and cytogenetic aberrations play a crucial role in disease diagnosis, classification, and risk stratification.

Aim

To describe the genetic profile of pediatric ALL patients at diagnosis and find correlations between the genetic profile at diagnosis and long-term treatment outcomes.

Methods

The genetic profile of 23 Estonian pediatric ALL patients treated according to the ALLTogether protocol during 2020-2023 at Tartu University Hospital and/or Tallinn Children´s Hospital was examined. Comprehensive genetic profiling included karyotyping, FISH analyses, RT-PCR screening test for translocations (HemaVision), NGS panel analysis (TruSight Myeloid, Illumina), and chromosomal microarray analysis (CMA; HumanCytoSNP-12, Illumina).

Results

Among the 23 patients (aged 1-12y; 13 males/10 females), pre-B ALL was diagnosed in 21, and T-ALL in two cases.

Cytogenetic testing revealed t(12;21) in 11/23 (48%) and high hyperdiploidy in 3/23 (13%)

patients, both known to be indicators of favorable prognosis. At least one (likely) pathogenic variant was detected by NGS in 14 (61%) patients. The most commonly affected genes detected by NGS and/or CMA were *KRAS*, *CDKN2A/B*, *ETV6*, and *NOTCH1*.

The complete remission rate in our cohort is 90%. Two patients with pre-B ALL diagnosis experienced at least one relapse. One of them has a germline variant causing Lynch syndrome and predisposing him to malignancies. The second patient (died at age 12,5y) had several risk factors: age at diagnosis 11 years, somatic *CDKN2A/B* deletions leading to poor copy number alteration risk profile according to the ALLTogether protocol and four pathogenic variants on NGS panel analysis at different levels of allele frequency.

Conclusion

Our study emphasizes the importance of comprehensive genetic profiling of ALL patients, which is important for disease treatment, identifying risk factors, and prognosis prediction.

HAEMOPHILIA A AND VON WILLEBRAND DISEASE IN ONE INDIVIDUAL: A FAMILY CASE OF COMPLEX INHERITANCE AND DISEASE PREDISPOSITION IN OFFSPRING

by Morkūnaitė Agnė | Preikšaitienė Eglė | Kryžauskaitė Lina | Šaulytė Trakymienė Sonata | 1Faculty of Medicine, Vilnius University, Lithuania | 2Vilnius University, Faculty of Medicine, Department of Human and Medical Genetics, Vilnius, Lithuania | 3Hematology, Oncology and Transfusion Medicine Center, Vilnius University Hospital Santaros Clinics, Vilnius, Lithuania | 4Clinic of Children's Diseases, Institute of Clinical Medicine, Faculty of Medicine, Vilnius University, Vilnius University Hospital Santaros Clinics, Vilnius, Lithuania

Abstract ID: 138
Themes: Benign Hematology
Presenter Name: Morkūnaitė Agnė
Keywords: FVIII, Haemophilia A, Next Generation Sequencing, von Willebrand disease

Introduction.
While both Hemophilia A (HA) and von Willebrand Disease (VWD) are inherited bleeding disorders, their coexistence in one individual is relatively rare. This case explores the phenotypic and genetic characteristics of HA and vWD in two siblings following their father's confirmed diagnosis of both conditions.

Aim.
To understand the inheritance patterns and phenotypic manifestations associated with the pathogenic variants identified in a family.

Methods.
A 10-year-old boy and a 1-year-old girl were referred to our centre for phenotypic hemostasis testing. Father's coagulation phenotype: FVIII (%): 2-4, vWF:Ag (%): 14-17, vWF:Ac (%): <15. Next Generation Sequencing of the father's blood DNA identified a hemizygous pathogenic variant c.1492G>A in the F8 gene, a c.2435del in the VWF gene, and a compound heterozygous variant c.4751A>G in the VWF gene, classified as possibly pathogenic by in-silico predictors. The father's maternal cousin has also been diagnosed with mild HA (FVIII level of 18%) with the same variant in the F8 gene, however, without any pathogenic variants in the vWF gene.

Results.
No significant bleeding episodes were recorded in the boy's history, aside from ecchymoses on his legs attributed to soccer. In contrast, the girl experienced a prolonged 6-hour bleeding episode from a cut lip. Coagulation tests for vWD showed lower/normal-limit values in both children, with the boy and the girl respectively exhibiting FVIII (%): 155 and 126, vWF:Ag (%) 49 and 57, vWF:Ac (%) 45.6 and 52.9. Additionally, the girl was diagnosed with and treated for iron deficiency anaemia.

Conclusion.

The genetic analysis of the father indicated pathogenic variants suggest a familial predisposition to HA and vWD. The phenotypic expressions observed in the children further support the suspicion of vWD. These findings underscore the necessity for additional genetic counselling and cascade testing to assess the broader family implications and guide future medical decisions.

HYPERKALEMIA: UNRAVELLING THE DIAGNOSTIC CONUNDRUM AND EXPLORING DEHYDRATED HEREDITARY STOMATOCYTOSIS

by Augustė Lukošaitytė | Eglė Preikšaitienė | Vilnius University, Faculty of Medicine, Vilnius, Lithuania | Vilnius University, Faculty of Medicine, Department of Human and Medical Genetics, Vilnius, Lithuania

Abstract ID: 104
Themes: Other
Presenter Name: Sonata Šaulytė Trakymienė
Keywords: PIEZO1, dehydrated hereditary stomatocytosis, pseudohyperkalemia

We describe a family of three generations carrying *PIEZO1* pathogenic variants, for which the DHSt diagnosis was suspected upon discovery of pseudohyperkalemia. We provide an example how early genetic testing can prevent contraindicated treatment resulting in adverse events and explore variability of the phenotypes associated with *PIEZO1*.

IMPACT OF MINIMAL RESIDUAL DISEASE BEFORE HEMATOPOIETIC STEM CELL TRANSPLANTATION ON ITS OUTCOMES IN PEDIATRIC ACUTE MYELOID LEUKEMIA

by Greta Urbonavičienė | Center for Pediatric Oncology and Hematology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

Abstract ID: 143
Themes: Leukemia
Presenter Name: Greta Urbonavičienė
Keywords: acute myeloid leukemia, hematopoietic stem cell transplantation, minimal residual disease, survival.

Background. Minimal residual disease (MRD) was reported to predict outcomes in pediatric ALL. We aimed to assess pre-transplant MRD impact on HSCT outcomes in pediatric AML.

Methods. A retrospective analysis of 23 patients who underwent allo-HSCT for AML using uniform conditioning (busulfan, cyclophosphamide and melphalan) in 2013–2023 was performed. MRD was assessed before HSCT, on day +28, +60, +100. Negative MRD was defined as lower than 0.0001% or undetectable assessed either by flow cytometry or PCR or double-negative.

Results. Five (22%) patients received HSCT from HLA-identical siblings, 18 (78%) from MUD. Ten recipients (43%) were MRD-negative before HSCT. Thirteen patients (57%) showed positive MRD before HSCT with a median pre-transplant level of 0.185% [range 0.001 – 1.99%, IQR 0.103 - 0.788%]. In the MRD-positive group, one patient died before day +28, ten out of twelve assessable (83%) patients became MRD-negative on day +28. On the day +60, positive MRD was found in three patients – two of them became negative later on, the third one died due to AML relapse. None of pre-transplant MRD-negative patients showed MRD positivity at any time.

1/23 (4.3%) children died on refractory AML, 3/23 patients (13%) succumbed on TRM. Outcome comparison in pre-transplant MRD-negative vs positive patients revealed no difference in all key endpoints ($p > 0.05$): cumulative incidence of TRM at 1-year was 0.10% (+/- 0.1) vs 0.21% (+/- 0.15), 1-year RFS 1.00 vs 0.909 (95% CI 0.754 – 1.00), 1-year EFS 0.900 (95% CI 0.732 – 1.00) vs 0.808 (95% CI0.595–1.00) and 5-year OS 0.900 (95% CI 0.732 – 1.00) vs 0.727 (95% CI 0.503 – 1.00), respectively. Median follow-up was 2.2 [1.15 – 6.06] years.

Conclusions: Positive pre-transplant MRD was frequent in children transplanted for AML, however in our small cohort it did not affect significantly transplant although long-term OS tended to be inferior.

Initiation of long-term follow-up for childhood cancer survivors at Vilnius University Hospital Santaros Klinikos

by Monika Kapitancuke | Goda Elizabeta Vaitkeviciene | Jelena Rascon | Clinic of Children's Diseases, Institute of Clinical Medicine, Vilnius University Faculty of Medicine, Vilnius, Lithuania; Center for Pediatric Oncology and Hematology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania | Clinic of Children's Diseases, Institute of Clinical Medicine, Vilnius University Faculty of Medicine, Vilnius, Lithuania; Center for Pediatric Oncology and Hematology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania | Clinic of Children's Diseases, Institute of Clinical Medicine, Vilnius University Faculty of Medicine, Vilnius, Lithuania; Center for Pediatric Oncology and Hematology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania

Abstract ID: 94
Themes: Late Effects
Presenter Name: Monika Kapitancuke
Keywords: ALL-STAR study, Survivorship Passport, TREL project, childhood cancer survivors, long-term follow-up

Introduction. More than 80% of children, adolescents, and young adults who undergo cancer treatment become long-term survivors. However, up to 75% of them may experience late effects of their cancer treatment. The survival rate at Vilnius University Hospital Santaros Klinikos (VULSK) has increased to 80-90% over the years. A synergy of several collaborative research initiatives such as the EU-funded Horizon 2020 project TREL 'Twinning in Research and Education to Improve Survival in Childhood Solid Tumors in Lithuania" and the Nordic ALL-STAR platform for a population-based acute lymphoblastic leukemia (ALL) survivor cohort enhanced care and research of childhood cancer survivors. We aimed to describe our experience in structured survivorship care.

Results. The TREL project run in 2021-2023 aimed to improve the quality of survivorship by implementing the Survivorship Passport at VULSK. Moreover, it offered a chance to collaborate with experienced institutions and partners across Europe, gain knowledge and experience in childhood cancer late effects surveillance.

In March 2023, an outpatient clinic for late effects was launched in VULSK, where patients are seen once a week by a pediatric oncologist. Since then, 16 survivors, who are 5 years after diagnosis and up to 18 years of age, have started to be followed-up in the Late Effects Clinic. Over half of the patients experienced late effects, particularly after treatment for Ewing sarcoma and allogeneic hematopoietic stem cell transplantation. Additionally, 3 patients received counseling for long-term follow-up recommendations before transitioning to adulthood. Survivorship passports were issued for 5 survivors. From April 2023 to January 2024 32 survivors were enrolled in the ALL-STAR study, with a target of reaching around 100.

Conclusions. The TREL project has successfully initiated long-term follow-up of childhood cancer survivors in VULSK. Survivorship Passport and ALL-STAR study enhance

opportunities to continue the activities of the Late Effects Clinic.

INTESTINAL MUCOSITIS, SYSTEMIC INFLAMMATION AND BLOODSTREAM INFECTIONS FOLLOWING HIGH-DOSE METHOTREXATE TREATMENT IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA

by Sarah Weischendorff | Silvia De Pietri | Mathias Rathe | Malene Johanne Petersen | Claus Henrik Nielsen | Claus Moser | Klaus Müller | Department of Paediatrics and Adolescent Medicine, Rigshospitalet, University of Copenhagen, Denmark | Department of Paediatrics and Adolescent Medicine, Rigshospitalet, University of Copenhagen, Denmark | Hans Christian Andersen Children's Hospital, Odense University Hospital, Odense, Denmark | Department of Paediatrics and Adolescent Medicine, Rigshospitalet, University of Copenhagen, Denmark | Institute for Inflammation Research, Centre for Rheumatology and Spine Disease, Rigshospitalet, University of Copenhagen, Denmark | Department of Clinical Microbiology, Rigshospitalet, University of Copenhagen, Denmark | Department of Paediatrics and Adolescent Medicine, Rigshospitalet, University of Copenhagen, Denmark

Abstract ID: 118
Themes: Leukemia
Presenter Name: Sarah Weischendorff
Keywords: Acute lymphoblastic leukaemia, Bloodstream infections, CCL20, Citrulline, High-dose methotrexate, Intestinal mucositis, Systemic inflammation

Introduction: Intestinal mucositis (IM) increases the risk of bloodstream infections (BSI) and inflammatory toxicity during acute lymphoblastic leukemia (ALL) induction treatment. However, the implications of IM in subsequent ALL therapy phases remain unknown.

This study investigated the relationship between IM (measured by plasma citrulline and the chemokine CCL20) and the development of bloodstream infections (BSI) and systemic inflammation (reflected by C-reactive protein, CRP) in children with ALL during high-dose methotrexate (HDMTX) treatment, an important part of ALL consolidation therapy.

Methods: The study included patients treated according to the NOPHO ALL 2008 protocol (n=52) and the ALLTogether1 protocol (n=42), both with identical HDMTX procedures but different scheduling. Plasma samples for citrulline and CCL20 analyses were collected on the day of initial HDMTX administration and one week after, along with the registration of CRP. BSI occurrence was registered within the first three weeks post-HDMTX. Data were analysed using mixed model repeated measures analyses for time and group comparisons and Spearman's rank-order correlation.

Results: Post-HDMTX, citrulline dropped to median levels of 14.5µM and 16.9µM for patients treated according to the NOPHO ALL 2008 and ALLTogether1 protocols, respectively (p=0.11). Patients with hypocitrullinaemia (<10µmol/L) had higher risk of BSI (4/14; 29%) than patients without hypocitrullinaemia (1/72; 1.4%) (OR=28.4, p=0.0021). Patients treated according to the NOPHO ALL 2008 protocol exhibited increased mucosal and systemic inflammation post-HDMTX compared to patients treated according to

ALLTogether1, with increased CCL20 (14.6pg/ml vs. 3.7pg/ml, $p<0.0001$) and CRP levels (10.0 mg/l vs. 1.0 mg/l, $p<0.0001$). Both citrulline and CCL20 correlated with CRP for these patients ($r_s=-0.44$, $p=0.0016$ and $r_s=0.35$, $p=0.016$, respectively).

Conclusion: These results suggest that hypocitrullinaemia (indicating severe IM) following HDMTX increases the risk of BSI, confirming previous observations from more intensive treatments. Moreover, the NOPHO ALL 2008 protocol caused a more severe mucosal and systemic inflammatory response after HDMTX compared to the ALLTogether1 protocol.

INVESTIGATING THE EFFECT OF COMBINING IMPDH INHIBITION WITH CYTARABINE IN KMT2A-FUSION AML

by Yolande Klootsema | Nikolas Herold | Ingrid Lilienthal | Division of pediatric oncology and surgery, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden | Division of pediatric oncology and surgery, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden, and Paediatric Oncology, Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm, Sweden | Division of pediatric oncology and surgery, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden

Abstract ID: 117
Themes: Leukemia
Presenter Name: Yolande Klootsema
Keywords: AML, Cytarabine, Drug resistance, Mycophenolate Acid

Rearrangement of the *KMT2A* gene occurs in up to 20% of children with acute myeloid leukaemia (AML). *KMT2A*-rearranged paediatric AML is more resistant to standard therapy and is associated with inferior outcomes. Despite the established use of cytarabine (ara-C) in AML induction and relapse therapy, resistance is common and hinders effective therapy. Our previous studies have defined SAMHD1 as a resistance factor for ara-C. SAMHD1 inhibition with hydroxyurea combined with ara-C increases active ara-C metabolites and improves its anti-leukemic effect in vitro, in vivo, and in a recent clinical trial for adults with primary AML. Inosine monophosphate dehydrogenase (IMPDH) is a crucial enzyme in guanine nucleotide synthesis, and recent studies have found that its inhibition is effective in limiting *KMT2A*-fusion AML proliferation in vitro and in vivo. We have data suggesting IMPDH inhibitors (IMPDHi) can inhibit SAMHD1. The goal of this research is to investigate the role of IMPDH inhibition in combination with ara-C in *KMT2A*-rearranged AML cell lines, and to characterize the role of SAMHD1 on the effect of IMPDHi and IMPDHi/ara-C combinations.

For these studies, we will use a panel of SAMHD1-positive or -negative AML cell lines with or without the *KMT2A*-rearrangement. We will use the IMPDHi mycophenolate acid both alone and in combination with ara-C. Cell proliferation inhibition will be assessed using an ATP-based viability assay and dose-response curves will be generated in GraphPad Prism. Drug synergy will be measured using an online tool. Depending on project progression, our investigation will delve into cellular mechanisms governing cell death, encompassing apoptosis, enzyme function, and checkpoint activation. Our preliminary results show that IMPDHi is effective in limiting AML proliferation, and that ara-C can be more effective in its presence, suggesting that this combination may be an effective therapy for *KMT2A*-rearranged AML.

Late Pulmonary Adverse Effects in Acute Lymphoblastic Leukemia Childhood Survivors; A national cross-sectional NOPHO ALL2008 study

by Sonja Izquierdo Meyer | Mette Tiedemann Skipper | Birgitte Klug Albertsen | Ruta Tuckuviene | Peder Skov Wehner | Thomas Leth Frandsen | Kjeld Schmiegelow | Liv Andrés-Jensen | Kim Gjerum Nielsen | Sune Leisgaard Mørck | Department of Clinical Medicine, Aarhus University. Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital | Department of Clinical Medicine, Aarhus University. Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital | Department of Clinical Medicine, Aarhus University. Center for Children and Adolescents with Cancer, Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital | Department of Paediatrics and Adolescent Medicine, Aalborg University Hospital | Department of Paediatric Hematology and Oncology, Odense University Hospital | Department of Paediatrics and Adolescent Medicine, Copenhagen University Hospital, Rigshospitalet | Department of Paediatrics and Adolescent Medicine, Copenhagen University Hospital, Rigshospitalet. Institute of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen | Department of Paediatrics and Adolescent Medicine, Copenhagen University Hospital, Rigshospitalet | Institute of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen. Danish PCD & chILD Centre, CF Centre Copenhagen, Copenhagen University Hospital, Rigshospitalet | Department of Clinical Medicine, Aarhus University. Danish Center of Paediatric Pulmonology and Allergology, Department of Paediatrics and Adolescent Medicine, Aarhus University Hospital

Abstract ID: 103
Themes: Late Effects
Presenter Name: Sonja Izquierdo Meyer
Keywords: Acute lymphoblastic leukemia, late effects, pulmonary adverse effects, pulmonary function

Enhanced survival rates in childhood acute lymphoblastic leukemia (ALL) are attributed to more intensified treatment protocols and improved supportive care, but unfortunately comes with a significant cost. Pulmonary toxicities are common during ALL treatment. Thus, long-term risk of late pulmonary adverse effects (LPAE), including pulmonary function (PF) deficit and pulmonary symptomatology (PS), may persist as significant concerns. Previous studies lack control matching and exclusion of obsolete radiation therapy. Addressing these gaps, we aim to uncover LPAE in a childhood ALL survivor cohort treated on the NOPHO ALL-2008 protocol.

This national cross-sectional study at Aarhus and Copenhagen University Hospital (Feb 2019 - Mar 2024) includes participants aged 5-17.9 at examination. ALL survivors (N=317) and age- and gender matched controls were recruited for anthropometric examination, PF testing and PS online questionnaires according to the danish ALL-STAR study protocol eligibility criteria. ALL survivors' disease and treatment characteristics were collected from the NOPHO registry. The primary and secondary outcomes are mean difference in PF and PS in ALL survivors vs. controls.

206 survivors (≥1 lung test, N=191) and 219 controls (≥1 lung test, N=206) have

participated. Preliminary descriptive statistics indicate groups with comparable mean age, sex, and smoking habits ($p<0.05$). Data collection completes by March 2024 and data will be analyzed for publication in 2024.

Irrespective of the study findings, this study is positioned to provide valuable insights into LPAE impact in childhood ALL survivors and to optimize pulmonary follow-up management strategies for clinicians in these patients concerning LPAE prevention, early diagnosis and treatment.

MALIGNANCY-ASSOCIATED HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN SWEDEN: INCIDENCE, CLINICAL CHARACTERISTICS AND SURVIVAL

by Henter, Jan-Inge | Löfstedt, Alexandra | Jädersten, Martin | Meeths, Marie | Childhood Cancer Research Unit, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden; Astrid Lindgrens Children's Hospital, Karolinska University Hospital, Stockholm, Sweden | Astrid Lindgrens Children's Hospital, Karolinska University Hospital, Stockholm, Sweden | Department of Hematology, Karolinska University Hospital, Stockholm, Sweden; Center for Hematology and Regenerative Medicine, Department of Medicine, Karolinska Institutet, Stockholm, Sweden | Childhood Cancer Research Unit, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden; Astrid Lindgrens Children's Hospital, Karolinska University Hospital, Stockholm, Sweden

Abstract ID: 101
Themes: Benign Hematology
Presenter Name: Jan-Inge Henter
Keywords: hemophagocytic lymphohistiocytosis, incidence, malignancy-associated

INTRODUCTION: We aimed to evaluate malignancy-associated hemophagocytic lymphohistiocytosis (mal-HLH) in Sweden regarding population-based incidence, clinical features, and survival.

METHODS: The entire Swedish population 1997-2018 was studied. With the Swedish National Patient Registry, we identified patients with HLH-associated diagnoses that also had malignancies. The ICD-10 diagnoses D76.0-D76.3 and C96.0 were used to identify histiocytic disorders, and those with a registered malignant diagnosis (C00-C97 in ICD-10) on 2018-12-31 were included.

RESULTS: During 1997-2018, we identified 307 adults (≥18 years old) and 9 children (209 males, 107 females; P<0.001) with both an HLH-related diagnosis and malignant disease, corresponding to 0.19/100,000 adults annually (0.15/100 000 for the entire population), increasing from 0.026 (1997-2007) to 0.34 (2008-2018) (P<0.001). In the latest 7-year period (2012-2018), the annual incidence was 0.45/100,000 adults (n=246). This incidence varied between the 6 health-care regions in Sweden, from 0.18 to 0.71 (Region Stockholm) per 100,000 adults annually (P<0.001), likely due to variable awareness.

Mal-HLH was reported in 0.6% of all hematological malignancies, with the highest proportion (2.5%) in young males. Among the 316 patients, the 1-month probability of survival, likely representing the HLH episode, increased significantly from 52% 1997-2007 to 71% 2008-2018, whereas 2-year survival remained poor (25%). Altogether, 52% were lymphomas, 29% leukemias, 8% other hematological malignancies, and 11% solid tumors. Males were more affected than females (P=0.0012).

Of the nine children (median age 8 years; 4-17), five had ALL, one AML, two B-cell lymphomas, and one a NK/T-cell lymphoma. The probability of survival at 1 and 2 months

was 89%, and at 1 and 2 years 64%; median follow-up 25 months (range 1-203).

CONCLUSIONS: The annual mal-HLH incidence increased 10-fold and was at least 0.71/100,000 adults 2012-2018, i.e., 0.62/100,000 adults considering 13% estimated HLH over-reporting, and that early survival improved significantly, likely due to increased awareness and more HLH-directed therapy.

MATCHED RELATED DONOR –DERIVED ACUTE LYMPHOBLASTIC LEUKEMIA IN A PATIENT WITH MYELODYSPLASIA AND ATAXIA CAUSED BY DE NOVO SAMD9 VARIANT

by Tekla Harju | Jussi-Pekka Tolonen | Elisa Rahikkala | Outi Kuismin | Maria Suo-Palosaari | Reetta Hinttala | Johanna Uusimaa | Riitta Niinimäki | 1. Research Unit of Clinical Medicine, University of Oulu, Oulu, Finland; 2. Department of Children and Adolescents, Oulu University Hospital, Oulu, Finland | 1. Research Unit of Clinical Medicine, University of Oulu, Oulu, Finland 2. Department of Children and Adolescents, Oulu University Hospital, Oulu, Finland 3. Medical Research Center, University of Oulu and Oulu University Hospital, Oulu, Finland | 1. Research Unit of Clinical Medicine, University of Oulu, Oulu, Finland 3. Medical Research Center, University of Oulu and Oulu University Hospital, Oulu, Finland 4. Department of Clinical Genetics, Oulu University Hospital, Oulu, Finland | 1. Research Unit of Clinical Medicine, University of Oulu, Oulu, Finland; 4. Department of Clinical Genetics, Oulu University Hospital, Oulu, Finland | 5. Department of Diagnostic Radiology, Oulu University Hospital, Oulu, Finland. 6. Research Unit of Health Sciences and Technology, Oulu University Hospital and University of Oulu, Oulu, Finland | 1. Research Unit of Clinical Medicine, University of Oulu, Oulu, Finland; 3. Medical Research Center, University of Oulu and Oulu University Hospital, Oulu, Finland; 7. Biocenter Oulu, University of Oulu, Oulu, Finland | 1. Research Unit of Clinical Medicine, University of Oulu, Oulu, Finland; 2. Department of Children and Adolescents, Oulu University Hospital, Oulu, Finland; 3. Medical Research Center, University of Oulu and Oulu University Hospital, Oulu, Finland | 1. Research Unit of Clinical Medicine, University of Oulu, Oulu, Finland; 2. Department of Children and Adolescents, Oulu University Hospital, Oulu, Finland

Abstract ID: 124
Themes: Leukemia
Presenter Name: Tekla Harju
Keywords: HSCT, SAMD9 gene, donor-derived leukemia, functional analysis, multiorgan syndrome

Germline *SAMD9* mutations predispose to childhood myelodysplastic syndrome (MDS) with monosomy 7 or deletion of 7q. Based on current understanding, constitutional variants in the *SAMD9* gene, or its paralog *SAMD9L* on the chromosome 7q21, cause a *SAMD9/9L* syndrome—multiorgan disorder spectrum—which includes MDS, neurological symptoms, growth restriction and organ dysfunctions. The proposed disease mechanism is caused by gain-of-function (GOF) variants enhancing the growth restriction quality of SAMD9/9L protein.

We describe a patient with *de novo SAMD9* variant c.4691G>A(p.(Gly1564Asp)). Genetic predisposing syndrome was suspected during an episode with severe infection and esophageal achalasia at the age of 13 years. At five months, the patient was diagnosed with MDS with monosomy 7 and treated with hematopoietic stem cell transplant (HSCT) from a matched sibling donor. Complete blood count had shown abnormalities already at two months of age. Other symptoms included intrauterine growth restriction, ataxia, spasticity, learning difficulties, severe infections, diarrhea, and bronchopulmonary symptoms. The patient’s variant is classified as likely pathogenic (PS2,PM2,PM5,PP3) based on the

American College of Medical Genetics and Genomics classification. Functional laboratory analyses show conflicting results of the variant's ability to inhibit HEK293 cell growth.

Fourteen years after the HSCT, acute lymphoblastic leukemia originated from the donor cells. Patient died after a relapse. No *SAMD9* variant was detected with high read depth sequencing from parents' fibroblasts. Karyotyping of the parents was normal. A less than 1 % risk of gonadal mosaicism could cause the sibling donor to have the same *SAMD9* variant as the patient. The healthy sibling donor was given genetic counseling, but no genetic testing has been done so far.

We hypothesize that constitutional *SAMD9* variants may affect the non-hematopoietic cells of the bone marrow niche and harbor a risk for developing hematological malignancies after HSCT. More information is needed on long-term HSCT survivors with germline predisposing syndromes.

MATURE CYSTIC GASTRIC TERATOMA: AN UNUSUAL PRESENTATION OF SEVERE ANAEMIA IN INFANCY

by Uža Tautvydas | Venckutė Greta | Rutkauskienė Giedrė | Klimaitė Justina | Hospital of Lithuanian University of Health Sciences - Kaunas Clinics, Lithuania | Hospital of Lithuanian University of Health Sciences - Kaunas Clinics, Lithuania | Hospital of Lithuanian University of Health Sciences - Kaunas Clinics, Lithuania | Hospital of Lithuanian University of Health Sciences - Kaunas Clinics, Lithuania

Abstract ID: 113
Themes: Solid Tumours
Presenter Name: Uža Tautvydas
Keywords: ANAEMIA, GASTRIC TERATOMA, MATURE TERATOMA

Gastric teratomas are rare and typically occur in infant boys.

A 4-month-old boy was admitted to the hospital for sluggishness, feeding difficulties and rhinorrhea. After a blood test, he was diagnosed with severe normocytic normochromic anaemia (Hb 63 g/l) with increased reticulocytes (9,98 %). Additional tests for causes of anaemia were performed: ferritin, vitamin B12, folic acid, bilirubins, LDH, and haptoglobin levels were normal. During physical evaluation, a palpable mass under the rib cage was detected. On abdominal ultrasound, a 9 x 6 cm (sized) polymorphic formation was observed in the upper part of the left lateral canal of the peritoneal cavity, most likely a gastric teratoma. Tumour markers were performed - Ca19-9 126,5 kU/l; CEA 2,5 mcg/l; AFP 120,1 kU/l; bHCG: 0,5 U/l. Abdominal computed tomography (CT) showed a 7,9 cm x 5,4 cm heterogeneous mass visible in the stomach wall, with a fatty component and some intratumoral polymorphous calcinates - gastric teratoma. Due to severe anaemia, a blood transfusion was given and the patient was prepared for the surgery. The tumour growing beyond the gastric fundus, both exo- and endophytically, was removed during laparotomy. Also, gastric fundus resection with anterior fundoplication was performed. Histologically, the tumour was identified as a mature cystic teratoma of the stomach. The resection margins were free of tumour. After 3 months follow-up: Ca19-9 13 kU/l, AFP 18,3 kU/l, Hb 117 g/l, abdominal ultrasound and CT - no recurrence or metastasis.

These embryonic neoplasms typically present with a palpable abdominal mass; they are benign and associated with a good prognosis.

PALLIATIVE ANALGESIA IN CHILDHOOD CANCER PATIENTS: A RETROSPECTIVE ANALYSIS

by Erika Rouhento | Susanna Vuorenoja | Maija Kalliomäki | Sauli Palmu | Tampere University Hospital, Finland | Tampere University Hospital, Finland | Tampere University Hospital, Finland | Tampere University Hospital, Finland

Abstract ID: 112
Themes: Other
Presenter Name: Erika Rouhento
Keywords: analgesia, paediatrics, palliative care

Brief introduction: Pain the most prominent symptom of paediatric palliative patients. Even though modern medicine provides multimodal approaches to treating pain, pain is undertreated in 30 % of these patients.

Aims: The objective of this study was to find out how pain was addressed and treated in a tertiary University Hospital paediatric palliative care during a ten-year-period 2013-2022.

Methods: This is a single center cohort study. All childhood cancer patients treated in palliative care in Tampere University Hospital were included. Patient records were sought for palliative diagnosis, age, sex, duration of palliative period, pain medication or other treatment modality, effects, and side effects.

Summary: We identified 35 patients, aged 1-19 years (median 9,1 years) of which 24 were female. Twenty-three patients had the ICD10 diagnosis of palliative care recorded in the diagnoses. The palliative phase lasted 1 - 491 days and was carried out at home in 15 cases. CNS tumours had affected 15 of the patients, other diagnoses were sarcoma, neuroblastoma, acute lymphoblastic leukaemia, and hepatocellular cancer. All patients were on acetaminophen. Non-steroidal anti-inflammatory drugs were given to 24, morphine to 29, oxycodone to 21, fentanyl to 31, methadone to 3, tramadol to 1, gabapentinoids to 13, amitriptyline to 9, anaesthetic blocks to 3, radiation therapy for analgesia to 10 patients and 5 patients had a procedure, such as drainage, to alleviate pain and discomfort. The patient data concerning effects and side effects was utterly heterogenous.

Conclusions: The WHO analgesic ladder was followed during the palliative care. Pain, its treatment, effects and side effects benefit from a systematic approach and this should be the basis for future studies.

PARIS-TROUSSEAU SYNDROME WITH MULTISYSTEM INVOLVEMENT IN A PATIENT WITH JACOBSEN SYNDROME

by Trakymas Gaudas Benediktas1 | Nemanienė Rolanda2 | Burnytė Birutė3 | 1Faculty of Medicine, Vilnius University, Lithuania | 2Center for Pediatric Oncology and Hematology, ilnius University Hospital Santaros Clinics, Vilnius, Lithuania | 3Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

Abstract ID: 141
Themes: Benign Hematology
Presenter Name: Trakymas Gaudas Benediktas
Keywords: 11 chromosome deletion, Jacobsen syndrome, Paris-Trousseau syndrome, thrombocytopenia

Introduction:

Jacobsen syndrome is a rare chromosomal disorder resulting from a deletion in the long arm of chromosome 11. While it is known for distinctive facial features, multisystem anomalies, and intellectual disability, the critical role of haematological surveillance and intervention cannot be overlooked due to associated blood disorders and platelet dysfunction.

Aim:

To explore the haematological complications and multisystem anomalies associated with Jacobsen and Paris-Trousseau syndromes.

Methods:

We evaluated a two-year-old girl with thrombocytopenia and neutropenia suspected of myelodysplastic syndrome (MDS). Her diagnostic workup included medical history review, laboratory tests, and genetic analysis.

Results:

The patient's haematological profile displayed persistent thrombocytopenia from birth (113 ×109/L) - a finding consistent with Paris-Trousseau syndrome, fluctuating platelet counts (32-70 ×109/L), and mild leukopenia (3-4 ×109/L) with neutropenia (1-1.5 ×109/L). Bone marrow trephine biopsy showed MDS characteristics, notably disturbed architecture and massive megakaryopoiesis hyperplasia/dysplasia. Flow cytometry revealed a low percentage of myeloid lineage blasts in bone marrow. Cytological examination showed hypocellular smears, with erythropoiesis displaying normoblastic features with minimal dysplasia. Despite these significant haematological findings, other system reviews revealed multiple congenital anomalies: hearing impairment, elevated anti-thyroid peroxidase antibody levels, omphalocele, kidney hydronephrosis and cardiac defects, such as ventricular and atrial septal defects, requiring surgical intervention - all aligning with Jacobsen syndrome's typical

multisystem involvement. Patient had distinctive facial features, such as short nose, depressed nasal bridge, and short neck. Single nucleotide polymorphism (SNP) array analysis revealed a deletion of 11.68 Mb in size of chromosome region 11q24.1q25.

Conclusion:

This case underscores the importance of early recognition and comprehensive management of Jacobsen and Paris-Trousseau syndromes, emphasising collaborative healthcare efforts to optimise patient outcomes. Further research is needed to enhance our understanding of its pathophysiology and improve therapeutic strategies.

POOR PERFORMANCE OF CLINICAL RISK MARKERS OF BLOOD STREAM INFECTIONS GUIDING ANTIBIOTIC TREATMENT IN CHILDREN WITH ACUTE MYELOID LEUKEMIA

by Carla Warley Kjær | Maria Ebbesen Sørum | Sarah Weischendorff | Marianne Hoffmann | Henrik Hasle | Klaus Müller | Department of Pediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen, Denmark | Department of Pediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen, Denmark | Department of Pediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen, Denmark | Department of Pediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen, Denmark | Department of Pediatrics, Aarhus University Hospital, Aarhus, Denmark | Department of Pediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen, Denmark

Abstract ID: 129
Themes: Leukemia
Presenter Name: Carla Warley Kjær
Keywords: AML, antibiotics, blood stream infections, fever, neutropenia

Introduction: Initiation of antibiotics during treatment of acute myeloid leukemia (AML) is guided by fever during periods of neutropenia. However, fever is a non-specific symptom and carries a risk of over-treatment with potentially significant side effects. This study described fever occurrence alongside dynamics of C-reactive protein (CRP), absolute neutrophil count (ANC), and clinical mucositis in relation to bacterial and fungal blood stream infections (BSI) during AML induction treatment.

Methods: Twenty children (1-16 years) with AML were studied during the first four weeks of Induction I treatment (NOPHO-DBH AML 2012). Clinical data were collected retrospectively. Results are presented as median (range).

Results: During Induction I, 5/20 patients (25%) developed BSI with median onset on day 14 (11-26). All 20 patients received intravenous antibiotics.

Fever occurred in 18/19 patients (95%). The number of fever days was similar in patients with and without BSI (4 [2-8] days vs. 4.5 [0-11] days), and only 17 (19%) of the 89 total fever days were BSI-related.

CRP levels $\geq$50 mg/L were observed in 16/20 (80%) patients and were similar in patients with and without BSI (prior to onset) with maximal levels of 45 (1-106) mg/L vs. 151 (3-210) mg/L, P=0.04. CRP was normal at the onset of BSI (9 mg/L [1-106]), and ANC was comparable between patients with and without BSI at the timepoint of debut (ANC day 14: $0.01x10^9$ cells/L [0.01-0.02] vs. $0.01x10^9$ cells/L [0.01-0.14]).

BSI was more frequent in patients with oral or intestinal mucositis than in patients without mucositis (43% vs. 13% and 40% vs. 0%, respectively).

Conclusion: Fever and CRP were poor at predicting antibiotic-requiring neutropenic infections. Clinical mucositis was associated with BSI, holding promise as a significant risk factor to improve targeted use of antibiotics. Measurements of plasma citrulline, a quantitative marker of intestinal mucositis, are pending and will be presented at the conference.

Abstract NOPHO 2024

QUALITY OF LIFE IN CHILDREN AND ADOLESCENTS AFTER TREATMENT FOR ACUTE LYMPHOBLASTIC LEUKEMIA ACCORDING TO THE NOPHO ALL2008 PROTOCOL

Authors: Mogensen, Nina[1,2*], Kreicbergs, Ulrika[1,3], Albertsen, Birgitte Klug [4,5], Lähteenmäki, Päivi M[6,7], Heyman, Mats [1,2], Harila, Arja[8]

[1] Childhood Cancer Research Unit, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden
[2] Department of Pediatric Oncology, Karolinska University Hospital, Stockholm, Sweden
[3] Department of Health Care Sciences, Palliative Research Centre, Marie Cederschiöld University, Stockholm, Sweden
[4] Department of Pediatrics and Adolescent Medicine, Aarhus University Hospital, Aarhus, Denmark
[5] Department of Clinical Medicine, Faculty of Health, Aarhus University, Aarhus, Denmark
[6] Turku University Hospital, University of Turku, and FICAN-West, Turku, Finland
[7] Swedish Childhood Cancer Registry, Karolinska Institutet, Stockholm, Sweden
[8] Department of Women's and Children's Health, Uppsala University and Pediatric Oncology, Uppsala University Hospital, Uppsala, Sweden

Keywords: Quality of life, leukemia, questionnaire, patient-reported outcome measures (PROM)

Introduction and aim: The improved outcome of childhood acute lymphoblastic leukemia (ALL) over the last decades has increased the importance of assessing late effects and health-related quality of life (HRQOL), particularly when evaluating and comparing outcomes in clinical trials. This study aimed to assess HRQOL in children treated for ALL according to the NOPHO ALL2008 protocol.
Methods: Children, aged 1- <18 years at diagnosis, alive in first remission, and their parents, were asked to complete PedsQL 4.0 Generic Core Scales (self and proxy-report) at ≥6 months after end of therapy. Data on socioeconomic factors and parent-reported toxicity were collected through a study-specific questionnaire, and the NOPHO ALL2008 database was used to identify eligible families and add additional disease- and treatment-related data. Data was collected during 2013-2019 in Sweden, Finland, and Denmark.
ANOVA was used to compare mean differences in HRQOL scores between treatment arms, simple linear regression was used to evaluate association between treatment-related and socioeconomic factors and HRQOL scores, and multiple linear regression analysis was used to model these associations.
Results: A total of 299 children were included. The older children (8 years and older) reported similar HRQOL scores compared to Finnish reference data, except lower scores for School Functioning in high risk patients. Scores from the parent-proxy and self-reports from 5–7-year-olds were notably lower than reference. Parent-reported toxicity was associated with lower total and physical HRQOL scores in adjusted models for younger as well as older children in the self-report and parent-proxy versions, and also with lower psychosocial score in the parent-proxy.
Conclusions: Self-reported HRQOL was similar to reference population. The most important determinant for HRQOL after end of ALL treatment was parent-reported toxicity during treatment. Thus, minimizing complications is an obvious focus for future treatment protocols.

REDUCED QUALITY OF LIFE AFTER CHILDHOOD LANGERHANS CELL HISTIOCYTOSIS: CAN WE MAKE A CHANGE?

by von Bahr Greenwood, Tatiana (1,2) | Sveijer, Malin (1,3) | Gavhed, Désirée (1) | Hertzberg, Helena (1) | Zander, Eric (4) | Henter, Jan-Inge | (1)Childhood Cancer Research Unit, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden; (2)Pediatric Oncology, Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm, Sweden | (1)Childhood Cancer Research Unit, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden; (3)Department of Pediatrics, Eskilstuna Hospital, Eskilstuna, Sweden | (1)Childhood Cancer Research Unit, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden | (1)Childhood Cancer Research Unit, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden | (4)Center of Neurodevelopmental Disorders Karolinska Institutet, Center for Psychiatry Research, Department of Women\'s and Children\'s Health, Stockholm, Sweden | (1)Childhood Cancer Research Unit, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden; (2)Pediatric Oncology, Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm, Sweden

Abstract ID: 134
Themes: Late Effects
Presenter Name: Tatiana von Bahr Greenwood
Keywords: Langerhans cell histiocytosis, depression, fatigue, pain, quality of life

Langerhans cell histiocytosis (LCH) is an inflammatory myeloid neoplasia with variable clinical presentation, from self-healing single lesions to multisystemic potentially fatal disease. Long-term consequences, including progressive central nervous system (CNS) neurodegeneration, are common. In this cross-sectional postal survey we aimed to investigate how LCH affects long-term everyday life. All individuals ≥10 years of age diagnosed with LCH in childhood ≥5 years ago in Stockholm during 1990-2014 were invited to participate, answering self- and parent-report questionnaires assessing health-related quality-of-life (HRQOL), fatigue, pain, depression, and attention deficits. Non-parametric statistics were used to analyze survey data and Pearsons' correlation for associations between variables. Thirty-two of 61 eligible individuals (52%) responded; they had more extensive disease, more often systemic treatment and CNS involvement than non-responders, who were not analyzed further. Responders' (n=32) median time from diagnosis was 17.5 years. Overall, 14/32 (44%) had had multisystemic disease, including four (12.5%) with risk organ involvement, and 17/32 (53%) had received systemic treatment. Five (16%) had CNS involvement, all with neurodegeneration. Mean total HRQOL score was 78.8 and mean total fatigue score 68.7 (Pediatric Quality of Life Inventory). Five (16%) had a neuropsychiatric diagnosis. In patients ≥15 years, 42% reported long-lasting pain and 27% had scores indicating depression. Poorer HRQOL correlated with fatigue, symptoms of depression and attention deficits. Interestingly, best HRQOL was reported from a majority of patients with single system disease and with multisystemic disease with longest duration of systemic treatment. We conclude that patients with childhood LCH report high

frequencies of fatigue, long-lasting pain, and symptoms of depression and attention deficit in the long-term, which are associated with poorer quality-of-life and should be evaluated at follow-up for early intervention. We also raise the question if longer treatment may reduce long-term consequences and have a positive impact on perceived quality of life.

Sacrococcygeal teratomas in children and adolescents – a Danish 26-year retrospective cohort study

by Line Walther Lundbæk Siggaard | Mark Bremholm Ellebæk | Jesper Sune Brok | Mathias Rathe | Department of Pediatric Oncology and Hematology, H. C. Andersen Children's Hospital, Odense University Hospital, Odense, Denmark | Department of Surgery, Odense University Hospital, Odense, Denmark | Department of Pediatric and Adolescent Hematology and Oncology, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark | Department of Pediatric Oncology and Hematology, H. C. Andersen Children's Hospital, Odense University Hospital, Odense, Denmark

Abstract ID: 96
Themes: Solid Tumours
Presenter Name: Line Walther Lundbæk Siggaard
Keywords: Sacrococcygeal teratoma, incidence, mortality, pediatric, recurrence, sequelae.

Background: Sacrococcygeal teratomas (SCT's) are the most common extragonadal germinal cell tumors in infants and neonates. Despite of curative treatment, a large part of the patients experience sequelae which affects quality of life. Objectives were to describe the incidence, recurrence- and mortality rates and sequelae of SCT's in children and adolescents in Denmark.

Materials and methods: We conducted a nationwide retrospective register-based cohort study of all Danish children aged ≤18 years diagnosed with pathologically verified SCT in the period 1995-2021 using four national databases on pathology, health, fetal medicine, and childhood cancer. Date of diagnosis was defined as the date of pathologically verified sacrococcygeal teratoma.

Results: We identified 62 patients with a gender ratio of 4.6:1 in favor of females, and a median age at diagnosis of 18 days (range 0 days-17 years). The incidence of SCT was 1 out of 27,513 live births. Mature tissue was found in 48%, 34% contained immature tissue, and 18% had malignant tumors. Associated anomalies in the nervous-, cardiac-, urogenital and/or musculoskeletal systems were identified in 16% of cases. At last follow-up, 27%, 25%, and 5% had urological sequelae, anorectal sequelae, and/or chronic pain, respectively. Ten recurrences occurred during the study period, corresponding to a recurrence rate of 16%, with a median time to recurrence of 1.76 years (range 0.27-6.56 years). Of these recurrences, 5/10 originated from a mature teratoma, 4/10 originated from an immature teratoma, and 1/10 originated from a malignant teratoma. The overall SCT-related mortality rate was 3% due to intraoperative complications (n=1) and progressive malignant SCT with yolk sack components and liver metastases (n=1).

Conclusion: The incidence of SCT's were stable among the Danish children during the study period. We found a recurrence rate of 16% and 3% SCT-related mortality. One in four children developed urological and/or anorectal sequelae.

T cell memory response to Varicella zoster virus in children at a haematological and oncological ward

by Eva Tiselius | Emil Sundberg | Hanna Andersson | Anna Höbinger | Peter Jahnmatz | Arja Harila | Josefine Palle | Shanie Saghafian-Hedengren | Anna Nilsson | Karolinska Institutet, Sweden | Uppsala University, Sweden | Karolinska Institutet, Sweden | Karolinska Institutet, Sweden | Mabtech AB, Sweden | Uppsala University, Sweden | Uppsala University, Sweden | Karolinska Institutet, Sweden | Karolinska Institutet, Sweden

Abstract ID: 91
Themes: Infections
Presenter Name: Eva Tiselius
Keywords: IFN-, chickenpox, human herpesviruses, memory T cell

Background: T cell memory in children develops gradually, through the impact of a variety of factors. A central factor is herpesvirus infection, such as Varicella Zoster Virus (VZV). Chickenpox, the primary VZV infection, is common in children and highly infectious. In the immunosuppressed patient undergoing haematological or oncological care, VZV infection and reactivation can cause severe complications. However, not enough is known regarding VZV-specific memory T cell responses in immunosuppressed children.

Aims: To assess memory T cell responses to VZV in children at a haematological and oncological ward.

Methods: 39 paediatric oncological and/or haematological patients as well as 14 children without malignancies were included in this study. Through ELISA, VZV IgG seropositivity was determined. T cell subsets were characterised through FACS. Finally, Fluorospot was used to analyse T cell memory responses through quantification of IFN-, IL-22, IL-10, IL-17A secretion.

Results: As expected, a diminished population of naïve CD8+ and CD4+ T-cell subset was seen in children with haematological malignancies or post-HSCT compared to children without malignancies. Furthermore, their memory T cell compartments were proportionally larger. These differences were partly related to age. Children with haematological malignancies or post-HSCT also showed diminished cytokine secretion upon polyclonal stimulation compared to children without malignancy. Interestingly, IFN- response to VZV was virtually depleted in these children.

Conclusion: As previously seen, our data shows that T cell phenotype is affected by both age and diagnosis. Remarkably, the almost depleted IFN- response to VZV alludes to a perturbed Th1 compartment. Therefore, it can be stipulated that there are qualitative differences in T cell response to VZV in children with haematological malignancies or post-HSCT, though the cause remains unknown.

The effect of high-dose methotrexate treatment on renal function of pediatric ALL patients

by Pinja Honkanen | University of Turku

Abstract ID: 95
Themes: Late Effects
Presenter Name: Marika Grönroos
Keywords: High-dose methotrexate, acute lymphoblastic leukemia, renal function

Background:

It is important to monitor the renal function of patients receiving high-dose methotrexate therapy because of methotrexate-induced nephrotoxicity. Our hypothesis is that in some children with delayed methotrexate elimination, the creatinine concentration in the blood increases and the glomerular filtration rate (GFR) decreases by more than 30% of the initial value during the high-dose methotrexate infusion period.

Material and methods:

This retrospective study investigated the renal function of children with acute lymphoblastic leukemia (ALL) who were treated with high-dose methotrexate at Turku University Central Hospital between 2006 and 2018. Renal function was monitored by measuring serum creatinine before, after, and at the end of high-dose methotrexate treatment. The GFR was determined from the serum creatinine concentration using the Schwartz calculation formula, which describes kidney function better than the serum creatinine value alone. A total of 76 patients participated in the study, most of whom were treated either according to the NOPHO ALL-2000 or NOPHO ALL-2008 treatment protocols.

Results:

No renal damage was found in any of the study patients during or after high-dose methotrexate treatment. However, at the start of high-dose methotrexate treatment, more than half of the patients experienced a decline in GFR compared to baseline. This decrease in GFR leveled off as the treatment periods progressed. The 30% increase in creatinine, which was considered significant, was the highest in percentage terms in the 7–12-year-old group. In addition, a significant 30% increase in creatinine occurred between the end of treatment visit and the last follow-up visit.

Conclusions:

This study gives indications that the high-dose methotrexate is well tolerated in terms of renal function. Effect of high-dose methotrexate treatment on renal function in the long term should be studied more.

The radiological and clinical course of osteonecrosis in children with acute lymphoblastic leukaemia

by Roosa Rokkanen | Henri Aarnivala | Sanna Huhtaniska | Maria Suo-Palosaari | Pauliina Utriainen | Tytti Pokka | Liisa Järvelä | Riitta Niinimäki | Research Unit of Clinical Medicine, University of Oulu, Oulu, Finland | Research Unit of Clinical Medicine, University of Oulu, Oulu, Finland 2Department of Paediatrics and Adolescent Medicine, Oulu University Hospital, Oulu, Finland | Department of Diagnostic Radiology, Oulu University Hospital and Research Unit of Medical Imaging, Physics, and Technology Medical Research Center Oulu, University of Oulu, Oulu, Finland | Department of Diagnostic Radiology, Oulu University Hospital and Research Unit of Medical Imaging, Physics, and Technology Medical Research Center Oulu, University of Oulu, Oulu, Finland | Department of Pediatric Hematology, Oncology and Stem Cell Transplantation (SCT), Children's Hospital, University of Helsinki and Helsinki University Hospital, Helsinki, Finland | Research Unit of Clinical Medicine, University of Oulu, Oulu, Finland | Department of Pediatrics and Adolescent Medicine, Turku University Hospital and University of Turku, Turku, Finland | Research Unit of Clinical Medicine, University of Oulu, Oulu, Finland 2Department of Paediatrics and Adolescent Medicine, Oulu University Hospital, Oulu, Finland

Abstract ID: 133
Themes: Leukemia
Presenter Name: Roosa Rokkanen
Keywords: Acute lymphoblastic leukaemia, children, magnetic resonance imaging, osteonecrosis

Introduction

In patients with acute lymphoblastic leukaemia (ALL), osteonecrosis (ON) can affect multiple sites throughout the skeleton. Although ON is a common sequel to cancer treatment, the prognosis of ON in childhood ALL remains underexplored.

Aim

This study describes the radiological evolution of ON lesions in patients treated according to the Nordic Society of Paediatric Hematology and Oncology (NOPHO) ALL2008 treatment protocol. Additionally, we aimed to identify factors associated with an adverse outcome of ON.

Subjects & methods

A total of 30 patients with ON treated in the three tertiary centers participating in the study were identified from the NOPHO toxicity registry. We reviewed their medical records and analyzed the magnetic resonance imaging scans of 177 ON lesions, out of which 65 were in the joints, and graded them according to the Niinimäki radiological classification.

Results

A total of 15 sites affected with ON were identified. The median time from ALL diagnosis to ON was 2.2 years (range: 0.0–7.9 years, interquartile range 0.65–2.4 years). The median follow-up time was 2.0 years (range: 0.0–13.5 years, interquartile range 0.6–3.5 years) from ON diagnosis, and a mean of three follow-up scans were evaluated. Follow-up images were available for 137 (77%) of ON lesions. Among these, 57% remained stable, 34% resolved completely, 7% improved to a lower grade, and 2% progressed. Joint collapse (grade 5) was observed in 11/65 joint lesions. Eight lesions required surgery: five hip lesions total joint arthroplasty, and three ankle lesions core decompression. The chance for spontaneous resolution of ON decreased with increasing patient age (20% for each year, adjusted for sex and stem cell transplant, $p<0.05$).

Conclusion

Joint ON demonstrates the most potential to both improve and progress, underscoring the high priority of grade 3-4 ON lesions regarding both follow-up and future interventional studies.

THE SWEDISH CHILDHOOD CANCER FUND'S NATIONAL WORKING GROUP FOR TOXICITY AND LATE COMPLICATIONS

by Weronica E Ek | Klas Blomgren | Jacob Engellau | Cecilia Folin | Päivi Lähteenmäki | Per Nyman | Aron Onerup | Kim Ramme | Per-Erik Sandström | Anna Sällfors Holmqvist | Ingrid Tonning Olsson | Arja Haila | The Swedish Childhood Cancer Fund | Department of Women's and Children's Health, Karolinska Institute, Sweden, Department of Pediatric Oncology, Karolinska University Hospital, Sweden | Dept. of Radiation Physics, Oncology and Hematology, Skane University Hospital, Sweden | Dept of Oncology, Skane University Hospital, Sweden, Institution of health science, Faculty of Medicine, Lund university, Sweden | Department of Women's and Children's Health, Karolinska Institute, Sweden, Department of Pediatric and Adolescent Medicine, Turku University Hospital, Finland | Crown Princess Victoria Children´s Hospital, Linköping University Hospital, and Department of Biomedical and Clinical Sciences, Linköping University, Linköping, Sweden | Department of Pediatrics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Sweden | Department of Women's and Childrens Health, Uppsala University, Sweden | Department of Clinical Sciences, Pediatrics, Umeå University, Sweden | Childhood Cancer Centre, Skane University Hospital, Sweden, Department of Clinical Sciences, Lund University, Sweden. | Childhood Cancer Centre, Skane University Hospital, Sweden, Department of Clinical Sciences, Lund University, Sweden. | Department of Women's and Childrens Health, Uppsala University, Sweden

Abstract ID: 98
Themes: Late Effects
Presenter Name: Weronica E Ek
Keywords: Swedish Childhood Cancer Fund, Toxicity, late complications, working group

Background and aims. Due to improvements in cancer treatment, 85% of Swedish children treated for cancer survive. Childhood cancer survivors also live longer than ever, but previous studies show that as many as 70% of all survivors suffer from health issues, many occurring later in life. The goal of the Swedish Childhood Cancer Fund's (Barncancerfonden) strategic investment in "toxicity and late complications" is survival with improved quality of life, and the long-term vision is survival with preserved quality of life for everyone who has been treated for childhood cancer. For this purpose, the Swedish Childhood Cancer Fund has appointed a national profession-led multidisciplinary working group with the main aim to improve the quality of research within the area of toxicity and late complications, as well as increase national and international collaborations.

Methods and Results. The main focus areas for the working group for Toxicity and Late Complications (arbetsgruppen för toxicitet och sena komplikationer, NAG-TSK) are: networking (to improve national and international collaboration), research grant calls (facilitate national research programs to improve the quality of research within the area), and infrastructures (to increase the quality and use of infrastructures in Sweden). NAG-TSK has organized two scientific meetings in Stockholm (2022 and 2023). A new two-stage grant call with a total budget of 16 million SEK opened in 2023, with the aim to stimulate national and multiprofessional collaborations. Out of 10 submitted applications, 5 were

recommended to submit a full application. Final decisions for the call will be announced in 2024.

Conclusions. Backed by a focused investment, the long-term goal of this working group is to ensure that individuals treated for childhood cancer will have a preserved quality of life.

Title:

Towards a mechanistic understanding of cell fate coordination: new insight from quantitative bio imaging, single cell transcriptomics and mathematical modeling

Authors:

Moreira Soares Oliveira, B., Asser, A., Hanel, A., Guerra, F., Raitaniemi, P., Santhan, S., and Tollis, S.

Affiliation:

Institute of Biomedicine, School of Medicine, University of Eastern Finland
Yliopistonranta 8, 70210 Kuopio, Finland

Abstract:

Cancers are a consequence of wrong cellular decisions, where proliferation is chosen over other cell fates. In healthy tissues, cell fate-specific signals restrict commitment to division. The hematopoietic system exemplifies cell fate choices, as developing immune cells switch between fast proliferation and cell cycle pausing phases during which they differentiate. This alternance is disrupted in leukemia, where over-proliferating non-differentiated cells saturate the bone marrow (BM). How can cells sharing the same (BM) microenvironment exhibit so strong difference in their abilities to proliferate or differentiate? To date, it is unknown how cell fate coordination is ensured, and which factors in the BM environment are critical, limiting our therapeutic abilities.

Our recent results in the budding yeast model organism demonstrated that single cells need to accumulate G1/S specific transcription factors as they grow, to become able to commit to division. We hypothesized that external signals (e.g. mitogens or differentiation factors) accelerate or slow down this accumulation, to favor cell proliferation or delay cell cycle commitment and increase the time window for acquisition of differentiation biases, effectively coordinating cell fate choices.

To study cell fate coordination at the molecular level, we used cutting edge Quantitative Bio-Imaging techniques to measure the concentration and localization of core G1/S proteins (E2F-RB1-CyclinD1-CDK inhibitor p27) in a leukemia cell line (NALM-6). CycD1 protein levels peaked in late G1 cells to 30-35nM, while p27 expression (that competes with CycD1 for cell cycle activation) was continuously decreasing in G1 from 30-40nM in small G1 cells to 6nM in larger cells (concentrations per genome copy). p27 levels were decreased to basal level (6nM) in cells of all sizes when exposed to Interleukin 6 (IL-6), representing a possible route by which IL-6 could act on cell proliferation.

To understand how similar microenvironmental signals affect differentially the proliferation of different cell types, we are integrating this unprecedented quantitative data into a mathematical model of the G1/S transition. Our model was constructed on a subset of 24 core G1/S genes that are sufficient to unambiguously define hematopoietic cell types in single-cell transcriptomics data. Model predicted that p27 levels decrease in G1 was sufficient to drive cell cycle activation when p27 levels drop, representing a novel quantitative determinant of human cell cycle commitment. We are currently analyzing how cell type-dependent gene expression profiles affect model predictions. This project will provide combinations of molecular targets adapted to particular medical situations (as based on transcriptomics profiles), and accurate quantitative requirements to pharmacologically control transitions between cell fates. We ascertain that this knowledge will address a shortcoming in current cancer treatment.

TUMOR LYSIS SYNDROME - PREVALENCE AND RISK FACTORS – IN PAEDIATRIC PATIENTS DIAGNOSED WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN LATVIA

by Fainveice Elina | Smirnova Olga | Cebura Elizabete | Riga Stradins University, Latvia | Riga Stradins University, Latvia | Riga Stradins University, Latvia; Children's Clinical University Hospital, Latvia

Abstract ID: 126
Themes: Leukemia
Presenter Name: Fainveice Elina
Keywords: Hyperuricemia, childhood leukemia, electrolyte disturbances

Objectives

Tumor lysis syndrome (TLS) emerges commonly in paediatric patients with acute lymphoblastic leukemia (ALL). According to the *Cairo-Bishop* model, laboratory TLS is diagnosed when the patient exhibits at least two of the following blood serum changes —hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia. Clinical TLS is diagnosed when laboratory TLS is accompanied by acute kidney failure, cardiac arrhythmias, or seizures.

This study aims to identify the prevalence and risk factors associated with TLS development in paediatric ALL patients.

Methods

We present a retrospective cross-sectional study. Patients aged 0–18 years, primarily diagnosed with ALL from January 1, 2011, to December 31, 2021, and undergoing primary or relapse chemotherapy, were included. Data, encompassing patients' gender, age, immunophenotyping of ALL, initial lymphadenopathy, organomegaly, leukocytosis, lactate dehydrogenase level, as well as uric acid, phosphorus, potassium, and calcium, were collected. Data were analyzed using SPSS, employing normal distribution (Shapiro-Wilk test), descriptive statistics, and Spearman's correlation coefficient.

Results

A total of 108 patients with a mean age of 5.96±4.62 years were included. Eleven of the included patients developed relapse during this period. Males constituted 62.04%, and females constituted 37.96%, with laboratory TLS observed in 1 female and 3 males, and clinical TLS in 2 males. TLS occurred in two precursor-B leukemia and two precursor-T leukemia cases. Initial lymphadenopathy was present in 75% of TLS cases, while initial hepatosplenomegaly was observed in all TLS cases. Initial leukocytosis appeared in 50% of TLS cases. Hypocalcemia and hyperphosphatemia were predominant in laboratory TLS. Clinical manifestations of TLS included cardiac arrhythmias.

Conclusions

Despite a significant number of high-risk patients, TLS manifested in only 3.36% of observed episodes. The findings underscore the importance of preventive measures and vigilant control of serum uric acid and electrolytes to avert life-threatening TLS complications in paediatric ALL.

TWO CASES OF JUVENILE MYELOMONOCYTIC LEUKAEMIA IN ESTONIA

by Triin Pohlak | Triin Paabo | Kadri Saks | Sirje Mikkel | Tartu University Hospital, Estonia | Tartu University Hospital, Estonia | Tallinn Children's Hospital, Estonia | Tartu University Hospital, Estonia

Abstract ID: 105
Themes: Leukemia
Presenter Name: Triin Pohlak
Keywords: GVHD, jmml, leukaemia, transplantation

Introduction

Juvenile myelomonocytic leukaemia (JMML) is a rare paediatric neoplasm with myelodysplastic and myeloproliferative features. With estimated incidence of 1.2 cases per million children aged 0-14, only few cases have been diagnosed in Estonia. Hereby we present two recent cases of JMML diagnosed in 2022.

Case descriptions

Our first patient (A) was diagnosed with JMML at the age of 1.5 years and second patient (B) at the age of 3 months. Patient A presented with severe infections and fluctuating cytopenias. Patient B had persisting bloody stool and BCGitis, raising suspicions of primary immunodeficiency. Both had significant splenomegaly and fulfilled WHO diagnostic criteria of JMML, which was confirmed by bone marrow genetic analyses: patient A had somatic mutation of PTPN11 and monosomy 7, and patient B somatic mutation of NRAS.

In both cases, allogeneic haematopoietic stem cell transplantation (allo-HSCT) was indicated. After bridging-therapy with azacitidine allo-HSCT was performed during clinically stable disease, with matched unrelated donor (12/12), BuCyMel+ATG conditioning, and cyclosporine as primary immunosuppressive agent. The post-transplantation period, however, proved to be challenging, and both children needed long-time treatment at intensive care unit.

Patient A developed acute steroid-refractory grade IV skin and gastrointestinal graft-versus-host disease (GVHD), which led to small-intestine ileus and bowel segment resection. Patient B had severe engraftment syndrome with pulmonary oedema, capillary leak syndrome and skin rash, that further developed into grade III skin aGVHD. Another challenge was treating tuberculosis due to active BCGitis.

Patient A was discharged at day +155, patient B at day +77. JMML is in remission, with complete donor chimerism in both patients.

Conclusion

JMML is a rare paediatric malignancy, with allo-HSCT being the only curative treatment for most patients. In our cases this has shown efficacy – despite developing acute life-threatening complications, both patients are now in complete remission, without signs of chronic GVHD.

UPREGULATION OF INSULIN-LIKE GROWTH FACTOR-I IN RESPONSE TO CHEMOTHERAPY IN CHILDEREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

by Helin Berna Kocadag | Sarah Weischendorff | Silvia de Pietri | Claus Nielsen | Mathias Rathe | Bodil Als-Nielsen | Henrik Hasle | Anders Juul | Klaus Müller | Maria Ebbesen Sørum | Department of Paediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen University Hospital, Denmark. | Department of Paediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen University Hospital, Denmark. | Department of Paediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen University Hospital, Denmark. | Institute for Inflammation Research, Rigshospitalet, Copenhagen University Hospital, Denmark. | Hans Christian Andersen Children's Hospital, Odense University Hospital, Odense, Denmark | Department of Paediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen University Hospital, Denmark. | Department of Paediatrics, Aarhus University Hospital, Aarhus, Denmark. | Department of Growth and Reproduction, Rigshospitalet, Copenhagen University Hospital, Denmark. | Department of Paediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen University Hospital, Denmark. | Department of Paediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen University Hospital, Denmark.

Abstract ID: 130
Themes: Leukemia
Presenter Name: Helin Berna Kocadag
Keywords: Acute lymphoblastic leukemia, IGF-I, citrulline, growth factors, inflammation, tissue damage.

Background: Pediatric cancer treatment is challenged by toxic side effects due to chemotherapy-induced tissue damage particularly involving the gut. Insulin-like growth factor I (IGF-I) plays a key role in tissue repair and protects against gut mucosa damage in chemotherapy-treated rodents.

Aim: To investigate associations between IGF-I levels and chemotherapy-related toxicities in pediatric acute lymphoblastic leukemia (ALL).

Methods: This prospective study, involving 114 patients with newly-diagnosed ALL, measuring plasma IGF-I weekly for five weeks together with citrulline, a marker for intestinal integrity. Statical analyses included mixed models, Mann-Whitney U-test and Spearman’s rank-order correlation.

Results: At the timepoint of ALL diagnosis, IGF-I levels were reduced (median (quartiles): -1.2 standard deviation score (SDS) (-1.89 to -0.53)). This was followed by an increase in IGF-I peaking at day 8 (median: 0.0 SDS (-0.84 to 0.71), $P < 0.001$). This increase correlated with C-reactive protein (CRP) (rho = 0.37, $P < 0.001$) and interleukin-6 (IL-6) (rho =0.39, $P = 0.03$) on day 15 where maximum levels of these markers were observed.
Citrulline levels reduced in response to chemotherapy reaching nadir at day 15. A greater IGF-I increase from day 1-15 correlated with slower recovery citrulline from day 15-29 (rho = -0.28, $P = 0.01$).

Conclusion: This study demonstrates reduced IGF-I levels in children newly diagnosed with ALL, but increases in response to chemotherapy, most pronounced in patients experiencing more severe inflammation and slower recovery of intestinal integrity. The observed rise in IGF-I preceding elevations in CRP and IL-6 suggests its potential as an early biomarker of chemotherapy-related tissue injury and inflammation. Moreover, these findings shed light on IGF-I as a potentially protective factor that increases in response to chemotherapy-induced tissue damage. Such insights may have implications for ALL patients as well as extending beyond the field of oncology and hematology.