medications such as liposomal amphotericin B, intravenous immunoglobulin therapy).

Pharmacological treatment included various diuretics, low-molecular-weight heparin, correction of coagulation abnormalities, thrombocyte transfusions, albumin supplementation, ursodeoxycholic acid, acetylcysteine and defibrotide. Fluid balance was carefully monitored. The only patient who received defibrotide had faster clinical recovery and normalization of laboratory parameters. In three patients abdominal drainage and in two patients thoracic drainage had to be performed.

hepatic sinusoidal obstruction syndrome is a severe complication of oncologic treatment with possible lethal outcome requiring rapid diagnosis and intensive treatment.

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ADMINISTRATION OF TARGETED THERAPY IN CHILDREN WITH NTRK REARRANGED MESENCHYMAL NEOPLASMS

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The aim of this report is to present 2 patients diagnosed with neoplasm of mesenchymal origin, in whom NTRK inhibitor entrectinib was successfully administered.

The first patient presented at the age of 9 months as recurrent chalazion.

During subsequent clinical and radiological follow-up a diagnosis of right upper eyelid tumor was made. Taking into account tumor localization, surgical procedure of a maximum possible tumor reduction was performed, unfortunately with positive resection margins. Histopathological analysis confirmed the diagnosis of „NTRK-rearranged spindle cell neoplasm“ according to the new 2020 WHO classification of soft tissue tumors. The neoplasm was characterized by increased cellularity and relatively low mitotic activity. The possibility of an aggressive clinical course could not be excluded. Molecular analysis (FusionPlex Sarcoma Kit SAR6) verified an LMNA-NTRK fusion and oral entrectinib therapy was initiated. The patient has tolerated the medication very well and is without the radiological signs of eventual local relapse (magnetic resonance imaging).

The second patient is a 12-year-old boy presenting with a solid expansive lesion of the lesser pelvis extending towards the groin and anterior abdominal wall (locoregional disease). Tumor tissue sampling confirmed malignant peripheral nerve sheath tumor. Neoadjuvant systemic chemotherapy according to the EpSSG-NRSTS protocol and radiotherapy accomplished only partial reduction of the tumor mass prompting next generation sequencing on formalin-fixed paraffin-embedded tissue blocks (FoundationOne®Heme) that confirmed LMNA-NTRK1 fusion. Oral entrectinib has been initiated leading to tumor shrinkage that enabled complete surgical resection. The adverse effects registered in this case are one forearm fracture and increased appetite accompanied by significant weight gain that are diminished after medication dose reduction.

In conclusion, implementation of the targeted therapy has enabled avoidance of mutilating surgery and adverse effects of conventional cytostatic agents in the first case. Excellent control of malignant mesenchymal tumor has been achieved in the second case.

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FANCONI ANEMIA: A CASE REPORT

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Background Fanconi anemia is a rare genetic inheritance disease. Although the transmission in most cases is autosomal recessive, in some instances, it can be X-linked. Congenital malformations are the first clinical presentation that could affect many organic systems like the skeletal, skin, cardiac, pulmonary, central nervous system, gastrointestinal and urogenital. Limb asymmetry, thenar hypoplasia, microcephaly and low stature and weight are very frequent. Patients may also present ear malformations with or without congenital deafness and intellectual disabilities. The most serious problem is early severe bone marrow failure which leads to pancytopenia and, some years later, to the progression of acute myeloid leukemia or myelodysplastic syndrome. Moreover, the presence of solid tumors (head and neck or anogenital) is more prevalent.

Case Report A 9 year old male child was born with polymalformations such as imperforate anus, micropenis, inverted nipples, low implanted ears, sacrococcygeal sinus, thenar and radius hypoplasia. His birth occurred under a supervised gestation of 42 weeks by caesarean because of fetal bradycardia. The Apgar index was 5/8/9 and reanimation was performed. The patient was hospitalized in intensive care and anus correction surgery was performed.

The child's parents were healthy but consanguineous (cousins). The boy is the couple's third child. The first one died at 7 years old with acute myeloid leukemia and had a previous diagnosis of Fanconi anemia. The second one had sudden death at 3 months old. Because of this, karyotype and evaluation of chromosomal breakage induced by diepoxybutane (DEB) was tested and the last one confirmed Fanconi anemia diagnosis. Until now, he developed pancytopenia and bone marrow failure without progression to leukemia. Later, he had a younger brother without Fanconi anemia. It should be noted that the child in question has a 17 year old male cousin also diagnosed with Fanconi anemia. The cousin has low stature, intellectual disability and performed Hematopoietic stem cell transplantation at 7 years old.

Currently, the child takes danazol and receives periodic transfusions. He has multidisciplinary follow-up and was proposed to Hematopoietic stem cell transplantation.

Conclusion Fanconi anemia is responsible for many malformations and inevitable bone marrow failure. The presence of an inheritance pattern increases the level of suspicion when other relatives have the disease.

After diagnosis, these patients need close multidisciplinary follow-up to improve the expectancy and quality of life. The prevention or early detection of neoplasia is the main objective for these patients, as it leads to poor prognosis.

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A GIRL WITH PRE-B ACUTE LYMPHOBLASTIC LEUKEMIA ON MAINTENANCE THERAPY WITH HEREDITARY COMPLEMENT-MEDIATED THROMBOTIC MICROANGIOPATHY (AHUS)

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A 3-year old girl suffering from acute lymphoblastic leukemia (pre-B immunophenotype, medium risk, treatment protocol ALL IC-BFM 2009) during maintenance therapy (MTX 10mg/weekly/and 6-mercaptopurine 50mg/m² daily) had sudden onset of pallor, oliguria, and microhematuria (128 RBC/mm³). Initial complete blood count revealed normocytic anemia (Hb 59 g/L, Htc 16.3%, MCV 85.3 fL, platelets 26 x10⁹/L) alongside elevated bilirubin (67 µmol/L), urea (17.6 µmol/L), creatinine (82 µmol/L) and LDH (2296 U/L) and a reduced haptoglobin level (0.03 g/L). Plasma-free hemoglobin was elevated (154 mg/L), as well as d-dimers (2.87 mg/L), antithrombin III (126.8%), and fibrinogen (6 g/L). Immunohematological analysis (direct and indirect Coombs test, antiplatelet antibodies) was negative.

Hematological data: Hb level (45g/L), minimum platelets count (3x10⁹/L), maximum LDH level units (704.8 U/L), schistocytes seen (no). Renal impairment: oliguria with macrohematuria, maximum serum creatinine (86 µmol/L), creatinine clearance (Schwartz formula) 23 ml/min/1.73m². Evidence of infective causes: no (stools O157:H7, Shigella sp, VTEC, Streptococcus pneumoniae). Endomysial antibodies (EMA), ANCA, methylmalonic aciduria, hyperhomocysteinemia negative. Renal histology: not done Laboratory investigation: reduced ADAMS-13 activity (40%, reference range 67-150 %) with normal C3 (0.75 g/L), C4 (0.27 g/L). Factor H level was high (1248 mg/L, reference range 250-880 mg/L) with terminal pathway activation marker level markedly increased (1315 ng/mL, ref. range 110-252 ng/mL), supporting pathological overactivation of the complement system.

Treatment: The girl was initially treated with fresh frozen plasma, periodic RBC transfusions, and single plasmapheresis. On the 2nd day of admission, she received a first eculizumab infusion (300 mg). After application, we noticed an immediate increase in platelets and reticulocytes with a decrease in free plasma hemoglobin and global renal function recovery. Moderate hypertension that occurred was treated with enalapril and amlodipine. The former maintenance therapy was immediately switched to cyclophosphamide. The girl is well, with continued eculizumab treatment on a recommended schedule.

Genetic analysis: The patient was found to be homozygous for the CFH H3 haplotype (involving the rare alleles of c.-331C>T, Q672Q, and E936D polymorphisms) reported as a risk factor of aHUS. The patient was homozygous for the MCPgaac haplotype of the CD46 gene reported as a risk factor of developing aHUS.

Conclusion A triggering factor for thrombotic microangiopathy was drug-mediated, causing complement activation on a predisposing genetic background. To our best knowledge, this is the third similar case found in literature, the first to receive eculizumab in such cases as well as following early onset of complement activation disease.

311 AUTOIMMUNE HEMOLYTIC ANEMIA WITH COMPLEMENT ACTIVATION MIMICKING AHUS

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A boy of 5 years was admitted into the Division for Pediatric Hematology and Oncology due to severe anemia. Initial complete blood count showed severe macrocytic anemia (Hb 44 g/

L, Htc 14.9%, MCV 112.6 fL), elevated Rtc count (34.7%, 158.7/1000 erythrocytes), and slightly reduced platelet count (110 x10⁹). The boy had hemolysis (low haptoglobin level (<0.10 g/L), elevated bilirubin, and LDH, with complement activation (C4 0.72 g/L, C3 0.02 g/L, CH50 13%). Urea (3.3 mmol/L) and creatinine (19 µmol/L) were within reference values. Exclusion diagnostics: malignant hematological disorders (bone marrow biopsy), folate deficiency anemia, and vitamin B12 deficiency. Immunohematological analysis: autoimmune hemolytic anemia with positive both direct and indirect anti-globulin (Coombs) test.

The erythrocytes were coated with warm IgG autoantibodies and IgM class autoantibodies in a wide temperature range (4 – 37°C) without erythrocyte specificity alongside activated complement components while the platelets were coated with IgM autoantibodies. ADAMTS13 activity was decreased (38%), but not deficient alongside low C1q antigen, low Factor H antigen (84 mg/L, ref. range 250-880 mg/L) and low sC5b-9 (terminal complement complex) (301 ng/mL, ref. range 110-252 ng/mL) Treatment: intravenous methylprednisolone (6 mg/kgBW/14 consecutive days) with periodical erythrocyte and platelet concentrate transfusions, rituximab once weekly (5 doses in total); plasmapheresis (6 cycles in total, with side effects which included increased tendency clotting). These therapeutic strategies showed no therapeutic benefit, and the child was dependant on periodic RBC and platelet transfusions. The therapy was switched to IVIg (4,7g/kg/5 days) and vitamin B12 (1000mcg/daily/7 days), with significant improvement of RBC and platelet count.

Genetic analysis: a heterozygous mutation for a rare intronic variation (c.600-14C>T) and heterozygous for the Y402H polymorphism of the CFH gene.

c.600-14C>T mutation is located near the 5' end of exon 6 in the gene encoding the complement C3 protein (C3). This rare variation was described previously in one patient with aHUS, in one patient with glomerulonephritis, in one subject suffering from C3-deficiency, and one patient with age-related macular degeneration. This rare variation was also identified in healthy subjects with a relatively low frequency (0.04-1.1%), but no functional studies were performed on its possible role.

Conclusion We believe that the underlying disease was autoimmune hemolytic anemia with both cold and warm autoantibodies complicated with complement activation on predisposing genetic background.

312 HEALTH-RELATED QUALITY OF LIFE IN INFANTS, TODDLERS AND YOUNG CHILDREN WITH SICKLE CELL DISEASE

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Little is known about health-related quality of life in children with sickle cell disease aged 0-7 years old living in an European country. In order to improve quality of life in these young children, these data are important and provide insight in potential areas that may benefit from interventions.

The primary aim of this study is to compare health-related quality of life between the general paediatric population and