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