

X-Linked Lymphoproliferative Disease Presenting as Pancytopenia in a 10 month Old Boy
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A previously healthy 10-month old boy was admitted with one week of fever, rash, and malaise. He appeared lethargic with a fever of 102 degrees F and a heart rate of 180 b/min. He had a purpuric petechial rash over his trunk and extremities and an erythematous bulging tympanic membrane on the right. His liver was palpable 4cm below the costal margin and he had no splenomegaly. His initial WBC was 3.9 with 68% lymphocytes and 13% atypical lymphocytes. His hemoglobin was 8.1 mg/dL and platelet count 36,000. His AST, ALT and LDH were all elevated at 152, 146, and 2041 respectively. EBV serology indicated acute infection. His immunoglobulins were normal.

He was treated with ceftriaxone for acute otitis media and possible bacteremia; over the next several days he improved clinically with less lethargy and improved appetite. However his pancytopenia worsened necessitating red blood cell and platelet transfusions. His bilirubin rose to 8, ALT to 1890, and AST to 7300. His triglycerides were elevated at 319 and fibrinogen low at 107. A bone marrow biopsy revealed hypocellular marrow with no evidence of hemophagocytosis.

He was treated with high dose IVIG, acyclovir, steroids, and chemotherapy according to the HLH-94 protocol. Three weeks into his illness he developed respiratory distress and was intubated. He developed progressive liver failure with coagulopathy and appeared septic. He passed away 24 days after the onset of his illness.

Gene sequencing at the University of Washington identified a point mutation in exon 1 resulting in a new splice and the deletion of 22bp's, frame shift, and early termination of SH2D1A confirming a diagnosis of XLP. His mother is a carrier of the mutation. His soluble interleukin-2 (sIL-2R) receptor level was 9311 U/mL and perforin studies were normal. Natural killer cell function was not able to be performed.

XLP is a rare genetic disorder which usually affects previously healthy males in their first decade. The defective gene responsible for this disease encodes the protein SAP (signaling lymphocyte activation molecule or SLAM-associated protein, also called DSHP or SH2D1A). XLP can have a similar clinical picture to hemophagocytic lymphohistiocytosis and in series of HLH patients mutations in SAP are frequently found.