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Epstein-Barr virus–associated hemophagocytic lymphohistiocytosis in X-linked lymphoproliferative disease

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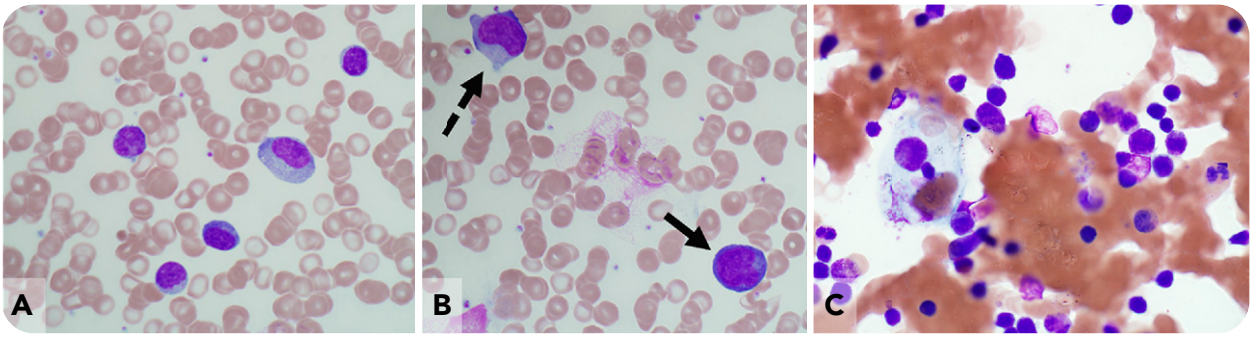

A 23-month-old boy presented with a 5-day history of fever, rash, and lymphadenopathy. Complete blood count revealed a white blood cell count of 69.4 K/μL, with lymphocytes of 88%. Peripheral blood smear showed a spectrum of mature, reactive, and plasmacytoid lymphocytes (panel A; Wright-Giemsa stain [WG], original magnification ×50; panel B; an immunoblast [solid arrow] and reactive lymphocyte [broken arrow], WG, original magnification ×100). Peripheral blood flow cytometry showed no evidence of malignancy. Bone marrow aspirate showed hemophagocytosis (panel C; WG, original magnification ×100). There was coagulopathy, hypofibrinogenemia, and hyperferritinemia, ferritin 1855 ng/mL (5-100 ng/mL). Epstein-Barr virus (EBV) serology showed evidence of recent EBV infection. EBV antibody to viral capsid antigen immunoglobulin M was >160.0 units/mL (0.0-43.9 units/mL), and EBV quantitative polymerase chain reaction was 96 800 copies per mL (<390 copies per mL). There was elevation of sCD25 4295 pg/mL (175-858 pg/mL) and sCD163 8257 ng/mL (range, 399-1968 ng/mL), decreased natural killer cell function by functional assay, and increased granzyme B expression, confirming hemophagocytic lymphohistiocytosis (HLH) diagnosis. Signaling lymphocytic activation molecule-associated protein (SAP) expression was abnormally absent, and *SH2D1A* gene mutation was detected leading to the diagnosis of X-linked lymphoproliferative disease (XLP1).

This is a rare, inherited immunodeficiency, characterized by immune dysregulation resulting in increased risk of HLH, lymphomas, and extreme vulnerability to EBV infection. XLP1 should be suspected if fulminant EBV infection occurs in a male.

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