A 7-year-old boy with flu-like symptoms treated with amoxicillin presented with cervical lymphadenopathy; maculopapular rash on arms, face, and trunk; and markedly high white blood cell (WBC) count (100 × 10^9/L) and high absolute lymphocyte count (85 × 10^9/L). The peripheral smear revealed a heterogeneous population of lymphocytes (panels A and B). Howell-Jolly bodies were also seen (panel B inset) consistent with his therapeutic splenectomy for hereditary spherocytosis. A monospot (heterophile) test was positive, and serum immunoglobulin M antibody to viral capsid antigen was elevated. Quantitative polymerase chain reaction for Epstein-Barr virus (EBV) was 19,360 copies/mL. Flow cytometry revealed a polyclonal population of T-lymphocytes (85% CD3⁺, 11% CD3/4⁺, 70% CD3/8⁺). Molecular studies showed T-cell receptor β and γ gene clonal rearrangements. The patient was treated supportively and improved clinically. The WBC count decreased to 13.9 × 10^9/L (Abs lymph: 8.8 × 10^9/L) over the next several weeks.

This case of infectious mononucleosis is highly unusual in that extreme leukocytosis is rarely associated with reactive conditions. Although clonal rearrangements of the T-cell receptor genes were positive, they were most likely secondary to EBV infection. The peripheral smear morphology demonstrated a reactive proliferation of lymphocytes consistent with EBV infection. Classic clinical findings were also exhibited including a morbilliform rash that developed after empiric ampicillin.
Epstein-Barr virus–associated lymphocytosis masquerading as lymphoma

Samuel I. McCash and Steven Marionneaux