Atypical lymphocytosis, cold agglutinin hemolytic anemia, and monoclonal gammopathy in an HIV patient with marrow involvement by diffuse large B-cell lymphoma

A 43-year-old man presented with fever, fatigue, and shortness of breath. Physical examination revealed bilateral axillary lymphadenopathy. Complete blood count showed hemoglobin of 9.8 g/dL, a white cell count of $4.4 \times 10^9/L$, and a platelet count of $195 \times 10^9/L$. Blood smear showed increased red blood cell agglutination, polychromasia with nucleated red cells, and atypical lymphocytosis (panel A). Hemolysis was evident, with raised serum bilirubin (2.3 mg/dL), low serum haptoglobin (4 mg/dL), high serum lactate dehydrogenase, direct Coombs test positive, and cold agglutinins (1:256). Serology studies for hepatitis B or hepatitis C were negative. Laboratory work-up detected hypergammaglobulinemia (3.9 g/dL) with increased serum immunoglobulin G (IgG) (2408 mg/dL), IgM (599 mg/dL), and IgE (175 mg/dL) with an IgG k monoclonal paraprotein. A bone marrow biopsy revealed dense nodular atypical lymphoid infiltrates, plasmacytosis, and megakaryocytic hyperplasia (panel B). Biopsy of the axillary lymph nodes showed diffuse large B-cell lymphoma. Subsequently, the patient was discovered to be positive for HIV type 1, with a viral load of 485 315 copies per microliter, and a CD4 cell count of 215 per microliter.

All patients with unexplained cold agglutination and hypergammaglobulinemia associated with lymphoma should undergo screening for HIV infection; peripheral blood analysis may be useful in the diagnosis of marrow involvement by lymphoma.
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