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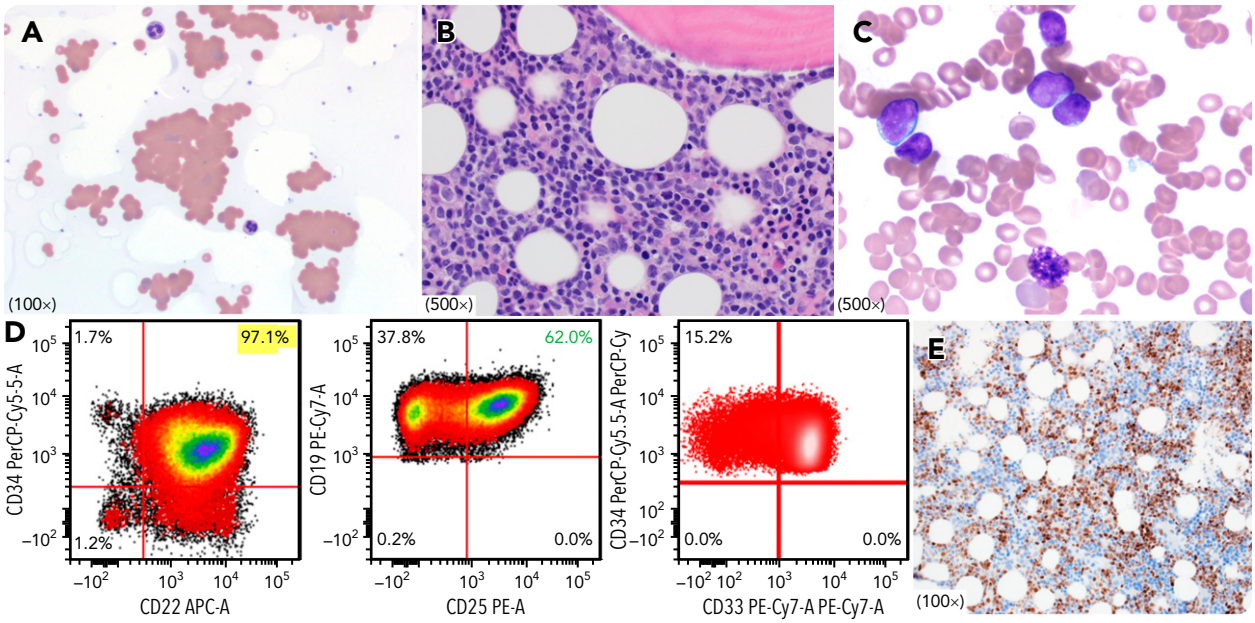
Unexpected presentation of cold agglutinin syndrome with B-acute lymphoblastic leukemia

Beenu Thakral and Carlos E. Bueso-Ramos, The University of Texas MD Anderson Cancer Center



A 44-year-old man presented to emergency department with sudden-onset dyspnea and fatigue. Complete blood count showed marked normocytic anemia (hemoglobin, 6.8 g/dL) with normal white blood cell and platelet counts. Peripheral blood smear showed marked red cell agglutination (Wright-Giemsa stain, panel A). Further work-up demonstrated cold autoimmune hemolytic anemia (cAIHA) with increased serum lactate dehydrogenase (653 U/L; range, 135-225), mild hyperbilirubinemia (total 2.6 mg/dL; indirect, 1.4), decreased haptoglobin (<3 mg/dL; range, 32-197), positive direct antiglobulin test for C3d only, and a cold agglutinin titer of 128. Bone marrow biopsy showed unexpected B-lymphoblastic leukemia (B-ALL) in a 70% cellular bone marrow with 40% blasts (panel B, hematoxylin and eosin stain; and panel C, May-Grunwald-Giemsa stain). Flow cytometry immunophenotyping identified aberrant B-lymphoblasts (36%) with CD10bright$^+$CD19$^+$CD22$^+$CD25partial$^+$CD33 partial$^+$CD34$^+$ CD79a$^+$ and negative for CD3, CD20, MPO, and CRLF2 (panel D). Blasts were positive for terminal deoxynucleotidyl transferase (TdT) immunostain (panel E). The patient was initially treated with steroids and rituximab for cAIHA followed by hyper CVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone), and blinatumomab for B-ALL.

Patients with cold agglutinin syndrome have cAIHA secondary to infection, autoimmune disorder, or overt B-cell lymphoma, with the latter usually indolent and lowgrade in most patients. This case illustrates a rare, unexpected initial presentation of cold agglutinin syndrome with B-ALL and emphasizes the importance of a comprehensive work-up because therapy needs to be directed for both cAIHA and B-ALL.

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