blood work
images in hematology

Cold agglutinin syndrome with unexpected bone marrow CD5$^+$ diffuse large B-cell lymphoma

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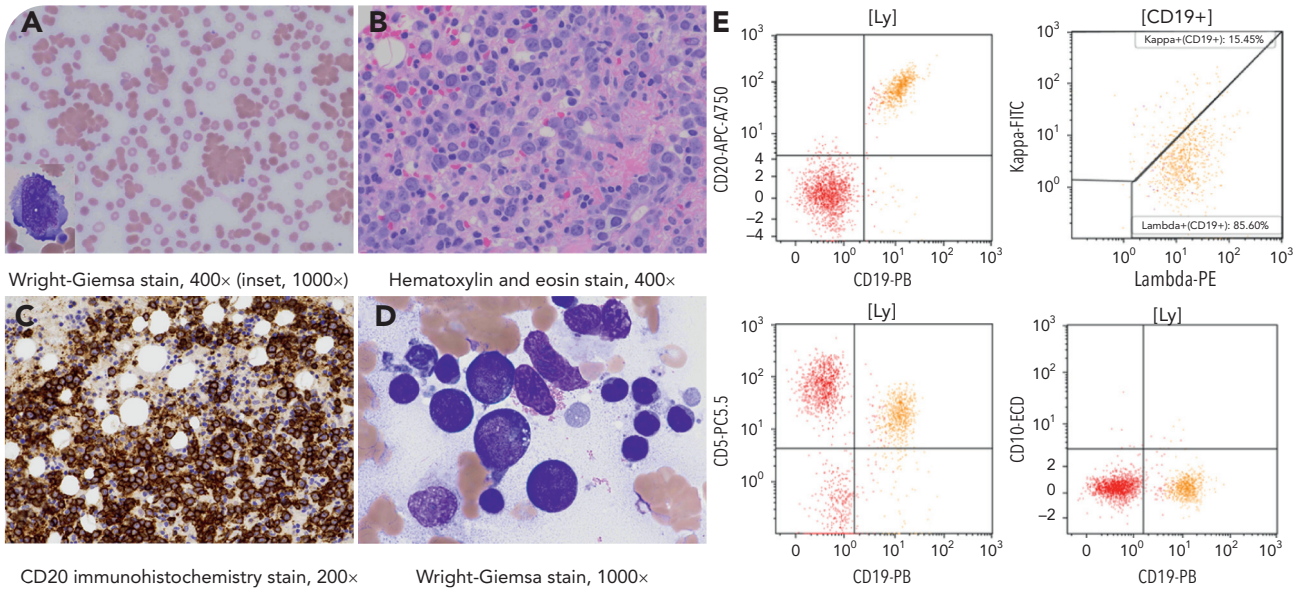

Wright-Giemsa stain, 400× (inset, 1000×)

Hematoxylin and eosin stain, 400×

CD20 immunohistochemistry stain, 200×

Wright-Giemsa stain, 1000×

A 57-year-old woman presented with a 1-week history of generalized weakness. Complete blood cell count revealed pancytopenia (hemoglobin, 8.7 g/dL; white blood cells, 2.2 × 10^9/L; platelets, 53 × 10^9/L). Peripheral blood smear showed marked red blood cell agglutination (panel A; 40× objective) with 2% atypical lymphoid cells (inset, 100× objective). Further workup demonstrated cold autoimmune hemolytic anemia (cAIHA) with increased serum lactate dehydrogenase (557-1500 U/L; range, 98-192 U/L) and a cold agglutinin titer of 160. There was no radiographic evidence of malignancy or lymphadenopathy. Bone marrow biopsy demonstrated unexpected diffuse large B-cell lymphoma (DLBCL) in a variably cellular (10%-90%) bone marrow (panels B [40× objective], C [20× objective], and D [100× objective]). Flow cytometry detected λ-restricted B cells (5%) with CD5$^+$/CD19$^+$/CD20$^+$/CD38$^+$/CD200$^+$, without CD10 or CD34 coexpression (panel E). Lymphoma cells were positive for B-cell lymphoma 2 (BCL2), B-cell lymphoma 6 (BCL6), and multiple myeloma 1 (MUM1), and negative for cyclin D1 and terminal deoxynucleotidyl transferase (TdT) (immunohistochemistry, not shown). Cytogenetics revealed abnormal complex karyotype (47,X,-X,-2,dic [3;6][p21;p25],del[5][q22],-7,add[7][q32],add[10][q22],+18,+2-6mar[cp8]), with negative fluorescent in situ hybridization for v-myc myelocytomatosis viral oncogene homolog (*MYC*), *BCL6*, and immunoglobulin heavy chain (*IGH*)::*BCL2* rearrangements.

Cold agglutinin syndrome is a rare type of autoimmune hemolytic anemia caused by cold-reacting autoantibodies secondary to infections, autoimmune diseases, or cancers. Lymphomas associated with cold agglutinin syndrome are usually indolent/low grade, with DLBCL extremely rare. This case emphasizes the importance of peripheral blood and bone marrow evaluation in patients diagnosed with cAIHA.

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