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CONTINUING MEDICAL EDUCATION
ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Hematology Quiz – Case 23

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2011, 28(2):285–286

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An 80-year-old man presented to the outpatient clinic with fatigue, difficulty in breathing, heartburn, chest pain and palpitations in effort, pain in fingers and toes during last week, as well as hemorrhagic dermal rash especially in the lower extremities (fig. 1). There was a history of mild anemia and episodes of acrocyanosis (blue discoloration of fingers and toes following exposure to cold) for the last ten years. A chronic non-deformans arthritis of the hands was diagnosed ten years ago with mild cervical lymphadenopathy and mild splenomegaly. No abnormal findings were detected in the CT of the upper and lower abdomen and of the chest.

The physical examination revealed pallor, tachycardia, splenomegaly (2 cm below the left costal margin) and hepatomegaly (3 cm below the right costal margin). Mild cervical and axillar lymphadenopathy were detected. The physical examination was otherwise unremarkable.

Laboratory tests were as follows: Hct: 21.3%, Hb: 6.1 g/dL, WBC: 2,800/μL (neutrophils 38%, lymphocytes 50%, monocytes 12%, reticulocytes: 6.1% and platelets 144.000/μL. Peripheral blood smear is shown in figures 2 and 3. Blood chemistry was Glu 1.50 mg/dL, BUN 0.70 mg/dL, creatinine 0.9 mg/dL, Na 135 mEq/L, K 4.0 mEq/L, Ca 4.6 mEq/L, SGOT 26 IU/L, SGPT 16 IU/L, bilirubin 2.52 mg/dL (indirect 1.8 mg/dL), ALP 105 IU/L, γGT 32 IU/L, uric acid 5.5 mg/dL, LDH 1,070 IU/L, CPK 10 IU/L. Total protein was 7.3 g/L (albumin 3 g/L, α_1-globulins 0.3 g/L, α_2-globulins 0.3 g/L, β-globulins 0.7 g/L and γ-globulins 2.5 g/L). The coagulation tests were normal (PT 11 sec, APTT 30 sec, fibrinogen 230 mg/dL). Direct Coombs test was positive for IgG, IgA, IgM, and C3; indirect Coombs test was also positive. Antibodies for *Mycoplasma*, EBV and other viruses were negative. ANA, anti-DNA tests were positive. Urine chemistry and microscopy were normal.

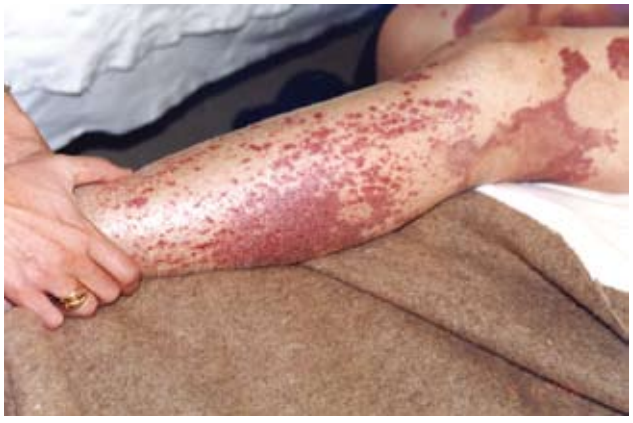

Figure 1

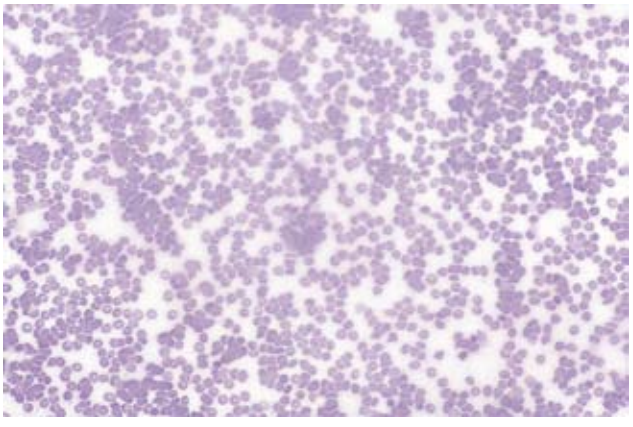

Figure 2

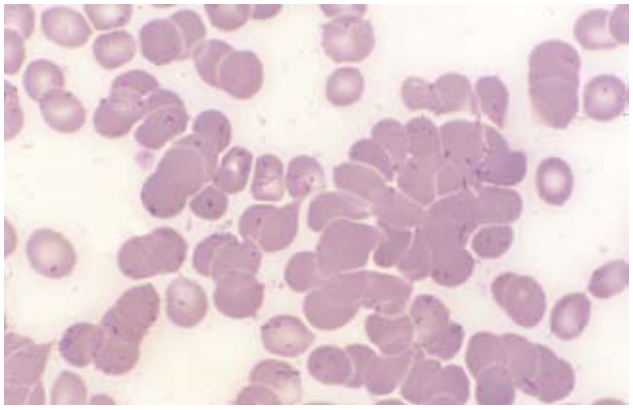

Figure 3

Comment

Anemia in systemic lypus erythematosus (SLE) is usually anemia of chronic diseases and/or autoimmune hemolytic anemia with a positive direct Coombs test. Cold agglutinin disease (CAD) is rarely the cause of anemia.

CAD is a type of hemolytic anemia characterized by the presence of cold agglutinins in the circulation. Cold agglutinins are IgM autoantibodies against carbohydrate antigen I producing erythrocytes agglutination during cold exposure and resulting in hemolysis. CAD usually accompanies lymphoproliferative neoplasms such as lymphomas, multiple myeloma, or monoclonal gammopathy of undetermined significance (MGUS).

Cold hemagglutinin disease (CHAD) is the main cause of the cold red cell autoantibody disorders; the second more common is paroxysmal cold hemoglobinuria (PCH). The IgM autoantibodies in CAD usually bind to red cells with complement activation resulting to hemolysis in vitro at the same temperature (monophasic hemolysins).

The characteristic IgG Donath-Landsteiner autoantibodies in PCH are usually biphasic hemolysins; they bind to red cells at low temperatures and activate complement at 37°C leading to hemolysis. The cold IgM autoantibodies of CAD can also cause biphasic hemolysis if they have a relatively low thermal range and a high complement fixing ability.

The disease is usually refractory to steroids and requires cytotoxic and/or immunosuppressive therapy, as well as anti-CD20 antibody administration in cases that did not respond to conventional treatment.

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