Case Report

Cold agglutinin-induced hemolytic anemia as the primary presentation in SLE - A case report

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Abstract

Cold agglutinin-induced hemolytic anemia as the primary presentation in systemic lupus erythematosus (SLE) is extremely rare. Only few cases have been reported in literature so far. Here, we report a 17-year-old girl who presented with features of hemolytic anemia and later diagnosed as a case of SLE.

Keywords: Autoimmune hemolytic anemia, cold agglutinin, Coombs test, systemic lupus erythematosus

Introduction

Autoimmune hemolytic anemia (AIHA) may be the first manifestation of systemic lupus erythematosus (SLE) and can appear several years before the diagnosis of SLE is made.[1] AIHA though rare in SLE is found more commonly in the childhood form of the disease than in adults.[2] Both American College of Rheumatology (ACR) and Systemic Lupus International Collaborating Clinics (SLICC) recognize AIHA as one of the diagnostic criteria for SLE. Antierythrocyte antibodies in SLE are mainly warm-type IgG, but mixed-type AIHA is also reported. Here, we are reporting a case who presented with features of AIHA with cold type IgG and later diagnosed to have SLE.

Case Summary

A seventeen year old girl was admitted with complaints of high-grade, intermittent, fever with chills, for 4–5 days. She also had multiple small and large joint pain symmetrically for 3–4 weeks, which was not associated with morning stiffness or restriction of movements. There was a history of fever with generalized nonpruritic rash several times prior to current admission and was managed as viral exanthematous fever. On examination, she had high-grade fever with tachycardia with normal blood pressure. There was pallor, bilateral pitting pedal edema and a 1 × 1 cm, nontender, firm, mobile right-sided cervical lymph node. There was no icterus, cyanosis, or clubbing. Respiratory system examination revealed bilateral basal crepitations with normal vesicular breath sounds. Cardiovascular system evaluation revealed normal heart sounds, grade 3 left parasternal systolic murmur, and no gallop. She had splenomegaly. There was no neurological deficit. Locomotor examination did not show signs of inflammation, restriction of movement, or deformity. On admission, her hemoglobin was 5.1 g/dL, MCV was 95.10 with a total leukocyte count 9,000/cumm and platelet count of 2,44,000/cumm. Serum creatinine was 0.7 mg/dL. Serum uric acid and serum electrolytes were within normal limits. Her serum bilirubin was 2.09 mg/dL (direct bilirubin - 1.09, indirect bilirubin - 1) with aspartate aminotransferase (AST) 125.4 IU, alanine aminotransferase (ALT)-35.4 IU, and alkaline phosphatase - 91.7 IU. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) values were also within normal range. Serum iron, ferritin, vitamin B12, and folic acid and thyroid stimulating hormone (TSH) level were normal. Peripheral smear for malaria and serology for dengue, viral hepatitis, chikungunya, and HIV were negative. Rheumatoid factor and anti-CCP were negative. Urine and blood culture were sterile. Chest X-ray revealed clear lung fields. Ultrasonography showed

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mild hepatosplenomegaly. Computed tomography (CT) thorax showed focal area of consolidation involving lateral basal segment of left lower lobe along with multiple subcentimetric mediastinal lymph node and axillary lymph nodes. Her electrocardiogram (ECG) and echocardiogram (ECHO) were normal. She was advised packed red blood cell transfusion, but the blood bank informed us about difficulty in cross matching due to presence of various autoantibodies in patient's blood. This led us to suspect AIHA. Further investigations revealed reduction in hemoglobin to 3 g/dL with a reticulocyte count of 13%. Serum bilirubin raised to 2.51 (direct - 1.23, indirect - 1.28), but liver enzyme levels remained within normal limits. Serum lactate dehydrogenase (LDH) was 1,052; direct Coomb's test was positive. Urine examination did not show RBCs or hemoglobin. Antinuclear antibody (ELISA) and anti-ds-DNA (high titer) were positive. Serum complement levels were low. C3 level was 76.21 mg/dL (normal = 90–180 mg/dL) and C4 level was <7.30 (normal = 10-40 mg/dL). Antiphospholipid antibodies (IgM and IgG) were <10 u/ml. Peripheral blood smear revealed features of normochromic normocytic anemia with anisocytosis, polychromatosis, and several microscopic agglutinated red cells. This was associated with cold agglutination in high titer. Serum protein electrophoresis was normal. Serology for cytomegalovirus, Epstein Bar virus, and mycoplasma were negative. FNAC of cervical lymph node depicted scanty aspirate of fat droplets and an occasional lymphocyte. Two units of least incompatible packed red cells were transfused with premedication. She was also treated with broad spectrum antibiotic and supportive care. Since the reports were in favor of a hemolytic process, we started inj. methylprednisolone 500 mg as intravenous pulse. Patient became afebrile with the second pulse of steroid. Follow-up investigations showed significant improvement in hemoglobin and normalization of reticulocyte count and LDH levels. After 3 days of pulse, she was switched over to tapering doses of oral prednisolone. She is doing well and is on regular follow-up.

Discussion

AIHA has been known to occur in 5%–10% of SLE patients. AIHA is a rare disease with an incidence of 1–3 per 1,00,000 people per year.[3] AIHA consist of warm, cold, or mixed reactive antibody types that are directed against antigens on the red blood cell surface.[4] Cold AIHA is distinguished from warm AIHA by a preponderance of immunoglobulin M autoantibodies known as cold agglutinins (CAs) that react strongly between 0°C and 4°C.[5] Cold AIHA can be primary or idiopathic and secondary to infection, malignancy or autoimmune conditions.[6] Pathophysiology is based on molecular mimicry of foreign antigens.[7] CAs activates classical complement pathway, leading to C3b deposition on the surface of red blood cells, which are phagocytosed in the liver.[8,9] Cold antibody-mediated hemolytic anemia is extremely rare in SLE. Only few cases have been reported in literature. There are different modalities of AIHA treatment, which includes corticosteroids, rituximab, IV immunoglobulin, or splenectomy. Although in cold-AIHA, steroid has less effect compared with warm AIHA to which our patient responded well. A similar case was reported by Chaubey *et al.*[10] and Srinivasan *et al.*[11] Patients presenting with anemia usually visit family physicians. Therefore, increased awareness among primary physicians about SLE presenting as hemolytic anemia especially in young ladies is important for the early diagnosis and appropriate management.

Conclusion

Though CA-induced AIHA as the primary clinical presentation of SLE is extremely rare, a high degree of clinical suspicion is the key to early diagnosis and adequate management.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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