Case Report

Cold Autoimmune Hemolytic Anemia as First Clinical Manifestations in Systemic Lupus Erythematosus (SLE) in Young Female Patient, a Rare Association: Case Report

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ABSTRACT

Background: Cold autoimmune hemolytic anemia" is very uncommon in systemic lupus erythematous (SLE), and until now a small number of similar reports have been published in scientific papers.

Case presentation: Here, we present a nineteen-year-old female patient who admitted with cold type hemolytic anemia, pancytopenia and was later diagnosed to have SLE.

Conclusion: Despite the very rare association between SLE and cold autoimmune hemolytic anemia (AIHA), this case report improves clinical practice regarding considering SLE as one of the differential diagnoses in cold AIHA, to provide early diagnosis and optimal management.

Keyword: Cold antibody AIHA, direct Coombs test, SLE, ANAs.

Introduction

Autoimmune hemolytic anemia (AIHA) is broadly classified as either "warm" or "cold" autoimmune hemolysis relies on the thermal degree at which the antibodies bind and destroy the patient's red blood cells (RBCs). Warm autoimmune hemolytic type is the most common, while cold type is an uncommon form of AIHA [1].

Cold autoimmune hemolytic anemia results when immunoglobulin M autoantibodies are directed against the patient's red blood cells at a temperature below 37°C, resulting in intravascular complex-mediated hemolysis [2]. Autoantibodies that bind and destroy the patient's red blood cells in systemic lupus erythematous (SLE) are mostly warm-type but cold autoantibodies are extremely rare [3].

Access this article online	
Quick Response Code:	Website: www.smh-j.com
	DOI: 10.54293/smhj.v4i2.101

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Received: 20 Feb 2024 **Received in revised form:** 26 Mar 2024 | **Accepted:** 30 Mar 2024

Please cite this article as: Alhashim H, Alsaleh HM, Alfayez RA, Alamin AM. Cold Autoimmune Hemolytic Anemia as First Clinical Manifestations in Systemic Lupus Erythematosus (SLE) in Young Female Patient, a Rare Association: Case Report. SMHJ [Internet]. 2024;4(2):109-111.

SMHJ
Saudi Medical Horizons Journal

Case Presentation

A nineteen-year-old Saudi single girl, not known to have any chronic medical illness, was admitted with complaints of easy fatigability, palpitation, exertional shortness of breath, and subjective fever for one week associated with generalized small and large joint pain bilaterally for nine months. There was no joint swelling, stiffness, or limitation of movement. There was no history of skin rash or mouth ulcer. There was no history of night sweats, weight loss, or anorexia. On examination, her vital signs were stable with no documented fever. There was pallor, jaundice, and bilateral lower limb pitting edema. There was no cyanosis, clubbing, or palpable lymphadenopathy. Respiratory and cardiovascular examinations were unremarkable apart from a hemic murmur. There was no focal neurological deficit. Musculoskeletal examination revealed no joint swelling, deformity or tenderness with normal range of movement. Upon admission, her total leukocytes count was 1.81 x 109/L, hemoglobin of 4.5 g/dl, mean corpuscular volume was 108.8 FL and platelet count of 46 x 109/L. Serum lactate dehydrogenase was 535. The erythrocyte sedimentation rate was 130. Urine examination showed +3 protein, 0-3 RBC, and 0-2 WBC. Serum creatinine was 88 µmol/L. Serum electrolytes including sodium, potassium, calcium, and phosphate were within normal range. Liver function test were unremarkable. Normal prothrombin and activated partial thromboplastin time. Serum iron was 9.21 µmol/L, and ferritin was 185 ng/ml. Serum folate and vitamin B12 levels were within reference range. Thyroid function test was unremarkable. Hemoglobin electrophoresis was normal. Urine protein 3.26 g/L, urine creatinine 3960 µmol/L, and spot urine protein/creatinine ratio 7.484. As the patient has symptomatic anemia and her hemoglobin level was below 7 g/dl, we requested a packed red blood cell transfusion (PRBC) to raise her hemoglobin level, but unfortunately the blood bank faced cross-matching difficulty as the patient found to have multiple autoantibodies so there was no compatible blood for her. Accordingly, we request direct and indirect Coomb's tests as we suspect AIHA, which came positive for the direct Coombs test. Peripheral blood smear showing RBC with marked auto-agglutination, moderate leukopenia with polymorphonuclear leukocytes shifting to the left, marked thrombocytopenia, and few reactive lymphocytes. Further investigations were requested to rule out secondary AIHA in the form of “Rheumatoid factor” and “anti-Cyclic Citrullinated Peptide antibody” were negative. Antinuclear antibody (ANA) was negative. Urine and blood culture showed no growth. Hepatitis profile and human immunodeficiency virus antigen/antibodies were negative. X-ray chest showed clear lung fields. Ultrasonography showed no hepatomegaly and no splenomegaly, both kidneys were normal in size, shape, and echo pattern with preserved corticomedullary differentiation, and no hydronephrosis is noted on either side. Contrast computed tomography (CT) of the chest, abdomen, pelvis, and neck showed bilateral multiple small sub-centimetric cervical lymphadenopathy, patchy areas of ground-glass opacification in the left upper and bilateral lower lung lobes, mild smooth interlobular septal thickening, mild subcutaneous chest wall edema, mild bilateral pleural effusion and mild pericardial effusion, no significant enlarged mediastinal, hilar or axillary lymph nodes. Two units of least incompatible packed red blood cells were transfused with pre-medications. Since the presentation was in favor of cold autoimmune hemolytic anemia, we kept the patient on a warm blanket, started her on intravenous immunoglobulin, and methylprednisolone 1g as intravenous pulse for 3 days then shifted to prednisolone 1mg/kg daily and hydroxychloroquine but hemoglobin level did not improve after 2 weeks. As we still suspect SLE we request to send another sample of ANA, C3, C4, and anti-double strand DNA (anti-dsDNA). We started her on a “Rituximab” 375 mg/m2 one dose weekly for 4 doses, with a dramatic response after the second dose as her hemoglobin level increased from 4.5 to 7.4 and then to 10g/dl. Her platelet count increased from 46 X 109 per litre to 184 X 109 per litre. Total white blood cell count increased from 1.81 to 3.6 X 109 per litre. Repeated investigations showed positive ANA (Pattern: homogenous, titer 1:1280) and anti-dsDNA with very low complement level, C3 was 0.305 g/L and C4 was less than 0.0695 g/L. Accordingly, we refer the patient to Rheumatology and Nephrology Department for further evaluation and management. A renal biopsy was done as the patient has nephrotic range proteinuria and showed morphologic features of focal mild mesangial hypercellularity and segmental sclerosis in four out of nine glomeruli with mild interstitial fibrosis and tubular atrophy. As we diagnosed and managed the patient in the early stage, she has currently been on follow-up with the Rheumatology and Nephrology clinic for about one year in stable condition.

Discussion

Anemia secondary to autoimmune hemolysis is caused by antibodies acting against self-RBCs antigens leading to premature RBC destruction and intravascular hemolysis [4]. Autoimmune hemolysis can present in either “warm” or “cold” form relies on the thermal degree at which the antibodies bind and destroy the patient's red blood cells (RBCs). [1]. Autoantibodies against red blood cells (RBCs) in SLE are mainly warm-form but cold autoantibodies are

very rare, therefore clinical practitioners should have high clinical suspicion to provide early diagnosis and management [3]. In SLE, AIHA is often refractory to standard first-line therapy, which is why we started second-line treatment with Rituximab, which showed a remarkable response [5].

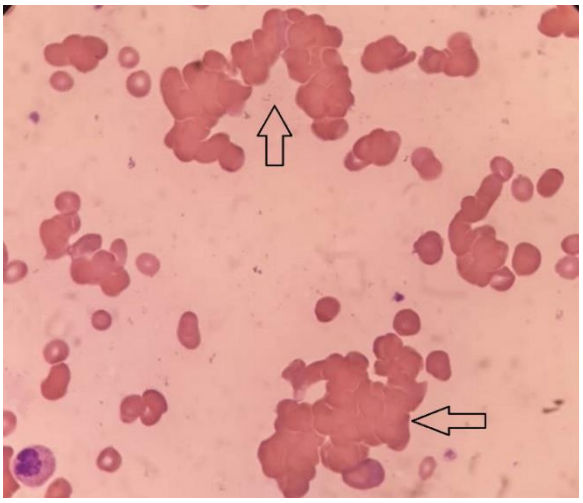

Figure 1: Peripheral blood smear showing RBC with marked auto-agglutination.

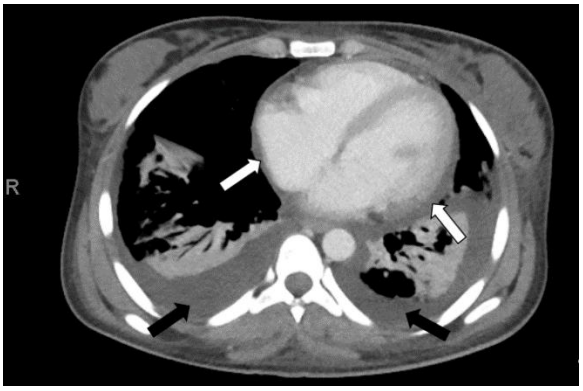

Figure 2: Chest computed tomography, axial view with intravenous contrast showed mild bilateral pleural effusion (black arrows) and mild pericardial effusion (white arrows).

Conclusion

Cold reactive autoimmune hemolysis as the first clinical manifestation of SLE is extremely uncommon. Raising the index of clinical suspicion is needed for prompt diagnosis and management. Repeated ANA testing should be considered in highly suspected cases to avoid false negative results. In SLE, AIHA is often refractory to first-line therapy like corticosteroid, so initiation of second-line therapy including Rituximab should not be delayed.

Conflict of Interest

None

Funding

None

References

1. Lechner K, Jager U. How I treat autoimmune hemolytic anemias in adults. Blood. 2010;116(11):1831-8

2. Despotovic JM, Kim TO. Cold AIHA and the best treatment strategies. Hematology Am Soc Hematol Educ Program. 2022;2022(1):90-5.

3. Mohanty B, Ansari M, Kumari P, Sunder A. Cold agglutinin-induced hemolytic anemia as the primary presentation in SLE - A case report. J Family Med Prim Care. 2019

4. Hill A, Hill QA. Autoimmune hemolytic anemia. Hematology Am Soc Hematol Educ Program. 2018;2018(1):382–9.

5. Pavo-Blanco M, Novella-Navarro M, Cáliz-Cáliz R, Ferrer-González MA. Rituximab en la anemia hemolítica autoinmune refractaria en lupus eritematoso sistémico. Reumatol Clin. 2018;14(4):248–9.