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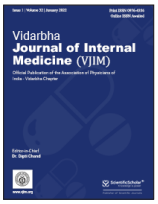

Case Report

Autoimmune Haemolytic Anaemia as Presenting Feature of Systemic Lupus Erythematosus

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ABSTRACT

Here, we describe a unique case of a 37-year-old woman who presented with a vague clinical presentation, found to have warm autoimmune haemolytic anaemia. Further immunological and inflammatory workup during hospitalisation lead to the diagnosis of systemic lupus erythematosus.

Keywords: 37 years, Systemic lupus erythematous, Warm autoimmune haemolytic anaemia

INTRODUCTION

Autoimmune haemolytic anaemia is a rare acquired disorder characterised by autoantibodies against red cell antigens resulting in haemolysis and anaemia due to a decrease in the red blood cell (RBC) life span.[1] It can be caused by warm, cold or mixed antibodies.[2] AIHA can occur as idiopathic (primary) or secondary to other malignancies (leukaemia, lymphoma or solid tumours), infections and autoimmune diseases (like SLE).[1,3] Incidence is 1–3 out of 100,000 patients/year, out of which 70–80% are caused by warm autoantibodies resulting in warm autoimmune haemolytic anaemia (wAIHA).[3] About half of all wAIHA cases are secondary to the above conditions.[3] Secondary AIHA may also occur in systemic lupus erythematosus (SLE) and it is reported that 10% of SLE patients have wAIHA; however, wAIHA as the initial presentation of SLE is rare.

CASE REPORT

A previously untransfused 37-year-old, resident of rural area, gravida 2, para 1 and one intrauterine death, woman with no other comorbidities presented to the outpatient department with fatigue, generalised weakness and shortness of breath on exertion for the past 2 months with worsening of symptoms for the past 2–3 weeks. The patient also mentioned decreased food intake and dark stools during the same period of time. She denied symptoms of arthritis and Raynaud's phenomenon to date. She denied taking any medications or supplements except iron supplements, which she started taking after visiting general practitioners. She had no family history of autoimmune diseases.

Vitals on presentation were temperature 98.1°F, heart rate of 120 beats/min, blood pressure of 150/90 mmHg, respiratory rate of 22/min, and oxygen saturation 97% on room air. Pallor was seen, no lymphadenopathy, anicteric sclera, and 1+ pitting oedema on both lower extremities were noted. Lungs were clear to auscultation and the abdomen was soft, non-tender, and mild splenomegaly with normal bowel sounds. No rash was identified.

ECG showed sinus tachycardia and a chest X-ray revealed left costophrenic angle blunting without cardiomegaly.

The sample for the direct Coombs test with IgG was positive. Haemoglobin was 5.9 g/dL. The stool was negative for occult blood. Peripheral smear showed RBC agglutination, moderate anisopoikilocytosis, polychromasia, spherocytes, teardrop cells, and occasional elliptocytes. Upper GI endoscopy was normal up to D2. Reticulocyte counts were 10% (high). LDH was increased. Vitamin B12 levels and serum ferritin were high. While managing with intravenous steroids, (Methylprednisolone - 1 mg/kg) additional haematology and rheumatology work-ups were continued. ANA (by IF) screen showed 1:3200 (very strong positive), titre with speckled nuclear pattern (typically associated with SLE or MCTD). Rheumatoid factor was negative. Anti-ds DNA, anti-Sm, and RNP were positive. HIV, hepatitis B surface antigen, and Hep C antibody are non-reactive. [Table 1] shows all laboratory results since the presentation.

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With the positive laboratory findings, a diagnosis of SLE was confirmed according to 2019 American College of Rheumatology (ACR) and 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria.

The patient reported improvement of her symptoms with steroid pulse therapy of 5 days. Her haemoglobin improved up to 7.3 g/dL; she discharged on prednisolone on tapering doses and azathioprine.

DISCUSSION

Warm autoimmune haemolytic anaemia occurs due to IgG antibodies causing haemolysis through Fc-mediated extravascular phagocytosis of the IgG-coated RBCs in the spleen, resulting in spherocytes due to loss of RBC membrane.[4] DAT is useful in differentiating immune- from non-immune-mediated haemolytic anaemia.[5]

Haematological manifestations occur in SLE affecting all three cell lines. The aetiology of anaemia is reported as multifactorial, including anaemia of chronic disease, autoimmune haemolysis, renal disease or treatment induced. Autoimmune haemolysis occurs in <10% of patients with SLE. Haemolytic anaemia can occur years before or after a diagnosis of SLE is made and rarely as an initial presenting feature of SLE.[6,7] Warm autoimmune haemolytic anaemia is more common than cold agglutinin type. No specific diagnostic criteria exist for haemolytic anaemia; however, the diagnosis is made if no other cause of anaemia is identified in the presence of signs of RBC destruction (e.g., elevated LDH, unconjugated bilirubin and low haptoglobin), signs of accelerated RBC production (e.g., increased reticulocyte count), positive DAT test and peripheral smear with schistocytes or spherocytes.

Both the 2019 ACR and 2012 SLICC classification criteria include haemolytic anaemia as one of the diagnostic criteria for SLE.[2]

Below is the application of ACR criteria to our patient (a score of at least 10 indicates SLE).

Entry criteria

It is positive for ANA (antinuclear antibody) at a titre of ≥1:80.

Additive criteria

1. Autoimmune haemolysis score 4;
2. Serosal effusion score 5;
3. Complement proteins, low C3 and C4 score 4;
4. SLE-specific antibody and anti-ds DNA score 6.

(double-stranded DNA)

Table 1: Laboratory parameters.

		Reference range
Haematocrit	15.1%	35–45
Mean corpuscular volume	98.1 FL	78.5–96.5
Platelets	3.23 LAC	1.5–4.5
Total leukocyte count	12,690/CUMM	4000–11,000
Reticulocyte count	10%	0.5–2.5
Ferritin	1235 ng/mL	10–280
Lactate dehydrogenase	519 U/L	135–214
VIT B12	1960 pg/mL	191–771
Urine albumin	Absent	Absent
HB electrophoresis	Normal pattern	
Direct Coombs test	Positive 4+	Negative
C3	25.30 mg/dL	90–180
C4	5.37	10–40
Bilirubin indirect	1.2 mg/dL	0–1
Ultrasound : Abdomen	Mild hepatosplenomegaly with mild ascites and pleural effusion	
2D Echocardiography	Normal	
Upper GI Endoscopy	Normal	
Antinuclear antibody (Immunofluorescence)	1:3200 (positive) speckled pattern	NO IF
Anti-ds DNA/SM/RNP/KU	++	
Stool occult blood	Negative	
Peripheral smear	Spherocytes, agglutination, polychromasia, teardrop and anisopoikilocytosis	

HCT: Haematocrit, MCV: Mean corpuscular volume, TLC: Total leukocyte count, LDH: Lactate dehydrogenase, USG ABDO: Ultrasound Abdomen, 2DECHO: 2D echocardiography, UGI endoscopy: Upper GI endoscopy, ANA(IF): Antinuclear antibody (Immunofluorescence)

With a total score of 19, our patient met the criteria for diagnosis.

Our patient also met the criteria of SLE per 2012 SLICC with the following positive findings.

1. ANA;
2. Clinical criteria: Serositis and haemolytic anaemia;
3. Immunological criteria: ANA, anti-ds DNA, low complement, and positive direct Coombs test.

Although both the criteria were met in our case, depending on the turnaround times for different tests, a presumed diagnosis is often made with pending work-up; thus, high suspicion and awareness of rare presentations of SLE are needed among clinicians. Autoimmune haemolytic anaemia can be part of another autoimmune disease spectrum; therefore, identifying it as part of other disease processes and considering wide differential is important.

Treatment of wAIHA in SLE is based on a few retrospective analyses and rare case reports in which the results of idiopathic AIHA were extrapolated to AIHA secondary to SLE, leading to similar treatment options such as corticosteroids, steroid-sparing immunomodulators such as rituximab, splenectomy, and immunoglobulins.[1,6,8,9] The steroid response rate in secondary wAIHA is reported to be around 80%; however, approximately 60% of patients lose response with weaning or discontinuation of steroids, requiring prolonged therapy or slow tapering with close surveillance.[9]

CONCLUSION

Although wAIHA as an initial presentation of SLE is rare, a high degree of suspicion followed by thorough investigation among clinicians is needed for accurate diagnosis and timely management. We aimed to highlight the importance of utilising clinical criteria to aid in the diagnosis of autoimmune diseases, especially in cases with vague presentations.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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