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Case Report

Internal Medicine Section

Autoimmune Haemolytic Anaemia, Acute Pericarditis with Cardiac Tamponade as Presenting Manifestations in Systemic Lupus Erythematosus- A Rare Case Report

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ABSTRACT

Systemic Lupus Erythematosus (SLE) is an autoimmune disorder that affects mostly young women in which tissue-binding autoantibodies and immune complexes cause damage to organs and tissues. SLE is characterised by aberrant immunological responses that result in the release of higher levels and immunogenic nucleic acids, proteins, and other self-antigens. Autoimmune Haemolytic Anaemia (AIHA) is a condition in which antibodies against red blood cells are present. It is classified as a warm and cold antibody AIHA. The causes of warm antibody AIHA are autoimmune illnesses, infections, or even malignancy. The presence of Immunoglobulin G (IgG) antibodies can indicate warm autoimmune haemolytic anaemia (warm agglutinin anaemia), which is characterised by fatigue and other constitutional symptoms. Although, autoimmune haemolytic anaemia can be a component of the SLE spectrum, warm autoimmune haemolytic anaemia as the first manifestation of SLE is exceedingly rare. This case report describes a case of a 23-year-old female who presented to the hospital with complaints of breathlessness and chest pain. After evaluation she was found to have pericardial tamponade and AIHA. Pericardiocentesis was done and further investigations confirmed the diagnosis of SLE. She was treated with injectable methylprednisolone, injectable antibiotics, Tab. hydroxychloroquine, Tab. febuxostat ,Tab. colchicine, oral antidiuretic, oral levothyroxine and other supportive management. The lack of unambiguous pathognomonic characteristics or tests, coupled with the variable presentation of SLE, makes diagnosis tricky. Overall, AIHA can be an initial presentation as well as a part of other disease processes, emphasising the significance of a comprehensive work in patients with AIHA.

Keywords: Haemolysis, Pericardiocentesis, Steroids

CASE REPORT

A 23-year-old female presented with fever (moderate grade, intermittent), swelling over face and both lower extremities for two months and breathlessness for the past two days.

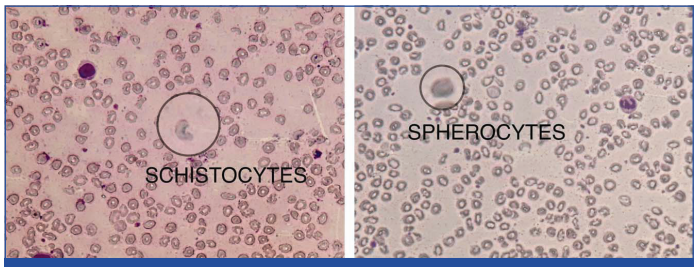
On admission, she was conscious, oriented {Glasgow coma score (GCS) of 15}, breathlessness {New York Heart Association (NYHA) grade IV}. General physical examination revealed axillary temperature of 101° Fahrenheit, pulse rate was 106 per minute, Blood Pressure was 100/70 mmHg taken in right arm supine position. Jugular Venous Pressure (JVP) was raised to 8.5 mm of water, pitting oedema and bluish discolouration of the nails were seen on both lower limbs. Bilateral macular oedema was revealed during a fundus examination. There was no rash observed over trunk and extremities. Auscultation revealed clear lungs and a soft, tender per abdomen examination with normal bowel sounds. Cardiovascular system examination revealed muffled heart sound and S3 gallop.

The haematological parameters revealed pancytopenia with haemoglobin of 6.4 gm%, Total Leucocyte Count (TLC) of 3100/cubic per mm, total platelet count was 0.53 lakh/cubic mm. Direct and indirect Coombs test was done by gel card method and Direct Coombs Test (DCT) was positive [Table/Fig-1]. The Antinuclear Antibodies (ANA) test revealed to be 2.8 (0.9 negative, >1.1 raised) with a homogeneous nuclear pattern (typically associated with SLE). Human Immunodeficiency Virus (HIV), hepatitis B surface antigen, and hepatitis C antibodies were non reactive. The peripheral blood smear revealed normocytic normochromic Red blood cells with anisopoikilocytosis in the form of schistocytes, spherocytes and both respectively, suggestive of haemolytic anaemia [Table/Fig-2a-c].

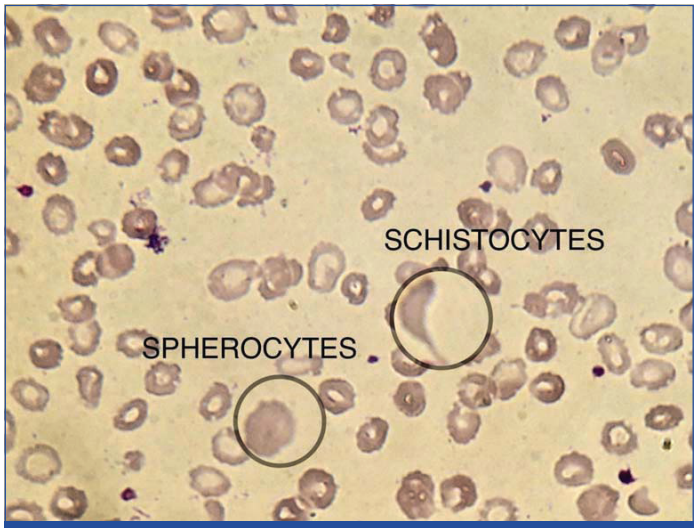
Test	Patients results (Reference range)	Test	Patients results (Reference range)
Haemoglobin (gm%)	6.4 (12-15)	Direct bilirubin (mg/dL)	1 (0-0.2)
Haematocrit (%)	18.8 (36-46)	Indirect bilirubin (mg/dL)	0.5 (0.2-0.8)
Mean corpuscular volume (fL)	104 (78.9-98.6)	Total bilirubin (mg/dL)	4.5 (0.3-1.0)
Mean corpuscular haemoglobin (pg)	19.6 (26.8-33.8)	Prothrombin time (seconds)	14.1 (9.4-12.5)
Mean corpuscular hemoglobin concentration (gm/dL)	33.07 (31.5-36.5)	International normalised ratio	1.19 (0.8-1.1)
Red cell distribution width (%)	24.2 (11.5-15.5)	Urine total protein (mg/dL)	628 (1-14)
Reticulocyte (%)	3.5 (0.5-2.17)	Protein/Creatinine (mg/dL)	1950 (1-249)
Iron (mcg/dL)	34 (50-170)		
Ferritin (ng/dL)	476.2 (11-307)	Vitamin B12 (pg/mL)	528 (180-914)

Total iron-binding capacity (mcg/dL)	240 (250-450)	Complement C3 (mg/dL)	25 (83-193)
Iron saturation (%)	14 (15-50)	Complement C4 (mg/dL)	3 (15-57)
Lactate dehydrogenase (U/L)	702 (100-190)	Erythrocyte Sedimentation Rate (ESR) (mm/hr)	102 (0-20)
White blood cells (/mm^3)	3100	Urine total protein (mg/g)	5150 (<150)
Platelets (lakh/mm^3)	0.53		
Potassium (mmol/L)	5.8 (3.5-5.1)	RA quantitative (IU/mL)	12.4 (12)
Blood urea nitrogen (pg/mL)	42 (0-100)	Anti-ds DNA (IU/mL)	260 (<4)
Creatinine (mg/dL)	2.5 (0.6-1.2)	Antinuclear antibodies	2.8(>1.1 raised)
Aspartate transaminase (U/L)	55 (13-39)	Thyroid stimulating hormone (UIU/mL)	4.37 (0.465-4.68)
Alanine transaminase (U/L)	12 (7-52)	Vitamin D (ng/mL)	8 (<20)
Alkaline phosphatase (U/L)	99 (34-104)	Serum protein electrophoresis g/dL (g/dL)	5.6 (6.1-8.1)

[Table/Fig-1]: Laboratory investigations results since the presentation.



[Table/Fig-2ab]: Peripheral smear findings. a): Leishman stain (40X) shows normocytic normochromic RBCs., and schistocytes; b): Leishman stain (40X) few spherocytes. (Images from left to right)

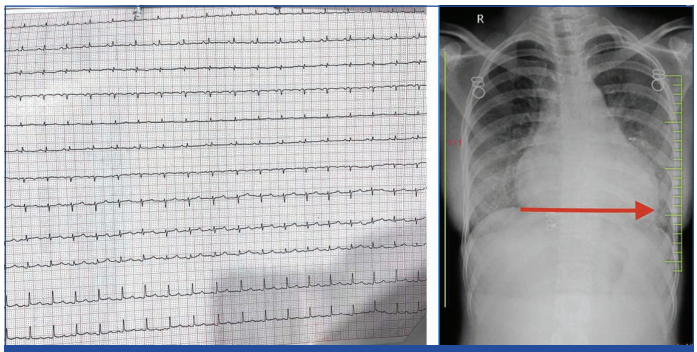


[Table/Fig-2c]: Peripheral smear findings Leishman stain (Oil immersion view: 100X) shows normocytic normochromic RBCs and along with spherocytes and schistocytes are also appreciated.

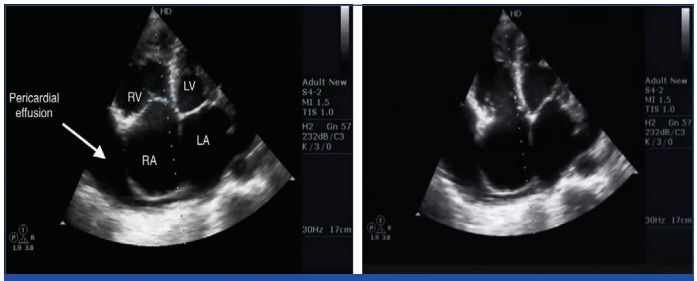
Blood group A+ with positive Coombs with warm antibodies, as well as several additional antibodies, was detected throughout the type, screen, and cross match process. The patient was hospitalised to the Intensive Care Unit (ICU), where her haemodynamics and transfusion reactivity were constantly scrutinised. Haematological and rheumatology work-ups were continued while ultrasound of abdomen and pelvis was suggestive of bilateral perirenal fluid collection associated with bilateral polycystic ovarian disease. Electrocardiogram (ECG) was suggestive of suggestive of low QRS voltages in limb leads and precordial leads with electrical alternans [Table/Fig-3].

Interstitial oedema, moderate cardiomegaly, enlarged cardiac silhouette or "water bottle sign" suggestive of pericardial effusion were noted on a chest X-ray [Table/Fig-4].

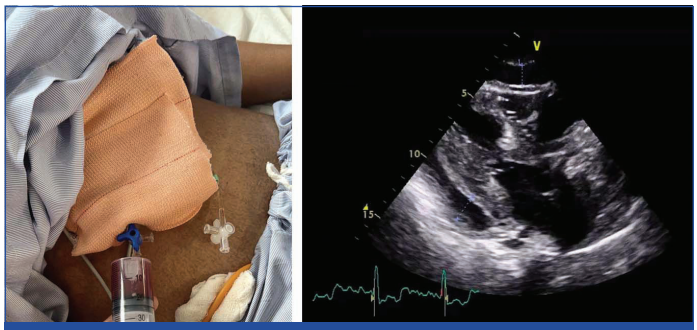
2D Echocardiogram (ECHO) was done which was suggestive of massive pericardial effusion with tamponade [Table/Fig-5]. [Video-1] shows Right ventricle (RV) free wall is collapsing in RV cavity. Diastolic collapse of RV, sign of cardiac tamponade [Table/Fig-6]. In view of polyserositis, pericarditis complicated in cardiac tamponade Urgent pericardiocentesis was done [Table/Fig-7].



[Table/Fig-3]: Electrocardiogram was suggestive of low QRS voltages in limb leads and Precordial leads with electrical alternans.
[Table/Fig-4]: Interstitial oedema, moderate cardiomegaly, enlarged cardiac silhouette or "water bottle sign" suggestive of pericardial effusion were noted on a chest X-ray. (Images from left to right)



[Table/Fig-5]: 2D ECHO was done which was suggestive of Massive Pericardial Effusion with Tamponade.
[Table/Fig-6]: Right Ventricle (RV) free wall is collapsing in RV cavity. Diastolic collapse of RV,sign of Cardiac Tamponade. (Images from left to right)



[Table/Fig-7]: Haemorrhagic pericardial effusion.
[Table/Fig-8]: Review 2D ECHO showing minimal pericardial effusion post pericardiocentesis. (Images from left to right)

In view of Polyserositis, Pericarditis complicated in cardiac tamponade urgent pericardiocentesis was done [Table/Fig-7].

Review 2D ECHO was done after pericardiocentesis suggestive of minimal anterior collection of pericardial effusion, posterior pericardial effusion 0.8 mm [Table/Fig-8].

Patient was advised kidney biopsy in view of evidence of severe nephritis but she denied. She was treated with injectable methylprednisolone (1 mg/kg/day for seven days followed by 1 mg/kg/day injectable prednisolone for next seven days), Injectable

antibiotics, tab. hydroxychloroquine, tab. febuxostat, tab. colchicine (in view of initial episode of acute pericarditis) 0.5 mg once daily, oral antidiuretic, oral levothyroxine and other supportive management. She was discharged after 15 days and was advised to continue oral corticosteroid like prednisolone 30 mg once a day till next follow-up, tab. hydroxychloroquine, tab. febuxostat, oral antidiuretic, oral levothyroxine on lower dose of 12.5 mcg once a day. On her first follow-up after 15 days her breathlessness significantly improved and there was no evidence of pericarditis, pancytopenia.

DISCUSSION

Systemic Lupus Erythematosus (SLE), is a chronic autoimmune inflammatory condition that impacts several organs and has an unexplained cause. Serosal involvement is prevalent in SLE [1], and it has been included in the American College of Rheumatology (ACR) lupus diagnostic criteria since1982, and later in the Systemic Lupus Collaborating Clinics (SLICC) 2012 classification criteria [2].

SLE is more common in women of childbearing age, such as in the present case report. Pericarditis is the most prevalent lupus cardiac symptom, affecting 9-54% of lupus patients. Cardiac tamponade is substantially less common, with an incidence of about 2.5% [3]. Predictive variables and the prevalence of tamponade in lupus patients were only briefly discussed in a few publications. Eric Dein et al., reported pericarditis is a manifestation of SLE serositis recognised in the ACR, SLICC classification criteria of SLE [4].

Chadia Chourabi et al., reported a case of 22-year-old female known case of SLE that manifested initially as cardiac tamponade, based on haemolytic anaemia, serositis, arthralgia, positive anti-nuclear, and low complement they diagnosed systemic lupus erythematosus, pericardiocentesis, intravenous methylprednisolone followed by daily oral prednisone with hydroxychloroquine administered to the patient [5]. SLE causes haematological symptoms in all three cell lines, resulting in anaemia, thrombocytopaenia, and leuckopenia, with anaemia being the most prevalent [6].

Anaemia can be caused by a variety of factors, including anaemia of chronic diseases, immunological hemolysis, nephropathy, or treatment-induced anaemia. Autoimmune hemolysis affects less than 10% of SLE patients [7]. Haemolytic anaemia can develop years before or after a diagnosis of SLE, and it is rarely the first manifestation of SLE [7]. Haemolytic anaemia is one of the diagnostic criteria for SLE in both the 2019 American College of Rheumatology (ACR) and the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria [8].

Hair P et al., concluded the persistence of circulating anti-erythrocyte antibodies in 90% of subjects with SLE and a history of AIHA [9]. The resulting erythrocyte complement opsonization and anaphylatoxin production raise the possibility that these complement effectors are involved in chronic morbidity and the risk of AIHA relapse [9]. Kanderi T et al., describes a rare case of a 32-year-old woman who had a muddled clinical picture and later diagnosed with warm autoimmune haemolytic anaemia. Additional immunological and inflammatory testing done both during and after the patient's hospitalisation resulted in the diagnosis of systemic lupus erythematosus [10].

Warm autoimmune haemolytic anaemia is more prevalent than cold agglutinin type autoimmune haemolytic anaemia. Haemolytic anaemia has no specific diagnostic criteria; however, it is diagnosed if there is no other cause of anaemia and signs of RBC destruction (like elevated LDH, unconjugated bilirubin, low haptoglobin), markers of expedited RBC production (like increased reticulocyte count), positive DAT test, and schistocytes or spherocytes on a peripheral smear. Warm autoimmune haemolytic anaemia is caused by IgG antibodies that cause hemolysis in the spleen by Fc-mediated extravascular phagocytosis of IgG-coated red blood cells, ultimately in spherocytes due to RBC membrane loss [11].

The application of ACR criteria in the present case is shown below (a score of at least 10 indicates SLE) [2]. Enrollment criteria Antinuclear antibody (ANA) with a titer greater than or equal to 1: 80 is required. In the present case report, the patient met the diagnosing criteria with a total score of 25.

With the following positive findings in the present case met the 2012 SLICC criteria [8] for SLE-

1. Lupus nephritis: ANA;
2. Clinical criteria: Serositis, renal and haemolytic anemia;
3. Immunological criteria: ANA, Anti-dsDNA, antiphospholipid antibody, low complement, positive direct Coombs test.

After ruling out other possibilities like infection, cancer, or heart failure, lupus-related serositis was confirmed. The diagnosis of pericarditis made with clinical features, clinical examination, 2D-echocardiogram, electrocardiography. Clinically typical precordial sharp pain; pericardial rub on auscultation; characteristic ECG changes (electrical alternans); also associated with features developed on echocardiography were suggestive of pericardial tamponade in this case report.

Mathian A et al., describes circulating regulatory T cells are rapidly, dramatically, and briefly increased by intravenous high dose methylprednisolone. This growth might contribute to methylprednisolone's ability to prevent future SLE flare-ups [12]. Cheng W et al., suggested early pericardiocentesis can save lives, hence it is important that cardiac tamponade be identified as soon as possible with comprehensive physical examination and the necessary investigations [13]. Immunosuppression, preferably with intravenous methylprednisolone and adjuvant pericardiocentesis, appears to be necessary and efficacious in lupus-related tamponade.

CONCLUSION(S)

The SLE can present as multiple symptoms, rarer presentations like refractory anaemia, breathlessness should raise the suspicion of autoimmune hemolysis and cardiac tamponade.The treating physician should keep these rare possibilities while treating cases of SLE.

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