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Case Report

Auto immune mixed haemolytic anaemia: a rare presentation of SLE

Mote Srikanth, S. Lokesh*, Anirban Dutta, Vaishnavi Danasekaran

Department of General Medicine, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed-to-be University) Pondicherry, India

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***Correspondence:**
Dr. S. Lokesh,
E-mail: lokeshdr@gmail.com

ABSTRACT

Auto Immune Mixed Haemolytic Anaemia (AIHA) is defined as presence of both warm and cold antibodies against patient's own red blood cells which is diagnosed by monospecific Direct anti-globulin test. Hereby we report a middle-aged women old women who was a known case of hypothyroidism on regular medication, presented with history of fatigability, exercise intolerance and exertional breathlessness of 1 month duration. The patient was subjected for preliminary investigations, which revealed severe anaemia with hemoglobin of 3.6 g% and an increased reticulocyte count of 12% with normal total leukocyte and platelet counts. Peripheral smear revealed anisopoikilocytosis, nucleated RBCs and schistocytes. Biochemical tests for haemolysis was evaluated which showed and elevated LDH levels (780U/L), and a reduced serum haptoglobulin levels. Liver Function test revealed a total bilirubin of 6.8mg/dl with indirect bilirubin of 5.4 mg/dl with normal liver enzymes. Baseline evaluation of Auto immune haemolytic anaemia with coombs test turned out to be positive. Patient was subjected for Mono specific DAT, Indirect Anti-globulin test (IAT) and antibody screening. Mono specific DAT showed both Anti IgG and anti C3 antibodies. IAT test was positive at 4^0C and negative at 22^0C and 39^0C which confirmed that the AIHA was of mixed warm and cold type. On evaluation for connective tissue diseases, patient serum was reactive for ANA and ds-DNA and found to have Systemic Lupus Erythematosus which is a rarity and was responded to corticosteroids.

Keywords: Autoimmune haemolytic anaemia, Direct anti-globulin test, Immunoglobulin (Ig), Intravenous immunoglobulin, Systemic lupus erythematosus

INTRODUCTION

Autoimmune haemolytic anaemia (AIHA) is characterized by the production of antibodies directed against self RBCs. AIHA is fairly uncommon disorder, with estimate of the incidence 1-3 cases 100,000 per year. AIHA is classified by the temperature at which autoantibodies bind optimally to RBCs. In warm antibody AIHA, which constitutes about 80-90% of adult cases, haemolysis is mediated by antibodies which bind to RBCs at 37°C (98.6°F). In cold antibody AIHA the antibodies are of IgM class which react at temperatures of <37°c, require complement for activity and produce spontaneous agglutination of red blood cells in vitro.

Mixed AIHA is the presence of both warm and cold antibodies.[1,2] Haematological abnormalities are frequently encountered in patients with Systemic lupus erythematosus (SLE).[3] Most patients have warm antibody AIHA. There have been some reports of adult AIHA secondary to SLE with involvement of not only warm antibodies but also cold antibodies, that is mixed -type AIHA (mixed AIHA).[4] Patient with SLE may develop several haematological complications including anemia, leukopenia, thrombocytopenia. Several case series have

shown that autoimmune haemolytic anemia occurs in 10% patients with SLE.[5,6] AIHA is often associated with extrahematological features, as sever renal and central nervous system involvement, which may require corticosteroid and immunosuppressive treatment.[7] Glucocorticoids can cause dramatic cessation or marked slowing of haemolysis in about two third of patients. The best responses are seen in idiopathic cases or in those related to SLE. Drugs reported in the treatment of refractory AIHA in SLE include IVIG, azathioprine and other immunosuppressive medications as well as danazol and rituximab.[8,9]

CASE REPORT

A thirty eight year old middle aged women who presented to our hospital with chief complaints of fever of ten days with easy fatigability, breathlessness and abdominal pain for seven days. Patient was apparently normal ten days back she developed fever which was acute in onset, high grade, intermittent, associated with chills and rigors and relived on medication. There was no evening rise in temperature. She developed easy fatigability and breathlessness for seven days which was insidious in onset and gradually progressed from class II to III grade according to New York Heart Association (NYHA) grades of dyspnea. Breathlessness was associated with bilateral pedal edema and palpitations. Patient had abdominal pain for seven days which was continuous, diffuse, dragging and non-radiating type of pain. She was a known case of hypothyroidism since 20 years on replacement therapy with L-thyroxine 75mcg once daily and also a known case of type 2 diabetes mellitus for 7 months and on oral hypoglycemic drugs (metformin and glimipride)

Patient achieved menarche at the age of 14 years. She had irregular menstrual cycles of 5/45 with bleeding period of 5 days. Married since 34 years with an obstetric score of G3P3, normal vaginal delivery with no complications. No history of any pregnancy loss and abortions.

She was taking mixed diet and had no disturbances in sleep and appetite. No disturbances in bowel habit and no addictions. No history of similar complaints in the family.

On general examination the patient was conscious, oriented to time, place and person, co-operative, moderately built and moderately nourished. Patient was anaemic, jaundiced (Figure 1) and was having bilateral pitting pedal edema (Figure 2). JVP was elevated by eight centimeters of H2O from the sternal angle. There was no clubbing, cyanosis, lymphadenopathy.

Patient pulse rate was 100/min which is regular, high volume with no specific character, no radio radial delay, no radio femoral delay, all peripheral pulses felt. Blood pressure: 130/80mmHg in supine position, Patient was tachypneic with respiratory rate of 22/min and febrile with temperature of 101ºF.

Cardiovascular examination revealed gallop rhythm and an ejection Systolic murmur at the base of the heart. On abdominal examination there was tender hepatomegaly of 16cm span and soft splenomegaly palpable for 6 cm's in the left hypochondrial region. Lung were clear with normal central nervous system examination. Fundoscopy revealed no disc edema, roth spots, fusiform dilatation of veins with extravasation and arteriolar haemorrhages. Clinically possibility of haemolytic anaemia was suspected and patient was evaluated for type and cause of hemolysis.

The peripheral smear examination showed evidence of hemolysis, anisopoikilocytosis with polychromasia increased nucleated RBC with spherocytes were present. Leukocytosis with normal distribution and adequate platelets with no haemoparasites. As depicted in Figure 3

Liver function shows increased indirect hyperbilirubinaemia with increased indirect bilirubin of 5.9mg/dl which is depicted in Table 2.

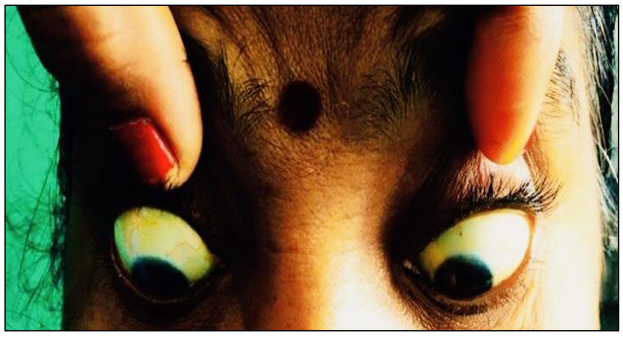

Figure 1: Photograph of the patient in the case report having icterus.

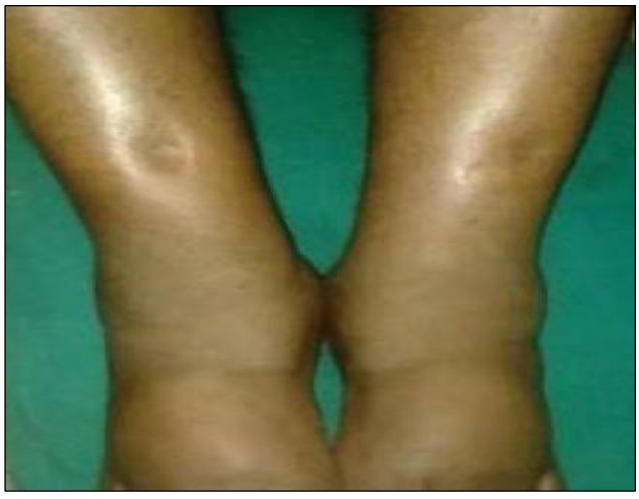

Figure 2: Photograph of this patient in the case report shows having bilateral pedal edema.

Baseline evaluation of Auto immune hemolytic anaemia with coombs test turned out to be positive. Patient was subjected for Mono specific DAT, Indirect Antiglobulin

test (IAT) and antibody screening. Mono specific DAT showed both Anti IgG and anti C3 antibodies. IAT test was positive at 4^0C and negative at 22^0C and 39^0C which confirmed that the AIHA was of mixed warm and cold type. Serum LDH, Serum haptoglobulins and Serum C3, C4was decreased which shows evidence of hemolyis and compliment activation. ANA and Anti-dsDNA was positive which was depicted in Table 3.

ECG showed normal sinus rhythm with sinus tachycardia which is depicted in Figure 4.

X ray chest dint not show any features of cardiomegaly which was depicted in figure 5Ultrasound Abdomen was suggestive of hepatosplenomegaly. There was no evidence of portal hypertension and para aortic lymphadenopathy. Serology for human immunodeficiency virus, syphilis, ebstein barr virus, cytomegalovirus, hepatitis A, B, C viruses and *Mycoplasma pneumonia* were negative. A final diagnosis of AIHA of mixed warm and cold variety due to SLE was made and treatment was initiated

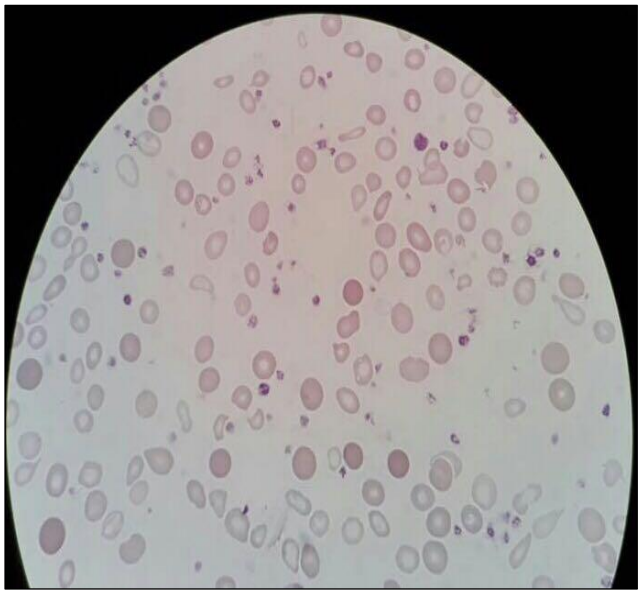

Figure 3: Evidence of hemolysis with Anisopoikilocytosis with polychromasia and spherocytes.

Table 1: Shows hematological parameters at the time of admission and discharge.

Hematological parameters	On admission	At discharge
Hemoglobin	3.8g/dl	7.8g/dl
MCV	128.8fl	98fl
MCH	52.9pg	33fl
MCHC	39.8g/dl	35g/dl
RBC	1.11million/cu mm	2.5 million/cu mm
Total Leukocyte Count	22,100/cu mm	10,200/cu mm
Platelet count	1.36 lakhs /cu mm	1.82 lakhs/cu mm
Differential Counts	N-63% E-3% L-30% M-2%	N-68% E-5% L-35% M-1%

Table 2: Shows the abnormal Liver function tests.

Liver Function Tests						
Total protein 7.8g/dl	Albumin 4.6g/dl	Globulin 3.2g/dl	A/G ratio: 1.4:1	Total Bilirubin 6.1mg/dl	Indirect Bilirubin 5.6mg/dl	Direct Bilirubin 0.5mg/dl

Table 3: Shows Immunological parameters at admission.

Test	Result	unit	Reference range
Serum Haptoglobulin	40	mg/dl	50-220
Serum LDH (lactate dehydrogenase)	4170	U/L	140/280 U/L
Serum C3	0.78	g/L	0.8-1.5
Serum C4	0.101	g/L	0.16-0.38
ANA (Anti-nuclear Antibody)	4.0		<1.5 Negative >1.5 Positive
Anti-ds DNA	Positive: 1:1280		<1:10 negative
Coombs Test	DAT/IAT= Positive		Negative

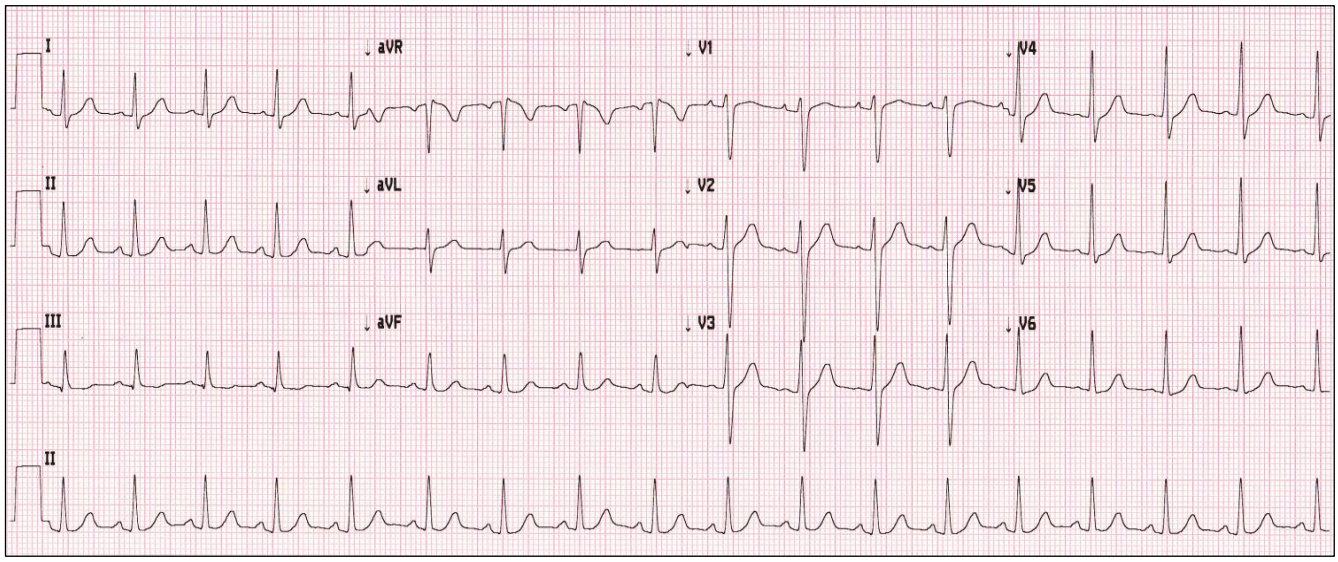

Figure 4: ECG - Normal standardisation with normal sinus rhythm, sinus tachycardia- HR of 100/min.

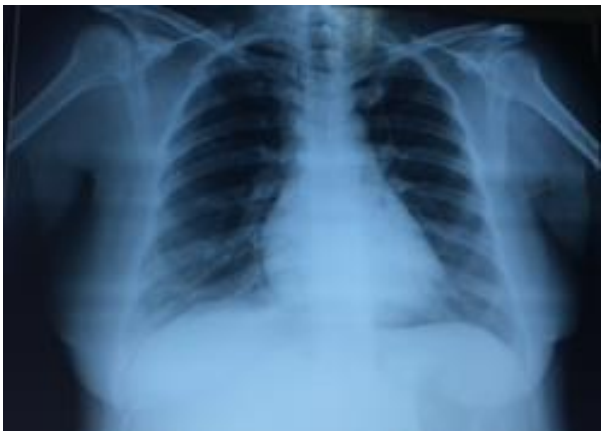

Figure 5: Chest X-ray of the patient shows no evidence of cardiomegaly with normal study.

The patient was initiated on pulse methyl prednisolone at 1g per day for 3 days and later switched over to oral prednisolone at 1mg/kg/day. After 48 hours patient's haemoglobin increased to 4.8 g/dl with slow regression of hepatosplenomegaly. The patient was on follow up for 3 weeks and Hemoglobin improved from 3.9 to 7.8 g/dl. There was no evidence of hemolysis on repeat Peripheral Smear. No blood transfusion was done during the entire course of treatment. Diabetes was controlled with insulin in view of patient on steroid therapy. Patient remained normotensive during the course of follow up and remained in in euthyroid. The patient was also remained weight neutral during the course of therapy

DISCUSSION

Haemolysis is defined as increased Red cell production or increased red cell destruction. Autoimmune haemolytic anaemia (AIHA) is characterized by the production of antibodies directed against self RBCs. AIHA is fairly uncommon disorder, with estimate of the incidence 1-3 cases 100,000 per year.[10] AIHA is classified by the temperature at which autoantibodies bind optimally to RBCs. In warm antibody AIHA, which constitutes about 80-90% of adult cases, haemolysis is mediated by antibodies which bind to RBCs at 37 °C (98.6 °F). In cold antibody AIHA the antibodies are of IgM class which react at temperatures of <37 °c, require complement for activity and produce spontaneous agglutination of red blood cells in vitro. Mixed AIHA is the presence of both warm and cold antibodies.[1,2]

Systemic lupus erythematosus is classified based on SLICC (Systemic Lupus International Collaborating Clinics) which requires ≥4 criteria (at least one clinical and one laboratory criteria) or biopsy proven lupus nephritis with positive ANA or Anti DNA. It is classified into clinical and immunological criteria. In which Clinical criteria (acute and chronic cutaneous lupus, leukopenia, thrombocytopenia, arthritis and serosistis) Immunological (ANA, Anti-ds DNA, Anti-Sm, Low compliment C3, C4). Systemic lupus erythematosus is considered a main cause for secondary AIHA, and most cases involve warm type antibody. In contrast, 25-42% of cases of mixed AIHA, which has both warm and cold antibodies, are associated with SLE.[5,11]

Haematological abnormalities are frequently encountered in patients with Systemic lupus erythematosus (SLE).[3] Most patients have warm antibody AIHA. There have been some reports of adult AIHA secondary to SLE with involvement of not only warm antibodies but also cold antibodies, that is mixed -type AIHA (mixed AIHA).[4] In our case patient had mixed AIHA with SLE which is a

rarity. Patient with SLE may develop several haematological complications including anemia, leukopenia, thrombocytopenia. Several case series have shown that autoimmune haemolytic anemia occurs in 10% patients with SLE.[5,6]

AIHA is often associated with extra hematological features, as sever renal and central nervous system involvement, which may require corticosteroid and immunosuppressive treatment.[7] Glucocorticoids can cause dramatic cessation or marked slowing of haemolysis in about two third of patients. The best responses are seen in idiopathic cases or in those related to SLE. Drugs reported in the treatment of refractory AIHA in SLE include IVIG, azathioprine and other immunosuppressive medications as well as danazol and rituximab.[8,9]

Diagnosis of AIHA is based on evidence of haemolytic anaemia consisting of anaemia, jaundice, splenomegaly, reticulocytosis, raised serum bilirubin and a positive DAT.[12] AIHA though rare SLE is found more commonly in the childhood form of the disease than in adults.[13] Here by we report a case of mixed autoimmune haemolytic anaemia as the hematologic manifestation in SLE which is a rarity. Systemic lupus erythematosus (SLE) and other autoimmune diseases account for a lesser but considerable proportion of secondary AHA cases. In our case patient was responded to Intravenous corticosteroids.

CONCLUSION

Autoimmune haemolytic anaemias are usually characterized by presence of either warm or cold auto antibodies. In this patient presence of both warm and cold auto antibodies along with complement C3 is present hence it is a case of mixed autoimmune haemolytic anaemia. The patient's serum is reactive for ANA, Anti-ds DNA and C3 which points towards SLE. Hence our diagnosis is Systemic Lupus Erythematosus (SLE) with mixed auto-immune haemolytic anemia. AIHA occurs in less than 5% of patients with SLE. Mixed AIHA occurs in less than 10% of patients with AIHA. Hence, a case of mixed autoimmune haemolytic anemia as the hematologic manifestation in SLE is a very rare entity.

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REFERENCES

1. Packman CH. The Clinical Pictures of Autoimmune Hemolytic Anemia. Transfus Med Hemotherapy. 2015;42(5):317-24.
2. Sudha Reddy VR, Samayam P, Ravichander B, Bai U. autoimmune hemolytic anemia: mixed type-a case report. Indian J Hematol Blood Transfus. 2011;27(2):107-10.
3. Nossent JC, Swaak AJ. Prevalence and significance of haematological abnormalities in patients with systemic lupus erythematosus. QJM: An Inter J Med. 1991 Jul 1;80(1):605-12.
4. Hirano Y, Itonaga T, Yasudo H, Isojima T, Miura K, Harita Y, et al. Systemic lupus erythematosus presenting with mixed-type fulminant autoimmune hemolytic anemia: SLE and mixed-type fulminant AIHA. Pediatr Int. 2016;58(6):527-30.
5. Kokori SI, Ioannidis JP, Voulgarelis M, Tzioufas AG, Moutsopoulos HM. Autoimmune hemolytic anemia in patients with systemic lupus erythematosus. Am J Med. 2000;108(3):198-204.
6. Hepburn AL, Narat S, Mason JC. The management of peripheral blood cytopenias in systemic lupus erythematosus. Rheumatol. 2010;49(12):2243-54.
7. Gomard-Mennesson E, Ruivard M, Koenig M, Woods A, Magy N, Ninet J, et al. Treatment of isolated severe immune hemolytic anaemia associated with systemic lupus erythematosus: 26 cases. Lupus. 2006;15(4):223-31.
8. Kaushansky K, Lichtman MA, Prchal JT, Levi MM, Burns LJ, Caligiuri M. Williams Hematology. 9th Ed. 2016:5094.
9. Fayyaz A, Igoe A, Kurien BT, Danda D, James JA, Stafford HA, et al. Haematological manifestations of lupus. Lupus Sci Med. 2015;2(1):e000078-e000078.
10. Gehrs BC, Friedberg RC. Autoimmune hemolytic anemia. Am J Hematol. 2002;69(4):258-71.
11. Haller W, Hind J, Height S, Mitry R, Dhawan A. Successful treatment of mixed-type autoimmune hemolytic anemia with rituximab in a child following liver transplantation. Pediatr Transplant. 2010;14(3):E20-5.
12. Lilleyman J. De Gruchy's Clinical Haematology in Medical Practice. J Clin Pathol. 1990;43(4):352.
13. Singh A, Mandal A, Patel A, Mishra S. Autoimmune Haemolytic Anaemia-A Spectrum of Presentation in Children. JCDR. 2017 Sep;11(9):SR01.

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