Case Report

Autoimmune Hemolytic Anemia in 62 Year Old Lady with Mixed Connective Tissue Disorder with Subclinical Hypothyroidism: A Rare Presentation

Vipin Porwal, Pulkit Jain, Ashish Sharma*

Mixed connective tissue disease (MCTD) is an overlap syndrome characterized by the presence of U1RNP antibody with features of polymyositis, scleroderma, and systemic lupus erythematosus. A female 62-year-old patient presented with generalized body weakness since 4 months and shortness of breath for 3 months. The patient had a history of repeated blood transfusions, in view of a clinical history of recurrent blood transfusion with hypothyroidism (anti-TPO positive) with direct coomb test positive with ANA positive. She is a case of autoimmune hemolytic anemia. ANA immunoblot shows U1RNP positive, suggestive of mixed connective tissue disorder. She responded well with prednisolone (1-mg/kg) with a tapering dose.

Access this article online

Website: www.cijmr.com

DOI: 10.58999/cijmr.v3i03.175

Keywords: Anaemia, Autoimmune hemolytic anemia, Mixed connective tissue disease, Subclinical hypothyroidism

Introduction

Autoimmune hemolytic anemia is an acquired disorder characterized by hemolysis and anemia, causing a decreased lifespan of RBC due to autoantibodies against red cells.[1] It can be due to warm, cold, or mixed antibodies.[2] Autoimmune hemolytic anemia can occur as idiopathic (primary) or secondary to other malignancies (leukemia, lymphoma, infections, or even autoimmune diseases).[1,3] Out of 1 to 3 out of 100000 patients per year incidence, warm autoantibodies resulting in AIHA constitute about 70 to 80%.[3] 50% of the above conditions are due to secondary causes.[3] Patients presenting with relevant history, symptoms of anemia and history of recurrent blood transfusion AIHA may be suspected. Patients need to undergo routine tests like CBC, reticulocyte count, and peripheral blood smear. LDH and haptoglobulin need to be tested to know the hemolytic anemia. Direct antiglobulin test may be performed in case of absence of other causes of hemolysis. AIHA is diagnosed by a positive direct antiglobulin test (direct Coombs test) in the absence of other possible causes of hemolysis. Sometimes, AIHA may follow years after severe SLE.[4] About two-thirds of patients of AIHA respond to steroids, which are used as first-line drugs. However, it is common that patients resent relapse and require close monitoring and slow, careful tapering.[5]

Case Report

A 62-year-old female patient presented with complaints of generalized body weakness for 4 months and shortness of breath for 3 months. History:- the patient had a history of hospitalization 5 months back with a complaint of loose stool. The patient had a history of recurrent blood transfusions. The patient had a history of subclinical hypothyroidism, diagnosed one month back and was on medication. No history of black stool, blood in vomitus, or fresh per rectal bleed. The patient had no history of chest pain, edema, palpitations, or cough. No history of anorexia, fever, weight loss, joint pain, rashes headache. The patient had no past history of coronary heart disease, hypertension and diabetes mellitus. The patient had no history of autoimmune disease. The patient had a bladder, bowel, and normal sleep pattern unaltered.

The patient's vital signs on presentation were blood pressure of 100/70 mmHg, temperature of 37.2°C, heart rate of 106 beats/min, regularly regular, normovolumic

RD Gardi Medical College , Ujjain, Madhya Pradesh, India.

Correspondence to: author, RD Gardi Medical College , Ujjain, Madhya Pradesh, India, E-mail: pulkitjaingwalior@gmail.com

Submitted: 06/05/2024 Revision: 29/07/2024

Accepted: 01/11/2024 Published: 17/12/2024

How to cite this article: Porwal V, Jain P, Sharma A. Autoimmune Hemolytic Anemia in 62 Year Old Lady with Mixed Connective Tissue Disorder with Subclinical Hypothyroidism: A Rare Presentation. Central India Journal of Medical Research. 2024;3(3):19-21.

Table 1: Routine investigations

Laboratory parameters		*At the time of admission*
CBC	HB	3.1 g/dl
	WBC	2.56 X 10^3/μL
	RBC	1.83 X 10^6 /μL
	Platelet	313 X 10^3 /μL
	ESR	64
Renal function test	Urea	20.5 mg/dl
	Creatinine	0.6 mg/dl
Urine analysis	Pus cells	1–2/hpf
	Urine sugar	-
Liver function test	Total protein	1.7 g/dl
	Albumin	3.6 g/dl
	Globulin	4.3 g/dl
	SGPT	83.1 U/L
	SGPT	30.5 U/L
	ALP	142.2 U/L
Serum Electrolytes	Sodium	139.5 mmol/l
	Potassium	4.1 mmol/l
TSH		10.85 mIU/L
LDH		783.0 U/L
Direct coomb test		Positive
Indirect coomb test		Negative
Vit B12.		>1000 PG/ML
Ferritin		534 NG/ML
Iron		99.5 microgram/DL
Sickling test		Early negative, late negative
Folate		>20 NG/ML
ANA immunoblot		U1 RNP antigen positive
Complement C3		163.56 MG/DL (Normal Range 90-180 MG/DL)
Anti TPO		Positive

pulse, no radio radial, no radio femoral delay, respiratory rate of 18 breaths/min, and oxygen saturation of 99% on room air.

On examination, the patient had severe pallor present, icterus absent, cyanosis absent, and edema in lower limbs absent. On physical examination, she had pallor nails and pale skin. On CNS examination patient had consciousness, oriented to time, place and person. CVS examination: - normal precordium, S1S2 present tachycardia present. Respiratory examination: - Bilateral chest symmetrical, bilateral chest air entry present. Per abdomen:- soft non tender, no organomegaly present, bowel sound present.

The patient's blood sample was preserved, and an urgent 2 RCC transfusion was done.

O positive blood group was found on type and screen and cross match process. For close monitoring of hemodynamic and transfusion reactions, the patient was admitted to the intensive care unit. Routine investigations are shown in Table 1.

Peripheral smear examination shows macrocytic anemia, thrombocytosis, and neutrophilic leucocytosis with left shift up to myelocytes. Toxic granules were seen in a few neutrophils. Stool occult blood was negative. G6PD 30 minutes. Vit B12 > 1000 pg/mL. Ferritin 534 ng/mL. ECHO reveals normal LV systolic function at 60%. No RWMA at rest. Concentric LVH with grade I LV diastolic dysfunction. MAC present (PML) with mild MR. Mildly sclerosed aortic valve with PG- 09 mmHg. Mild TR , RVSP 18 mmHg + RAP. No clot/pericardial effusion (Annexure 1).

Reticulocyte count 9% (Annexure 2) positive direct and negative indirect Coombs with warm antibodies in addition to several other antibodies (Annexure 3).

HIV, hepatitis B surface antigen, and Hep C antibody are non-reactive. ANA ELSIA 34.04 AU/mL (Annexure 4) rheumatoid factor positive 40 IV/mL (Annexure 5); CCP IgG 11.78 AU/mL. ANA immunoblot shows U1RNP positive (Annexure 10).

In view of a clinical history of recurrent blood transfusion with hypothyroidism (anti-TPO positive) with direct coomb test positive with ANA positive. She is a case of Autoimmune hemolytic anemia.

She responded well with prednisolone (1-mg/kg) with a tapering dose. She now has hemoglobin 10 g.

Discussion

Infection and stressful event can be a precipitating factor for autoimmune disorders.

Mixed connective disorders is a rare autoimmune disease that has features overlapping one of the connective disease like rheumatoid arthritis, systemic sclerosis, dermatomyosistis, and polymyositis. Due to variable presentation, diagnosis is difficult. Initial presentation of MCTD as hematological manifectation is still rare.

Patient had severe anaemia, which found to be a case of autoimmune hemolytic anemia on investigation. Autoimmune hemolytic anaemia is rare disorder with incidence of 1 to 3 per 100000 per year. AIHA is classified according to the temperature at which autoantibodies optimally bind to red blood cells. AIHA warm antibody it accounts for about 80 to 90% of cases in adults and 10% of cases have cold agglutinin disease.[6]

Autoimmune hemolytic anemia can occur due to various reasons, including genetics, malignancies, infections or other autoimmune disorders. The patient undergoes an investigation to find out the cause of AIHA. On ANA screening, find to be positive patient underwent immunoblot ANA and was found to be Serum u1RNP positive.

AIHA is known to occur in 5 to 10% of patients with connective tissue disease. But initial presentation of MCTD as Autoimmune hemolytic anemia is very rare. Our patient had no other symptoms of MCTD, such as myositis or, polyarthritis or Raynaud's phenomenon. Rajashree S. Khot *et al*. show the presence of an old lady with MCTD with warm Autoimmune hemolytic anemia with tuberculosis.[7]

A patient has the involvement of wrist joint and elbow, with RA factor low positive with low positive anti-CCP with high ESR, with a duration of symptoms of > 6 weeks, which follows the criteria of rheumatoid arthritis.

Espinosa-Orantes A *et al*., show the presence of rheumatoid arthritis with warm immune hemolytic anemia. RA and SLE disease unusual overlap is found in Rhupus syndrome. This syndrome shows less SLE-associated damage and more RA-associated manifestations.

Here is a case of overlap syndrome with an initial presentation due to the presence of AIHA, elevated levels of anti-CCP and no erosive arthritis.[8]

Karki P Prasai P. shows the presence of Hashimoto thyroidis with autoimmune hemolytic anemia.[9]

The patient was started on steroid prednisone (1-mg/kg per day) as medical treatment and was tapered after 2 weeks. And the patient improved.

Conclusion

Mixed connective disorder is an autoimmune chronic inflammatory disease with unclear etiology.

Other disease processes can present as autoimmune hemolytic anemia, highlighting the importance of work-up to be done thoroughly for timely diagnosis and management of underlying conditions.

Autoimmune hemolytic anemia can present as various spectrums and physicians need to be aware of it.

References

1. Liebman HA, Weitz IC. Autoimmune hemolytic anemia. Medical Clinics. 2017 Mar 1;101(2):351-9.
2. Mohanty B, Ansari MZ, Kumari P, Sunder A. Cold agglutinin-induced hemolytic anemia as the primary presentation in SLE-A case report. Journal of Family Medicine and Primary Care. 2019 May 1;8(5):1807-8.
3. Kalfa TA. Warm antibody autoimmune hemolytic anemia. Hematology 2014, the American Society of Hematology Education Program Book. 2016 Dec 2;2016(1):690-7.
4. Firestein GS, Budd RC, Gabriel SE, McInnes IB, O'Dell JR. Kelley and Firestein's textbook of rheumatology. Elsevier Health Sciences; 2016 Jun 21..
5. Bass GF, Tuscano ET, Tuscano JM. Diagnosis and classification of autoimmune hemolytic anemia. Autoimmunity reviews. 2014 Apr 1;13(4-5):560-4.
6. Srikanth M, Lokesh S, Dutta A, Danasekaran V. Auto Immune Mixed Haemolytic anaemia: A rare presentation of SLE.
7. Khot RS, Patil A, Rathod BD, Patidar M, Joshi PP. Uncovering the unusual: a case of mixed connective tissue disease with rare presentation, atypical complications, and therapeutic dilemmas. Cureus. 2023 Mar;15(3).
8. Espinosa-Orantes A, Hernandez-Vera MA, Juarez-Villa JD, Anahí Guadalupe GE, Flores G. Rheumatoid arthritis and autoimmune hemolytic anemia as first manifestation of rhupus. Case reports in rheumatology. 2020;2020(1):8870643.
9. Karki P, Prasai P, Chetri VA, Gautam A, Maskey R. Autoimmune Hemolytic Anemia with Autoimmune Hypothyroidism: A Case Report. JNMA: Journal of the Nepal Medical Association. 2023 Jul;61(263):614.