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A Rare Association of Autoimmune Hemolytic Anemia in Abdominal Tuberculosis

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ABSTRACT

Tuberculosis is the most common infectious disease caused by Mycobacterium tuberculosis which can affect any system in our body. Hence, tuberculosis can present with wide variety of manifestations which may sometimes be over or under diagnosed. Anemia is frequently seen in TB patients, and it is commonly anemia of chronic disease [1]. Association of autoimmune hemolytic anemia and tuberculosis is exceedingly rare. Here we are presenting such a rare case of abdominal tuberculosis complicated by coombs positive hemolytic anemia.

Keywords: Autoimmune hemolytic anemias, Tuberculosis, Pancytopenia, Coomb's test

INTRODUCTION

Autoimmune hemolytic anemias (AIHA) are a group of disorders in which auto antibodies are directed against RBCs resulting in early and excessive destruction of RBCs due to reduced lifespan and presents with clinical features of anemia, jaundice and splenomegaly [1]. AIHA can be primary or secondary to many underlying diseases [2] including infections like mycoplasma, infectious mononucleosis etc., However, the incidence of autoimmune hemolytic anemia in tuberculosis is rare. To diagnose AIHA clinical history is essential to find out any underlying illness or drugs which may lead to the disease.

Next, laboratory investigations are carried out to determine the etiology. A positive direct anti globulin test (DAT) test is not specific for AIHA [7]. Hence, additional serological investigations are required to establish the cause of the positive reaction. Tests used are a complete blood count (CBC), peripheral smear, bilirubin, lactate dehydrogenase (LDH) particularly isoenzyme 1, haptoglobin and urine hemoglobin. Diagnosis is made by first ruling out other common causes of hemolytic anemia such as thalassemia, sickle-cell disease and G6PD deficiency.

CASE REPORT

A 33 years old unmarried female presented with history of fever for 2 months. Fever was low grade, intermittent, not associated with chills and rigor. Patient was admitted elsewhere and treated as enteric fever by family physician. Patient recovered from fever. But she noticed high colored urine, abdominal distension and easy fatigability during subsequent month. USG abdomen done outside reported as chronic parenchymal liver disease and free fluid in the abdomen. Patient was referred to our institute for further management.

On examination patient was conscious, oriented and afebrile. Pallor and icterus were present. No pedal edema and lymphadenopathy. Abdomen was distended with mild splenomegaly and there was evidence of free fluid in the form of shifting dullness. There was diffuse tenderness over the abdomen. Hemic murmur was present in cardiovascular system.

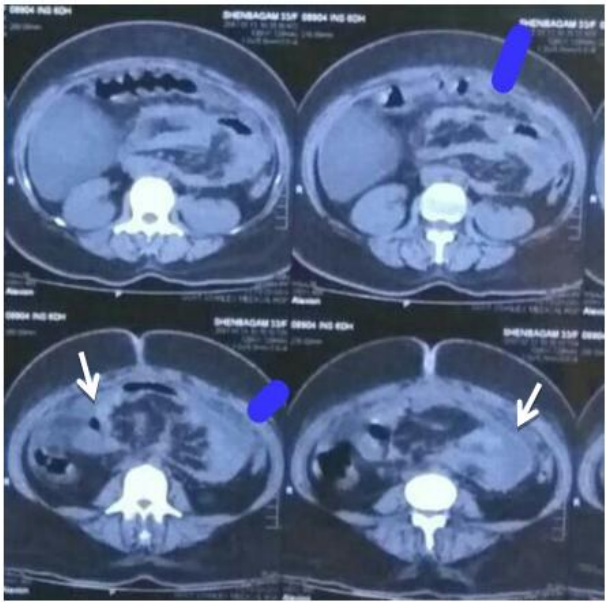
Investigations revealed a hemoglobin of 4 gm% with total leucocyte count of 2600/mm3 and normal differential percentage. MCV - 104fl, platelet - 1.2 lakhs. We sent the blood sample for grouping and cross matching. Peripheral smear showed pancytopenia with macrocytic RBCs, anisopoikilocytosis, tear drop cells and polychromatic cells. Reticulocyte count was 0.5%. Total bilirubin 3.4 mg/dl with indirect bilirubin 2.4 mg/dl. Total protein 6.0 gm/dl, Serum albumin 2.4 gm/dl, SGOT, SGPT and alkaline phosphatase were within normal limits. Renal function tests were normal. Patient had low Vitamin B12 (106 pg/ml) and normal folic acid level. Patient had high serum ferritin (674 ng/ml) and normal serum iron and total iron binding capacity.

Patient was having pancytopenia with macrocytic RBCs and low reticulocyte count, probably due to chronic infection and vitamin B12 deficiency. Vitamin B12 injection was started. While doing cross matching sample lysed repeatedly. Serum LDH was 1887U/L.

A possibility of autoimmune hemolytic anemia was thought of and direct anti globulin test (Coomb's test) was done which was positive. Repeated tests on three occasions within a week were also positive for IgG (warm type of AIHA). Hence, blood transfusion was withheld.

USG abdomen showed hepatosplenomegaly and ascites. Ascitic fluid was exudative with high lymphocyte count and elevated ADA (84 U/l). No malignant cells in ascitic fluid. Montoux test was positive. CECT abdomen showed omental thickening suggestive of tuberculosis (Fig. 1). Gene xpert was sent.

Figure. 1 CECT abdomen shows omental thickening



G6PD was normal. Viral markers (HbsAg, anti HCV, HSV, CMV, EBV, parvo virus & HIV) were negative. ANA - negative. Anti parietal and intrinsic factor antibodies were negative. Bone marrow study showed erythroid hyperplasia.

Based on clinical features, ascitic fluid analysis and CECT abdomen anti tubercular treatment was started. Later gene xpert came positive for MTB (Rifampicin sensitive).

Patient recovered from cardiac failure and mobilized. Patient was registered for anti tuberculous treatment (ATT) and discharged with oral prednisolone. Patient was on regular follow up. After six weeks prednisolone dose was tapered and stopped. At the end of two months there was no abdominal distension and no free fluid in abdomen in repeat USG. Complete haemogramand peripheral smear were also normal. Repeat ANA, anti ds DNA and anti Sm antibody were negative. ANA repeated after 6 months was also negative. Patient is doing well.

.**DISCUSSION**

Tuberculosis may present with a wide variety of hematological manifestations including anemia. Various pathogenic mechanisms have been explained in tuberculosis associated anemia. However, the most common is normocytic normochromic anemia [1] of chronic disease due to suppression of erythropoiesis by inflammatory mediators. Other causes would be malnutrition, malabsorption syndromes, failure of iron utilization and vitamin B12/ folate deficiency [3], [4]. TB associated anemia is generally mild and resolves with ATT.

Initially we suspected hemolytic anemia due to vitamin B12 deficiency in view of pancytopenia with low reticulocyte count. Though vitamin B12 deficiency usually causes coomb's negative hemolytic anemia due to ineffective erythropoiesis, it is rarely associated with autoimmune hemolytic anemia. Pernicious anemia is less likely in this patient due to negative anti parietal and intrinsic factor antibody. Moreover bone marrow study is also not consistent with B12 deficiency.

Another possibility of autoimmune hemolytic anemia is systemic lupus erythematosus. But screening ANA test was negative. ANA may be negative in cases with high clinical suspicion of SLE either due to inaccurate technique or sometimes ANA bound in the form of immune complexes not detected in serum. Hence, we did additional antibody tests such as anti ds DNA and anti sm antibody.

But TB associated autoimmune hemolytic anemia is very rarely reported. Autoimmune hemolytic anemia (AIHA) is a disorder in which antibodies against erythrocyte membrane reduces the life span of RBCs. AIHA can occur as a primary disorder or secondary to other causes like drugs and infections. AIHA is exceedingly rare in tuberculosis. On review of literature we found that autoimmune hemolytic anemia has been rarely associated with various form of tuberculosis. Most of them responded to ATT with or without steroids without need of blood transfusions.[2], [5]. If corticosteroid is indicated it should be used cautiously [6].

Animal study discovered that the inoculation of tubercle bacilli or their products produce hemolytic anemia, myelofibrosis and pancytopenia [4].

The majority of the reported cases were extra pulmonary or disseminated tuberculosis. In our case we found that almost all types of anemia in a single case which made us baffled during work up.

Disseminated TB may induce a marked proliferation of reticuloendothelial tissues, resulting in wide range of severe hematological disorders through immune mechanisms. Besides, there have been reports of drug-induced AIHA, especially to rifampicin and isoniazid [8].

CONCLUSION

Though rare, tuberculosis should be considered as one of the possible infectious causes of autoimmune hemolytic anemia. Beforehand, the most common causes of autoimmune hemolytic anemia have to be ruled out. This case emphasizes the need for meticulous work up of anemia in tuberculosis patients and to consider AIHA in the differential diagnosis of anemia. If tuberculosis patients present with features of hemolysis, autoimmune hemolytic anemia should be ruled out even in the presence of other possible causes of ineffective erythropoiesis like vitamin B12 deficiency.

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