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Case report Open access

COLD AGGLUTININ INDUCED HEMOLYTIC ANEMIA IN A PATIENT WITH PULMONARY TUBERCULOSIS

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ABSTRACT

Autoimmune hemolytic anemias (AIHA) are an uncommon group of disorders characterized by red cell destruction due to autoantibodies. Though usually idiopathic, AIHA is commonly associated with lymphoproliferative disorders, infections, autoimmune disease, and some drugs. This report describes a case of 25 year old female presenting history of fever associated with cough and fatigue. There was a past history of receiving blood transfusion on four occasions. The HRCT thorax demonstrated fine nodular densities in right upper lobe, suggestive of tuberculosis. Abdominal ultrasonography revealed mild splenomegaly. A bone marrow biopsy performed on the patient revealed erythroid hyperplasia. There was no evidence of any malignancy. Diagnosis of cold autoantibody hemolytic anemia complicated by pulmonary tuberculosis was made. The patient was managed with blood transfusions and treated with anti-tubercular agents. The occurrence of AIHA in pulmonary tuberculosis is rare.

INTRODUCTION

Autoimmune hemolytic anemia (AIHA) occurs when a patient produces pathologic antibodies that attach to and lead to the destruction of their RBCs with consequent anemia. AIHA can be classified as warm AIHA and cold AIHA according to the characteristic temperature activity of the antibodies [1]. Occasionally, a patient may have mixed cold and warm active antibodies. Primary (idiopathic) AIHA is less frequent than secondary AIHA [2]. Autoimmune antibodies, particularly cold-reactive antibodies, are sometimes produced following an infection or immune defects or lympho proliferative disorders or drugs [3,4,5,6]. These secondary cases are often challenging since not only AIHA, but also the underlying disease must be diagnosed and treated. Association of autoimmune haemolytic anaemia with pulmonary tuberculosis has been seldom reported. Tuberculosis being a common disease, the association with hemolytic anemia should be recognized and treated judiciously.

CASE REPORT

A 25 year old female presented to our department with a history of fever associated with cough and fatigue. Physical examination revealed pallor and mild splenomegaly. Blood pressure, pulse rate and temperature were within normal limits. Bilateral crepitations could be heard on chest auscultation. Other findings on physical examination were unremarkable. There was a past history of receiving blood transfusion on four occasions. The laboratory investigations demonstrated severe anemia (Hemoglobin 4.5 g/dl; MCV 74.3fl MCH 18.4pg MCHC 24.7g/dl) with a normal white blood count and platelet count. The peripheral blood smear showed microcytic hypochromic RBCs with anisopoikilocytosis, elliptocytes, tear drop cells, target cells. The reticulocyte count was 5.82% and reticulocyte index was calculated to be 2.0. Serum LDH was raised (991 U/L). The Direct Coombs test was positive with anti-C3d specificity; anti-IgG was negative. The cold agglutinin titre was 1:256. The patient tested negative for anti nuclear antibodies and ds-DNA antibodies, HIV, Hepatitis B surface antigen and anti HCV antibodies. Sputum was positive for acid fast bacilli. Chest X-ray showed diffuse small nodular infiltrates over right lung fields. The HRCT thorax demonstrated fine nodular densities in right upper lobe, suggestive of tuberculosis. Abdominal ultrasonography revealed mild splenomegaly. A bone marrow biopsy performed on the patient revealed erythroid hyperplasia. There was no evidence of any malignancy. Based on the characteristics discussed in the preceding paragraphs and available literature, a diagnosis of cold autoantibody hemolytic anemia complicated by pulmonary tuberculosis was made. The patient was managed with blood transfusions and treated with anti-tubercular agents.

DISCUSSION

Autoimmune hemolytic anemia (AIHA) is a rare disease. In a recent population based study [7] the incidence was 0.8/100.000/year, but the prevalence is 17/100.000[8]. There are two main types of autoimmune hemolytic anemia: warm antibody and cold antibody induced hemolytic anemia

based on the ability of the autoantibodies to attach to and destroy red blood cells at different temperatures.

Cold active autoantibodies have the capability to agglutinate red blood cells at temperatures well below the normal body temperatures, fix complement, and lead to immediate intravascular RBC destruction or hepatic mediated clearance. Two different clinical syndromes are manifested from cold auto immune antibodies. Cold Agglutinin Disease is associated with IgM antibodies usually directed at the RBC *I* antigen. The responsible pathologic IgM antibodies are distinguished from naturally occurring cold autoantibodies by their titre and thermal amplitude. Natural cold autoantibodies occur in titres less than 1:64 at 4° C and have no activity at temperatures much higher than that. However, pathologic cold agglutinins typically have titres well over 1:1000 and may react at 28-31° C or even up to 37° C [1]. An IgG type of cold reactive autoantibody with anti P specificity, known as Donath Landsteiner antibody, characterizes Paroxysmal Cold Hemoglobinuria.

In contrast, warm active antibodies are typically IgG, may or may not fix complement, and primarily lead to RBC loss by splenic removal of sensitized cells. Both CAD and PCH are less common than warm AIHA and make up approximately 20% or less of AIHAs.[1]

Almost all cases of cold AIHA in adults seem to be secondary. The underlying conditions in most cases are lymphoproliferative diseases, less commonly autoimmune diseases(SLE) or infections(infectious mononucleosis, Mycoplasma pneumonia, advanced HIV infections) , and rarely drugs[3,4,5,6].In some of the cases , the etiology remains obscured labeling them as primary or idiopathic. The key component to treatment remains avoidance of exposure to cold and management of underlying infectious or malignant process. In contrast to warm AIHA, cold AIHA does not respond well to steroids and/or splenectomy[2]. Transfusion of red cells in AIHA can result in rapid in vivo destruction of transfused cells due to the presence of auto antibodies, hence it is of transient benefit, but may be required initially in managing severe anemia.[2]

In tuberculosis, hematologic abnormalities like anemia are common. Possible mechanisms include nutritional deficiency, malabsorption syndrome, marrow suppression, and failure of iron utilization [9]. However, the association of immune hemolytic anemia with tuberculosis is relatively rare [10]. The majority of the cases reported in literature are disseminated or extra pulmonary tuberculosis.

In our patient with cold autoantibody induced hemolytic anemia, the work up for secondary causes of AIHA like lymphoproliferative disorders and SLE was negative, and tuberculosis was diagnosed on the basis of isolation of organism in sputum and clinical and radiological findings. The patient responded to anti tubercular treatment, steroids were not given.

CONCLUSION

Although rare, pulmonary tuberculosis may be associated with autoimmune hemolytic anemia. Tuberculosis should be considered as a differential diagnosis of the etiology of secondary AIHA because administration of steroids alone to treat AIHA in such untreated tuberculosis cases may be detrimental to the patient.

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