A Case Report **Pathology**

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COLD AGGLUTININ DISEASE WITH MALARIA – A CASE REPORT

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ABSTRACT

Aim of the case report was to present a rare case of CAD with Malaria. Methods and materials were as per the clinical protocol and investigations done in the department of pathology.Cold Agglutinin Disease (CAD) is a subgroup of autoimmune Haemolytic Anemia (AIHA). Cold reactive immune globulins (agglutinins) which are directed against erythrocyte surface antigen ('1' antigen) are essential for the pathogenesis of CAD. Classically, the patients with CAD present with chronic anemia and acrocyanosis. Several factors like the antibody titre and the temperature range determine the ability of Cold agglutinin to induce haemolysis. The conclusion of study was that,the specific problem that occurs in the laboratory due to pathologic cold agglutinins need to be kept in mind for the accurate diagnosis. Here, we are reporting a case with of CAD in association with malaria in a 13 yrs old female.

KEYWORDS: **Auto-immune haemolytic anemia, Malaria, Cold agglutinin disease,Autoantibody.**

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INTRODUCTION

Haemolytic anaemias are due to excessive destruction of red blood cells. In the immune cases of hemolytic anaemia, AIHA is important, which is characterized by an immune reaction against red blood cell self antigen. AIHA is classified into warm antibody and cold antibody types [1].

Cold agglutinins were first described by Landsteiner in 1903. The association of cold agglutination with haemolysis was described by Rosenthal and Corten in 1937.

Cold antibody haemolytic anemia can be of two types – cold agglutinin diseases and paroxysmal cold haemoglibinunia. CAD again subclassified in to primary (idiopathic) and secondary. CAD can occur after exposure to infections like mycoplasma pnuemoniae, viral infection, malaria or secondary to neoplasms. Cases of secondary CAD have been reported due to different etiology (2-3).

Case Report

A 13 yrs old female presented with severe anemia, jaundice, splenomegaly and mild hepatomegaly. She had been taking treatment for this for 2 months. She had received 4 units of blood during that period. The automated hematology analyzer showed MCV-133 ft., MCHC-69.7g/dL, and RDW – 18.1%, with very low RBC count 0.81 millions/cmm.

Patients blood group was A+ tve, but she was reported as AB + tve due to spontaneous agglutination. Peripheral smear showed agglutination and coombs test was negative. Under experts opinion, all test were repeated after washing RBC's with warm saline.

Then peripheral blood smear showed dimorphic picture with macrocytes, few spherocytes(Fig.1), increased reticulocytes up to 4 %, and presence of gamet of P. falciparum(Fig.2). So, the patient was diagnosed as case of chronic malaria causing haemolysis.

Direct coombs test was repeated which showed positive result. Then keeping in the mind autoimmune hemolytic anemia (AIHA) further investigation were done, in which osmotic fragility was increased, test for warm antibody was negative while test for cold antibody was positive. Primary CAD is more common in middle age while in this case patient was 13 years old female. In the absence of other etiology of secondary CAD and in the presence of gamet in the peripheral smear, finally the case was diagnosed as cold agglutinin disease in associate with malaria.

DISCUSSION

The incidence of AIHA is estimated to be approximately 1:1,00,000 in adults [4]. Among these warm reactive antibodies are responsible for 87% of cases and cold reactive antibodies are responsible for 13% of the cases [4].

In contrast, the South Indian data shows that cold AIHA is rare and that it contributes to only 1% of the total cases of AIHA [5].

Cold Agglutinins may be found in the sera of healthy individuals in the titre which is less than 1:64 at 40^0 c, while pathologic cold agglutinin have titre more than 1:1,000 and they may act even up to 37^0 c [6]. In this case titre was > 1:1000.

Patients with high titres or wide thermal amplitude, antibodies can have difficult serological problem for the blood bank laboratory which happened in this case. Often, incompatible units are released due to residual agglutination from the cold antibodies [6].

These problems can be solved by washing the patient's cell with warm saline in the direct grouping and by using normal AB positive serum on the control slide [6].

In the present case, 13 yrs female presented with severe anaemia, hepatosplenomegaly and jaundice. The haemogram showed erratic values of the RBC count and the blood indices. The problem was encountered while the patient's various tests were being determined. This problem was solved by washing the RBC's

with warm normal saline. The cold agglutinin titre was more than 1:1000.

In this case of secondary CAD, the cause was malaria. Shoron Georgy et al have mentioned that hyperactive malarial splenomegaly (HMS) is an immunopathologic complication of recurrent malaria infection. Patients with HMS develop splenomegaly acquired clinical immunity to malaria, high serum concentration of anti-plasmodium antibodies and high titre of IgM, with a complement fixing IgM , that acts as cold agglutinin [7]. This was the first case seen in this institute.

CONCLUSION

CAD is a rare disorder and patient may suffer with quality of life, if not diagnosed properly. The plethora of problems that occure during the lab testing of CAD should be known to pathologist and technicians to make an early and accurate diagnosis for correct treatment. Also clinicians should keep in mind that such type of presentation of CAD can be in association with diseases like malaria.

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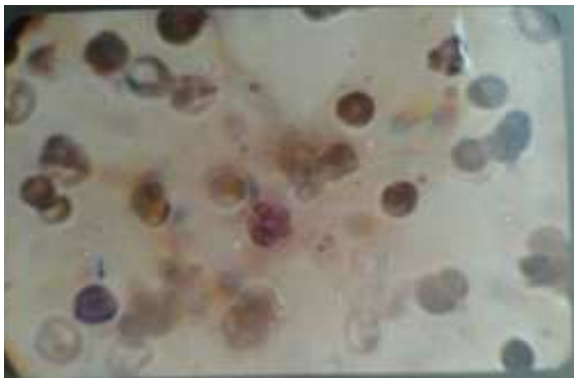

Fig.1
Peripheral blood smears of CAD showing mild anisocytosis with deeply stained spherocytes and normoblast.

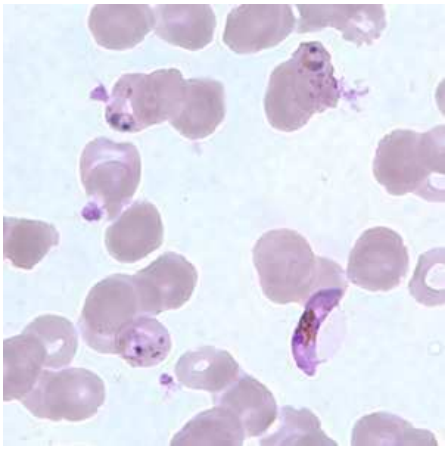

Fig.2
Peripheral smears of CAD showing gamet of P. falciparum.

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