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A report of a rare case of autoimmune haemolytic anaemia in a patient with hodgkin's disease in whom routine serology was negative

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Abstract---Autoimmune haemolytic anaemia can be negative for direct antiglobulin test. Hence the DAT negative patients cannot be ruled out from having AIHA when there is clinical suspicion of AIHA. We hereby report our case of AIHA with Hodgkin's lymphoma who is DAT- negative.

Keywords---DAT, AIHA, Hodgkin's disease, IgA.

Introduction

Autoimmune haemolytic anaemia is characterised by production of auto-antibodies against the circulating erythrocytes causing destruction of the RBC's. DAT (Direct antiglobulin test) is diagnostic for AIHA but 10-15% cases of AIHA can be DAT negative. The reason for this situation can be because of- 1) red cell bound IgA and rare warm IgM autoantibodies that are not detectable by the routine anti-human globulin reagent [3]. 2) red blood cell bound IgG molecules, below the threshold of detection of the DAT. 3) low-affinity IgG autoantibodies that are washed off the red cells during the washing phase for the test.

Case Report

A 35 years old male came with complaints of generalised weakness, fever of low grade, abdominal discomfort. Patient also complains of swelling over the neck.

On examination patient had cervical lymphadenopathy. Cervical lymph node biopsy was taken and showed mixed-cellularity Hodgkin's disease. CT abdomen scan was done and showed enlarged para-aortic lymph nodes and multiple hypodense space-occupying lesions in the liver and spleen. Bone marrow biopsy was conducted for staging purpose and revealed no signs of bone marrow infiltration hence the disease was classified as stage IIIB Hodgkin's disease. Patient was started on chemotherapy and completed eight cycles. Recheck CT scan was done following completion of chemotherapy and showed complete resolution. Patient's blood picture was within normal limits.

Patient presented to the hospital 3 years later with complaints of low-grade fever, generalised weakness, generalised body ache, yellowish discolouration of sclera and high coloured urine since past 15 days. Laboratory investigations were done and showed a haemoglobin concentration of 4.8 g/dL, haematocrit 12%, mean corpuscular volume 118 fL, reticulocyte count 35%, white blood cell count 13.7×10^9 /L and platelet count 201×10^9 /L. His plasma haemoglobin was 29.0 mg/dL and his lactate dehydrogenase level was 1,302 IU/L. Liver function tests showed albumin 4.1 g/dL, total proteins 7.5 g/dL, total bilirubin 7.5 mg/dL, an elevated indirect bilirubin level of 6.3 mg/dL, alkaline phosphatase 120 IU/L, alanine transaminase 25 IU/L and aspartate transaminase 77 IU/L. His peripheral blood smear showed marked anisocytosis, macrocytosis and 6-9 normoblasts/100 white blood cells. Abdominal PET-CT was done and showed a space occupying lesion in the liver. Patient was diagnosed as a relapsed case of Hodgkin's disease. Bone marrow aspirate and biopsy was conducted and showed megaloblastic red cell hyperplasia.

Patient tested negative for direct antiglobulin test (DAT) and indirect antiglobulin test (IAT). Patient was given multiple blood transfusion of 10 units packed red blood cells. Donath-Landsteiner antibody test turned out to be negative ruling out paroxysmal nocturnal haemoglobinuria. All the above investigations give a strong suspicion of Coomb's negative AIHA. A DAT, performed after washing the red blood cells in cold saline to rule out low affinity antibodies, was negative. Subsequently, DAT was performed using a monospecific antiglobulin gel card (DiaMed GmbH, Switzerland) and showed a grade 3 reaction with IgA antiglobulin. The reactions in other columns containing antiglobulin for IgG, IgM, C3c, C3d and control were negative, which established the diagnosis of secondary IgA-mediated AIHA. Patient was started treatment with gemcitabine, dexamethasone and cisplatin (GDC) and was given six cycles of the regime along with full dosage of oral steroids was tapered and stopped after one year. Patient improved well and there was no further evidence of haemolysis.

Discussions

The AIHA is not considered in the absence of a positive DAT, and other causes of haemolysis are investigated, thus overlooking the Coomb's negative AIHA which is relatively uncommon. The standard Coombs' reagent is done by polyclonal rabbit antiserum binding to human IgG and complement, i.e., C3. If warm IgM or IgA antibody is in the process, a standard DAT elucidates negative. This shows importance of monospecific antiglobulin test if a suspicion of AIHA in DAT-negative cases has.

In many case studies reported that IgA-mediated AIHA at first presents as severe haemolytic anaemia and negative DAT. In Petz and Garratty study, 7.8% of all AIHA cases and 11% of warm-reactive AIHA cases had negative DAT. Therefore 3 to 11% of cases of AIHA are estimated as DAT-negative. In this case the patient plasma haemoglobin is 29 mg/dL and red cell destruction is by complement-dependent mechanisms leading to intravascular haemolysis. In chronic lymphocytic leukaemia and non-Hodgkin's lymphoma the AIHA may occur but in HD10 it is rare. IgA-mediated AIHA in HD is rarest. Sporadically in case reports it is stated that AIHA occurs in HD, that also in stages III and IV of nodular sclerosis HD or mixed cellularity HD11. This case is a severe IgA-mediated AIHA in a relapsed IIIB HD patient, stating that AIHA in Hodgkin's lymphoma does not always present in classical form with positive DAT. Corticosteroids for warm-reactive AIHA is the treatment of choice. There is rapid and sustained response to oral steroids though serology is different from classical case of AIHA. Patient showed good response with rise in haemoglobin concentration, decreased reticulocyte counts, serum lactate dehydrogenase levels and there is no need of packed red blood cell transfusions. In conclusion, even in unusual presentation of haemolytic anaemia and negative DAT, to identify the IgA autoantibodies on the surface of circulating erythrocytes, which causes clinically significant haemolytic anaemia additional testing has to be done. Therefore, by considering AIHA in DAT negative case we can avoid unnecessary transfusions to a patient.

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