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INTERESTING CASE REPORT OF HEREDITARY SPHEROCYTOSIS AT AJIMS, MANGALURU

General Medicine

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ABSTRACT

Aims and objectives: Reporting a case of Hereditary Spherocytosis at AJIMS, Mangaluru.

Materials and methods : Hereditary Spherocytosis is genetically determined hemolytic disorder with marked heterogenesity of clinical features ranging from asymptomatic condition to fulminant haemolytic anemia.The etiology of the disease is a deficiency in the membrane proteins resulting in the instability of the cytoskeleton. A 27 year old male presented with anemia, jaundice, splenomegaly with history of blood transfusions in the past.

Results and conclusion: Blood film showed microspherocytes, reticulocytosis of 6% and negative direct antiglobulin test. Patient was managed conservatively with folic acid supplement and advised follow up for the need of splenectomy in near future as per severity of haemolysis.

KEYWORDS

hereditary spherocytosis, jaundice, microspherocytes, splenomegaly, haemolytic anemia

INTRODUCTION

Hereditary Spherocytosis is relatively rare type of genetically determined haemolytic anemia and it is characterized by marked heterogenesity in which there is defect in red cell membrane proteins predisposing them to haemolysis. It is the most common inherited hemolytic anemia in Caucasians with an incidence of 1: 2500-5000 population. [1, 2] Most cases are inherited in autosomal dominant fashion [3] and most severe forms are instead autosomal recessive with patient being homozygous.[4] Hereditary Spherocytosis silent carrier state might exist in 1.4% of the population.[3] Most of the cases will have positive family history. Clinical course of disease is variable ranging from asymptomatic state to severe haemolysis. This case of 27 year old male who presented with fatigue and jaundice is reported in view of the rarity of this disorder to diagnose and manage such a disorder.

CASE REPORT

27 year old male patient hailing from Orissa presented with complaints of easy fatigability since 4 months and yellowish discolouration of urine since 2 months with previous history of 2 units of blood transfusion .Patient also had history of recurrent yellowish discolouration of eyes. Patient's sibling also had similar complaints with history of blood transfusion. No history of sickle cell disease in family. No history of neonatal jaundice and he was not taking any drugs. Patient denied history of fever, generalized itching, pale coloured stools, right hypochondriac pain.

On examination young male who is moderately built, severely pale with icterus present. Spleen was enlarged massively 6cm below the left costal margin , soft in consistency but liver was not palpably enlarged. He had no lymphadenopathy and other systemic examinations were normal.

Laboratory investigations revealed Hb of 4.4 g/dL , Hct 13.2%, WBC 4.2 x 10^9/L ,platelet 201 x 10^9 /L, Total Bilirubin - 2.7mg/dl , Indirect bilirubin - 2.4mg/dl, LDH 901, MCV 81.5Fl, MCHC 33.3 g/dl with increased reticulocyte count of 6%. Peripheral blood smear showed predominant microspherocytosis with WBC and platelets of normal morphology. Autoimmune cause was ruled out as direct coombs test sent was negative. Hb electrophoresis sent revealed no evidence of β-thalassemia/ haemoglobinopathy. Bone marrow aspiration and biopsy was suggestive of micronormoblastic erythropoiesis with microspherocytes present majority in number. Osmotic fragility test was on the higher side of normal limits. USG abdomen revealed massive splenomegaly and gallstones.

Hereditary Spherocytosis diagnosis was made, received 3 units of blood transfusion , supplemented with folic acid,multivitamins and was counselled regarding pneumococcal vaccination , splenectomy and every 3 months follow up visit but patient failed to follow up.

DIFFERENTIAL DIAGNOSIS

The major differential diagnosis was autoimmune haemolytic anemia which mimics HS due to the presence of a large number of microspherocytes in the peripheral blood film. . A positive direct Coomb's test demonstrates autoimmune haemolytic anaemia. Haemolytic anaemia is also a feature of haemoglobinopathies, which can be diagnosed by haemoglobin electrophoresis. In HS, the electrophoresis will be normal, and the presence of microspherocytes on the blood smear confirms the diagnosis. The differentials focus on the causes of fall in the RBC surface area/volume that occur in autoimmune haemolytic anaemia, HS, and microangiopathic anaemia. However, in this scenario , there were no features, such as fragmented RBC, which is suggestive of microangiopathy. Hence a negative direct Combs test, positive osmotic fragility test, blood smear showing microspherocytes, and presence of raised reticulocyte count all show that hereditary spherocytosis was the most likely diagnosis.

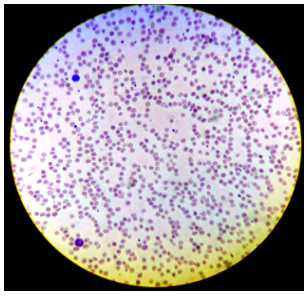

Figure 1.Peripheral blood smear showing spherocytes

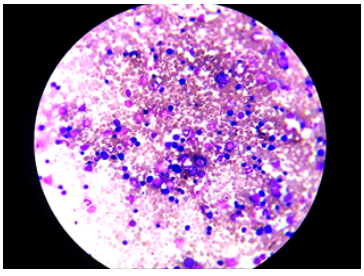

Figure 2.Bone marrow picture showing erythroid hyperplasia with micronormoblastic erythropoiesis with microspherocytes

DISCUSSION

Hereditary Spherocytosis was first described in 1871[5] and identification is credited to Minkowsky and Chauffard. [4]Microspherocytosis is the morphological hallmark of hereditary spherocytosis which is caused by loss of membrane surface area with abnormal osmotic fragility in vitro.[6] An intrinsic genetic defect causing defect in cytoskeletal proteins :Ankyrin , Spectrin ,Band 3,Band 4.1,Band 4.2 leading to weak interaction between proteins and cause red cells to lose membrane fragments and to accommodate the change in ratio of surface area to volume leading to red cells adopt spherical shape and thus spherocytic cells get trapped in splenic cords where they are phagocytosed and extravascular haemolysis occur. [5]

This defective protein can be detected by sodium dodecyl sulphate polyacrilamide gel electrophoresis (SDS-PAGE).[7]

Spectrin deficiency is the most common defect. The defects are associated with variety of mutations that result in different abnormalities and varied clinical expression. Most cases are heterozygous because homozygous states are lethal.[1, 2, 3,10]

Severity of Hereditary Spherocytosis can vary from symptom free carrier state to severe haemolysis. Mild Hereditary Spherocytosis patients can have normal levels of Hb. Diagnosis of Hereditary Spherocytosis is often made in young adulthood, although it may be diagnosed at any age.[7,9]

Spectrin deficiency is frequently detected in childhood and Band 3 deficiency usually in adulthood .Hb is slightly low, spherocyte numbers ,haemolysis high in Spectrin deficiency than Band 3 deficiency. Anemia, neonatal jaundice ,transfusion requirement is more common in patients with Spectrin / Ankyrin deficiency whereas splenomegaly ,gallstones more frequent in Band 3 deficiency patients. [7,8,9]

Lab investigations show anemia of mild-moderate degree reticulocytosis usually 5-20% with peripheral smear showing numerous microspherocytes characterised by lack of central pallor, MCHC is usually increased ,with levels >35g/dl, MCV is normal /slightly decreased. [5]

The osmotic fragility test(OFT) can be helpful in establishing the diagnosis of Hereditary Spherocytosis and normal OFT can occur in 10-20% cases and hence normal OFT doesn't exclude the diagnosis of Hereditary Spherocytosis. Cell dehydration in the spherocytes of patients with Hereditary Spherocytosis can be the cause of normal OFT in nonsplenectomized patients. A positive osmotic fragility result may also be obtained in patients with hereditary elliptocytosis and hemolysis[9]

More specific flow cytometric tests, detecting binding of eosin-5-maleimide to red cells is recommended.[4]

Complications of hereditary spherocytosis include pigment gallstones, aplastic, haemolytic and megaloblastic crises, poor growth, skeletal deformities, and less commonly skin ulceration, chronic dermatitis.

[1, 2] High RBC turn over and increased erythroid marrow activity in Hereditary Spherocytosis make children vulnerable to develop aplastic crisis due to Parvovirus and other infections.

As spherocytes are solely destroyed in spleen, haemolysis can be prevented by splenectomy and it is usually not recommended in patients with Hb >10 and retic count <10%. When it is indicated which is done in age group of atleast 5-6 years, administration of vaccines against Pneumococcal, Haemophilus influenza, Meningococcal 2-3 weeks before surgery is recommended. Patient is also supplemented with 2.5 mg to 5mg folic acid daily to avoid folic acid deficiency. Families with affected child counselled that 50% probability to next child having Hereditary Spherocytosis.[11]

HS is rare disorder and when suspected detailed hematological assessment is necessary to prevent pitfalls in diagnosis and to avoid mismanagement. It is hoped that this report will bring awareness on the existence of HS and hence an increased index of suspicion and prompt referral to haematologist and to avoid unnecessary use of blood transfusion.

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