Hereditary Spherocytosis - A Rare Case Report

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Abstract

Eleven years old female child presented with severe anemia, jaundice and moderate splenomegaly. Her hematological parameters supported diagnosis of hereditary spherocytosis. Father died of similar illness at the age of 40 years. Appropriate treatment was started with an advice to patient to undergo splenectomy as an active part of management of the disorder. Mother ard other siblings were normal.

Key words : *Hereditary spherocytosis, Osmotic fragility, Gall stones, Splenectomy.*

Introduction

Hereditary spherocytosis is a rare hereditary hemolytic anemia in Indian population. The exact data is not available but it seems quite uncommon. The incidence is 1:4500 in Caucasians (North Africa, West Asia, and Europe). It is inherited as autosomal dominant but few cases of autosomal recessive are also seen. Splenectomy almost cures anemia but should be deferred till 5 to 6 years of age due to fear of fulminant sepsis.[1,2, 3, 4]

Case report

Eleven years old female child reported from a remote village in a tribal area of Bhandardara to Pravara Rural Hospital on 8th June 2010 with complaints of weakness, yellowish discoloration of eyes since early childhood. She also had exertional breathlessness and easy fatigability. Father had similar complaints of prolonged jaundice since childhood. He died at the age of 40 years. Further details were not available. Other three siblings are normal. No past history of blood transfusion or hospitalization.

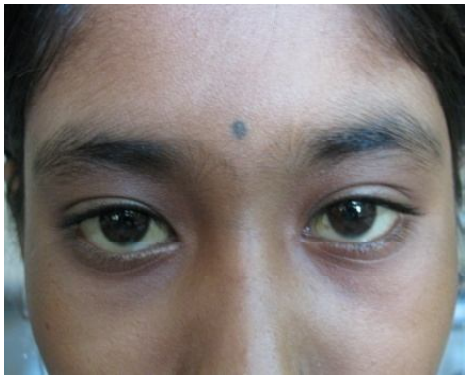

Fig1: Showing Icteric tinge

Fig 2: Hemolytic facies

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Examination

On examination she had severe pallor, deep icterus with lemon yellow tinge (Fig1), mild changes of hemolytic facies (Fig 2). Per abdominal examination showed mild hepatomegaly and moderate splenomegaly (Fig3). Other systems were normal. A provisional diagnosis of chronic hemolytic anemia was made and the case was investigated.

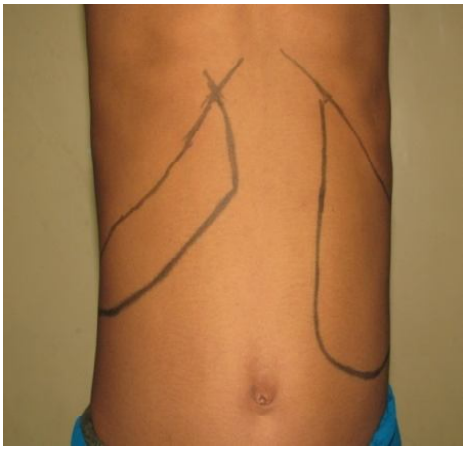

Fig 3: Hepatosplenomegaly

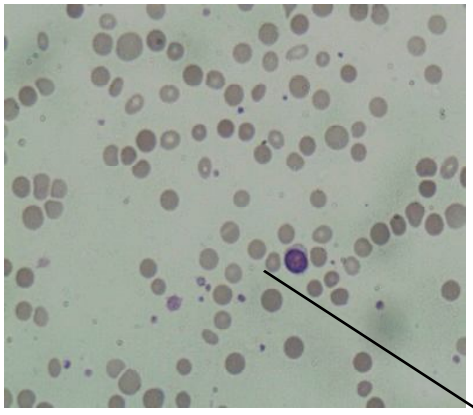

Fig 4 showing spherocytosis

Investigations

i) Haemogram – hemoglobin 5.3g/dl.

ii) Peripheral blood smear- RBCs showed anisopoikilocytosis, few spherocytes, mild polychromasia, 2 nucleated RBCs/100 WBCs, hypochromasia of mild degree. WBCs and platelets were normal. (Fig 4)

iii) Red cell indices - MCHC- 39.3 % MCV -75.3 fl RDW – 42%

iv) Reticulocyte count – 4%

v) Osmotic fragility –started at 0.96% of NaCl and ended at 0.28% of NaCl. (Markedly increased)

vi) Bone marrow- showed erythroid hyperplasia consistent with hemolytic anemia

vii) Hemoglobin electrophoresis- normal

viii) Direct coomb's test- negative

ix) Liver function tests- S.bilirubin- total 10 mg/dl and indirect 8.8 mg/dl (unconjugated hyperbilirubinimia).

x) X-ray skull lateral view showed mild widening of diploe with thining of cortex (suggestive of extramedulary hemopoiesis) (Fig5).

xi) Abdominal sonography revealed multiple gall stones, largest stone was 5 mm in diameter (Fig6).

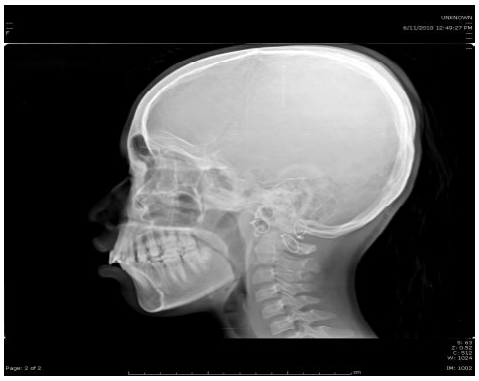

Fig 5: X ray skull showing widening of diploe

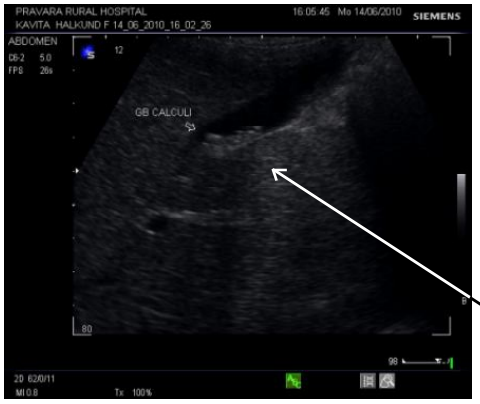

Fig 6: USG abdomen showing gallstone

Diagnosis and management

Based on family history, clinical findings and investigations the diagnosis of hereditary spherocytosis was confirmed. As child had severe anemia, she was given two units of blood transfusions. She was put on folic acid supplement 1 mg daily. Child is under consideration for total splenectomy.

Discussion

Hereditary spherocytosis is a chronic haemolytic anemia due to defect in red cell membrane. It is common in west Asia, North Africa and Europe with incidence of 1: 1000 to 1:4500. It is quite rare in India but exact data is not available. First clinical description was given by Vanlair and Mesius in 1871. Hereditary spherocytosis has wide spectrum of severity from asymptomatic disease without anemia with minimal hemolysis to severe hemolytic anemia requiring frequent blood transfusions to sustain life.

Hereditary spherocytosis is usually transmitted as autosomal dominant trait and less frequently as autosomal recessive trait. As many as 25% have no family history and are fresh mutants. The most common molecular defects are of spectrins and ankyrin which are major component of cytoskeleton responsible for RBC shape. Spherical shape of RBC impairs smooth passing from splenic cord to splenic sinuses and the spherocytic RBCs are destroyed prematurely in spleen.

Various clinical presentations

1) New born: May present with anemia and hyperbilirubinemia sufficiently severe to require phototherapy or even exchange transfusion. Though rare, hereditary spherocytosis should always be considered as a cause of neonatal hyperbilirubinimia.
2) Infant and children: Severity is variable. Some children remain asymptomatic till adult hood. Others may have severe anemia, pallor, jaundice, fatigue, and exercise intolerance. Severe cases may have marked expansion of skull marrow diploe and hemolytic facies. Similar findings are also seen in thalassemia major where they are more enhanced.
3) Pigmentary gall stones may be seen by the age of 4-5 years. At least 50% of unsplenectomised patients ultimately develop gall stones, though they may be asymptomatic.
4) Aplastic crisis may be seen, as in other hemolytic anemias, due to parvovirus infection, and hypoplastic crisis due to other infections. Aplastic crisis presents with rapid onset of severe anemia, high output congestive cardiac failure, hypoxia, cardiovascular collapse and sudden death.
5) Leg ulcers described in adults are not seen in children.

Severity of hereditary spherocytosis

Hereditary spherocytosis may present in mild, moderate or severe form.[5] Mild hereditary spherocytosis occurs in 20 to 30 percent of cases. These patients have no anemia, modest reticulocytosis, and little splenomegaly or jaundice, and may not be detected until adolescence or adult life. They maintain normal hemoglobin levels in the face of accelerated erythrocyte destruction via an erythropoietin driven increase in erythropoiesis. The stimulus for increased production of erythropoietin is not known but does not appear to be hypoxia.

Moderate hereditary spherocytosis accounts for 60 to 75 percent of cases. Moderately affected individuals are more anemic, have higher reticulocyte counts, and elevated serum bilirubin concentrations. They may require occasional transfusions, and are usually detected

in infancy or childhood. Although this group of anemic patients display an appropriate increase in serum erythropoietin, the reticulocyte response may be blunted, contributing to the degree of their anemia.

Severe hereditary spherocytosis occurs in approximately 5% of cases. It is characterized by marked hemolysis, anemia, hyperbilirubinemia, splenomegaly, and a regular requirement for red cell transfusions. The pattern of inheritance is almost always recessive and the parents of affected patients are usually asymptomatic.

Unconjugated hyperbilirubinimia occurs due to on going hemolysis, large amount hemoglobin is released which is broken down into heme and globin. Heme is converted to biliverdin which is converted to bilirubin. All these processes are carried out in reticuloendothelial system. Bilirubin is then taken up by hepatocytes and conjugated with glucoronic acid and secreted in bile. The bilirubin formation exceeds the capacity of liver to conjugate, so indirect hyperbilirubinimia (unconjugated bilirubin) occurs.

Gall stones formation Black pigmentary gall stones occur because of superabundance of unconjugated bilirubin in bile. When solubility of bile is exceeded, the excess unconjugated bilirubin precipitated as calcium bilirubinate. Calcium bilirubinate then polymerizes, binds to mucin produced by gallbladder mucosa and is retained. Gallstone formation depends upon bile supersaturation with unconjugate bilirubin and available free calcium. Calcium salt and mucin act as nidus to initiate stone growth.[1]

Diagnostic features

History hereditary spherocytosis is typically diagnosed in infancy or childhood but it may occur at any age. Anemia is often asymptomatic except some fatigue. A positive family history is usually present.

Examination

Pallor is seen in almost all patients but may vary in degree. Jaundice is seen in about half the patients. Jaundice is acholuric. Spleen is enlarged in half of the infants and 75 to 95 % in adolescence. Usually it is increased 5-6 cms bellow costal margin. (Fig.3)

Investigations : Hemoglobin level is usually 9-12 gm/dl but may be as low as 4-5 gm/dl. Reticulocyte count may vary from 6-20% with mean value of 10%. Spherocytes are the hall mark of the disease. They are dense, round, hyperchromic, lack central pallor and has decreased mean cell diameter. Red cell indices- MCHC is high > 36% (due to relative cellular dehydration). Increased MCHC and wide RDW suggest diagnosis of hereditary spherocytosis.[2]

Osmotic fragility is markedly increased. RBCs are incubated in progressive dilution of an isotonic buffer salt solution. Exposure to hypotonic saline cause RBCs to swell and spherocytic cells break more readily compared to normal biconvex RBCs. The osmotic fragility test is not specific for spherocytosis.

Incubated AGLT (acidified glycerol lysis test) is specific and sensitivity is 100%. It is >30 minutes for normal sample and < 5 minutes in hereditary spherocytosis. Simplicity of this test allows its use for rapid screening of large number of blood samples. [2] Newer specific tests such as osmotic gradient ektacytometry, the Eosin-5-maleimide test, membrane protein measurement are more sensitive but expensive and not readily available.

Management

Medical management consists of maintaining normal hemoglobin which is necessary in severe cases. Due to accelerated erythopoiesis, these children are susceptible to folic acid deficiency, therefore folic acid supplements are administered in a dose of 1mg daily. Intercurrent infections are promptly treated. Blood transfusions are made as per need of the patient.

Splenectomy: As spherocytes are destroyed exclusively in the spleen, splenectomy eliminates most of the hemolysis in hereditary spherocytsis. After splenectomy

RBCs life span improves, hyperbilirubinimia reduces.Whether all patients need splenectomy is controversial. Some do not recommend splenectomy if hemoglobin is > 10gms and reticulocyte count < 10%. If the child develops a crisis or has poor growth or cardiomegaly then these are indications for splenectomy. Splenectomy should be deferred till the age of five years as fulminant sepsis can occur before this age. Laparoscopic splenectomy when performed by experienced surgeons can result in a shorter hospital stay and less complications.[3] Splenectomy eliminates repeated blood transfusions, freedom from aplastic crisis and gallstones.

Patient should be vaccinated for haemophilus influenzae Type b, meningococcal and pneumococcal vaccines at least four weeks before splenectomy. After splenectomy patient should be put on life long prophylaxis with oral penicillinV 125mg bid (age below 5 years) and 250mg bid (age more than 5 years).[3]

Prognosis

Complications develop during course of illness. Fifty percent of unsplenectomised patients develop gallstones. Various crisis such as hemolytic crisis, aplastic crisis, megaloblastic crisis occur. Gout, leg ulcers, extramedulary hemopoiesis, hematological malignancies, cardiomyopathy, hypogonadism are also seen.

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