

Hereditary Spherocytosis – A Case Report

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Abstract

Hereditary spherocytosis is the most common cause of chronic hemolytic anemia. Deficiency in predominantly spectrin and also in other protein such as band 3, protein 4.2 and ankyrin is the main etiology. Clinical presentation varies from anemia, reticulocytosis, splenomegaly to symptoms and signs arising due to its complications such as chronic leg ulcers, hemolytic crisis, aplastic and megaloblastic crisis and cholelithiasis. Peripheral blood smear, reticulocyte counts, osmotic fragility studies and ultra sonography of abdomen are essential investigations for the diagnosis of hereditary spherocytosis. Milder forms of hereditary spherocytosis are asymptomatic. We present a case of a 24 year old male who presented with pain in abdomen and icterus. Investigations revealed the case to be of hereditary spherocytosis. The patient was posted for splenectomy and was on post splenectomy prophylaxis.

Keywords: Spherocytosis, anaemia, osmotic fragility, splenomegaly.

Introduction

Hereditary spherocytosis is a rare inherited red cell membrane disorder. It is characterized by defect in spectrin, a red cell membrane protein and is transmitted as an autosomal dominant disorder.⁽¹⁾ It is a cause of chronic hemolytic

anemia and is characterized by marked heterogeneity. The incidence is estimated to be 1:2000 to 1:5000.⁽²⁾ The characteristic presentation is of hemolytic anemia showing characteristic spherocytes, reticulocytosis, jaundice, moderate to severe splenomegaly and

increased osmotic fragility.⁽³⁾ The patient can present with aplastic or megaloblastic crisis, cholecystitis and cholelithiasis, leg ulcers, extramedullary hematopoiesis and hematochromatosis.⁽⁴⁾ However cases of arterial and venous thrombosis have also been described. The investigative sequence involves peripheral blood examination, reticulocyte count, ultra sonography abdomen, fresh blood or incubated NaCl osmotic fragility studies, sodium dodecyl sulfate polyacrylamide gel electrophoresis(SDS-PAGE) and exclusion of secondary cause of spherocytosis.⁽⁵⁾

Case Report

A 24 year old male presented to the medicine OPD with complaints of intermittent dull aching left hypochondriac pain in abdomen and yellow discoloration of eyes since 5 years. General examination revealed to be patient slightly tachycardic. There was no history of any blood transfusion in the past. They were no gross signs of liver cell failure or sternal tenderness. Per abdominal examination revealed massive splenomegaly of 12 cm below the left costal margin and hepatomegaly of 4 cm below the right costal margin. Both the sites were soft and tender. Rest of the systemic examination was unremarkable.

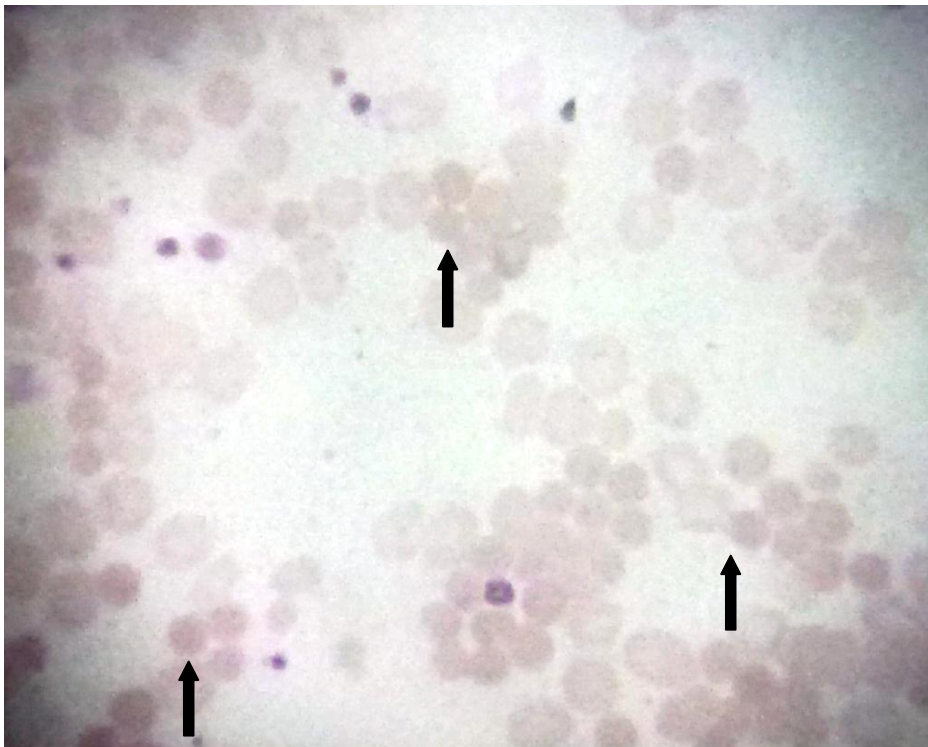


Figure 1: Photomicrograph showing numerous micro-spherocytes (arrows) along with anisopoikilocytosis. (Leishman stain, 400x)

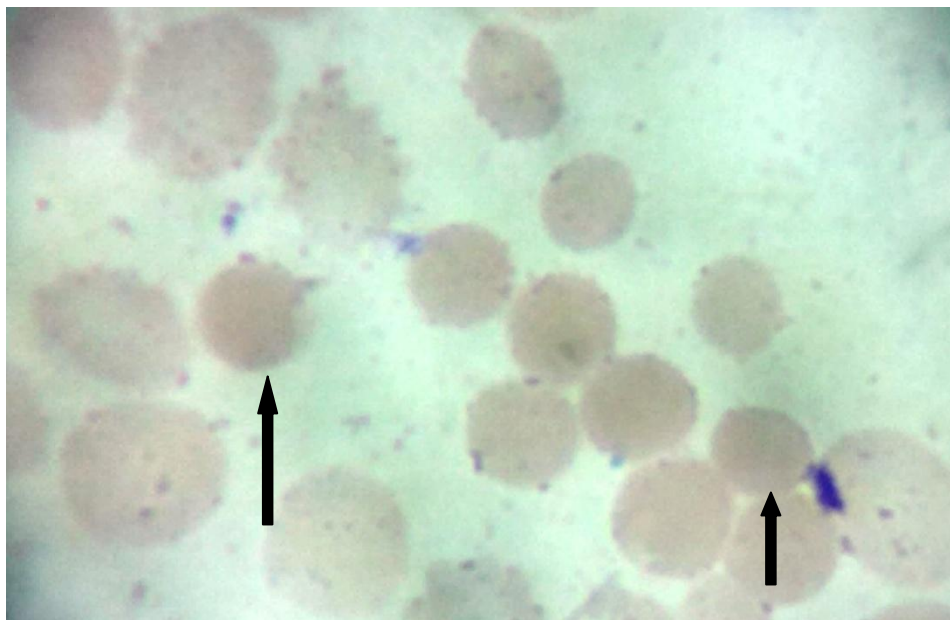


Figure 2: Photomicrograph showing oil immersion view of the spherocytes (arrows). (Leishman stain, 1000x)

Routine hematological examination revealed the patient to be severely anemic with hemoglobin 6.1 gm/dl. Peripheral blood smear revealed anisopoikilocytosis consisting of macrocytes, normocytes and numerous micro spherocytes (Figure 1, Figure 2). His total leucocyte count was within normal limit but he had neutrophilia. The platelet count were within normal limit. However, giant platelets were noted throughout the field. Fragmented cells/ schistocytes were not seen. He had reticulocytosis (9.5%). His total bilirubin was 12 mg/dl with indirect being 11 mg/dl. Serum protein, alkaline phosphatase and rest of the liver enzymes were within normal limits ruling out any liver disease. His serum iron, serum ferritin, serum TIBC were within normal limits. Direct Coomb's test was negative thus ruling out immune hemolytic anemia. NaCl incubated osmotic fragility showed increased fragility.

Family history revealed the father to have similar signs and symptoms. He was diagnosed with hereditary spherocytosis and was not alive.

Abdominal ultra sonography revealed splenomegaly 12 cm below the left costal margin along with hepatomegaly 4 cm below the right costal margin and cholelithiasis. Based on all the above findings, diagnosis of hereditary spherocytosis was considered

Discussion

Hereditary spherocytosis is a rare, inherited red cell membrane disorder.⁽⁶⁾ The abnormality being deficiency and disorder in predominantly spectrin. However abnormality in other protein such as ankyrin, band 3 and protein 4.2. Hereditary spherocytosis is a hemolytic condition leading to chronic anemia which can present as an autosomal dominant, recessive or as a sporadic (25%) cases.^(1,6) It can present with varying degree of severity, membrane protein defects and modes of

inheritance. It can remain undiagnosed for years if not decades. The classical clinical features seen are anemia, jaundice and splenomegaly. However, anemia could be masked as in mild to moderate spherocytosis due to the capacity of the marrow to compensate 6-8 folds.⁽⁷⁾ There is increase reticulocyte count due to prolific destruction of RBCs which reflectsthe hyperplasia ofthe marrow. Jaundice is often evident in moderate to severe degree of spherocytosis and conditions in which the marrow is stressed with superadded infections. Those cases which have moderate to severe hemolysis can present with cholelithiasis, hemolytic crisis and similar complication as a result of increase breakdown of RBCs.⁽³⁾

The age of presentation of hereditary spherocytosis varies from the neonatal period to the ninth decade of life.⁽⁷⁾

About 20-30% patients have mild disease, 60-70% have moderate disease, 10% have moderately severe disease where as 3-5% of patient have severe disease course.⁽⁸⁾

Laboratory investigations include a thorough peripheral blood smear examination for presence of spherocytes and exclusion of other disease conditions in which spherocytes are noted such as immune hemolytic anemia, hemolytic transfusion reaction, liver disease, bacterial sepsis, snake - spider & hymenoptera evenomation, severe hypophosphatemia, prolonged blood sample storage and hypersplenism.⁽⁹⁾ Tests which detect abnormal red cell surface area to volume ratio and hence fragility such as osmotic fragility studies are also helpful as supportive tests in the final diagnosis. However, flow cytometric EMA (eosin-5' maleimide) labelled intact red blood cell test is

a quicker and more sensitive and specific test for identifying spherocytosis.⁽¹⁰⁾ Sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE) is also used for analysis of red cell membrane proteins which helps in the categorization as deficiency of band 3, spectrin or ankyrin, combined spectrin ankyrin deficiency and no detectable defect.⁽²⁾ Other tests such as glycerol lysis test (GLT), acidified glycerol lysis test and pink test can also be applied in the diagnostic array.⁽¹¹⁾

However in routine hematology, a combination of presence of familial history, peripheral blood smear examination, ultrasonography abdomen for splenomegaly and osmotic fragility studies, is used where flowcytometric EMA binding tests are not available as in the present case.

Those cases presenting in the neonatal period can be treated with phototherapy and/or blood transfusion depending on the severity of anemia.

However splenectomy is to be deferred up to 5 years in children less than 5 years of age due to risk of pneumococcal infections. Cholecystectomy is also indicated at the same time of splenectomy as cholelithiasis is a proven complication of this disease. Patients who undergo splenectomy should be vaccinated with multivalent hemophilus and other vaccine before the procedure.

Our patient was posted for splenectomy and was on post splenectomy antibiotic prophylaxis.

Conclusion

Hereditary spherocytosis is a rare form of hemolytic anemia due to defect in red cell membrane proteins seen generally in children but can also be noted in adults. The milder form is

generally asymptomatic where as signs and symptoms begin to appear with increasing severity of the disease. Repeated blood transfusions may be required to compensate the decreasing hemoglobin levels. However, splenectomy offers definitive treatment. Complications arising as a result of hemolysis such as cholelithiasis can be averted by timely intervention. Generally, familial forms are predominant, however recessive and sporadic forms also do occur. Exclusion of all the secondary causes of spherocytosis is of prime importance to arrive at a diagnosis of hereditary spherocytosis as treatment modalities differ.

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