Chronic Diseases Journal

Hereditary spherocytosis in an 18-month-old boy with pancytopenia: A case report

Borhan Moradveisi[1], Soran Ghafouri[2], Abdollah Sedaghat[2]

1 Assistant Professor, Department of Pediatrics Hematology and Oncology Diseases, School of Medicine, Kurdistan University of Medical Sciences and Health Services, Sanandaj, Iran
2 Resident, School of Medicine, Kurdistan University of Medical Sciences and Health Services, Sanandaj, Iran

Case Report

Abstract

Hereditary spherocytosis (HS) is a familial hemolytic disorder with marked heterogeneity of clinical features, ranging from an asymptomatic condition to a fulminant hemolytic anemia. Although a positive family history of spherocytosis increases the risk for this disorder, it may be sporadic in some cases. In severe cases the disorder may be detected in early childhood, but in mild cases it may go unnoticed until later in adulthood. The case was an 18-month-old boy from Sanandaj, Iran with 3 days decreased activity movement, poor feeding, pallor and urine discoloration since 3 days ego following an episode of fever. He was a case of anemia who was managed conservatively on nutritional supplements. Blood film showed 80% spherocytes, reticulocyte was 0.5%, increased osmotic fragility test and a negative direct Coombs.

KEYWORDS: Hereditary Spherocytosis, Familial Hemolytic Disorder, Hemolytic Disorder, Anemia, Spherocytes, Reticulocyte, Osmotic Fragility Test

Date of submission: 16 Feb 2013, ***Date of acceptance:*** 20 May 2013

Citation: Moradveisi B, Ghafouri S, Sedaghat A. **Hereditary spherocytosis in an 18-month-old boy with pancytopenia: A case report.** Chron Dis J 2013; 1(2): 92-5.

Introduction

Hereditary spherocytosis (HS) is a hemolytic disorder with marked heterogeneity of clinical features. It is a dominant inherited disorders characterized by the presence of sphere-shaped red blood cells.[1] HS has been commonly presented in northern Europe, North America, and Japan. It seems to be less common among African-Americans.[1,2]

HS is a result of deficiency of membrane surface area and an in vitro abnormal osmotic fragility. The intrinsic genetic defect is on the red blood cell along with spectrin defects.[3] Overall α-spectrin mutation occurs in recessive HS, whereas β-spectrin mutation occurs in the dominant HS.[4] Mild to moderately severe cases with ß-spectrin deficiency do not need a transfusion.[3] HS is categorized as mild, moderate, moderately severe, and severe in line with basic clinical laboratory variables, including primarily on the concentration of hemoglobin, as well as the reticulocyte count.[5] Clinical symptoms are hemolysis with anemia, jaundice, reticulocytosis, gallstones, splenomegaly, spherocytes on the peripheral blood smear, increased erythrocyte osmotic fragility, and a positive family history for the disease.[6] Intact spleen and intrinsic membrane-protein defect leads to abnormal red blood-cell and hemolysis. Most of the patients have moderate disease presenting with fatigue, pallor, or both due to anemia, otherwise it is asymptomatic. In case of a viral infection, jaundice arises in about 50% of the cases. Laboratory findings include

Corresponding Author:
Soran Ghafouri
Email: soranghafuri@gmail.com

hemoglobin concentration between 6 to 11 g/dl, and increased proportion of reticulocytes.[7]

Case Report

An 18-month-old boy from Sanandaj was brought by to the Pediatric Emergency Ward of Be'sat Hospital by his parents on 30th December-2012, with decreased activity and movement, poor feeding, pallor and urine discoloration following an episode of fever which occurred three days ago.

Previous medical history included hospitalization with the diagnosis of pneumonia and incidental finding of relatively severe anemia when the patient was 6 months old; despite bone marrow aspiration (BMA) and other evaluation, no definite cause for anemia was established and the patients discharged with oral iron supplementation.

His father had been assessed for anemia and splenomegaly 20 years ago with no definite diagnosis. His sister was assessed for anemia resulting in decreased serum B12 levels which treated with parenteral supplementation of vitamin B12. The patient was breast fed for 12 months, six months of which was exclusive breast feeding.

In the physical exam, his weight was 12.5 kg (70th percentile for weight). Vital sign was stable with no signs of fever with only mild tachycardia. Skin and mucosal membrane were apparently pale, with no significant skin lesion. No significant lymphadenopathy was detected. Liver size was normal; however tip of spleen was palpable 3 cm below the costal margin.

Laboratory results were as follows in table 1.

Liver function tests [(LFT): aspartate aminotransferase (ALT), alanine aminotransferase (AST), alkaline phosphatase (ALKP), bilirubin total and direct)], erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were normal, direct Coombs was negative and Glucose-6-phosphate dehydrogenase (G_6PD) was sufficient.

Peripheral blood smear (PBS) showed numerous spherocytes with marked anisocytosis and severe hypochromic and microscopic red blood cells. Bone marrow aspiration detected red-cell hyperplasia. Abdominal Ultrasound revealed mild splenomegaly and gallbladder sludge.

Four days after hospitalization, his 10-year-old brother referred to the hospital with fatigue, fever, sore throat, lack of energy and significant pallor, without any history of anemia or hospitalization. His physical examination showed splenomegaly (4 cm below costal margin) and marked pallor. Laboratory results were shown in the table 1.

LFT (ALT, AST, ALKP, bilirubin total and direct), ESR, CRP were normal, D-Coombs was negative and G_6PD was sufficient.

The parents' complete blood count (CBC) were normal. Increasing initial lysis occurs in the osmotic fragility test with and without incubation. A serum folate level typically was normal and B_{12} serum level fall below the normal

Table 1. Laboratory results of the case and his brother

White blood cells (WBC)	Patient's laboratory results 5400 (Neutrophil: 26%; Lymphocyte: 74%)	Patient's brother laboratory results 7400 (Neutrophil: 35%; Lymphocyte: 65%)
Red blood cells (RBC)	1.3 × 106	1.7 × 106
Hemoglobin (Hb)	2.7 mg/dl	4.4 mg/dl
Hematocrit (Hct)	8.5	12.7
Mean corpuscular volume (MCV)	64.3	72
Mean corpuscular hemoglobin concentration (MCHC)	20	34.6
Platelets (PLT)	31	214000
Red cell distribution width (RDW)	108000	20
Reticulocyte	26.9	1.2

limits. Patient's condition at discharge was likely to improve after transfusions of three units of packed-cell.

Discussion

Osmotic fragility test is a useful diagnostic test for this disorder. It is widely proposed that the membrane defect, fluidity and cytoskeletal change, is the main etiology for increased fragility of red blood cell. Hereditary spherocytosis is globally rare inherited red cell membrane disorder.[8-10] This is caused by a molecular defect in one or more of the proteins of the red blood cell cytoskeleton.[8] Spectrin deficiency is the most common defect. The defects are associated with a variety of mutations that result in different protein abnormalities and varied clinical expression. Most cases of HS are heterozygous because homozygous states are deadly.[8-11] In pedigrees that have a dominant defect, affected family members tend to have similar degrees of hemolysis and clinical severity.[12-14] Regardless of the molecular basis for a case of HS, the resulting spherocytes become trapped in the spleen as they course through the sinuses, and the red cells were engulfed by macrophages.[12-14]

Several reports and text books have associated a triad of anemia, jaundice and splenomegaly to the morphological findings of spherocytes as the hallmark to the diagnosis of HS like the finding in our case.[8-9,11-13] Our diagnosis was supported by an increased osmotic fragility and a negative direct Coomb's test, although a negative result may be obtained especially for osmotic fragility where a high reticulocytes count of more than 10% interferes with the test.[4]

Bone marrow suppression due to infection with parvovirus B19 can be presented with low reticulocyte count that is matched with our case.[4,8]

In the first few postnatal months, anemia can be developed in children who do not mount an adequate reticulocyte response.[4]

Later in the childhood, HS can manifest with anemia, jaundice, and splenomegaly.[4-8]

Affected patients may have mild, moderate, or severe anemia. Children who have moderate to severe anemia may have poor exercise tolerance, growth failure, and academic difficulties.[2-5] Older individuals develop bilirubin stones and may present with cholecystitis.[2-5] It is often not uncommon for the diagnosis to be missed until adulthood.

The peripheral blood smear in HS shows numerous spherocytes. Larger bluish cells (polychromasia) also may be seen. The CBC and reticulocyte count reveals a low hemoglobin concentration and elevated reticulocyte count.[1-3] The mean corpuscular hemoglobin concentration is usually high at greater than 35 g/dl (350 g/l). The mean corpuscular volume may be low or high if there is substantial reticulocytosis.[1-3] The test of the osmotic fragility can be useful in establishing the diagnosis of HS. Spherocytes have reduced cell membranes and thus they swell at higher concentrations of saline than do normal red cells. The direct antiglobulin (Coombs) test is usually negative. Other test includes elevated unconjugated bilirubin, elevated lactic dehydrogenase, and low haptoglobin levels. However, these findings are associated with any case of haemolysis and are nonspecific for HS.[1-3,6] Thus this might be recessively inherited or sporadic as it occurs in 25% of the cases or a silent carrier state, as it has been suggested to exist in 1.4% of the population.[4] The patient was managed conservatively with nutritional supplementation consisting of folic acid, ascorbic acid.

Specific indications for transfusion included exacerbation of anemia due to blood loss such as related to trauma or surgery, hypersplenism, and infection with parvovirus B19.[4]

Cure is achieved with splenectomy[4] but there was no indication for this in our patient. Splenectomy is carried out in cases with severe anemia and extramedullary hematopoiesis.[4-11]

Complications of hereditary spherocytosis include pigment gallstones, aplastic, haemolytic and megaloblastic crises, growth failure, skeletal deformities, and less commonly skin ulceration, and chronic dermatitis.[1-8]

As we noticed earlier in our case, the patient's 36-year-old father and 6-year-old sister had a history of anemia after a diagnostic work-up. However, they were not diagnosed correctly which caused anemia for a period of time. On the other hand, the patient's brother did not have any history of anemia or hospitalization despite suffering from this sickness for a long period of time. He had pallor and some complaint including fatigue, lack of energy, anorexia, significant pallor, splenomegaly, and growth failure.

Although HS is rare, it does occur in our environment and when suspected hematological assessment is necessary to avoid diagnostic pitfalls and mismanagement.

Conflict of Interests

Authors have no conflict of interests.

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