Case Report

A case report of hereditary spherocytosis (HS): Approach to diagnosis and management of HS

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ABSTRACT

Hereditary spherocytosis (HS) is a type of congenital hemolytic anemia, in which heterogeneous alterations in one of the six genes that encode for proteins involved in vertical associations which tie the red blood cell (RBC) membrane skeleton to the lipid bilayer causes dysfunction or deficiency of cell membrane protein resulting in spherical-shaped, hyper-dense, and poorly deformable RBCs with a shortened life span. We report a case of HS in a 2-month-old female who presented with severe anemia, jaundice, and hepatosplenomegaly. The peripheral blood smear showed spherocytosis and reticulocytosis. The osmotic fragility was positive and direct antiglobin test was negative. The osmotic fragility test and direct antiglobulin test were positive. She was managed with packed RBCs (PRBCs) transfusion and folic acid supplementation.

Key words: Direct antiglobulin test, Hemolytic anemia, Osmotic fragility, Spherocytosis

Hereditary spherocytosis (HS) is the most common hemolytic anemia due to a red cell membrane defect [1]. The prevalence is as high as 1 in 5000 in certain ethnic groups, especially in people of North European or Japanese descent [2]. It results from heterogeneous alterations in one of the six genes involved in vertical associations that tie the membrane skeleton to the lipid bilayer [3]. Various mutations in the genes encoding these membrane proteins have been described, the most important ones being ankyrin-1, β-spectrin, α-spectrin, band 3, and protein 4.2 (Fig. 1) [1,4]. Family studies indicate an autosomal dominant inheritance in approximately 75% of patients, with recessive and spontaneous mutations occurring in the remaining patients [3].

CASE REPORT

A 2-month-old female infant was referred for evaluation of severe anemia, poor feeding, and lethargy. She was born by normal vaginal delivery with a birth weight of 3.1 kg and Apgar scores of 9/10 and 10/10 at 1 and 5 min, respectively. The maternal weight gain during pregnancy was 9.5 kg and the maternal weight at the time of delivery was 69 kg. The dating and anomaly scans were reported as normal and she had an uneventful antenatal period. The parents were non-consanguineous. On detailed history taking, the father revealed that he required frequent blood transfusions during childhood and also had undergone splenectomy at the age of 10 years and cholecystectomy at the age of 17 years and has been asymptomatic since then. No one else in the family is affected with a similar illness.

On examination, in addition to severe pallor, the baby also had icterus and moderate hepatosplenomegaly. Her heart rate (HR) was 110/min, respiratory rate was 42/min, peripheral perfusion was adequate, and she was euthermic.

Her blood investigations revealed hemoglobin (Hb) of 3.9 g% and peripheral blood smear examination showed features suggestive of hemolysis in the form of significant spherocytosis (15%), occasional nucleated red blood cells (RBCs), and marked reticulocytosis (10.5%) with corrected reticulocyte count of 6%. The remaining relevant hematological and biochemical parameters are elucidated in Table 1. Osmotic fragility testing (OFT) showed that hemolysis begins at a concentration of 0.55% NaCl and completes in 0.2% NaCl, which confirms the presence of spherocytes. A direct antiglobulin test (DAT) was negative, but the osmotic fragility was increased.

She was managed conservatively with folic acid supplementation and packed RBCs (PRBCs) transfusion.

DISCUSSION

The clinical spectrum of HS during the perinatal period ranges from asymptomatic baby to severe fetal anemia with hydrops fetalis. Symptoms can range from mild-to-severe and may include anemia, fatigue, jaundice, gallstones, and/or enlargement of the

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Table 1: Hematological and biochemical investigations

Hematological parameters	Results	Normal value
Hemoglobin	3.9 g/dL	12–13 g/dL
Mean corpuscular hemoglobin concentration	37 g/dL	29–37 g/dL
Mean corpuscular volume	75 fL	80–100 fL
Neonatal HS ratio (MCHC/MCV)	**0.49**	**<0.36**
Mean corpuscular hemoglobin	26.7 pg	27-32 pg
Packed cell volume	20.1%	36–56%
Red cell distribution width	28.9%	10–16.5%
Reticulocyte count	10.5%	<2%
Total bilirubin	4 mg/dL	<1.2 mg/dL
Direct bilirubin	0.46 mg/dL	<0.3 mg/dL
Lactate dehydrogenase	333 IU/L	<150 IU/L
Serum iron	169 microgram/dL	35–150
Total iron binding capacity	368 microgram/L	240–450
Serum ferritin	520 ng/mL	24–336 ng/mL
Direct antiglobulin test	Negative	
Osmotic fragility	Increased	

HS: Hereditary spherocytosis

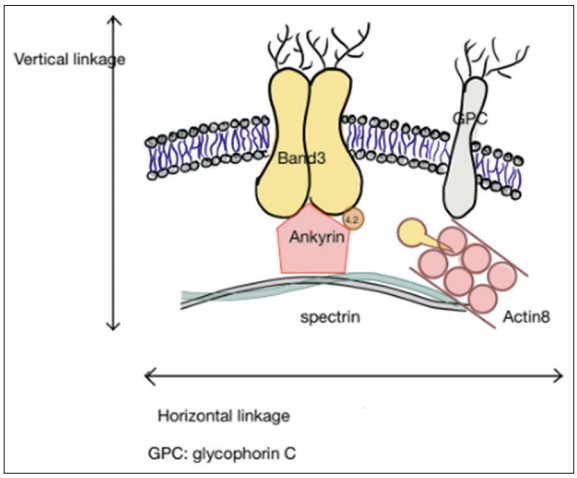

Figure 1: Horizontal and vertical linkage of various red blood cell membrane proteins (GPC: Glycophorin C) [4]

spleen. About 75% of cases are inherited as an autosomal dominant pattern, while 25% occur sporadically. The prevalence of HS is approximately 1 in 10,000 to 1 in 40,000, whereas in Northern Europe and North America, it is as high as one in 5000 [5].

HS is generally classified into three forms based on the severity of the disease process [5]. Mild HS occurs in 20–30% of cases. These patients have no anemia, or modest reticulocytosis and the disorder may not be detected until adolescence or adult life. Moderate HS accounts for 60–75% of cases, who present with anemia, high reticulocyte counts, and elevated serum bilirubin concentrations. They usually require occasional red cell transfusions. Severe HS occurs in approximately 5% of cases. It is characterized by marked hemolysis, anemia, hyperbilirubinemia, and splenomegaly. Such patients require red cell transfusions on a regular basis [5].

HS is most likely if a patient has DAT-negative jaundice, elevated mean corpuscular Hb concentration (MCHC) (36.5–37 g/dL), and low mean corpuscular volume (MCV) [1,6]. Based on this scenario, the Neonatal HS ratio (NHSR) can be calculated by dividing the MCHC by the MCV. As per the Intermountain Healthcare database, an NHSR of more than 0.36 is 97% sensitive and 99% specific for making a diagnosis of HS with a 99% negative predictive value [7]. In our case, the NHSR was 0.49. When the diagnosis of HS is uncertain, eosin-5-maleimide (EMA) binding or OFT is helpful. EMA binding is a flow cytometry-based test that measures the relative amount of fluorescently labeled EMA dye bound to band 3 and Rh-related proteins in the erythrocyte membranes [8].

When signs of anemia appear, PRBC transfusions are helpful. In a few reports, recombinant erythropoietin (rEPO), or long-acting darbepoetin therapy has been used as an alternative or adjunct to transfusion [9]. Folic acid supplementation is recommended in treating HS [10,11] These children should be closely observed for hematologic decompensation during acute illnesses as some of them may experience hemolytic or aplastic crises. This outcome is particularly true after 6 months of age when maternally derived immunoglobulin G antibodies to microbes have waned.

CONCLUSION

HS is the third most common yet frequently underdiagnosed congenital hemolytic anemia with 75% autosomal dominant inheritance. It is important to give appropriate genetic counseling to expectant parents with HS. Prompt treatment and anticipatory guidance are essential to prevent adverse outcomes related to HS.

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