



## Case Report

# Hereditary Spherocytosis in a 22 Month Old Child

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### Abstract

Hereditary spherocytosis (HS) is a familial hemolytic disorder with marked heterogeneity of clinical features, ranging from 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 case. A 22-month old girl was admitted in Rajshahi Medical College Hospital with pallor and jaundice. Her parents gave history of repeated episodes of pallor and jaundice since 8 month of age with negative family history. Blood film showed plenty of spherocytes, reticulocytosis of 15.0%, negative direct antiglobulin test & positive osmotic fragility test. She was managed conservatively on nutritional supplements & one unit of blood transfusion. To the best of our knowledge, this is the first reported case of hereditary spherocytosis from Rajshahi Medical College Hospital.

**Key words:** Anaemia, Jaundice, Spherocytosis, Hereditary

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### Introduction:

Hereditary spherocytosis (HS) is a familial hemolytic disorder with marked heterogeneity of clinical features range from asymptomatic to fulminant hemolytic anemia. The condition was first described in 1871.<sup>1</sup> HS is the commonest cause of inherited chronic hemolysis in Northern Europe and North America, with a reported incidence of 1 in 5,000 births.<sup>2</sup> In 80% of the instances, the inheritance of HS is autosomal dominant and in others autosomal recessive.<sup>3</sup> In North India, both autosomal dominant and recessive patterns have been reported with presentation similar to that in other populations but the underlying protein defect has not been characterized.<sup>4</sup> To our knowledge, no case has been reported from Rajshahi, Bangladesh. A family history and typical clinical and laboratory findings make the diagnosis possible without

much difficulty, and additional investigations are not required. Atypical cases may require measurement of erythrocyte membrane proteins to clarify the nature of the membrane disorder, and occasionally, molecular genetic tests are required to determine the mode of inheritance. In autosomal dominant form, the deficiency is mild, and hence, the anemia is mild while in the recessive form, the deficiency is greater and the anemia is profound.

### Case summary

In April 2017, a 22-month old girl was brought to the Rajshahi Medical College Hospital and was admitted with a severe pallor, mild jaundice and weakness. The girl's family lives in Nachol, Chapainawabgonj, and her parents are non-consanguineous. Before attending the hospital, the child was treated with some unspecified medicines. Systemic enquiry revealed that she had been suffering from repeated attacks of jaundice

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and pallor since she was 7 months old. This long-standing illness was usually managed locally but she was occasionally given folic acid and 1 unit of blood transfusion when she was 12 months old. Her birth history was uneventful, and she did not have neonatal jaundice. The girl was immunized as per the Expanded Programmed on Immunization schedule. She has one elder brother and there was no same type of illness in her other family member. At admission, the girl looked sick, pale and icteric. She was afebrile. Her pulse rate was 110 per minute, blood pressure 90/60 mmHg, and respiration rate 22 per minute. On abdominal examination, liver was palpable 2 cm from the right subcostal margin in the right mid-clavicular line which was soft and non-tender. Her spleen was also palpable 2 cm below from the left costal margin in anterior axillary line along its long axis towards the right iliac fossa which was soft in consistency, non-tender, moves with respiration. Other system examinations revealed no abnormality. So our provisional diagnosis was congenital hemolytic anaemia. On investigation during admission hemoglobin was 5.3 g/L, white blood cell count of 16,000/mm<sup>3</sup> with unremarkable differential counts. Red cell indices revealed that mean corpuscular volume (MCV)100.5 fl, mean corpuscular hemoglobin (MCH)24.8 pg & mean corpuscular hemoglobin concentration (MCHC)was 28.62 g/dL that were within normal limit and raised reticulocyte count (15.0%) and serum bilirubin (3.4 mg/dl). Peripheral blood film showed moderate rouleaux formation with anisopoikilocytosis, spherocytosis, poly chromatic cells and few nucleated red cells. Hemoglobin electrophoresis was normal. Coombs test—both direct and indirect—was also negative. In osmotic fragility test of red blood cell (RBC) showed that lysis started at 0.6% NaCl solution and 50% lysis was completed at 0.4% NaCl solution; osmotic fragility test was positive. Ultrasonographic examination of her abdomen revealed hepatosplenomegaly but no gallstones were found. During her hospital stay, the patient received folic acid and multivitamins and got 1 unit of blood transfusion.

## Discussion

In the presence of a large number of spherocytes in the peripheral blood film, a major alternative differential diagnosis was autoimmune haemolysis (which can mimic HS). A positive direct Coomb's test (detection of antibody on RBCs using direct antiglobulin) indicates autoimmune hemolytic anemia. Other rare causes of spherocytosis include thermal injury, Clostridial septicaemia with exotoxaemia, and Wilson's disease, which may present with transient hemolytic anemia. Hemolytic anemia is also a feature of haemoglobinopathies, which are diagnosed by hemoglobin electrophoresis. In HS, the haemoglobin electrophoresis is normal, and presence of microspherocytes on the blood smear confirms the diagnosis. The differentials focus on the causes of a fall in the RBC surface area/volume that occur in autoimmune hemolytic anemia, HS, and microangiopathic anemia. However, in our presented case, there were no suggestive features, such as fragmented RBC, which is in favor of microangiopathy. Therefore, a negative direct Coombs test, positive osmotic fragility test, a blood smear showing spherocytes, and a raised reticulocyte count all suggest that hereditary spherocytosis was the likely diagnosis.

Microspherocytosis is the morphological hallmark of HS, which is caused by loss of membrane surface area, with abnormal osmotic fragility *in vitro*. The pathophysiology of HS involves 5 proteins, which are key components of the cytoskeleton responsible for RBC shape. Abnormalities of spectrin or ankyrin are the most common molecular defects. The decreased deformability of the spherocytic RBCs impairs cell passage from the splenic cords to the splenic sinuses, and the spherocytic RBCs are destroyed prematurely in the spleen. Hereditary spherocytosis usually is transmitted as an autosomal dominant or, less commonly, as an autosomal recessive disorder. In about 25% of cases, there is no previous family history. In the neonatal period, HS is a significant cause of hemolytic disease and can be manifest as anemia

and hyperbilirubinemia sufficiently severe to require phototherapy or exchange transfusions.

Although some children are asymptomatic in childhood, others may have pallor (anemia), fatigue, and exercise intolerance. In severe cases, marked expansion of the diploic spaces skull bones and medullary region of other bones is observed but to a much lesser extent than observed in patients with thalassemia. After infancy, splenomegaly is common; there is no correlation between spleen size and disease severity. Bilirubin gallstone formation is a function of age; they can form as early as age 4-5 yrs. and are present in the majority of adult patients. The diagnosis of HS can be established from a positive family history and the presence of typical clinical and laboratory features of the disease: splenomegaly, spherocytes on the blood smear, reticulocytosis, and an elevated mean corpuscular hemoglobin concentration. If these are present, no additional testing is necessary to confirm the diagnosis. Although no test for HS is 100% reliable, the EMA binding test had a diagnostic sensitivity and specificity of 93% and 98%, respectively, in a recent large study. The classic incubated osmotic fragility test can detect the presence of spherocytes in the blood; it is not specific to HS and may be abnormal in other hemolytic anemia. Children with HS are susceptible to aplastic crises, primarily as a result of parvovirus B19 infection, and to hypoplastic crises associated with various other infections. High RBC turnover in the setting of erythroid marrow failure can result in profound anemia (hematocrit <10%), high-output heart failure, cardiovascular collapse, and death. White blood cell and platelet counts can also fall. Rare complications associated with HS include splenic sequestration crisis, gout, cardiomyopathy, priapism, leg ulcers, and spinocerebellar degeneration. Once the baseline level of disease severity is reached, an annual visit to the hematologist usually is sufficient. Growth should be monitored; exercise tolerance and spleen size documented, and parents should receive anticipatory guidance regarding the risk of aplastic crisis secondary to parvovirus, and hypoplastic crises with other infections. The spherocytes are

destroyed almost exclusively in the spleen; splenectomy eliminates most of the hemolysis. After splenectomy, the anemia, hyperbilirubinemia, and incidence of gallstones are significantly lessened, but not completely eradicated. Splenectomy is associated with immediate surgical morbidities in addition to a lifelong increased risk for sepsis, particularly by pneumococcal species. This risk is not completely eliminated with the requisite preoperative and postoperative vaccination against *Pneumococcus*, *Meningococcus*, and *Haemophilus influenzae* type b. Splenectomy is recommended for patients with severe HS. It should be considered for patients with moderate HS and frequent hypoplastic or aplastic crises, poor growth, or cardiomegaly. It is generally not recommended for patients with mild HS. When splenectomy is indicated, it should be performed after the age of 6 years, if possible, to avoid the heightened risk of post-splenectomy sepsis in younger children. Patients should be given 1 mg of folic acid daily for preventing secondary folic acid deficiency, and oral penicillin (penicillin V) for preventing secondary infection until reaching adulthood. Since patients are more prone to hemolysis, a bracelet or card indicating the diagnosis should be worn to alert health professionals. HS, as the name suggests, is inherited and can pass down from parents to children. Families with an affected child should be counseled about up to 50% probability of each subsequent child having HS. Although genetic counseling is difficult to do in most developing countries due to the non-availability of genetic testing, HS is a relatively straightforward clinical diagnosis of a genetic condition; so, parents have the opportunity to receive counseling about the consequences of the diagnosis, the prognosis, and the risk of another child being affected.<sup>2</sup>

### **Conclusion**

Hereditary spherocytosis should be considered in the differential diagnosis in patients with Coomb's-negative haemolytic anaemia.

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