

## CASE REPORT

# AUTOSOMAL DOMINANT HEREDITARY SPHEROCYTOSIS IN AN ELDERLY PATIENT

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### Abstract:

*Hereditary spherocytosis (HS) is an autosomal dominant inherited hemolytic anemia that usually manifests in early adolescence. A very small proportion (5%) may undergo de novo mutations and present at an elderly age without any positive family history. The disease is characterized by anemia, jaundice, splenomegaly, and the presence of spherocytes in peripheral blood, which are osmotically fragile. A 55-year-old elderly male presented with generalized weakness and a history of repeated blood transfusions for 5 months. He had recurrent jaundice for 8 years. There was no relevant family or drug history. He was anemic, icteric, and had mild splenomegaly. Investigation revealed persistently low Hb with normal red cell indices. There were a lot of spherocytes with polychromasia on the peripheral blood film. There was also evidence of hemolysis with a high reticulocyte count and higher levels of total and indirect bilirubin. Autoimmune hemolysis was excluded by negative direct and indirect Coomb's tests, and Hb defect was excluded by normal Hb electrophoresis. We also ruled out other infectious causes. The ultrasound confirmed splenomegaly. The osmotic fragility test showed increased osmotic fragility of the patient's red cells. History, symptoms, and test results strongly point to autosomal dominant hereditary spherocytosis with new mutations. An eosin-5-Maleimide binding test was advised, along with family screening of the patient.*

**Keywords:** Autosomal Dominant, Hereditary Spherocytosis, inherited hemolytic anemia

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### Introduction:

Hereditary spherocytosis (HS) is typically an autosomal dominant trait<sup>1</sup>. It is more common among people of northern European descent<sup>2</sup>. It is a disease of red blood cell morphology, characterized by a stiff, spherical form of RBC. This morphological alteration confines and subsequently eliminates the cells within the spleen, resulting in hemolysis and anemia<sup>3,4</sup>. Hereditary spherocytosis commonly presents itself in the early stages of adolescence.

However, it can manifest in the senior population, particularly those over the age of 65, as a new mutation without any prior family history. The severity of membrane protein abnormalities (spectrin and

ankyrin) correlates with the manifestation. The characteristic clinical features are anemia, jaundice, and splenomegaly<sup>5</sup>. Spherical red blood cells in peripheral blood and increased RBC osmotic fragility are the hematological features. In cases of mild hemolysis or when hemolysis is effectively compensated, not all classical symptoms are always present due to the bone marrow's ability to enhance red cell production<sup>6</sup>. Stress or other infections can sometimes lead to an elevation in hemolysis, resulting in temporary anemia or jaundice. Patients with undetected latent HS may only exhibit transitory anemia or jaundice as their initial manifestation. If there is clinical suspicion of HS, the peripheral blood

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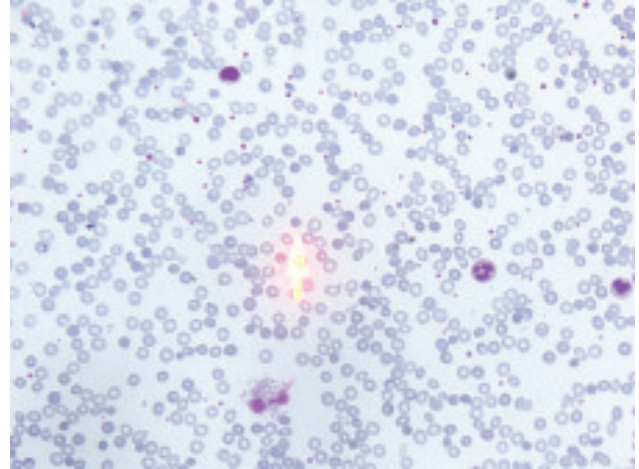
smear is the most straightforward and essential diagnostic. Patients with HS may experience severe medical conditions due to the presence of two comorbidities, even though HS itself is not considered a life-threatening condition. The most worrisome concomitant disease in patients with HS is parvovirus B19 infection <sup>7</sup>.

#### Case report:

A 55-year-old normotensive, nondiabetic man presented to our hospital with generalized weakness, a history of repeated blood transfusions, and mild abdominal pain for 5 months. He also gave a history of recurrent jaundice for 8 years, which subsided spontaneously on each occasion. Routine blood investigations incidentally diagnosed him with severe anemia following a 4-day episode of dry cough and fever, which manifested his weakness. He then received multiple blood transfusions in the form of 2 units of whole blood and 8 units of red cell concentrate over the next 5 months, but his symptoms did not subside. He did not reveal any history of bleeding, chronic diarrhea, constipation, weight loss, altered bowel habits, high-colored urine, rash, or joint pain. Recently, his elevated serum creatinine and ultrasonography (USG) evidence of renal parenchymal disease led to a diagnosis of chronic kidney disease (CKD). He has no family history of hemolytic diseases. On query, he did not give any drug history of antimalarials, antibiotics, dapsone, anticonvulsants, etc., or any history of chemical exposure or burns. On examination, the patient had a generalized dark complexion, was moderately anemic, mildly icteric, had a temperature of 98 °F, a blood pressure of 140/70 mmHg, and a pulse of 80 bpm with the presence of drop beats. There was no bone tenderness, lymphadenopathy, or skin rash. The abdomen was soft and non-tender, and the spleen was enlarged 1 cm from the left costal margin towards the right iliac fossa along its long axis. The rest of the systemic examination revealed no abnormalities.

On investigation, Hb was found to be persistently low, the lowest being 5.5 g/dL, while MCV: 84.4 fL; MCH:

27.9 pg, and MCHC: 33 g/L; there was eosinophilia with an absolute count of 2,200/cmm. PBF-dimorphic with plenty of spherocytes (Fig. 1), with polychromasia. WBCs were mature, with eosinophilia and an adequate number of platelets. A reticulocyte count of 12.29%, a raised total bilirubin of 3.01 mg/dl, an indirect bilirubin of 1.71 mg/dl, an uric acid of 10 mg/dL, and an LDH of 156 U/L revealed evidence of hemolysis. Transferrin saturation was 60%, with a very high serum ferritin level of 2579.81 ng/mL. Autoimmune hemolytic anemia was excluded by negative direct and indirect



**Figure 1:** Hereditary spherocytosis on peripheral blood film

Coomb's tests. ANA was negative. Osmotic fragility test was done which was increased osmotic fragility (Table 1). Stool OBT, fecal calprotectin, CEA, CA-19.9, and colonoscopy were normal, while upper gastrointestinal endoscopy revealed antral gastritis. Other causes of anemia were excluded by normal Hb electrophoresis, serum vitamin B12 (596 pg/mL), and folate assay (>20 ng/mL). S. creatinine was 1.84 mg/dL with normal urine R/E, and HbA1C was 5.7%. USG revealed splenomegaly (14 cm) with a Grade 1 fatty liver and poor cortico-medullary differentiation of both kidneys. The ECG revealed premature atrial contraction, but the echocardiogram and chest X-ray were normal.

**Table-I**  
Osmotic fragility test

Osmotic fragility test of fresh blood sample of the patient	Osmotic fragility of patient's blood sample- g/L NaCl	Normal Range- g/L NaCl
Initial Lysis	4.5	5.0
Complete Lysis	4.5	3.0
MCF (50% Lysis)	5.25	4.0-4.5
Comment	Increased Osmotic Fragility	

Other conditions associated with hemolysis, such as infectious mononucleosis, malaria, and Weil syndrome (leptospirosis), were tested negative. For eosinophilia, anthelmintic was prescribed orally, and ICT for filaria was negative. Based on the clinical features and peripheral blood smear findings, HS was strongly suspected. We prescribed oral folic acid to the patient, advised an Eosin-5 Maleimide binding test, and recommended family screening for HS.

#### Discussion:

HS is a prevalent hereditary form of hemolytic anemia characterized by the atypical shape of red blood cells (RBCs). A mutation in one of the five genes responsible for encoding proteins crucial for the cytoskeleton of the phospholipid bilayer in the RBC membrane causes the spherical shape of red blood cells (RBCs). The protein deficits that occur most frequently are band 3 and spectrin<sup>8</sup>

Autosomal dominant accounts for about 70% of HS cases, autosomal recessive for 25%, and de novo mutations account for 5%<sup>9</sup> For years, HS patients with modest hemolysis may go undetected. Timely detection will aid in the surveillance of an individual with hereditary spherocytosis, thereby diminishing the likelihood of difficulties in the future. Older children and adults may exhibit hemolytic anemia, high indirect bilirubin, splenomegaly, and cholelithiasis. Additionally, they may experience an aplastic crisis accompanied by infection<sup>8</sup> Patients can be diagnosed with HS without additional testing if they have a positive family history, clinical features of anemia, jaundice, splenomegaly, and a raised MCHC and reticulocyte level, as well as the presence of spherocytes.

Hemolysis, which is a result of an increased rate of red blood cell turnover and an enhanced concentration of pigments in the liver, can lead to gallstone formation<sup>5,6</sup> The treatment for people with clinically severe HS is splenectomy, however, it can be safely postponed in patients with mild, uncomplicated HS (hemoglobin level > 11 g/dL). Splenectomy typically leads to complete management of HS, except for the atypical autosomal recessive form of the condition<sup>10</sup>.

#### Conclusion:

Hereditary spherocytosis is a disease of adolescence. But when elderly patients are present with unexplained anemia HS shouldn't be ruled out merely just because of age. We want to enlighten the possibility of HS occurring in older people.

#### Conflict of Interest:

The author stated that there is no conflict of interest in this study

#### Funding:

No specific funding was received for this study.

#### Consent for publication:

Informed written consent was taken from the patient to publish details relevant to the disease and management.

#### Ethical consideration:

The study was conducted after approval from the Institutional Review Board of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. The confidentiality and anonymity of the study participant was maintained

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