Hereditary Spherocytosis and Gallstones Formation

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INTRODUCTION

Primary red blood cell (RBC) membrane disorders lead to numerous clinical syndromes including hereditary spherocytosis (HS). HS syndromes are considered as a group of inherited disorders associated with a primary defect in RBC membrane proteins.[1]

Patients with HS are at more risk of developing gallstones because their bodies make extra bilirubin in bile that is stored in the gallbladder. When it hardens in the bile, they can form little stone-like objects (Figure 1). Prevention of gallstones represents a major impetus for splenectomy and the development of bilirubin gallstones is considered as one of the most common complications in HS patients.[2]

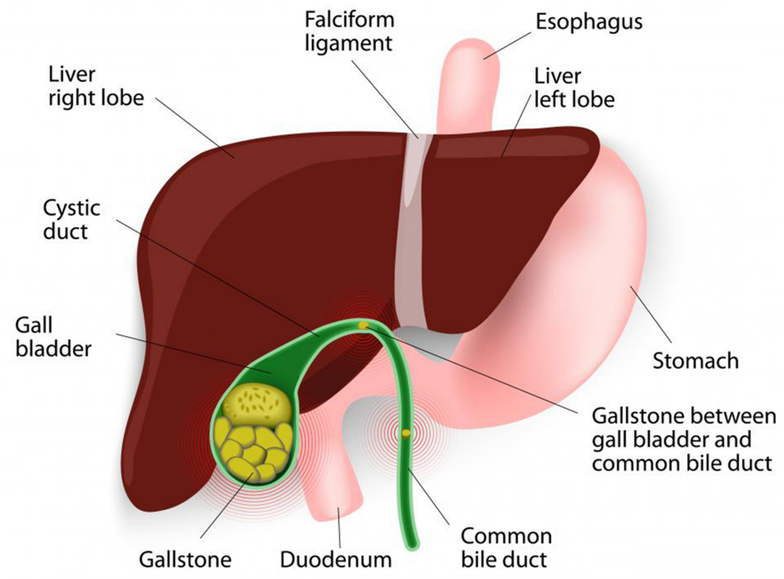

Figure 1. Formation of Gallstones

METHODS

The initial assessment of patients with suspected HS includes the medical history of their family members about the occurrences of anemia, gallstones, jaundice, and splenomegaly. Physical examinations also draw attention to the signs of any disorder like jaundice, splenomegaly, and scleral icterus (Table 1).

RESULTS

Patients with typical HS contain obvious spherocytes that lack central pallor on the PB smear, and most of the HS patients suffer from mild to moderate anemia with reticulocytosis.[3] In approximately 50% of HS patients, the mean corpuscular haemoglobin concentration(MCHC) increases due to relative cellular dehydration. The red cell distribution width (RDW) also increases (>14) in these patients.

Incubated osmotic fragility (OF) test is the gold standard test for diagnosing HS in patients with Coombs-negative spherocytic hemolytic anemia (HA). After incubating HS erythrocytes at 37°C for 24 hours, they start losing their membrane surface area more readily than that of normal cells because of their unstable and leaky characteristics.[4] However, the results of this OF test suffer from poor sensitivity as nearly 20% of the mild HS cases are missed out after this incubation period.

The increased level of bilirubin, reticulocytosis, lactate dehydrogenase (LDH), fecal, and urinary urobilinogen along with the decreased level of haptoglobin reflects the increased erythrocyte production or destruction in HS patients.[4]

DISCUSSION

The development of bilirubin gallstones is considered as one of the most common complications of HS.[2] About 6-50% of HS patients develop symptomatic gallbladder disease and experience cholecystectomy at the age of 10-30 years old.[5] Around 40-50% of patients with gallstones develop symptoms of gallbladder disorder or biliary obstruction. The treatment of gallbladder disorder in HS patients is controversial, particularly in patients with asymptomatic or mild HS gallstones.[6]

Cholescystectomy is suggested for patients with symptomatic gallstones with recurrent biliary colic or cholecystitis (Figure 2). Combined surgical procedures of cholecystectomy and prophylactic offer a considerable gain in the life expectancies of young patients and adults having mild HS and gallstones.[7] Yet, the use of concomitant splenectomy is controversial and considered on an individual basis, considering the severity of HA versus the post-splenectomy risks.

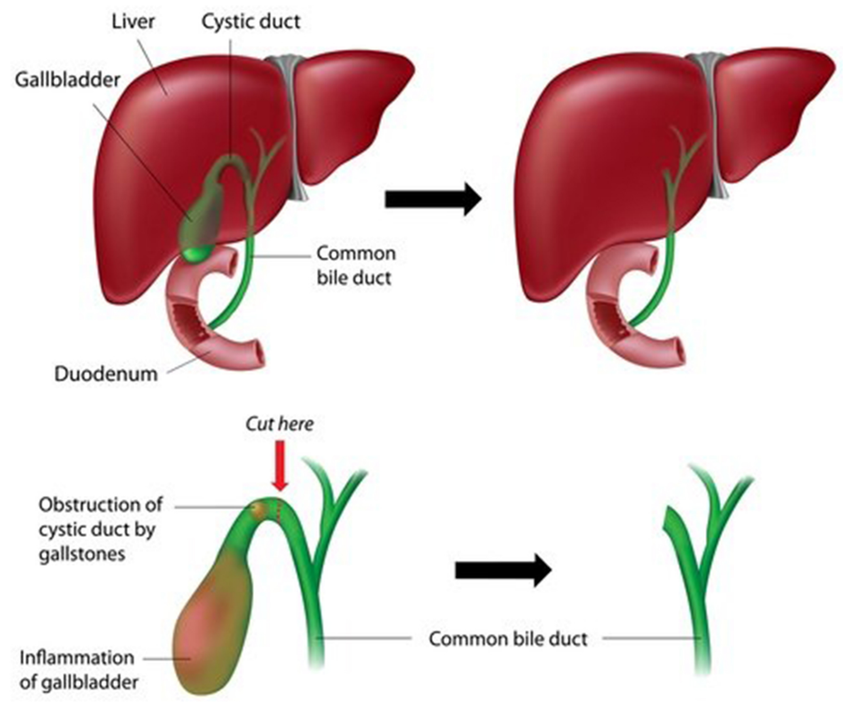

Figure 2. Technique of removing Gallbladder stones through Cholecystectomy

Table 1. Assessment of Patients with suspected hereditary spherocytosis.

Age Group	Presentation	Likely clinical severity of HS
Neonatal period	Hydrops fetalis (rare) Neonatal anaemia (rare) Neonatal jaundice	Severe Severe Not necessarily related to severity
Early childhood	Severe haemolytic anaemia	Severe
Childhood	Anaemia, jaundice Parvovirus infection Incidentai finding on blood count	Moderate Mild or moderate Mild
Adulthood	Parvovirus infection Incidental finding on blood count Extra-medullary haemopoiesis Anaemia unmasked by pregnancy	Mild

CONCLUSIONS

The red blood cell membrane diseases like hereditary spherocytosis are inherited because of the mutations in various membrane proteins, thereby, resulting in the decreased red cell deformability, reduction in the life span, and premature removal of the red cells from the circulation. The variations in the incidences of gallstones or cholelithiasis are in accordance with the different types of inherited hemolytic disorders and the ethnicity of the patients with HS. Therefore, regular ultrasound and other diagnostic examinations are recommended for timely detection of any presence of gallstones in patients with HS.

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