Hereditary Spherocytosis with Splenomegaly and Cholelithiasis in a Young Male of Western Region of Nepal - A Case Report

Ghimire P, Gurung NV, Shrestha S, Gurung A, Poudel SR, Chapagain A

Department of Surgery

Western Regional Hospital

Pokhara, Nepal

Corresponding Author

Prajwal Ghimire

Department of Surgery

Western Regional Hospital

Pokhara, Nepal.

E-mail: prazgh@gmail.com

Citation

Ghimire P, Gurung NV, Shrestha S, Gurung A, Poudel SR, Chapagain A. Hereditary Spherocytosis with Splenomegaly and Cholelithiasis in a Young Male of Western Region of Nepal: A Rare Case Report. *Kathmandu Univ Med J* 2015;52(4):366-8.

ABSTRACT

Hereditary spherocytosis is an autosomal dominant congenital hemolytic anemia due to defect in RBC membrane protein that commonly presents with intermittent jaundice, anemia, abdominal pain, splenomegaly and sometimes cholelithiasis. Due to the membrane defect, there is increased fragility, hemolytic anemia, marked splenomegaly and hyperbilirubinemia. This is a report of an 11 years old male diagnosed case of hereditary spherocytosis who presented with jaundice, splenomegaly and cholelithiasis. He underwent elective open splenectomy and cholecystectomy after prophylactic immunization for capsulated organisms and was advised lifelong oral penicillin prophylaxis post-splenectomy.

KEY WORDS

Cholelithiasis, hemolytic anemia, prophylaxis, splenectomy, splenomegaly

INTRODUCTION

Hereditary spherocytosis is an autosomal dominant hereditary disorder, a type of hemolytic anemia, characterized by the presence of spherocytic red blood cells, caused by various molecular defects in the genes that code for alpha- and beta-spectrin, ankyrin, band 3 protein, protein 4.2 and other erythrocyte membrane proteins.[1] It has a wide spectrum of severity and a prevalence of approximately 1/5,000 in people of Northern European descent.[2] The prevalence is not known in Nepal till date but seems rare. The clinical presentation is generally in childhood, but may be delayed until later life. Mild intermittent jaundice is associated with mild anemia, splenomegaly and gallstones.[1] This case is one of the few that has been reported in Nepal.

CASE REPORTS

An 11 years old male, the second child of non-consanguineous parents from Western Nepal was admitted to General Surgery ward of Western Regional Hospital, Pokhara, Nepal with complaints of yellow discoloration of eyes and recurrent pain in upper quadrant of abdomen for the last 2 years. He had history of neonatal jaundice and had multiple blood transfusions in the past for anemia. He was diagnosed as Hereditary Spherocytosis one year back and was advised for surgical consultation. He visited the hospital for elective surgery (Splenectomy and Cholecystectomy) as advised.

On examination, he was icteric. His vitals were stable and abdominal examination revealed splenomegaly eight cm from left subcostal margin. There was no pallor or raised temperature.

His investigations showed total White Blood Cell (WBC) count as 13,500 cells/cu.mm with the differential count as Neutrophils 71%, Lymphocytes 27 % and Eosinophil 2%. Hemoglobin level was 11.3 gm/dl with normal bands seen in Hemoglobin electrophoresis with platelets count of 2, 68,000 cells/cu.mm and Hemoglobin F 0.2. Peripheral blood smear showed Red Blood Cell (RBC) morphology as anisopoikilocytosis, normocytic normochromic cells with polychromasia and spherocytes; WBC morphology within normal limits and adequate platelets with no parasites in the smear. RBC count was 3360000 cells/cu.mm with retics of 10% and Osmotic fragility was increased initially from 0.60% to a total of 0.3%. Mean Corpuscular Volume (MCV) was as 80.6 fl and Mean Corpuscular Hemoglobin Concentration (MCHC) was 36.1 g/dl. Direct Coombs test, Antineutrophil Antibody (ANA) were both negative. Prothrombin time (PT) was 14.9 sec, Activated Plasma Thromboplastin time (APTT) 25.7 sec, International Normalized Ratio (INR) 1.32, Random Blood Sugar 73 mg/dl, urea 29 mg/dl, creatinine 0.8 gm/dl, Na+ 144 meq/l, k+ 4.3 meq/l, bleeding time 2 min, clotting time 10 min, total protein 7.0, Total bilirubin 11.2, direct bilirubin 0.6, SGPT 40, Alkaline Phosphatase 690. Serological markers of HIV-1,2, Hepatitis B Surface Antigen, Hepatitis C virus and Widal test were all negative. Urine Urobilinogen was positive with no Pus cells or Red Blood Cells in urine. Chest X-ray Posterior-Anterior view was within normal limits and Abdominal Sonography revealed contracted gall bladder with multiple calculi in the gall bladder and splenomegaly (14.6 cm). His blood group was B positive and weighed 27 kg. He received prophylactic vaccines for Hemophilus influenzae B and Pneumococcus 2 weeks prior to elective surgery.

He underwent elective open splenectomy and cholecystectomy with a midline abdominal incision under general anesthesia in a single setting. Operative findings were spleen of size 15 cm* 8 cm* 3 cm with splenunculi on the grater omentum and multiple small gallbladder calculi (Fig. 1). He was discharged on 3rd post-operative day and was followed up 1 week later. He presented with improvement of icterus and investigations revealed Hemoglobin 11.5 gm/dl, Reticulocyte count 2.8 %, White Blood Cells Count 6,600 cells/cu.mm (N36L58), Total protein 8.0, Total Bilirubin 0.8, Direct Bilirubin 0.2, SGPT 36 and Alkaline Phosphatase 193 U/L. He was advised to take oral penicillin daily for life long period post-operative.

DISCUSSION

Hereditary spherocytosis is mostly an autosomal dominant condition.[1] The most common molecular defects are spectrin or Ankyrin abnormalities, which act as the major components of the cytoskeleton for Red Blood Cell (RBC) shape.[1,2] Dominant defects is present in β-spectrin and protein three.[3] The genes responsible are localized on chromosomes 1, 2, 8, 15 and 17 for membrane

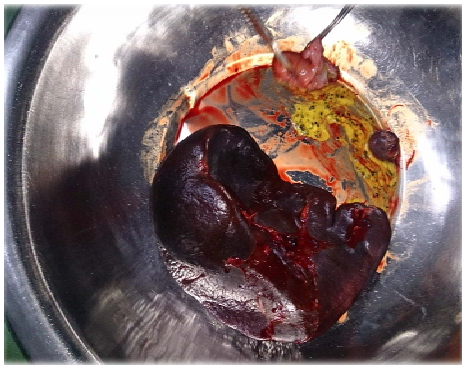

Figure 1. Splenectomy Specimen with Spelnunculi and Gall bladder with multiple small calculi.

proteins.[3] The loss of membrane surface area without a proportional loss of cell volume causes sphering of the RBCs and an associated increase in cation permeability, cation transport, adenosine triphosphate use and glycolysis.[3] The decreased deformability of the spherocytic RBCs impairs cell passage from the splenic cords to the splenic sinuses, and there is premature destruction of spherocytic RBCs in the spleen.[2,3] Splenectomy markedly improves RBC life span and cures the anemia.[2]

Clinical Features

It causes of hemolytic disease in the newborn and can manifest as anemia and hyperbilirubinemia requiring phototherapy or exchange transfusions.[2] Hemolysis may be more prominent in the newborn because hemoglobin F binds 2, 3-diphosphoglycerate poorly, and the increased level of free 2, 3-diphosphoglycerate destabilizes interactions among RBC membrane protiens.[2] The severity of symptoms vary in infants and children. Some patients remain asymptomatic into adulthood, but others have severe anemia with pallor, jaundice, fatigue, and exercise intolerance. Severe cases are marked by expansion of the diploë of the skull and the medullary region of other bones.[2] After infancy, the spleen is usually enlarged, and pigmentary gallstones can form as early as four years of age.[2] Because of the high RBC turnover and heightened erythroid marrow activity, affected children are susceptible to aplastic crisis, primarily as a result of parvovirus B19 infection.[2] The erythroid marrow failure can rapidly result in severe anemia (hematocrit <10%), fall in WBC and platelets counts, high output heart failure, hypoxia, cardiovascular collapse, and death.[2]

Laboratory investigations and findings

Evidence of hemolysis includes reticulocytosis and indirect hyperbilirubinemia.[2] The hemoglobin level usually is 6-10 g/dL, but it can be in the normal range.[2] The reticulocyte percentage often is increased to 6-20%.[2] The mean corpuscular volume (MCV) is normal, although the mean corpuscular hemoglobin concentration (MCHC) often is increased to 36-38 g/dL RBCs.[2] The RBCs on the blood film vary in size and include polychromatophilic reticulocytes and spherocytes.[2] Spherocytes usually account for >15

-20% of the cells when hemolytic anemia is present.[2] Erythroid hyperplasia is seen in the marrow aspirate or biopsy.[2] Marrow expansion may be evident on routine x-ray examination. Other evidence of hemolysis can include decreased haptoglobin and the presence of gallstones on ultrasonography. The diagnosis of hereditary spherocytosis usually is established clinically from the blood film, from the family history, and from splenomegaly.[2] The presence of spherocytes in the blood can be confirmed with an osmotic fragility test (the spherocytes lyse more readily than biconcave cells in hypotonic solutions).[2] A normal test result also may be found in 10-20% of patients. Other tests, such as the cryohemolysis test, osmotic gradient ektacytometry, and the eocin-5-maleimide test, may be more sensitive but are not readily available.[2] As a research tool, the specific protein abnormality can be established in 80% of these patients by RBC membrane protein analysis using gel electrophoresis and densitometric quantitation.[2] The protein abnormalities are more evident in patients who have had a splenectomy.[2] Radioactive chromium (51 Cr) labelling of the patient's own red cells will demonstrate the severity of red cell destruction.[1] Daily scanning over the spleen will show the degree of red cell sequestration by the spleen.[1] The presence of high levels of splenic radioactivity generally predicts a good response to splenectomy, but this test is used less commonly.[1]

Treatment

Splenectomy eliminates most of the hemolysis associated with this disorder.[2] After splenectomy, osmotic fragility mostly improves because of diminished splenic conditioning and less RBC membrane loss.[2] The resolution of anemia, reticulocytosis, and hyperbilirubinemia follows.[2] The criteria for patients to undergo splenectomy is still controversial.[2] Folic acid (1 mg daily) should be administered to prevent deficiency and the resultant decrease in erythropoiesis.[2] For patients with more severe anemia and reticulocytosis or those with hypoplastic or aplastic crises, poor growth, or cardiomegaly, splenectomy is recommended after age 5-6 years to avoid the heightened risk of post splenectomy sepsis in younger children.[2] Laparoscopic splenectomy decreases the length of hospital stay and has replaced open splenectomy for many patients.[1] Vaccines for encapsulated organisms (pneumococcus, meningococcus, Haemophilus influenza type b) should be administered before splenectomy following which prophylactic oral penicillin V (age <5 yr., 125 mg twice daily; age 5 yr. through adulthood, 250 mg twice daily) should be administered.[2] Post splenectomy thrombocytosis needs no treatment and usually resolves spontaneously.[2] Partial (near total) splenectomy also may be useful in children younger than age 5 years and can provide some increase in hemoglobin and reduction in the reticulocyte count, without hampering the splenic phagocytic and immune function.[2] Cholecystectomy is also indicated at the same time of splenectomy as the patient is very prone to develop cholelithiasis.[4]

Prognosis

Fifty percent of unsplenectomised patients develop cholelithiasis.[5] Complications are Hemolytic crisis, aplastic crisis, megaloblastic crisis, Gout, leg ulcers, extra medullary hemopoiesis, hematological malignancies, cardiomyopathy and hypogonadism.[2]

REFERENCES

1. Garden OJ. The Spleen. In: Williams NS, editor. Bailey & Love's Short Practice of Surgery. 26th Ed. New York: CRC Press; 2013.1087-96.
2. Segel GB. Hereditary Spherocytosis. In: Kliegman RM, editor. Nelson Textbook of Pediatrics. 19th ed. Philadelphia: Elsevier Inc.; 2011. 1659-61.
3. Kanellopoulou T, Kontopidou FN, Dourakis SP. Hereditary spherocytosis in a young male Report of an unusual case. *Archives of Hellenic Medicine* 2011; 28(6):814-8.
4. Bajracharya BL, Giri A, Baral MR. Hereditary Spherocytosis. *Kathmandu University Medical Journal* 2003; 2(6): 145-8.
5. Nigwekar P, Shrikhande DY, Niranjan BK, Shah N, Shukla T. Hereditary Spherocytosis - A Rare Case Report. *Pravara Med Rev* 2010; 2(4).