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Anaesthetic Management of a Case of Hereditary Spherocytosis for Splenectomy and open Cholecystectomy

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ABSTRACT

Hereditary spherocytosis is a familial hemolytic disorder with an autosomal dominant transmission mainly although recessive inheritance is also seen. The heterogeneity of clinical features ranges from an asymptomatic condition to a fulminant haemolytic anaemia. It was first described in 1871 and is the most common cause of inherited haemolysis in Europe and North America within the Caucasian population, with an incidence of 1 in 5000 births. We report a case of a fifteen years old Indian male child with hereditary spherocytosis with anaemia, jaundice, splenomegaly and calculus cholecystitis who was posted for splenectomy and cholecystectomy.

KEYWORDS : Hereditary Spherocytosis, splenectomy, cholecystectomy, haemolytic anaemia, jaundice

Introduction

Hereditary spherocytosis is also known as Minkowski–Chauffard syndrome[1]. It was first described in 1871 by two Belgian physicians, Vanlair and Masius, and is the most common cause of inherited hemolysis in Europe and North America within the Caucasian population, with an incidence of 1 in 5000 births [8, 9]. The clinical severity of hereditary spherocytosis varies from an asymptomatic carrier to severe haemolytic anaemia. Hereditary spherocytosis is an inherited blood disorder caused by a variety of molecular defects in the genes that code for the red blood cell proteins spectrin (alpha and beta), ankyrin, band 3 protein, protein 4.2 and other red blood cell membrane proteins which result in RBC cytoskeleton instability and loss of erythrocyte surface area leading to the production of spherical RBCs known as spherocytes with decreased deformability[3, 4, 6]. These proteins are necessary to maintain the normal shape of a red blood cell, which is a biconcave disk. The integrating protein that is most commonly defective is ankyrin which is responsible for incorporation and binding of spectrin, thus in its dysfunction cytoskeletal instabilities ensue.[1,3,4,5,6,7,8] The primary defect in hereditary spherocytosis is a deficiency of membrane surface area. Decreased surface area may be produced by two different mechanisms: 1) Defects of spectrin, ankyrin (most commonly), or protein 4.2 lead to reduced density of the membrane skeleton, destabilizing the overlying lipid bilayer and releasing band 3-containing micro vesicles. 2) Defects of band 3 lead to band 3 deficiency and loss of its lipid-stabilizing effect. This results in the loss of band 3-free micro vesicles. Both pathways result in membrane loss, decreased surface area, and formation of spherocytes with decreased deformability[1,2,3,4,5,6,9,11,12,13]. As the spleen normally targets abnormally shaped red cells which are typically older, it also destroys spherocytes[5, 6, 7,9,10]. The clinical severity of hereditary spherocytosis varies from symptom-free carrier to severe haemolysis. Symptoms include anemia, jaundice, splenomegaly, and fatigue. Primary treatment for patients with symptomatic has been total splenectomy[1, 11,12,13,15], which eliminates the hemolytic process, allowing normal hemoglobin, reticulocyte and bilirubin levels.

In hereditary spherocytosis, red blood cells fail to pass from the cords of Billroth into the sinusoids may be seen as a bottleneck through and get phagocytosed, causing extravascular hemolysis[12,13,15]. Spherocytic RBCs are removed rapidly from the circulation and destroyed by the spleen leading to anaemia, jaundice, enlarged spleen, and cholelithiasis. Complications include haemolytic crisis, with more pronounced jaundice due to accelerated hemolysis which may be precipitated by infection, aplastic crisis with dramatic fall in hemoglobin level and reticulocyte count usually due to maturation arrest and megaloblastic crisis which may be precipitated by infection and folate deficiency caused by increased bone marrow requirement[12,13,15,17]. Folate therapy is recommended in severe and moderate hereditary spherocytosis in order to prevent megaloblastic crisis. A characteristic feature of hereditary spherocytosis is an increase in mean corpuscular haemoglobin concentration (MCHC). Peripheral smear shows microspherocytes and presence of Howell-Jolly bodies within red blood cells[1, 9,20,21,22].

Pigmented gallstones occur in approximately half of untreated patients. Increased hemolysis of red blood cells leads to increased bilirubin levels, because bilirubin is a breakdown product of heme. The high levels of bilirubin must be excreted into the bile by the liver, which may cause the formation of a pigmented gallstone, which is composed of calcium bilirubinate[10, 11,12,13,14]. Since these stones contain high levels of calcium carbonates and phosphate, they are radiopaque and are visible on x-ray. Haemoglobin A1C (glycosylated haemoglobin) is a test for determining the average blood glucose levels over an extended period of time, and is often used to evaluate glucose control in diabetics. The haemoglobin A1C levels are abnormally low because the life span of the red blood cells is decreased, providing less time for the non-enzymatic glycosylation of hemoglobin. Thus, even with high overall blood sugar, the Hb A1C will be lower than expected[20]. There is no cure for the genetic defect that causes hereditary spherocytosis and management focuses on interventions that limit the severity of the disease. Splenectomy is indicated for moderate to severe cases, but not mild cases[16, 18, 19]. To decrease the risk of sepsis, post-splenectomy spherocytosis patients require immunization against the pneumococcus bacterium, influenza virus, and prophylactic antibiotic treatment. Since the spleen is important for protecting against encapsulated organisms, sepsis caused by encapsulated organisms is a possible complication of splenectomy. The option of partial splenectomy may be considered in the interest of preserving immune function[16, 17, 18, 19]. If gallstones are present, cholecystectomy may be performed simultaneously or at a later date. Severe cases may present as neonates. Moderate hereditary spherocytosis is the most common form, accounting for 60-75% of all cases. It is associated with mild-to-moderate anaemia, modest splenomegaly, and intermittent jaundice[15, 16]. Mild hereditary spherocytosis may not present until adulthood until environmental stress factors uncovers the disorder[1].

Case report

We report the case of a fifteen years old male patient weighing 39 kg, a known case of hereditary spherocytosis who underwent splenectomy and open cholecystectomy under general anaesthesia. The chief considerations in perioperative management include proper hydration and avoidance of hypoxia, hypercarbia and acidosis and peri operative erythrocyte transfusion. To decrease the risk of sepsis, post-splenectomy spherocytosis patients require immunization against the pneumococcus bacterium and human influenza virus, and prophylactic antibiotic treatment. This 15 years old male child

presented with pain in abdomen, yellowish discolouration of sclera, high coloured urine, nausea and vomiting. On physical examination he had pallor, icterus and splenomegaly. The child's parents gave history of neonatal jaundice on the third day of birth. He had an episode of anaemia and jaundice four years back for which blood transfusion was given at a district hospital. There was no history of consanguineous marriage between the parents. On performing ultrasound examination of abdomen he was found to have splenomegaly extending up to right iliac fossa and acute calculous cholecystitis.

His preoperative investigations revealed a haemoglobin of 9.5 gm%, reticulocyte count of 21.5% and peripheral smear showed microspherocytes .Liver function tests revealed a total serum bilirubin of 13.98 mg/dl (normal – 0.2-1.2 mg/dl) and conjugated bilirubin of 2.82 mg/dl (normal – 0.1-0.4 mg/dl). PT/INR was 27sec/1.67 (Control 13.5 sec).SGOT was 47 IU/L ,SGPT was 46 IU/L and Alkaline phosphatase was 239 IU/L. Total proteins and albumin was within normal levels. Platelet count was 1.18 lakh /cu mm. Osmotic fragility was increased and Coombs test was negative. The rest of investigations were within normal limits. Before surgery patient was given vaccine against pneumococci and H-influenza. He received 1unit of PCV and vitamin K 30mg IV the day before surgery. His baseline heart rate was 90 beats per minute and regular, blood pressure was 110/65 mm hg and respiratory rate was 16 per minute. His exercise tolerance was good and he had a metabolic equivalent (MET) value of 6. Chest radiography and ECG were normal. Ultrasound abdomen showed a massively enlarged spleen extending to the right iliac fossa and cholelithiasis.

On the day of surgery after obtaining an informed written consent from his parents he was kept fasting for a period of six hours prior to surgery. In the operating room he was connected to a multipara monitor displaying ECG, NIBP, SPO2, EtCO2 and core temperature and then 1 mg midazolam, 0.2 mg glycopyrrolate & 60 micrograms fentanyl were given intravenously. After preoxygenation with 100% oxygen for five minutes intravenous induction was done with 80 mg thiopentone sodium and 75 mg of succinylcholine. Endotracheal intubation was done with a 6.5 size cuffed portex tube. After confirming the tube position by capnography and auscultation the tube was fixed and anaesthesia was maintained with 50:50 air oxygen mixture with 1 MAC sevoflurane on controlled ventilation. 20 mg atracurium was given for muscle relaxation and incremental doses were given afterwards. Surgery lasted for three hours and his vital parameters were stable throughout surgery. The arterial blood gas sampling done intra operatively showed normal values. Intraoperatively hypoxia, hypothermia and acidosis were avoided and patient received a unit of packed red blood cells, FFP, platelet concentrates after clamping of splenic vessels. Neuromuscular blockade was reversed with neostigmine and glycopyrrolate. Post-operative analgesia was given with bilateral transversus abdominal plane block done under ultrasound guidance using 10 ml of 0.5 % ropivacaine on each side. He was extubated awake and shifted to the recovery room. He was subsequently transferred to high dependency unit for overnight stay and shifted to the ward on the third post-operative day. His haemoglobin became 11 gm/dl and platelet count was102000/ cu mm and PT/INR was 16 sec /1.2. His bilirubin levels came down and he started taking oral fluids from the fourth post-operative day.

Discussion

Hereditary spherocytosis is the commonest cause of inherited haemolytic anaemia in North America (1:5000 Births) but comparatively rare in Asians. Most cases are inherited as autosomal dominant; approximately 25% are sporadic and may be due to spontaneous mutations. Diagnosis is generally made in childhood or young adult life. Hereditary spherocytosis results in the formation of abnormal red blood cells with fragile cell walls leading to anaemia, jaundice, splenomegaly and ultimately, gall stone formation. Intrinsic membrane defect results in increased fragility of RBCs predisposing to hemolysis.

Four abnormalities in red cell membrane proteins have been identified-

(1) Spectrin deficiency alone (most common defect)
(2) Combined spectrin and ankyrin deficiency,
(3) Band 3 deficiency, and
(4) Protein 4.2 defects.

These defects result in uncoupling in the vertical interactions in the lipid bilayer skeleton and loss of membrane micro vesicles. This leads to loss of membrane surface area without a proportional loss of cell volume and causes sphering of the RBCs. Diagnosis of HS is based on increased osmotic fragility, spherocytes on peripheral blood smear and increased MCHC.

Complications include

(1) Cholelithiasis, a consequence of chronic hemolysis (2) aplastic crisis- most commonly after Parvovirus B19 infection (3) hemolytic crisis during intercurrent Infection and (4) megaloblastic crisis in presence of folic acid deficiency. Acute chest syndrome onset of new lobar infiltration on chest x-ray (excluding atelectasis) associated with fever, respiratory distress or chest pain has been reported.

Severe cases accounting for 5% of all patients may present as neonates. The pattern of inheritance is recessive and requires red cell transfusions and an incomplete response to splenectomy. The parents of affected patients have no signs of hereditary spherocytosis or have only a mild increase in the reticulocyte count, a few spherocytes on peripheral blood smear, a minimally abnormal incubated osmotic fragility test result, or an abnormal spectrin content detected by sensitive methods Moderate HS is the most common form, accounting for 60-75% of all HS cases is associated with mild-to-moderate anemia, modest splenomegaly, and intermittent jaundice. Mild HS may not present until adulthood and accounts for 20-30% of cases of autosomal dominant HS. Anemia generally is not present because the bone marrow is able to fully compensate for the persistent destruction of red cells. There is little or no splenomegaly and the patients usually are asymptomatic. The disease is not uncovered until they experience hemolytic or aplastic episodes triggered by infection or other stresses. The morphologic hallmark of hereditary spherocytosis is the microspherocyte, which is caused by loss of RBC membrane surface area and has abnormal osmotic fragility in vitro .Splenectomy is the standard treatment for patients with clinically severe hereditary spherocytosis , but can be deferred safely in patients with mild uncomplicated (hemoglobin level >11 g/dL). Splenectomy usually results in full control of hereditary spherocytosis except in the unusual autosomal recessive variant of the disorder.

Conclusion

Anaesthetic goals include avoidance of hypoxia, acidosis, and hypothermia. Vaccination against pneumococcus and H influenza before splenectomy is a must to prevent postoperative infections. In our patient vitamin K was given preoperatively as the PT/INR values were high and his liver functions were deranged too. Since the spleen protects infection against encapsulated organisms, sepsis caused by encapsulated organisms is a possible complication of splenectomy. The option of partial splenectomy may be considered in the interest of preserving immune function[21]. There is no cure for this genetic disease but the severity of the disease can be reduced by splenectomy in selected cases.

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