Case Report

Subtotal Splenectomy in Hereditary Spherocytosis - Advantages and Disadvantages

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ABSTRACT: Hereditary spherocytosis (HS) represents the most frequent hemolytic anemia in Central and Northern Europe consisting in an inherited abnormality of the red blood cell (RBC) membrane. It is usually transmitted as an autosomal dominant disorder; 25% of cases are without family history. Splenectomy is the classical conception and it can cure hemolysis, being the treatment of choice for moderate to severe forms of HS. A new approach is accepted nowadays, subtotal splenectomy, thus eliminating the lifelong risk of postsplenectomy infections. We present two cases of HS treated by subtotal splenectomy, alongside the advantages and disadvantages of this therapy.

KEYWORDS: *hereditary spherocytosis, splenectomy, subtotal*

Introduction

Hereditary spherocytosis (HS) is a familial hemolytic disorder associated with a variety of mutations that lead to defects in red blood cell (RBC) membrane proteins. It is usually transmitted as a less severe *autosomal dominant disorder* or, less commonly, as an *autosomal recessive* disease, with severe clinical form. 25% of patients are cases with new mutations. The molecular defects conduct to abnormalities of the major components of the RBC cytoskeleton, spectrin or ankyrin. The morphologic hallmarks of HS are the spherocytes that remain trapped in the spleen and become phagocytized, resulting in chronic hemolysis. Clinically, HS shows marked heterogeneity, ranging from an asymptomatic condition to fulminant hemolytic anemia. [1,2] Splenectomy is the classical conception and can be the treatment of choice for moderate to severe forms of HS. This usually results in full control of HS. [1] A new approach is accepted nowadays, *subtotal splenectomy*, thus eliminating the lifelong risk of postsplenectomy infections.

The authors present 2 cases of HS in whom subtotal splenectomy was performed with favorable results. Advantages and disadvantages of this therapy are discussed.

Case presentation

Patient 1, 16 year old female, physiologic and pathologic antecedents without importance, height and weight over the age average (78 kg, 172 cm) is admitted for a respiratory infection; moderate anemia, (9g/dl) jaundice and splenomegaly are also detected. She is reffered to our clinic with the suspicion of beta-thalassemia syndrome. The diagnosis was rapidly established as HS, after clinical consult, family history (father and paternal grandmother were both splenectomized for HS), complete blood count (spherocytes present, Fig.1) and abdominal ultrasound showing splenomegaly (200 mm length) and fibrosis at ARFI (Acoustic Radiation Force Impulse) assessment (3,15 m/sec at 3 cm depth; normal 1,3 m/sec). (Fig.2,3).

The patient underwent robotic subtotal splenectomy and cholecystectomy. The postoperative evolution was good, without complications. The case particularity is the lack of symptoms over a period of 16 years but with marked splenomegaly and advanced level of fibrosis.

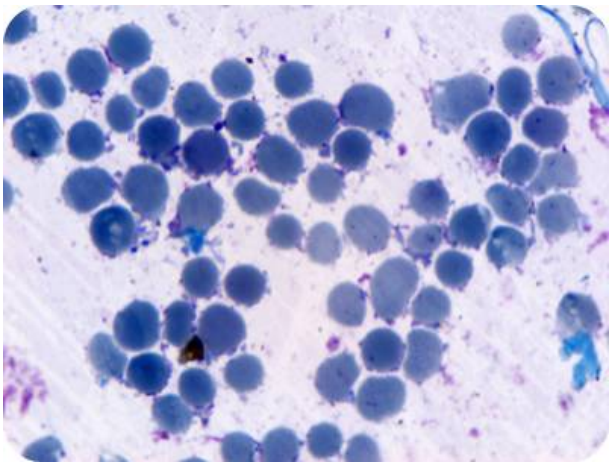

Fig.1.Spherocytes on peripheral blood smear, May-Grumwald-Giemsa stain.

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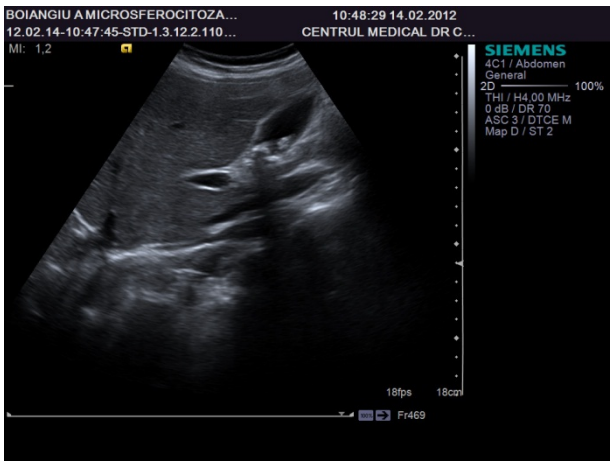

Fig.2.Ultrasonography showing gallstones.

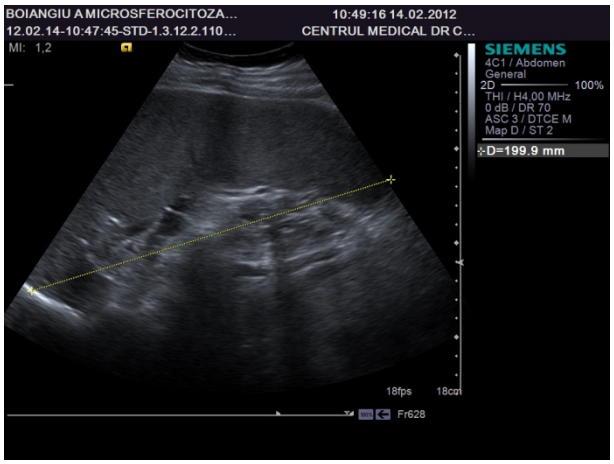

Fig.3.Ultrasonography showing splenomegaly.

Patient 2, 14 year old female, diagnosed with HS at the age of 3, with repetitive episodes of jaundice, anemia, abdominal pain and vomiting. At the admission she presented jaundice, ogival palate and moderate splenomegaly. The complete blood count revealed spherocytes, macrocytes and reticulocytosis 31%. The osmotic fragility test begun at 0,62 NaCl‰ and ended at 0,4 NaCl‰. Other laboratory investigation showed an elevated alkaline phosphatase, 544 U/l and negative tests for viral hepatitis B and C. The abdominal ultrasound found a moderately increased spleen, 117 mm, no cholecyst stones and renal microlithiasis. The patient underwent a laparoscopic subtotal splenectomy with the preservation of the lower pole of the spleen. The postoperative evolution was favorable. She was also vaccinated against *Streptococcus pneumoniae*. As side effects the patient presented thrombocytosis up to 800000/mmc. Four years after splenectomy the level of thrombocytes settled at a value of 493000-511000/mmc.

Discussion

HS onset is variable from newborn to scolar children, more often the diagnosis being established during the middle or late childhood. The anamnesis of a patient with HS can highlight the presence of anemia, splenectomy or gallstone in relatives, but 25% of cases have no family history. The clinical expression is heterogeneous, varying from chronic hemolysis to severe transfusion dependent anemia. In newborns, HS can cause anemia and hyperbilirubinemia sufficiently severe to require phototherapy or exchange transfusions. Some patients remain asymptomatic until adulthood, others may present moderate anemia (8-10g/dl) pallor, jaundice, fatigue, splenomegaly, gallstones. Sometimes, the only sign of HS in childhood is the presence of splenomegaly. Because of high RBC turnover and increased erythroid marrow activity, children with HS are predisposed to aplastic crises, associated with parvovirus B19 infection, or hypoplastic crises as a result of other infections. Severe anemia (hematocrit <10%) tachypnea, tachycardia, hypoxia, cardiovascular collapse and even death can occur especially in aplastic crises. Laboratory findings include the presence of spherocytes on the peripheral blood smear, as a constant sign, varying from 10-20% until 80%. The spherocytes are smaller in diameter and appear hyperchromic without the central pallor characteristic of the normal RBC. Other sign of increased erythropoiesis are reticulocytosis, erythroblastosis, and polychromatophilia. The hemoglobin level usually is 6-10 g/dl, but it can also be in the normal range. Other evidences of hemolysis include indirect hyperbilirubinemia, increased urinary urobilinogen and hypersideremy. The presence of spherocytes in the blood smear can be confirmed with an osmotic fragility test, when the exposure to hypotonic saline causes spherocytes to lyse more rapidly than the normal RBC. This quality can be enhanced by depriving cells of glucose overnight by incubation at 37°C, known as the incubated osmotic fragility test. More recently, osmotic fragility testing is based on flow-cytometry with greater efficiency than the conventional test and could be the method of choice for routine diagnostic use to screen HS and assess its clinical severity. [1,2,3,4]

A 1986 publication suggested that splenectomy is indicated in virtually every patient with HS, but recent guidelines recommend that *splenectomy should be performed in children with severe HS,*

considered in those who have a moderate form and should probably not be performed in those with mild disease. [5] One of the advantages of performing total splenectomy, even the accessory spleens, is that it assures the cure of the anemia by stopping the hemolysis in practically every case. The hemoglobin level will rise slightly at a level above that of non-affected family members. [5] Also, the pain or discomfort due to splenomegaly will be relieved and the risk of splenic rupture will be decreased. Another important advantage, especially in smaller children is that growth failure and skeleton changes due to exuberant erythropoiesis will be reversed, although there are cited cases like our 16 years old patient where growth was not affected despite the lack of treatment.

Today is it being recognized the life-long risk of bacterial infection and other non-infectious hazards after splenectomy, like vascular events, atherosclerosis, thrombosis, thromboembolism, pulmonary hypertension. [5,6] From the multitude of germs capable of sepsis, the most important are encapsulated bacteria like *pneumococcus*, *meningococcus* or *haemophilus influenza type b.* Although immunization and prophylactic antibiotics have decreased the overall risk, there are concerns about serotypes that there are not in vaccines, penicillin-resistant pneumococcal strains and compliance. Also, the risk for life-threatening infection persists for decades after splenectomy.[3,5,6] Besides encapsulated bacteria, there are being identified other pathogens like *falciparum malaria*, *anaplasma phagocytophilum* or *babesia* in persons who have had their spleen removed. There is no vaccination available yet for these pathogens.[5]

Regarding vascular events after splenectomy, in 1997 was reported for the first time atherosclerosis. Ten years later after further observations, Schilling reported more extensive vascular events, including venous events, thrombophlebitis, deep vein thrombosis and pulmonary embolus.[5,6] Other, more rarely, vascular events include pulmonary hypertension, osteonecrosis and priapism. A study recently published, aiming to identify risk factors for vascular events after splenectomy found that there is no evidence of pulmonary hypertension, elevated fibrinogen or dyslipidemia 4-5 years after surgery, although persistent thrombocytosis and elevated D-dimer were found in 73%, respectively 23% of patients.[7] Postsplenectomy thrombocytosis is commonly observed but it needs no treatment and usually resolved spontaneously, like in our case.[3,6]

All these arguments reinforced the idea of searching alternative treatment strategies. The first one proposed was *the implantation of splenic tissue in the epiploon*, but further analysis did not support the efficacy of this method. The second strategy was *subtotal splenectomy* that is a recognized procedure since 1995. Subtotal splenectomy represents the resection of 60-90% of splenic tissue, with the preservation more often of the lower lobe.[6,8,9] There were cases when the upper lobe of the spleen was preserved, subsequent this technique was abandoned because of concerning of correct intraoperative evaluation of the remnant splenic volume.[8,10] In the present time, about 85-90% of the spleen is removed, although it was recognized that for children with very large spleens, more extensive parenchymal resection was required to attain this desired resection.[8,9]

Maintaining a small amount of splenic tissue in a child is a great advantage if we take into consideration that the spleen represents 25% of the lymphatic tissue. Also, it decreases hemolysis, as evidenced by an increase in ^{51}Cr-labeled RBC life span and subsequently increase in hemoglobin values and decrease in reticulocytes counts.[3,6,8] A mild state of hemolysis can be still persistent and the risk for aplastic crises is not abolished. Various analyses observed the hemoglobin raised after partial splenectomy, usually over 12g/dl (Solimar *et al*, 2005 from 9,1g/dl±2,5 to 12,4 g/dl ±1,2; Bader-Meunier *et al* 2001, over 12 g/dl in 6 from 8 pacients; Stoehr et al, 2006 -mean hemoglobin raised over 12 g/dl in mild, moderate and severe forms; Seims et al., 2013 from 10.5 ± 1.7 vs 13.8 ± 1.1 g/dL). [6,9,11,12] The consequence is a reduced need of blood transfusions from 0,32U/year to 0,02U/year after subtotal splenectomy.

Another advantage of subtotal splenectomy is a low risk of thrombotic events as observed by recent analysis.[5] A 2001 publication observed that from 40 cases who underwent partial splenectomy, thrombocythemia was observed in 30 patients, although the platelets count returned to normal range within 2 years in all patients.[6] In our report thrombocytosis rose until 800.000/mmc without vascular events and with minimal therapy (aspirin 1 tb/day).

Regarding disadvantages of subtotal splenectomy, the most important is the fast regrowth of the spleen in the first 2 years and the restart of hemolysis. It was observed that growth

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velocity was higher in the first year, subsequently slowed and during following years the splenic volume stabilizes.[6] There are cited cases with regrowth up to 500% compared to weight-dependent standard sizes and sometimes, a second splenectomy could be necessary in one third of the patients.[6,9] Bader-Meunier *et al.* reported hematological complications in 25-38% of the patients who lead to a second operation in 21-40% of cases.[6] Rice *et al.* published a longitudinal cohort study following 25 symptomatic children with various congenital anemias study and observed that after 4 years of follow-up, the splenic regrowth was more pronounced, averaging 40% of original splenic size. Four children with HS have regrown their spleens up to 75% to 100% of their original size, but regrowth of the spleen was not associated necessarily with recurrent hemolysis.[13] Other studies noticed that a resection of 98% of splenic tissue, *near-total splenectomy,* seems to have a reduced regrowth of the remament spleen, without recurence of postoperative anemia and a very reduced rate of a second intervention, 7%.[9] This conclusion is reinforced by Rice *et al* who also observed that in two children in whom 95% to 97% of the spleen was removed, there has been regrowth of the splenic from 5% to 20% of baseline splenic volume within 2 years after surgery.[13] Another disadvantage of subtotal splenectomy is gallstone formation risk who persists in patients in whom cholecystectomy had not been performed, due to persistent mild hemolysis. However, splenectomy is not indicated as a prophilaxie method for gallstone formation.[5,6,10,13]

Except for very large spleens, *laparoscopic splenectomy* has become the method of choice in most of the centers. Recently, Vasilescu *et al*. reported a robotic approach with main benefits of lower blood loss rate, vascular dissection time and a better evaluation of the splenic remnant tissue.[14]

Although HS represents the most frequent hemolytic anemia in the Central and Northern Europe, in Romania β-thalassemia syndromes prevail over HS. In our experience of over 40 years we detected only 5 cases with HS and 26 cases with major β-thalassemia. 3 cases underwent total splenectomy and in the last 2 cases subtotal splenectomy was performed.

Since 1995, when subtotal splenectomy was proposed for the first time more and more countries report excellent results in the treatment of HS by this method.[5,6,8,15-17] In Romania, the first interventions were performed in 2003 at the Surgery Clinic of Fundeni Institute, Bucharest with great results.[8,10,14]

We can conclude that subtotal splenectomy represents an effective alternative for moderate and severe HS treatment that has proven to provide a persistent decrease of hemolytic rate and the preservation of splenic immune and phagocytic functions.

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