Evaluation of Subtotal Splenectomy in the Management of Hereditary Spherocytosis

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Background/Purpose: To evaluate the clinical and hematological response to subtotal splenectomy in children with hereditary spherocytosis (HS).

Materials and Methods: The authors analyzed the main clinical and hematological features in 18 patients with HS treated by subtotal splenectomy. The average age at the time of operation was 4 years. The indications for subtotal splenectomy were hypersplenism and severe anemia. The diagnosis of HS was made according to standard methods. The lower three fourth of the spleen were removed and the upper pole was preserved. The effect on hemolytic rate was assessed by comparing the presurgical and postsurgical values of hemoglobin, reticulocyte number and RBC life span. The residual splenic phagocytic function was assessed using technetium 99m scan and number of pitted red cells. The splenic regrowth were measured by ultrasonography.

Results: There were no complications related to the surgical procedure in any of the 18 children. The mean follow up period was 30±8 months. At the end of follow up hemoglobin increased on the average by 3 gm/dl, reticulocyte count decreased by 300x10⁶/L, and bilirubin level decreased. Normal technetium uptake was noted in the splenic remnant. Splenic regrowth were noted in 4 patients, two of them still need more than 2 transfusion/year. No postoperative overwhelming infection occurred.

Conclusion: Subtotal splenectomy can be performed without major blood loss in patients with HS. Up to 95% of the spleen can be safely removed. It is effective in decreasing the hemolytic rate while maintaining residual splenic function.

Index Word: Spherocytosis, Subtotal Splenectomy

INTRODUCTION

Hereditary spherocytosis is a relatively common inherited hemolytic anemia.¹ Removal of the spleen results in increased life span of red cell, decreased transfusion requirement, and decreased incidence of gallstone formation. Splenectomy is the treatment of choice for moderate-to-severe forms of the disease.²,³ Increased awareness that splenectomized patients face a lifelong risk of overwhelming life-threatening infections has dampened enthusiasm for the routine use of total...

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spleenectomy for management of HS.4-7 The phagocytic activity of splenic macrophages and the synthesis of antipolysaccharide antibodies by splenic B-lymphocytes both are necessary to mount an optimal defense against infection.8 With subtotal splenectomy there is a sustained decrease in hemolytic rate that can transform a severe hemolytic anemia to mild chronic hemolytic anemia.8

This study was carried out to evaluate the effect of subtotal splenectomy on hemolysis, splenic phagocytic and immune function, and splenic regrowth in patients with HS.

MATERIAL AND METHODS

This study included 18 patients (10 boys and 8 girls) with HS, managed over a 3-years period between March 1999 to march 2002 at Children Insurance Hospital (Abu-El Rish). Their ages ranged from 2.5 to 8 years, mean age 5.1±1.3 years. The clinical and hematological features of these 18 patients were monitored throughout the study. The diagnosis of HS was confirmed by complete blood picture, reticulocyte count and osmotic fragility test. The indications for surgery were severe anemia with frequent need for blood transfusion (10 patients), huge splenomegally and chronic anemia (4 patients). Cholecystectomy was done in conjunction with subtotal splenectomy in 4 patients due to presence of gallstones with huge splenomegally and chronic anemia.

Surgical technique:

A subtotal resection of 80% to 90% of the enlarged spleen with preservation of the upper pole was performed through a transverse left upper abdominal incision. The lesser sac was entered and vessel sling were placed around the splenic artery and vein (Fig. 1). The spleen was then mobilized by division of lienorenal ligament (Fig. 2). Subtotal splenectomy was based on ligation of polar arteries supplying the part of the spleen to be resected and control of intersegmental venous bleeding following splenic division. Occasionally, a single polar artery was present and intracapsular dissection with ligation of the segmental lobar vessels was required. A line of ischemic demarcation appeared on the spleen (Fig. 3). This line was superficially marked with electrocoagulation (Fig 4) followed by intracapsular dissection. Venous connections between segments were meticulously ligated during excision. Hemostasis of the raw surface was achieved with interrupted suturing of the splenic capsule (Fig 5). In 5 cases omentum was placed around the splenic ruminant. A single vascular pedicle provides blood supply to the remnant spleen. Also preservation of short gastric vessels to the splenic remnant provides good blood supply. In cases of a narrow vascular pedicle, the splenic remnant was fixed to the posterior abdominal wall by securing the splenic remnant within the retroperitoneum.

The patients received prophylactic antibiotics at induction of anesthesia and for five days postoperatively. The postoperative hospital stay ranged between two to five days with average three days.

Follow up

The follow up period ranged between 2 to 5 years with a mean of 30±8 months. Mean value of Hb, reticulocyte counts, and bilirubin levels at one month and every 6 months for 2.5 years. Quantitated red blood cells life span was measured before and one year after surgery using Cr51- labeled autologous erythrocytes in all patients.

The phagocytic function of the splenic remnant was assessed by sequential evaluation of the number of circulating pitted red cells. Immunological profile by assessment of serum levels of IgG and IgM preoperatively by and one year postoperatively.

Postoperative growth of the splenic remnant was quantitated by repeated abdominal ultrasonography using a broad band 7.5–MHz curved array or 10.5–MHz linear array transducers every 6 months to the end of follow up (2-5 years). The splenic volume was calculated using a formula for the volume of a prolate ellipsoid.10

\[
\text{Volume (mL)} = \text{Length (cm)} \times \text{width (cm)} \times \text{height (cm)} \times 0.52
\]

Study of splenic function with radionuclide scanning (splenic uptake of technetium99) was performed for all patients at one year postoperatively. The results were statistically analyzed using systec 9.0 software (SPSS Inc, Chicago, IL, USA).
Fig 1. The lesser sac is entered and vessel sling is placed around the splenic vessels.

Fig 2. Delivery of the spleen after division of the lienorenal ligament in a 4 year-old child with hereditary spheroctysis.

Fig 3. Operative photograph of the spleen following devascularization of the lower pole and the major splenic vessels. The upper pole of the spleen is perfused by retained vasculature from the short gastric vessels and uppermost polar branch.

Fig 4. The line of ischemic demarcation is marked with electrocoagulation followed by intra capsular dissection.

Fig 5. The remnant spleen (upper pole) in a HS patient during surgery. It can be seen that a single vascular pedicle provides blood supply to the remnant spleen. Haemostasis of the raw surface is achieved by interrupted suturing of the splenic capsule.

Fig 6. Measurement of the splenic volium 3 years after subtotal splenectomy.

RESULTS
The mean duration of operative time was 50 minutes ± 30 minutes for subtotal splenectomy, and 80 minutes ± 20 minutes for subtotal splenectomy in conjunction with cholecystectomy. No preoperative complications occurred in this series. There were no wound infections or other wound complications in the early postoperative period.

Hematoglobin values, reticulocyte count, serum bilirubin and platelet count were assessed before surgery and one month after subtotal splenectomy then every 6 months to the end of follow up. (Table 1)

The hematoglobin mean value increased significantly from a preoperative mean value of 9.1 ± 2.5 gm/dL to 12.4 ± 1.2 gm/dL (P < 0.001) at 12 to 18 months after surgery and this difference had persisted throughout 2 to 5 years of follow up.

The reticulocyte count decreased significantly from 518 ± 437 x 10^9/L before surgery to 268 ± 128 x 10^9/L at 12 to 18 months after surgery. This decrease in reticulocyte count persisted during subsequent 3 years. Mean serum bilirubin levels also decreased after subtotal splenectomy for these children from a level of 2.6 ± 1.1 mg/dL preoperatively to 1.3 ± 0.7 mg/dL at the most recent postoperative follow-up. Six of the 18 patients (33.33%) continued to suffer from attacks of hemolysis. Four patients need 1-2 transfusion/year, and two require more than 2 transfusion/year. Two patients (11.1%) developed gallstone two years after subtotal splenectomy.

Platelet counts: The mean platelet count in all patients was elevated 600 x 10^9/L during the first month after surgery. However, the platelet count returned to normal values of less than 400 x 10^9/L in all patients within 18 months.

All patients have been evaluated at 6 months intervals for 3 years. They showed persisted normal serum levels of IgG and IgM. No overwhelming infection was documented in children with splenic remnant during follow up period. In the first month postoperatively, most children had circulating Howell-Jolly bodies. However, this finding disappeared 6 months after surgery in all patients. The percentage of pitted erythrocytes was in normal range (Less than 2%) in all patients at the end of follow up. All patients had normal radionuclide uptake of the splenic remnant, and the size of the radionuclide image approximated the spleen size as determined by ultrasonography.

**Growth of splenic remnant:**

Serial evaluation of splenic volume every 6 months following subtotal splenectomy using ultrasonography showed that four children developed increase in splenic volume 4 times than the estimated volume one month postoperatively (Fig. 6). At the end of follow up, 2 patients need more than 2 transfusions/year (Table 2).

**Table 1: Laboratory data before and after subtotal splenectomy**

<table>
<thead>
<tr>
<th></th>
<th>Preoperative (Mean value)</th>
<th>Postoperative (Mean value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>One month</td>
<td>3 months</td>
</tr>
<tr>
<td>Hb (gm/dl)</td>
<td>9.1 ± 2.5</td>
<td>11.5 ± 1.1</td>
</tr>
<tr>
<td>Reticulocyte count /L</td>
<td>518 ± 437 x 10^9</td>
<td>375 ± 135 x 10^9</td>
</tr>
<tr>
<td>Serum bilirubin (mg/dL)</td>
<td>2.6 ± 1.1 mg</td>
<td>2.0 ± 1.1</td>
</tr>
<tr>
<td>Platelet count /L</td>
<td>200 ± 50 x 10^9</td>
<td>600 ± 70 x 10^9</td>
</tr>
</tbody>
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Table (2): Complications of subtotal splenectomy.

<table>
<thead>
<tr>
<th>Complications</th>
<th>No of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative need for blood transfusion</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Wound infection</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Recurrence of hemolysis</td>
<td>4 (1-2 transfusion / year)</td>
<td>22.2%</td>
</tr>
<tr>
<td>(6 patients, 33.3%)</td>
<td>2 (more than 2 transfusion / year)</td>
<td>11.1%</td>
</tr>
<tr>
<td>Re-growth of splenic remnant</td>
<td>4</td>
<td>22.2%</td>
</tr>
<tr>
<td>New gall stone formation</td>
<td>2</td>
<td>11.1%</td>
</tr>
<tr>
<td>Overwhelming infection</td>
<td>0</td>
<td>0%</td>
</tr>
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DISCUSSION

Anaemia, jaundice, splenomegally, and cholelithiasis are the clinical features of HS. Bilirubin gallstones are found in approximately 50% of patients with HS and frequently occur in patients with very mild disease. Six of 18 patients in our study revealed cholelithiasis (33.3%). Therefore periodic ultrasonic evaluation of the gallbladder should be performed.

Total splenectomy, which abrogates hemolysis, is the most attractive option. Yet, it is likely to expose the patient to a lifelong risk for potential lethal infection. Another interesting approach has been the use of subtotal splenectomy to retain splenic immunologic and phagocytic function while at the same time reducing the rate of hemolysis. Subtotal Splenectomy entails removal of 80% to 90% of the enlarged spleen, so less than 25% of the normal spleen volume is retained to preserve the phagocytic and immune function of the spleen and to decrease erythrocyte destruction.

Recent anatomic studies have demonstrated that the spleen is made of two primary lobes, one accessory lobe, and three to five segment. Each segmental artery supplies the correspondent segment in a wedge shape with relative avascular planes between segments. Lobar arterial branching occurs usually close to the surface of the splenic hilum necessitating a careful dissection before devascularization. Extensive splenic resection is possible even in the presence of massive splenomegally. The vasculature of the cut surface should be coagulated by monopolar diathermy or clamped and ligated. It is advisable to cover the cut surface with the greater omentum. When the upper pole of the spleen needs to be preserved, the blood supply can be supported by the short gastric vessels as described by Fonkalsrude et al. For all 18 patients with HS, the surgery was feasible with no preoperative morbidity. During the surgical procedure the minute vascular pedicle needs to be handled with great caution. Section of the parenchyma is better performed with a knife rather than with a thermocautery, so as to prevent electric burns of the single persistent narrow pedicle.

Classic indications for splenectomy in children with HS include repeated transfusions or anemic crisis. For subtotal splenectomy, our goal of reinoving 80% to 90% of splenic tissue is designed to gain the desired hematologic effect while preserving enough tissue for phagocytic and immune function. In a rat model of incriminated partial splenic resection, animals could survive intravenous injection of S-pneumoniae as long as 25% to 50% of the normal splenic tissue was preserved. In humans, optimal protection is likely to depend on the residual splenic mass and on the preservation of adequate blood flow. To obtain a splenic remnant accounting for 25% of the volume of a normal spleen, it requires that approximately 90% of the volume of an enlarged spleen be removed. This is achieved by preserving the splenic tissue supplied by a single pedicle.

Children less than one year of age with function spleens have a risk of septicemia of 0.3%, and those of one to seven years of age have risk of 0.07%. Before two years of age, the children are not able to make
antipolysaccharide antibodies in response to the polysaccharide capsular antigens of encapsulated bacteria.25 After total splenectomy, children become more prone to wound infections or infectious complications, especially before the age of 5 years, because of the immaturity of the immune system.26,27 The risk of septicemia associated with meningitis can be as high as 5% after total splenectomy, with a mortality risk of 1.5%.9,14,28-31 In the first year of life, this risk reaches 30% to 50% overwhelming sepsis caused by Streptococcus pneumoniae, H influenza and Neisseria meningitidis can be fatal, often within 12 to 24 hours of onset. S pneumonia is the most important pathogen and causes about 60% of postsplenectomy infections. H influenzae type B and N meningitidis account for about 25% of the cases. The rest are caused by a variety of organisms, including Escherichia Coli, staphylococcus and streptococcus.25 King and Shumacker reported the first 5 cases of severe infection in children after splenectomy for HS,26 and Erakis and Filler stated that the infection occurred twice as frequently in children younger than 4 years of age as opposed to those older than 4.32 Therefore, the indication for total splenectomy is limited to few cases, and conservative treatment is mandatory, even after trauma.33

Subtotal splenectomy preserves, to a certain degree the immune function of the spleen, which is essential to young children.34 Preoperative vaccination is recommended before subtotal splenectomy, in the event that total splenectomy is necessary. Antipneumococcus, antihemophilus, and antimeningococcus vaccines are used. Vaccines will provide protection for 3 to 5 years, and children should be vaccinated 3 months before surgery and every 3 to 5 years with polysaccharide vaccine against 24 sero-types of S pneumonia, vaccine against H influenza type B, and vaccine against N meningitides. Vaccine against N meningitidis is not administered in our patient. In recognition of the fact that most cases of postsplenectomy sepsis are caused by S pneumoniae, oral prophylactic penicilline must be given after total splenectomy and subtotal splenectomy, and probably until the patient is grown up25 or the normal phagocytic function of the splenic remnant is documented.

Previous reports have shown decreased immunoglobulin levels and impaired pneumococcal antibody responses in children undergoing total splenectomy for a variety of hematologic disorders.35,36 Although the spleen is the principal site of immunoglobulin production, the significance of preserved antibody levels following partial splenectomy is unclear given the multiple sites of antibody production.37

None of our patients with subtotal splenectomy encountered a severe infection during follow up. The assessment of pitted red cells, which decreased significantly 6 to 18 months after surgery provide strong indirect evidence that the filtering function of the spleen is being sustained. Also failure to observe Hoell-Jolly bodies may indicate the presence of functional splenic activity. However, it has to be stressed that the ability of such patients to produce antipolysaccharide antibodies that are involved in humoral defence against encapsulated bacteria and are synthesized by a spleen B-lymphocyte subpopulation has still to be evaluated.38,39

After subtotal splenectomy, platelets counts returned to normal values, hemoglobin values were found to be in the low normal range, and severely abnormal red cells are still being cleared from circulation. On the basis of these findings, Meunier et al., 2001 suggested that subtotal splenectomy is likely to carry a lower risk of thrombotic events than total splenectomy.8

Subtotal splenectomy leads to a decrease in hemolysis, as evidenced by an increase in 51Cr-labeled red blood cell life span, an increase in haemoglobin values, and a decrease in reticulocyte count and bilirubin. Rice et al found that the hematologic improvement after subtotal splenectomy for children with HS, approaches the hematologic responses observed after total splenectomy.21 Children with HS undergoing total splenectomy generally achieve an increase in hemoglobin of 1.5 to 3.0 gm/dl, slightly higher than the response seen in series of Rice et al. 21 Similarly, persistent hemolysis following subtotal splenectomy is reflected by persistent high reticulocyte count and bilirubin in contrast to patients with total splenectomy, in which the reticulocyte count is generally below 3% and the bilirubin levels are less than 1.0 mg/dl.40,41 The haemoglobin responses following subtotal splenectomy appear to be sustained over a prolonged period and in most cases do not lead to significant recurrent symptoms.37 In our study, gallstone formation occurred in two patients in whom cholecystectomy had not been
performed, as a result of persistent mild hemolysis.

The subtotal splenectomy is a safe surgical procedure that reduced the number for blood transfusions needed by children suffering from HS. However; this treatment appears to be effective for a relatively short period, because of the regrowth of the spleen. Therefore its indication must be carefully evaluated. Total splenectomy with appropriate vaccination and postoperative prophylactic antibiotics could be a better option, although the benefit of postponing total splenectomy in young children should be taken into consideration. In series of Bader-Meunier et al, the size of the remnant spleen increased in all patients, and the growth velocity was high during the first postsurgical year, it subsequently slowed. During the subsequent years, the volume of the splenic remnant stabilized. In our series 4 of 18 patients developed increase in the size of the splenic remnant and two of them needed more than two transfusion per year. So the patient's families should be aware of such a possibility.

The long term effects of subtotal splenectomy are not well established. Because of chronic hemolysis, the size of the splenic remnant has a tendency to increase, and this enlargement is especially rapid in young children. Subtotal splenectomy makes an important decrease in the number of blood transfusion in children suffering from chronic hemolysis possible. But, with subtotal splenectomy, there is a real possibility that a second operation for a total splenectomy will be needed a few years later because of the regrowth of the splenic remnant, especially in case of subtotal splenectomy in very young children. In deciding whether there is an indication for subtotal splenectomy, one must, therefore, take into consideration the age of the child and weigh the benefit of a decrease in the number of necessary blood transfusion with their related risks and a reduction of the number of hospitalization days against the risk of having to perform a total splenectomy either during subtotal splenectomy or a few years later.

In the European experience, which has limited follow-up to 14 years, a small number of children undergoing subtotal splenectomy. Although importantly the regrowth of the splenic remnant does not necessarily correlate with recurrent hemolysis. The reason for the discrepancy between splenic regrowth and hematologic status are unclear, although it may be due to altered blood flow or parenchymal remodelling after partial resection. The hematologic responses following a subtotal splenectomy in our patients appear to be sustained over a follow-up period and in most cases do not lead to significant recurrent symptoms. No child in our cases has required conversion to total splenectomy. We closely follow these children to identify symptoms that would warrant secondary conversion to a total splenectomy. Longer follow-up will define the need for later surgical procedures. Rice et al believed that the potential benefits of retaining functional splenic tissue in a young child even if only for a few years, outweigh the risk of possible secondary surgical procedure.

CONCLUSION

The procedure of subtotal splenectomy in treatment of HS is safe, and can be performed without the need for preoperative blood transfusion. Up to 95% of the spleen can be safely removed with adequate postoperative filtration function. Subtotal splenectomy has proven in our series, to provide a persistent decrease in the hemolytic rate, while preserving the integrity of splenic phagocytic function. On the basis of our results, we favour subtotal splenectomy in treatment of HS patients in which splenectomy is being considered for transfusion-dependent patients. Hopefully, this alternative management strategy for HS will partly solve the distressing dilemma between the risk of long-term severe infectious complications and the prompt necessity to decrease anemia and provide a better quality of life. Although our experience has been limited to 18 cases, we conclude that subtotal splenectomy in HS is associated with a decrease in the number of blood transfusions needed, and that in spite of the risk of regrowth of the splenic remnant, particularly in young children, it can be justified by the benefit of postponing total splenectomy with its concomitant risk of severe septicemia in very young children.

REFERENCES


