SPLENECTOMY FOR HEMATOLOGICAL DISEASES: THE QATIF CENTRAL HOSPITAL EXPERIENCE

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Background: In the Eastern Province of Saudi Arabia, an area known for various hemoglobinopathies, splenectomy is performed rather frequently. This study is an analysis of our experience with splenectomy performed for various hematological disorders between 1988 and 1997, outlining the indications, complications and outcome.

Patients and Methods: This is a retrospective analysis of all patients who had splenectomy at our hospital during this period. One hundred and forty-three patients were treated for various hematological disorders at our hospital. These disorders included sickle cell disease (SCD) (100 patients), sickle β-thalassemia (S-β-thal) (13 patients), β-thalassemia major (15 patients), Hb H disease (3 patients), idiopathic thrombocytopenic purpura (ITP) (5 patients), Gaucher's disease (2 patients), hereditary spherocytosis (1 patient), autoimmune hemolytic anemia (1 patient), thalassemia intermediate (2 patients) and chronic myeloid leukemia (1 patient).

Results: The indications for splenectomy in those with SCD and S-β-thal were: hypersplenism (26 patients), major splenic sequestration crisis (23 patients), minor recurrent splenic sequestration crisis (50 patients), splenic abscess (12 patients), and massive splenic infarction (2 patients). Splenectomy in these patients was beneficial in reducing their transfusion requirements and its attendant risks, eliminating the discomfort from mechanical pressure of the enlarged spleen, avoiding the risks of acute splenic sequestration crisis, and managing splenic abscess. For those with thalassemia, total splenectomy was beneficial in reducing their transfusion requirements, while partial splenectomy was beneficial only as a temporary measure, as regrowth of splenic remnant in these patients subsequently led to increase in their transfusion requirements. Those with ITP, hereditary spherocytosis, and autoimmune hemolytic anemia showed excellent response following splenectomy. There was no mortality, and the postoperative morbidity was 5.6%.

Conclusion: With careful perioperative management, splenectomy is both safe and beneficial in a selected group of patients with hematological diseases.

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Key Words: Splenectomy, hematological diseases, sickle cell disease, thalassemia.

The normal human spleen performs several important physiological and immunological functions.[1] Morris and Bullock in 1919[2] suggested that splenectomy would increase susceptibility to infection. This was documented by King and Schumacker in 1952.[3] They described an increased susceptibility to infection and death from sepsis following splenectomy in five infants who had splenectomy for congenital hemolytic anemia. Since then, our understanding of the role of the spleen and the dangers following splenectomy has changed, and as a result of this, various methods of prophylaxis against postsplenectomy sepsis and alternatives to total splenectomy have been adopted.[1,4]

Although our aim is usually to preserve the spleen, there remains a definite place for splenectomy in the management of many hematological diseases.[5-7] The decision for splenectomy in these patients requires a careful assessment, especially in children, who are at a greater risk of post-splenectomy sepsis. In the Eastern Province of Saudi Arabia, an area known for various hemoglobinopathies, splenectomy is performed rather frequently.[5,8-10] This study is an analysis of our experience with splenectomy performed for various hematological disorders over a period of nine years, outlining the indications, complications and outcome.

Patients and Methods

Patients who had splenectomy for hematological diseases at Qatif Central Hospital between 1988 and 1997 were analyzed. The medical records of these patients were reviewed for age at operation, sex, hematological

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diagnosis, indication for splenectomy, operative procedure, preoperative management, complications, and outcome. Patients with hypersplenism resulting from portal hypertension were excluded from the study.

The diagnosis of hereditary hemolytic anemia was established using standard laboratory methods on the patients and sometimes their families, including sickling test and hemoglobin electrophoresis (Helena Laboratories Super Z electrophoresis kit). The diagnosis of hypersplenism was based on the presence of splenomegaly with accompanying anemia, as judged by the transfusion requirements exceeding 250 mL/kg of packed RBC per year, or when the fall of Hb exceeded a frequency of 0.5 g per week, platelets count below 100,000/mm^3, or leukocyte count below 4000/mm^3, either singly or in combination. For the evaluation of the hematological response to splenectomy in hypersplenism, the pretransfusion level nearest to the date of splenectomy was taken as the preoperative value, and the mean of multiple estimations performed postoperatively and during outpatient follow-ups as the postoperative value.

Acute splenic sequestration crisis (SSC) is divided into major and minor attacks. The minor attacks are characterized by moderate increase in splenic size associated with a decrease of hemoglobin level of 2-3 g/dL, while major attacks are associated with a greater drop in hemoglobin level, sometimes reaching a level of less than 2 g/dL with large splenomegaly. This may lead to circulatory collapse and death. In both major and minor attacks, the spleen size regresses after blood transfusions.

Preoperatively, all patients received polyvalent pneumovax (0.5 mL of PMY Immune 23, Lederle), in addition to benzyl penicillin intravenously, which was continued postoperatively for 5-7 days, and when available, meningococcal and *H. influenza* vaccines. Preoperative hydration with IV fluids at 1½ the maintenance rate was given to those with SCD and S-β-thal, and when necessary, blood transfusions were given to restore their Hb to 10-12 g/dL and their hematocrit to 30%-40%. Exchange blood transfusion was not routinely performed.

Postoperatively, all patients were put on long-acting penicillin G (Benzathine penicillin), IM every three weeks, or oral penicillin twice daily, and parents were advised to bring their children to the hospital immediately for any febrile illness.

Results

A total of 143 patients had splenectomy for various hematological diseases at our hospital. There were 83 males and 60 females. Their ages ranged from 1½ to 60 years (mean 12.5 years), and 80.4% were less than 18 years of age (Table 1). The indications for splenectomy are shown in Table 2. The most common indication was SCD (70%). The indications for splenectomy in those with SCD and S-β-thal are shown in Table 3. In those with SCD and S-β-thal, splenic sequestration crisis was the most common indication for splenectomy (64.6%). In 23 patients (20 SCD and 3 S-β-thal), the indication for splenectomy was major SSC. There were 14 males and 9 females. Their ages ranged from 4 to 12 years (mean 7.3 years). All presented with severe anemia and huge splenomegaly. Their Hb on presentation ranged from 1.7 to 3.9 g/dL (mean 2.4 g/dL). There was no mortality, but two of the patients were comatosed on admission because of hypoxic encephalopathy due to severe anemia. Both patients recovered subsequently, but one had residual weakness of his lower limbs and decreased visual acuity which improved gradually.

Out of the 23 patients with major SSC, 18 had minor recurrent SSC with major attacks prior to their presentation, and only five patients presented with major attacks only. Their minor recurrent SSC ranged from 2 to 10 attacks (mean 4.4). Four patients had 2 major SSC in addition to 3, 5, 6 and 7 minor recurrent SSC, one patient had 2 major attacks only, and one patient had 3 major attacks. Fifty patients had MRSSC (46 SCD and 4 S-β-thal), ranging from 2 to 11 attacks (mean 3.6). Those with MRSSC were offered splenectomy after two attacks, but some of the parents were initially reluctant.

In 26 patients (20 SCD and 6 S-β-thal), the indication for splenectomy was hypersplenism in the form of frequent blood transfusions. In no patient was the indication for splenectomy due to thrombocytopenia or neutropenia alone. The blood parameters of these patients improved

TABLE 1. *Age distribution (n=143).*

Age range	Number of patients (%)
1-5	31 (21.7)
6-10	51 (35.7)
11-15	26 (18.9)
16-20	10 (7)
21-25	12 (8.4)
26-30	5 (3.5)
>30	8 (5.6)

TABLE 2. *Indications for splenectomy.*

Indication	Number of patients (%)
Sickle cell disease	100 (70)
Sickle-β-thalassemia	13 (9)
β-thalassemia major	15 (10.5)
Hb H disease	3 (2)
Idiopathic thrombocytopenic purpura	5 (3.5)
Gaucher's disease	2 (1.4)
Hereditary spherocytosis	1 (0.7)
Autoimmune hemolytic anemia	1 (0.7)
Thalassemia intermediate	2 (1.4)
Chronic myeloid leukemia	1 (0.7)

significantly after splenectomy, and their transfusion requirements decreased markedly (Table 4). On follow-up ranging from 3.5-8.5 years (mean 5.8), 21 patients (80.8%) received no further blood transfusions, one patient received five blood transfusions over a period of 5.5 years, three patients received 3-4 blood transfusions every year over a period of six years, while one patient continued to receive blood transfusions every month. Twelve of our patients with SCD had splenectomy for splenic abscess. All of them presented with fever and abdominal pain, and were found to have tender enlarged spleen. Their demographic and laboratory parameters are shown in Table 5. Two of our patients had splenectomy for massive splenic infarction. Twenty-four patients with SCD (24%) had splenectomy and cholecystectomy due to concomitant gallstones, and one patient had splenectomy and incidental appendectomy.

Twenty patients with thalassemia (15 β-thalassemia major, 3 Hb H disease, 2 thalassemia intermediate) underwent splenectomy because of increased blood transfusion requirements. Six patients with β-thalassemia major and one patient with thalassemia intermediate underwent total splenectomy, while 13 patients (9 β-thalassemia major, 3 Hb H disease and 1 thalassemia intermediate) had partial splenectomy. On follow-up ranging from 1.8-7.8 years (mean 4.5 years), 2 of the 3 patients with Hb H disease, as well as the two patients with thalassemia intermediate, required no more blood transfusions, while the third patient with Hb H disease continues to receive blood transfusions but at a lower frequency (11 blood transfusions/year instead of 15 blood transfusions/year and a hemoglobin drop of 0.7 g/week instead of 1.2 g/week). This patient subsequently had total splenectomy about two years after the partial splenectomy. There was also a marked reduction in the transfusion requirements in the 9 patients with β-thalassemia major who had partial splenectomy during the first two years following partial splenectomy (from a mean of 15.2 transfusions/year to a mean of 8.2 transfusions/year, P= 0.0034), but after that their transfusion requirements increased gradually as a result of increase in the size of the splenic remnant. Two of the six patients with β-thalassemia major who had total splenectomy required no more blood transfusions, while a third received only one blood transfusion postoperatively. The remaining three patients continued to receive blood transfusions, but at a lower frequency, from a mean of 22 transfusions to a mean of 10 transfusions/year.

The five patients with idiopathic thrombocytopenic purpura, aged 5, 10, 15, 25 and 50 years, respectively, who were not responding to steroids showed marked improvement in their platelets following splenectomy (from a mean platelet count of 35,000/mm^3 preoperatively to a mean platelet count of 308,000/mm^3 postoperatively). Two patients with Gaucher's disease, a brother and a sister aged 1.5 years and 3 years, were treated for hypersplenism with partial splenectomy and total splenectomy, respectively. Both showed marked improvement in their blood parameters. On the last follow-up, the younger patient was seven years old with massive hepatomegaly and increase in splenic remnant but no hypersplenism, while the brother was doing well with no hypersplenism. One patient aged 22 years had splenectomy for hereditary spherocytosis and another aged four years had splenectomy for autoimmune hemolytic anemia. Both responded well to splenectomy with no more blood transfusion requirements.

There was no postoperative mortality, but eight patients (5.6%) developed postoperative complications, and on follow-up ranging from 8 months to 8.7 years (mean 4.5 years), six patients developed complications (Table 6). Two of them had septicemia, due to salmonella in one and β-hemolytic streptococci in the other.

Discussion

Over a period of nine years, we performed 143 splenectomies for various hematological disorders. The indications for splenectomy in hematological disorders vary from one part of the world to the other, based on the prevalence of such diseases in that region.[5-7,11,12] While there are certain hematological disorders that are common all over the world, some hemoglobinopathies are localized to specific regions. The most common indications for splenectomy in our series were SCD and S-β-thal, which formed 79% of the total number of splenectomies.

Sickle cell disease is one of the commonly inherited hemoglobinopathies in the Eastern Province of Saudi

TABLE 3. *Indications for splenectomy in patients with sickle cell disease and sickle* ***b****-thalassemia.*

Indication	Sickle cell disease (n=100)	Sickle-β-thalassemia (n=13)
Hypersplenism	20	6
Sequestration crisis		
Major	20	3
Minor recurrent	46	4
Splenic abscess	12	–
Massive splenic infarction	2	–

TABLE 4. *Pre- and postsplenectomy hematological parameter in patients with hypersplenism (n=26).*

	Preoperative		Postoperative		
Parameter	Mean±SD	Range	Mean±SD	Range	*P*-value*
Hb (g/dL)	5±0.9	3.5-6.6	10±1.2	8-12.8	<0.0001
Hct (%)	16.9±3.6	12-25.6	31.2±2.6	26.6-36.3	<0.0001
WBC (10^3/mm^3)	7.2±3.9	3.3-15.4	15.6±3.8	10.4-25.1	<0.0001
Platelets (10^3/mm^3)	106±42.6	62-185	586.8±137.6	286-734.7	<0.0001
Reticulocytes (10^3/mm^3)	16.3±11.1	3-43	8.1±3.8	2.5-15	0.0035

*Using two-tailed paired t-test.

TABLE 5. *Demographic and laboratory parameters of patients with splenic abscess.*

Age/sex	Temp. (°C)	WBC	Splenic size (cm BCM)	Platelets	HJB	Blood culture	Peritoneal fluid and pus culture
21/M	38	$21.1x10^3$	14	1,385,000	Yes	*Enterobacter sakazakii*	*Enterobacter cloacae*
11/M	38.5	$17.3x10^3$	6	48,000	Yes	*Salmonella* group D	No growth
15/M	38	$21x10^3$	10	132,000	Yes	*Salmonella* group D	No growth
26/F	37.8	$6.2x10^3$	8	141,000	No	Salmonella	No growth
17/M	38.5	$20.3x10^3$	12	693,000	Yes	No growth	*Salmonella* group D
4/M	38.6	$23.4x10^3$	10	866,000	Yes	No growth	*Salmonella* group D
18/M	38.3	$12.4x10^3$	6	732,000	Yes	No growth	No growth
14/F	40	$11.4x10^3$	7	398,000	No	No growth	*Enterobacter cloacae* and *Enterobacter sakazakii*
19/M	38	$24.5x10^3$	7	667,000	Yes	No growth	Coliforms
18/M	39	$4.4x10^3$	8	102,000	Yes	*Salmonella paratyphi* group B	No growth
16/M	38.5	$12x10^3$	9	749,000	No	No growth	No growth

BCM=below costal margin; HJB=Howell-Jolly bodies.

Arabia, with a sickle cell trait frequency of nearly 20% in some areas.[13-15] The high level of hemoglobin F and the frequently associated α-thalassemia contribute to the benign nature of SCD in the Eastern Province of Saudi Arabia.[15-17] In SCD, the spleen enlarges during the first decade of life, but then undergoes progressive atrophy and autosplenectomy due to repeated attacks of vaso-occlusion and infarction, but not uncommonly, splenomegaly may persist even into adult life. This is the case in Saudi patients with SCD,[9,16] which makes it prone to developing splenic complications necessitating splenectomy.[8-10]

Acute splenic sequestration crisis (ASSC) formed the main indication for splenectomy in our patients with SCD and S-β-thalassemia. This is a serious complication of SCD, which if not recognized and treated early may cause sudden collapse and death. Twenty-three of our patients had major ASSC in addition to recurrent minor attacks, while 50 had recurrent minor attacks. Whereas ASSC is commonly seen in infants and young children between five months and two years of age,[18] our patients were older. This was due to the persistence of splenomegaly into an older age group in our patients. The role of splenectomy in major attacks is well established. To obviate a recurrence risk of 40%-50% and a mortality of 20%,[19,20] we advocate splenectomy if the child develops one major attack.[9,21-23] This is in contrast to minor attacks, where the criteria for splenectomy are not clear.

Several authors have recommended chronic blood transfusion therapy as a form of treatment, but on a short-term basis this proved to be ineffective, as the majority of patients developed ASSC when attempts were made to stop the transfusion program or shortly after completing the program.[21,24,25] We advocate splenectomy after two recurrent minor attacks. This is especially so in situations like ours where blood transfusion is not readily available. In addition, the poor compliance of parents, of allosensitization, hepatitis and other blood-borne infections do not make chronic blood transfusion a suitable form of therapy for these patients.[24-26] Splenectomy in such patients is beneficial, with no mortality or serious operative morbidity.

TABLE 6. *Postoperative and follow-up complications.*

Complication	#of patients	Time postoperatively
Acute chest syndrome	2	Six months, two days
Minor wound infection*	3	First week
Adhesive intestinal obstruction	1	Three weeks
Septicemia**	2	Four and eight months
CNS infarction and hematoma	1	Two months
Hematoma splenic bed	2	First week
Left pleural effusion and left lung collapse	2	First week

*Patients with splenic abscess; **salmonella in one, and β-hemolytic streptococci in the other; CNS=central nervous system.

Hypersplenism was the second indication in our patients with SCD and S-β-thal. This was in the form of frequent blood transfusions. While alternatives to total splenectomy for the treatment of hypersplenism, including partial splenectomy, percutaneous intraluminal occlusion of the splenic artery and embolic therapy, have been tried,[27-29] the associated complications, including splenic abscess, splenic rupture, pneumonia, pleural effusion, septicemia, and pancreatitis, make them an unsuitable form of treatment in patients with SCD.[30-32] We found splenectomy to be a beneficial remedy in these patients. Not only did their transfusion requirements decrease markedly postoperatively, but it also eliminated the discomfort from the mechanical pressure of the enlarged spleen. The fact that 24 (24%) of those with SCD had splenectomy and cholecystectomy due to concomitant gallstones calls for ultrasound screening for all those undergoing splenectomy for the presence of gallstones. We feel that if gallstones are discovered, even if they are asymptomatic, simultaneous cholecystectomy and splenectomy should be done.

Splenic abscess is considered to be rare, but it is not an uncommon complication of SCD.[10,33] Splenic infarction is common in patients with SCD and in the presence of bacteremia predisposed to by functional asplenia, which is not uncommon in these patients, making them liable to splenic infection and abscess formation. The reason for the high incidence of splenic abscess in our patients with SCD compared to other series is not known. Persistence of splenomegaly in our patients into an older age group and regional variations in SCD manifestations are two contributing factors. Many organisms cause splenic abscess, but the most frequently encountered organisms are *Staphylococci*, *Streptococci*, and gram-positive bacilli.[34,35] Salmonella accounted for only 11% of the causative organisms of splenic abscess as a whole,[34,35] but in our patients with SCD, salmonella was isolated in two patients from the abscess and in five from the blood. This is not unusual, as salmonella is known to cause various infections in patients with SCD, including septicemia, osteomyelitis, and septic arthritis.[36,37]

The role of splenectomy in the management of patients with thalassemia is well established. In patients with evidence of hypersplenism, splenectomy reduces the frequency of blood transfusions, and in turn helps to prevent iron overload, which is common in these patients.[38,39] Splenectomy, on the other hand, is associated with an increased risk of post-splenectomy sepsis.[40] To obviate this, alternatives to total splenectomy have been tried.[41-44] We performed partial splenectomy in nine patients with β-thalassemia major, and three patients with Hb H disease. Two of the three patients with Hb H disease required no more blood transfusions, while the third continued to receive blood transfusions but at a lower frequency. For those with β-thalassemia major, partial splenectomy proved beneficial in the first two postoperative years in significantly reducing their transfusion requirements, but subsequently, these requirements increased as a result of increase in the size of the splenic remnant. Therefore, partial splenectomy is recommended as a temporary measure in these patients and in children who are under five years of age, as they are at a higher risk of developing postsplenectomy sepsis.

The incidence of idiopathic thrombocytopenic purpura (ITP), hereditary spherocytosis, and autoimmune hemolytic anemia was low in our series. This may reflect a low prevalence of these disorders in our community, as previously reported.[5] Also, many of those with ITP are treated medically. For patients with ITP who fail to respond to immunoglobulins and corticosteroids, splenectomy has been shown to be beneficial in the majority of patients.[45,46] The five patients in our series with ITP showed marked improvement in their platelet count following splenectomy.

There was no postoperative mortality in our series. Thirteen patients (9%) developed postoperative complications on short- and long-term follow-up. This compares favorably with other series.[5-7,12,47] One reason for this is that our series did not include patients with hypersplenism secondary to portal hypertension, and none of our patients had hematological malignancy, which is associated with increased mortality and morbidity. On the other hand, the majority of our patients had SCD and S-β-thal. These patients are a surgical risk group, but with good perioperative management, splenectomy in these patients proved to be safe and beneficial. Two of our patients developed septicemia on follow-up, but in neither was it due to pneumococci. This may be due to the protective effect of polyvalent pneumococcal vaccine and postoperative penicillin prophylaxis given routinely to our patients. To obviate the risk of postsplenectomy sepsis, these patients should be immunized preoperatively with pneumococcal vaccine, as well as meningococcal and *H. influenza* vaccines, if available. We routinely cover our patients with penicillin prophylaxis, given either IM every three weeks, or orally twice daily, based on the age and compliance of the patients. The fact that salmonella infection is a serious and common complication in patients with SCD calls for anti-salmonella prophylaxis and the development of vaccine against salmonella for these patients. This, however, requires further evaluation and assessment.

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