

THE ROLE OF SPLENECTOMY IN PATIENTS WITH SICKLE CELL DISEASE

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Galen described the spleen as an organ full of mystery,¹ and in the absence of a clear understanding of splenic functions, Aristotle concluded that the spleen was not essential for life.² As a result of this, splenectomy was taken lightly, without a clear understanding of subsequent effects. In 1919, Morris and Bullock³ stressed the value of the spleen in resistance to infection, but it was only 30 years later when the importance of this was made clear by King and Schumacker,⁴ who reported an increased susceptibility to infection and death from sepsis in children following splenectomy.

The spleen is an organ with many important hematological and immunological functions,¹ including: 1) hemopoiesis during intrauterine life and compensatory hemopoiesis later in life, as in myeloproliferative disorders; 2) red blood cells remodeling and maturation; 3) destruction of old and abnormal red blood cells; 4) removal and filtration of particles, including red blood cell inclusions; 5) phagocytosis; 6) antibody production; 7) psonin production; 8) cell-mediated immune response; 9) removal of particulate antigens and clearance of immune complexes; and 10) storage of platelets, iron and factor VIII.

The Spleen and Sickle Cell Disease

Sickle cell disease, which was first described by Herrick in 1910,⁵ is due to homozygous inheritance of the HbS variant. It results from a single amino-acid substitution of valine for glutamic acid in the sixth position of the amino-acid sequence of the β -chain of hemoglobin. Sickle cell disease is one of the commonly inherited hemoglobinopathies worldwide, with a variable spectrum of severity. In the Eastern Province of Saudi Arabia, sickle cell disease (SCD) is common and has been reported to be more benign than in other parts of the world. This has

been attributed to high levels of HbF and the frequently associated alpha thalassemia.^{6,7}

The standard treatment of SCD has remained largely unchanged. It involves general preventive measures, as well as therapy for specific complications. One of the main organs to be affected early in SCD is the spleen, which is commonly enlarged during the first decade of life, but then undergoes progressive atrophy due to repeated attacks of vaso-occlusion and infarction, leading to siderofibrotic nodules (autosplenectomy) (Figure 1). Sometimes splenomegaly persists into the older age group and in some, into adult life.⁷⁻⁹ Those affected are liable to develop splenic complications, which are associated with morbidity and in some, with mortality. In these selected groups of patients, splenectomy is indicated.

Indications for Splenectomy

As a general rule, splenectomy should be avoided in patients with SCD, as these patients are already susceptible to infection, especially during the first three years of life.¹⁰ This is attributed to several factors, which include early splenic dysfunction. Functional asplenia is defined as the inability of an enlarged spleen to remove Howell-Jolly bodies, to take up colloidal sulphur-labeled particles or combat infection.¹¹ It usually manifests during the first six months to three years of life and contributes to the increased susceptibility to acute bacterial infections in these patients. Other contributory factors include defective opsonization due to abnormality of the alternate pathway complement activation,¹² neutrophil dysfunction,¹³ deficiency in heat-labile serum opsonizing activity¹⁴ and lack of circulating specific antibodies characteristic of early infancy.¹⁵

To obviate the risks of splenectomy, and especially of overwhelming postsplenectomy infection (OPSI), splenic preservation is being increasingly advocated. But in selected patients and with careful perioperative management, including prophylaxis against OPSI, splenectomy becomes an important part of the management in SCD. The main indications for splenectomy in SCD are: 1) acute splenic sequestration crisis, 2) hypersplenism, and 3) splenic abscess.

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Accepted for publication 7 July 1996. Date received 6 April 1996.

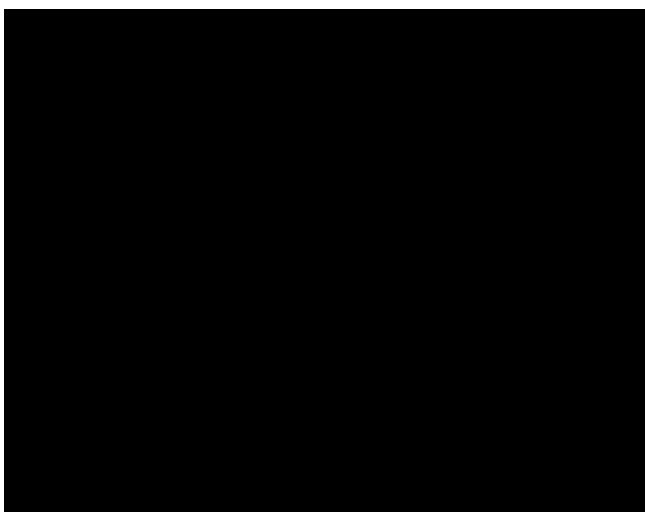


FIGURE 1. CT scan of the abdomen showing a small calcified spleen (siderofibrotic nodule, autosplenectomy).

Acute Splenic Sequestration Crisis (ASSC)

This is a fairly common and serious complication of SCD, and if not detected and treated early, it can cause circulatory collapse and sudden death from the rapid sequestration of circulating red blood cells in the spleen. It is characterized by the sudden onset of acute anemia, splenomegaly and active bone marrow response. Commonly, it is seen in infants and young children between five months and two years of age,¹⁶ but there are reports of ASSC in older children. In the Eastern Province of Saudi Arabia, we observed that ASSC occurs in older children, because Saudi patients with SCD are known to have splenomegaly that persists into the older age group.^{17,18} It is considered the second leading cause of death in patients with SCD in the first decade of life, after infection. The incidence of ASSC is variable, ranging from 7.3% to 30%, and contributes to 15% to 44% of deaths in the first decade of life.^{10,19-21} The clinical manifestations of ASSC are weakness, pallor, breathlessness, tachycardia, faintness and abdominal distention, and it is divided into major and minor attacks. The minor attacks are characterized by moderate increase in splenic size associated with a drop in the hemoglobin level of 2 to 3 g/dL, while major attacks are associated with a greater drop in hemoglobin, sometimes reaching a level of less than 2 g/dL.¹⁸ In major attacks, hypovolemic shock and death can occur. In both major and minor attacks, the spleen size regresses after blood transfusions.

The treatment of ASSC is directed toward correction of hypovolemia with blood transfusion. A dramatic response to treatment is seen in a rise in the hemoglobin level and regression of the spleen size, which must be measured. The role of splenectomy in major attacks is well established.^{19,22,23} We advocate splenectomy if the child

develops one major attack, as the survivors of these first episodes are then exposed to a recurrence risk of 40% to 50%, with a mortality rate of 20%.^{18,21,24} The role of splenectomy in minor attacks is, however, still controversial. Several investigators have recommended chronic blood transfusion therapy to prevent recurrent episodes, but in addition to allosensitization and hepatitis from blood transfusions, a significant number develop acute splenic sequestration crisis when attempts are made to stop the transfusions.²⁵ Whereas the criteria for splenectomy in minor attacks of ASSC are not clear, we agree with others that splenectomy should be considered after two such attacks.^{18,26} This is especially so in situations like ours, where blood transfusions are not readily available and poor compliance of the parents makes chronic blood transfusion an unsuitable form of treatment. Patients with SCD tend to develop splenic hypofunction as part of the natural course of their disease. Pearson et al.²⁷ have demonstrated progressive hyposplenism in patients with SCD, shown by an increase in pitted red blood cell counts as early as eight months of life. Sudden death from ASSC remains a significant threat to these patients and removal of a poorly functioning or nonfunctioning spleen does not add to increased susceptibility to infections.

The importance of newborn screening and parents' education about the dangers of ASSC cannot be overemphasized. The parents must be taught how to palpate the spleen and recognize sudden enlargement. This was shown clearly in the Jamaican study,²¹ which showed an increase in the incidence of ASSC from a mean of 4.6 to 11.3 per 100 patient years, with a decrease in the mortality rate from 29.4 to 3.1 per 100 events.

Hypersplenism

Hypersplenism is defined as a chronic state characterized by splenomegaly, associated anemia, and leukopenia with the WBC count below 4000/mm³, and thrombocytopenia with a platelet count below 100,000/mm³, either singly or in combination.²⁸ These result from pooling of the blood in the enlarged spleen with increased cell destruction. In patients with SCD, the extent of anemia is judged by the transfusion requirements exceeding 250 mL/kg of packed RBCs per year and/or a fall in hemoglobin exceeding 0.5 g/week.²⁸

Hypersplenism may remit spontaneously in some patients, but therapy often requires an increasing number of blood transfusions. The benefits of blood transfusion have to be weighed against the attendant risks, particularly RBC alloimmunization, which occurs in up to 20% of transfused sickle cell disease patients, and transmission of hepatitis and other blood-borne infections.²⁹ Add to this the poor compliance of these patients, which makes chronic blood transfusion an unsuitable form of therapy for them. To obviate the risks of splenectomy, especially

OPSI, total splenectomy should be avoided if possible. Consequently, alternatives to total splenectomy in the treatment of hypersplenism have been tried. They include partial splenectomy, percutaneous intraluminal occlusion of the splenic artery and embolization of the spleen.³⁰⁻³⁴ Although partial splenic embolization has been shown to be a safe and reliable method of treatment for hypersplenism,³⁵ it has its own complications, which makes it unsuitable in SCD. We found splenectomy to be beneficial in decreasing transfusion requirements and also in eliminating the discomfort from mechanical pressure of the enlarged spleen.^{28,36} Laparoscopic splenectomy has been described recently as a safe and feasible alternative to open splenectomy, both in children and adults.^{37,38} However, this requires further evaluation. The presence of an excessively large spleen or multiple adhesions, which are not uncommon in patients with SCD, would make laparoscopic splenectomy difficult and contraindicated in these patients.

Splenic Abscess

Splenic abscess is a rare, but known complication of SCD, in which there is a high incidence of splenic infarction in addition to the opportunity for bacteremia, for which there is predisposition in these patients due to functional asplenia.^{39,40}

The clinical presentations of splenic abscess are not specific, and a high degree of clinical awareness is essential for early diagnosis.⁴¹ The classic presentation is that of fever, abdominal pain and tender splenomegaly.⁴⁰ Radiographic signs of splenic abscess on abdominal x-ray include extraintestinal gas in the left upper quadrant, left upper quadrant soft tissue mass displacing the gastric air bubble, and downward displacement of the left kidney. The chest radiograph may show elevation of the left hemidiaphragm, left basal atelectasis, pneumonia and left pleural effusion. Ultrasonography and computerized tomography are the most useful imaging techniques in diagnosis (Figure 2). We found computerized tomography to be more reliable, as it allows more accurate anatomical localization.^{39,40}

Many organisms can cause splenic abscess, but the most frequently encountered organisms are *Staphylococcus aureus*, *Streptococci* and gram-negative bacilli. Other less common organisms include anaerobes, *Mycobacterium tuberculosis* and *Serratia marcescens*. An interesting finding is the isolation of *Salmonella* in the splenic abscess of patients with sickle cell disease.^{40,41} Splenic abscess secondary to *Salmonella* is now rarely reported, except in patients with SCD, who are known to have various infections due to *Salmonella*, including septicemia, osteomyelitis and septic arthritis.⁴²

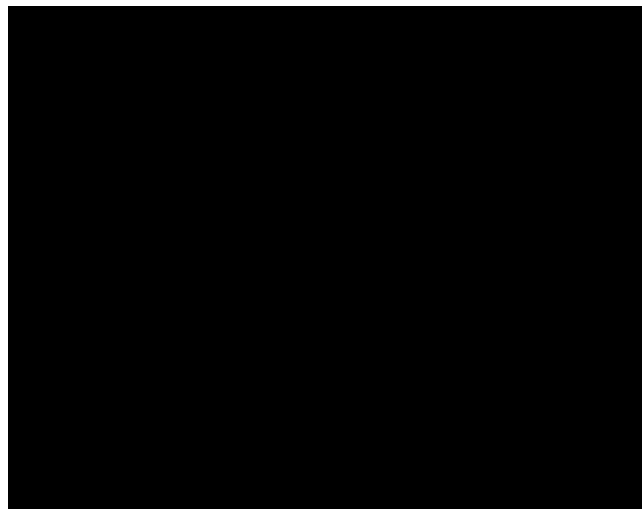


FIGURE 2. Abdominal CT scan showing a large splenic abscess.

The treatment of choice for splenic abscess is splenectomy and appropriate antibiotics.^{43,44,47,48} However, recent reports have established the effectiveness of percutaneous abscess drainage (PAD), both in children and adults, as preservation of splenic tissue is of value in reducing the late susceptibility to postsplenectomy sepsis.⁴⁵⁻⁴⁷ The success of PAD depends on several factors, namely the morphology and localization of the abscess and personnel skilled in PAD.^{48,49} Percutaneous abscess drainage should be of value in patients with SCD, who are at high risk for general anesthesia and major surgery; however, the presence of functional asplenia in these patients makes splenectomy together with prophylactic pneumococcal vaccination and antibiotics more rational.⁴⁰

Prophylaxis Against Postsplenectomy Sepsis

In 1952, King and Schumacker reported the severe and fatal bacterial sepsis in five infants following splenectomy for hereditary spherocytosis.⁴ Since then, there has been an increasing awareness of the risk of severe postsplenectomy infection. Although asplenic patients should be considered to have a life-long risk of acquiring severe late postsplenectomy infection, infections are more frequent in the first and second year of life after splenectomy.^{50,51} The single most important organism responsible for postsplenectomy sepsis was *Streptococcus pneumoniae*, accounting for 57% of infections.^{52,53} Other causative organisms include *Haemophilus influenzae*, *Neisseria meningitidis*, *Escherichia coli* and *Pseudomonas*.^{52,53}

All patients undergoing splenectomy should receive polyvalent pneumococcal vaccine. This should be given in elective cases as early as the decision for splenectomy is

made, and in emergency cases just before discharge from the hospital.⁵² *Meningococcal* and *Haemophilus* vaccines, although they have a narrow serotype coverage, should be given when available. Regarding long-term prophylactic antibiotics, the current recommendations in splenectomized children include prophylactic long-acting benzathine penicillin 600,000 U IM every three weeks for those under six years of age or 1.2×10^6 U IM every three weeks for those over six years of age, or preferably oral penicillin 125-250 b.i.d. for those under six years of age, and 500 mg b.i.d. for those over six years of age. The duration of prophylactic antibiotics remains controversial,^{26,54,55} but since infection is most likely to occur within two to three years of surgery, most people recommend giving it for at least two to three years postsplenectomy.⁵⁰⁻⁵³

References

- Cooper MJ, Williamson RCN. Splenectomy: indications, hazards and alternatives. *Br J Surg* 1984;71:173-80.
- Buntain WL, Lynn HB. Splenorhaphy: changing concepts for the traumatized spleen. *Surgery* 1979;86:748-60.
- Morris DH, Bullock FD. The importance of the spleen in the resistance to infection. *Ann Surg* 1919;70:513-21.
- King H, Schumacker HB. Splenic studies: susceptibility to infection after splenectomy performed in infancy. *Ann Surg* 1952;136:239-42.
- Herrick JB. Peculiar elongated and sickle shaped red blood corpuscles in a case of severe anemia. *Arch Inter Med* 1910;6:517-21.
- Perrine RP, Pembrey ME, John P, Perrine S, Shoup F. Natural history of sickle cell disease in the Eastern Province of Saudi Arabia. *Ann Intern Med* 1978;88:1-6.
- Al-Awamy BH, Naem MA. Splenic and hepatic function in sickle cell anemia, with emphasis on patients from the Eastern Province of Saudi Arabia. *Saudi Med J* 1986;7:434-42.
- Mallouh A, Burke M, Salamah M, et al. Splenic function in Saudi children with sickle cell disease. *Ann Trop Pediatr* 1984;43:87-91.
- Al-Awamy B, Wilson WA, Pearson HA. Splenic function in sickle cell disease in the Eastern Province of Saudi Arabia. *J Pediatr* 1984;104:714-7.
- Rogers DW, Clarke JM, Cupidore L, et al. Early deaths in Jamaican children with sickle cell disease. *Br Med J* 1978;1:1515-6.
- Pearson HA, Spencer RP, Cornelius EA. Functional asplenia in sickle cell anemia. *N Engl J Med* 1969;28:923-6.
- Johnston RB Jr, Newman SK, Struth AG. An abnormality of the alternative pathway of complement activation in sickle cell disease. *N Engl J Med* 1973;288:803-8.
- Dimitrov NV, Douwes FR, Bartolotta B, et al. Metabolic activity of polymorphonuclear leukocytes in sickle cell anemia. *Acta Haemat* 1972;47:283-91.
- Winkelstein JA, Dradman RH. Deficiency of pneumococcal serum opsonizing activity in sickle cell disease. *N Engl J Med* 1968;279:459-66.
- Fothergill LD, Wright J. Influenza meningitis. The relation of age incidence of the bacterial power of blood against causal organism. *J Immunol* 1933;24:273-84.
- Seeler RA, Shwiaki MZ. Acute splenic sequestration crisis (ASSC) in young children with sickle cell anemia. *Clin Pediatr* 1972;11:701-4.
- Salamah MM, Mallouh AA, Hamdan JA. Acute splenic sequestration crisis in Saudi children with sickle cell disease. *Ann Trop Pediatr* 1989;9:115-7.
- Al-Salem AH, Qaisaruddin S, Nasserullah Z, et al. Splenectomy and acute splenic sequestration crises in sickle cell disease. *Pediatr Surg Int* 1995;11:26-8.
- Powell RW, Levine GL, Yang Y, Mankad VN. Acute splenic sequestration crisis in sickle cell disease: early detection and treatment. *J Pediatr Surg* 1992;27:215-9.
- Topley JM, Rogers DW, Stevens MC, et al. Acute splenic sequestration and hypersplenism in the first five years in homozygous sickle cell disease. *Arch Dis Child* 1981;56:765-9.
- Emond AM, Collis R, Davill D, et al. Acute splenic sequestration in homozygous sickle cell disease: natural history and management. *J Pediatr* 1985;107:201-6.
- Powars DR. Natural history of sickle cell disease: the first ten years. *Semin Hematol* 1975;12:267-85.
- Topley JM, Rogers DW, Stevens MC, et al. Acute splenic sequestration in homozygous sickle cell disease: early detection and treatment. *J Pediatr Surg* 1992;27:215-9.
- Mills ML. Life-threatening complications of sickle cell disease in children. *JAMA* 1985;254:1487-91.
- Kinney TR, Ware RE, Schultz WH, et al. Long-term management of splenic sequestration in children with sickle cell disease. *J Pediatr* 1990;117:194-9.
- Emond AM, Morais P, Venugopal S, Carpenter RG, Serjeant GR. Role of splenectomy in homozygous sickle cell disease in childhood. *Lancet* 1984;14:88-90.
- Pearson HA, McIntosh S, Ritchey AK, et al. Developmental aspects of splenic function in sickle cell disease. *Blood* 1979;53:358-65.
- Al-Salem AH, Qaisaruddin S, Nasserullah Z, et al. Splenectomy in patients with sickle cell disease. *Am J Surg* 1996;172:254-8.
- Davies SC, McWilliams AC, Hewitt RE, Devenish A, Brozovic M. Red cell alloimmunization in sickle cell disease. *Br J Hematol* 1986;3:29-44.
- Dixon JA, Miller F, McCloskey D, et al. Anatomy and techniques in segmental splenectomy. *Surg Gynecol Obstet* 1980;150:516-20.
- Witte CL, Van Wyck DB, Mitte MH, et al. Ischaemia and partial resection for control of splenic hyperfunction. *Br J Surg* 1982;69:531-5.
- Levy JM, Wasserwan P, Pitha N. Presplenectomy transcatheter occlusion of the splenic artery. *Arch Surg* 1979;114:198-9.
- Alwmark KA, Bengmark S, Gullstrand P, et al. Evaluation of splenic embolization in patients with portal hypertension and hypersplenism. *Ann Surg* 1982;196:518-24.
- Maddison FE. Embolic therapy of hypersplenism. *Invest Radiol* 1973;8:280-1.
- Spigos DB, Jonasson O, Mozes M, Capek V. Partial splenic embolization in the treatment of hypersplenism. *Am J Roentgenol* 1979;132:777-82.
- Al-Salem AH, Khwaja MS, Al-Fadel M, Grant C, Al-Awamy B. Splenectomy in children with sickle cell disease and thalassemia. *Indian J Pediatr* 1989;56:747-52.
- Moore DC, McKee MA, Wang H, et al. Pediatric laparoscopic splenectomy. *J Pediatr Surg* 1995;30:1201-5.
- Thibault C, Mamazza J, Letourneau R, et al. Laparoscopic splenectomy: operative techniques and preliminary report. *Surg Laparosc Endosc* 1992;2:248-53.
- Grant CS, Al-Salem A, Khwaja MS, Sumer T, Al-Awamy B. Splenic abscess in children: aspects of management. *J R Coll Surg Edinb* 1987;32:342-5.
- Al-Salem AH, Kadappa Mallapa K, Qaisaruddin S, Al-Jam'a A, El-Bashier A. Splenic abscess in children with sickle cell disease. *Pediatr Surg Int* 1994;9:489-91.
- Debenckelaere S, Schoors DF, Buydens P, et al. Splenic abscess: a diagnostic challenge. *Am J Gastroenterol* 1991;86:1675-8.
- Al-Salem AH, Ahmed HA, Qaisaruddin S, et al. Osteomyelitis and septic arthritis in sickle cell disease in the Eastern Province of Saudi Arabia. *International Orthopaedic* 1992;1:398-402.
- Chun CH, Raff MF, Contreras L, et al. Splenic abscess. *Medicine* 1980;50:5.
- Sarr MG, Zuidema GD. Splenic abscess: presentation, diagnosis and treatment. *Surgery* 1912;92:480-5.
- Berkman WA, Harris SA, Bernardino ME. Nonsurgical drainage of splenic abscess. *Am J Roentgenol* 1983;141:395-6.
- Lerner RM, Spataro RF. Splenic abscess: percutaneous drainage. *Radiology* 1984;153:643-5.

47. Ramakrishnan MR, Sarathy TKP, Balu M. Percutaneous drainage of splenic abscess. Case report and review of literature. *Pediatrics* 1987;79:1029-31.
48. Gerzot SG, Robbins AH, Johnsons WC, et al. Percutaneous drainage of abdominal abscesses. *N Engl J Med* 1981;305:653-7.
49. Gerzot SG, Johnson WC, Robbins AH, et al. Expanded criteria for percutaneous abscess drainage. *Arch Surg* 1985;120:227-32.
50. Walker W. Splenectomy in childhood. A review in England and Wales, 1960-4. *Br J Surg* 1976;63:36-43.
51. Philipport A, Hight DW. Splenectomy in childhood. Altered concepts of management. *Am J Pediatr Hematol Oncol* 1980;2:62-8.
52. Cullinford GL, Watkins DN, Watts ADJ, Mallou DF. Severe late postsplenectomy infection. *Br J Surg* 1991;78:716-21.
53. Holdsworth RJ, Irving AD, Cuschieri A. Postsplenectomy sepsis and its mortality rate. Actual versus perceived risks. *Br J Surg* 1991;78:1031-8.
54. Schwartz PE, Sterioff S, Mucha P, et al. Post-splenectomy sepsis and mortality in adults. *JAMA* 1982;248:2279-83.
55. Craig RP, Bate CM, Humphries G. Some surgical aspects of homozygous beta thalassemia. *Br J Surg* 1977;64:277-80.