Invited Commentary

Indications for Splenectomy

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In the new millennium, indications for splenectomy have expanded. Proper patient selection based on an understanding of the biology of each individual's disease is essential for a favorable outcome. We review the most common diseases for which surgeons may be called on to perform splenectomy and while highlighting potential pitfalls and caveats.

THE SPLEEN MEDITATES important immunologic and hematologic functions as well as contributing to numerous pathologic processes. When the spleen is involved in disease, splenectomy may be performed with the intent of either altering the clinical course or providing symptomatic relief. In the new millennium, indications for splenectomy have expanded, and splenectomy may be beneficial to patients with a broad spectrum of benign and malignant diseases. Proper patient selection based on an understanding of the biology of each individual's disease is essential for a favorable outcome.

Splenectomy is not without potential complications, the most feared of which being overwhelming post-splenectomy infection (OPSI). Mortality rates of OPSI may exceed 50 per cent in unvaccinated patients.[1] Therefore, removal of the spleen should be performed only when the potential benefits to the patient clearly exceed the risks. Recent advances in surgical techniques allow for a laparoscopic approach in many patients who require splenectomy, thereby minimizing operative morbidity and patient discomfort associated with open splenectomy. However, a minimally invasive approach to splenectomy is not always feasible or desirable and therefore familiarity with the traditional approach remains vital. We review the spectrum of disease processes for which splenectomy may be indicated. Prerequisites for successful therapeutic or palliative splenectomy are a thorough understanding of splenic anatomy, physiology, and pathophysiology. We discuss the most common diseases for which surgeons may be called on to perform splenectomy and consider the various surgical approaches while highlighting potential pitfalls and caveats.

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Development and Anatomy

The spleen forms as a mesenchymal condensation of the dorsal mesogastrium during the fifth week of development. Initially, the spleen functions as a hematopoietic organ and assumes its more mature lymphoid characteristics at 15 to 18 weeks.[2] The spleen is related to the posterior wall of the stomach and is connected to the stomach and kidney by the gastrosplenic and splenorenal ligaments. With the exception of the hilum, the spleen is surrounded by peritoneum. On average, the spleen is 12 cm long and 7 cm wide. The splenic artery originates from the celiac axis and divides into 5 or more terminal branches that enter the splenic hilum. Several tributaries join to form the splenic vein, which joins the superior mesenteric vein to form the portal vein posterior to the neck of the pancreas.

A dense fibrous capsule surrounds the spleen and trabeculae form incomplete parenchymal compartments within the splenic pulp. Stretching of the capsule may cause pain in patients with splenomegaly. On cross-section, the spleen contains both red and white pulp. Arteries within the white pulp, central arteries, are surrounded by a sheath of lymphocytes known as the periarteriolar lymphatic sheath (PALS).[3] The PALS is comprised primarily of T cells, whereas adjacent lymphoid follicles are abundant in B cells. The marginal zone lies between the white and red pulp containing dendritic cells, which capture and present antigen to lymphocytes. Within the red pulp, the sinusoids are lined by a fenestrated endothelium similar to the lumen of the hepatic sinusoids.[4]

Normal Splenic Function

Although many functions of the spleen are redundant or can be assumed by other organs, splenectomy can lead to adverse consequences. An appreciation of

normal spleen function is important for the physician seeking to understand the potential consequences of splenectomy in a given disease process. Under normal conditions, the spleen contains less than 50 mL of blood and does not serve as a depot for intravascular volume, platelets, leukocytes, or erythrocytes. In the setting of splenomegaly or portal hypertension, the storage volume of the spleen expands and formed elements of the blood are sequestered.[5] As much as one third of the total platelet mass may be stored in the spleen and released during inflammatory states.[6]

Although active hematopoiesis occurs in the fetal spleen, it does not normally occur in postnatal life. However, in certain pathologic states such as myelofibrosis, extramedullary hematopoiesis may indeed take place within the spleen. The splenic white pulp is the largest accumulation of lymphoid tissue in the body and is a site of lymphocyte production and activation, from which cells migrate into the red pulp to reach the lumen of the splenic sinusoids. Dendritic cells and macrophages in the marginal zone are involved with antigen trapping, processing, and presentation. Splenic macrophages are particularly adept at recognizing and clearing opsonized bacteria.[7] Both dendritic cells[8] and T lymphocytes[9] within the spleen appear to have potent immunologic function.

In addition to its role in the immune system, the spleen is the site of senescent erythrocyte destruction. Macrophages in the splenic cords phagocytose erythrocytes and metabolize hemoglobin. Aged erythrocytes are more sensitive to the relatively acidotic, hypoxic, and hypoglycemic milieu of the spleen. The heightened sensitivity of senescent erythrocytes to the hostile splenic environment leads to alterations in membrane carbohydrate moieties,[10] thereby facilitating recognition by macrophages and subsequent culling or destruction of damaged cells. In addition to culling, pitting leads to removal of intracellular inclusions from erythrocytes. The loss of pitting after splenectomy accounts for the appearance of particulate matter such as Howell-Jolly bodies within erythrocytes postoperatively. Furthermore, asplenia limits bacterial clearance[11] and production of IgM and other opsonin proteins.[12]

Hematologic Conditions

Autoimmune Thrombocytopenia and Hemolytic Anemia

The pathogenesis of autoimmune thrombocytopenia or idiopathic thrombocytopenic purpura (ITP) involves the formation of antibodies to several antigenic determinants, including glycoproteins IIb/IIIa and Ia/IIa.[13] The spleen is both a site of autoantibody production and platelet destruction. Although ITP tends to be a self-limiting disorder in the pediatric population, adults often require specific therapeutic intervention. In the event of persistent or recurrent disease after treatment with glucocorticoids, cytotoxic agents, or immunoglobulin, patients with ITP may benefit from splenectomy. Demonstration of megakaryocytes in the bone marrow and the absence of splenomegaly are essential for establishing the diagnosis of ITP before splenectomy is undertaken. Musser reported that after splenectomy for ITP, up to 77 per cent of patients show a complete response. In addition, 14 per cent of patients show a partial response, whereas only 9 per cent failed to demonstrate a significant improvement in platelet count.[14] Unfortunately, preoperative characteristics do not necessarily predict which patients with ITP will respond to splenectomy.[15] Failure of splenectomy to improve the thrombocytopenia may be the result of an unappreciated accessory spleen or intraabdominal implantation of splenic tissue should fragmentation occur during surgery or extraction after a laparoscopic approach. Particular attention should be paid to the latter, especially during the "morselization" process used to facilitate removal while limiting the size of the incision.

Similarly, autoimmune hemolytic anemia may result in the need for splenectomy if the patient fails to respond to medical management, including oral corticosteroids.[16] Like with ITP, the pathogenesis of autoimmune hemolysis involves antibody-mediated cellular destruction and complement activation within the splenic substance. In patients with warm-reacting antibodies, favorable responses to splenectomy can be expected in 50 per cent to 80 per cent.[17]

Felty's Syndrome

Felty's syndrome is the occurrence of neutropenia and splenomegaly in patients with rheumatoid arthritis (RA). These manifestations are present in less than 1 per cent of patients with RA. Patients with Felty's syndrome face an increased risk of infection as a result of granulocytopenia, which results, in part, from intrasplenic destruction of granulocytes.[18] Granulocyte–macrophage colony-stimulating factor may ameliorate the neutropenia in some cases.[19] Splenectomy is indicated only in patients with severe or recurrent neutropenia or in those patients demonstrating recurrent and resistant infections.[20] Splenectomy results in increased granulocyte levels in 80 per cent of patients, with 55 per cent of patients experiencing no further infections.[21]

Thrombocytopenic Purpura

Thrombocytopenic purpura (TTP) presents with the pentad of fever, thrombocytopenia, hemolytic anemia, neurologic manifestations, and renal failure. TTP may

result from an excess of subendothelial collagen, resulting in systemic platelet trapping. Splenectomy is indicated only for patients in whom plasmapheresis fails or who relapse when this therapy is discontinued. Excellent results may be achieved in refractory cases.[22] Over 50 per cent of patients with TTP who undergo splenectomy may respond favorably.[23]

Erythrocyte Membrane Disorders

Hereditary spherocytosis (HS) is the most common erythrocyte membrane disorder for which splenectomy is indicated. An autosomal-dominant mutation results in a defective erythrocyte membrane resulting from derangements in spectrin and ankyrin, rendering the cells less deformable and thus susceptible to intrasplenic destruction. As a result of erythrocyte destruction within the spleen, patients with HS present with anemia, jaundice, and splenomegaly. The anemia may be relatively mild with jaundice being the only clinical manifestation.

The role of splenectomy in HS is to treat the underlying anemia and prevent the development of biliary pathology, aplastic crises, and late hemachromatosis.[16] Being that erythrocytes are destroyed within the spleen in patients with HS, splenectomy represents a highly effective treatment modality.[24] Splenectomy for HS is generally deferred until the patient is 4 to 6 years old to minimize the risks of OPSI. Splenectomy results in correction of the anemia associated with HS and prevents subsequent hemolytic episodes.[25] Response rates as high as 90 per cent have been reported.[14] Hereditary elliptocytosis is generally a nonpathologic trait, but when more than 90 per cent of the erythrocytes are affected, the disease manifestations may become significant. Indications for and results of splenectomy are similar to those of HS.[24]

Erythrocyte Enzyme Deficiencies

Pyruvate kinase deficiency (PKD) is an autosomal-recessive disorder associated with hemolysis and reduced red blood cell deformability. Consequently, erythrocytes are sequestered and destroyed in the spleen. The severity of disease ranges from fully compensated hemolysis to potentially fatal anemia and jaundice in the neonate. Although splenectomy does not eliminate hemolysis in patients with PKD, it does result in increased hemoglobin levels. As a result, transfusion requirements are greatly decreased or even eliminated.[26] Patients with PKD may also develop cholelithiasis and associated biliary tract pathology as a result of chronic hemolysis. Therefore, cholecystectomy may be indicated in patients with PKD. In patients with PKD undergoing cholecystectomy, concomitant splenectomy merits serious consideration to effectuate a decrease in the rate of hemolysis and subsequent transfusion requirements.[27]

Glucose-6-phosphate dehydrogenase deficiency (G6PD) is an X-linked disorder that renders the patient susceptible to hemolysis after exposure to certain drugs or chemicals such as methylene blue and fava beans. Deficiency of glutathione leads to the destabilization of red blood cell membrane skeletons through oxidative mechanisms.[28] Splenectomy plays little, if any, role in patients with G6PD deficiency and therefore should not be undertaken. The cornerstone of therapy in this unusual disease remains avoidance of inciting drugs or physiological stressors, particularly infections.

Hemoglobinopathies

In sickle cell disease, a single mutation in the beta-hemoglobin chain of Hb A results in rigid, nondeformable erythrocytes that are sequestered and destroyed in the spleen. Although the spleen may be enlarged early in life, the organ tends to shrink and autoinfarct as a result of recurring ischemic insults. Likewise, thalassemia involves a defect in hemoglobin synthesis and is most prevalent among Mediterranean populations. Thalassemia major, the homozygous form, presents in childhood with failure to thrive, ulcers, and anemia. Fetal hemoglobin (Hb F) persists and a relative paucity of adult hemoglobin (Hb A) can be demonstrated.

The indications for splenectomy in sickle cell disease and thalassemia include hypersplenism, sequestration crises, splenic abscesses, and massive splenic infarction.[29] Acute splenic sequestration crises are life-threatening events for which the transfusion requirement may be substantial and pain may be the most significant component of the overall presentation.[30] The features of acute splenic sequestration crises include severe anemia, splenomegaly, and abdominal pain. The patient's hemodynamic status may deteriorate into frank circulatory collapse. These patients require aggressive resuscitation with crystalloid and blood products before urgent splenectomy. In addition to relieving the acute sequestration crises, splenectomy also alleviates mechanical symptoms resulting from splenomegaly and may improve protein and energy metabolism in children with sickle cell disease.[31] Postoperatively, although these patients benefit from decreased transfusion requirements and increased circulating erythrocyte mass,[32] they are particularly at high risk for postsplenectomy infections.

Primary Hypersplenism

Hypersplenism refers to splenomegaly associated with a decrease in one or more of the formed blood elements. Although hypersplenism is most often a sec-

ondary manifestation of an underlying disorder such as portal hypertension, primary or idiopathic hypersplenism may occur. Primary hypersplenism or hypersplenism in the absence of a specific disease process was diagnosed more frequently in the past as a result of our limited inability to detect the presence of lymphoma or leukemia. The sensitivity of modern diagnostic modalities to detect lymphoma or leukemia has improved to the extent that primary hypersplenism is now an uncommon diagnosis. In instances in which hypersplenism is symptomatic and truly idiopathic, splenectomy is indicated to relieve the mechanical symptoms of splenomegaly, effect improvement of cytopenias, and eliminate the possibility of an underlying malignancy. Lymphoma has been pathologically detected in 40 per cent to 70 per cent of patients undergoing splenectomy for presumed primary hypersplenism.[33, 34] The frequency of this occurrence, as noted earlier, may be significantly lower as a result of advances in diagnostic imaging and the liberal use of fine-needle aspiration with flow cytometry.

Neoplastic Conditions Requiring Splenectomy

Hodgkin's Disease

The role of splenectomy in the management of patients with Hodgkin's lymphoma has undergone significant modifications. In the past, staging laparotomy, which included splenectomy, was an important component in the evaluation of these patients. Detection of disease below the diaphragm has important prognostic and therapeutic implications. When splenectomy was performed as part of a staging laparotomy for Hodgkin's disease, over one third of spleens removed were found to be involved with Hodgkin's disease. As a result, patients were upstaged by information obtained during staging laparotomy.[35] However, improvements in computed tomography, positron emission tomography, and magnetic resonance imaging techniques have limited the need for staging laparotomy.[36] Moreover, given improved toxicity profiles of chemotherapeutic agents, patients with a high likelihood of stage III or IV disease may undergo systemic therapy without being subjected to staging laparotomy. Yet, patients with early disease and equivocal radiologic findings may still be referred for operative staging. Surgical staging should be limited to patients with stage I or II disease in whom a negative result may permit withholding chemotherapy after radiation therapy.[37] Staging laparotomy is now performed, at most, in 30 per cent of patient's with Hodgkin's disease. When surgery is required, the laparoscopic approach is used with increasing frequency.[38]

Non-Hodgkin's Lymphoma

Splenectomy may be performed for non-Hodgkin's lymphoma (NHL) with either therapeutic or diagnostic intent. Indications for splenectomy include relief of symptoms resulting from splenic enlargement, cytopenias, facilitation of chemotherapy administration, and to establish a tissue diagnosis. In a single study, splenectomy improved cytopenias in up to 72 per cent of patients and may contribute to durable remission.[39] However, the surgical mortality and morbidity were 2.9 per cent and 37 per cent, respectively. When lymphoma primarily involves the spleen, cytopenias are frequent and are reversed by early splenectomy in 82 per cent of cases.[40] Berman and colleagues found that in patients with hematologic malignancies, splenectomy resulted in sustained normalization of platelet levels and thereby decreased the need for platelet infusions.[41]

Chronic Myelogenous Leukemia

Chronic myelogenous leukemia (CML) is a myeloproliferative disease in which the normal bone marrow elements are progressively replaced by neoplastic myeloid cells. CML is characterized by the Philadelphia chromosome, which involves fusion of fragments from chromosomes 9 and 22.[42] CML is typically indolent in onset with a progressive phase heralded by fever and splenomegaly. The progressive phase may culminate in a blast crisis with splenic sequestration of blood elements contributing to the anemia, infection, and hemorrhagic complications.

The primary therapy for CML includes hydroxyurea, interferon-alpha, and chemotherapy with bone marrow transplantation. There is clearly a role for palliative splenectomy to relieve compressive symptoms and improve cytopenias (Fig. 1).[43] However, splenectomy does not improve survival in patients with CML, and thromboembolic and vascular events are more common in patients with CML after splenectomy when compared with those managed nonoperatively.[44] Therefore, a heightened suspicion for thrombotic complications is appropriate when splenectomy is performed in patients with CML and this concern is discussed in greater detail subsequently.

Chronic Lymphocytic Leukemia

Splenectomy is performed for complications of chronic lymphocytic leukemia (CLL), including hypersplenism and the mechanical effects of splenomegaly. Anemia and thrombocytopenia may be significantly improved in patients with CLL after splenectomy. Moreover, in contrast to CML, in certain subgroups of patients such as those with hemoglobin levels

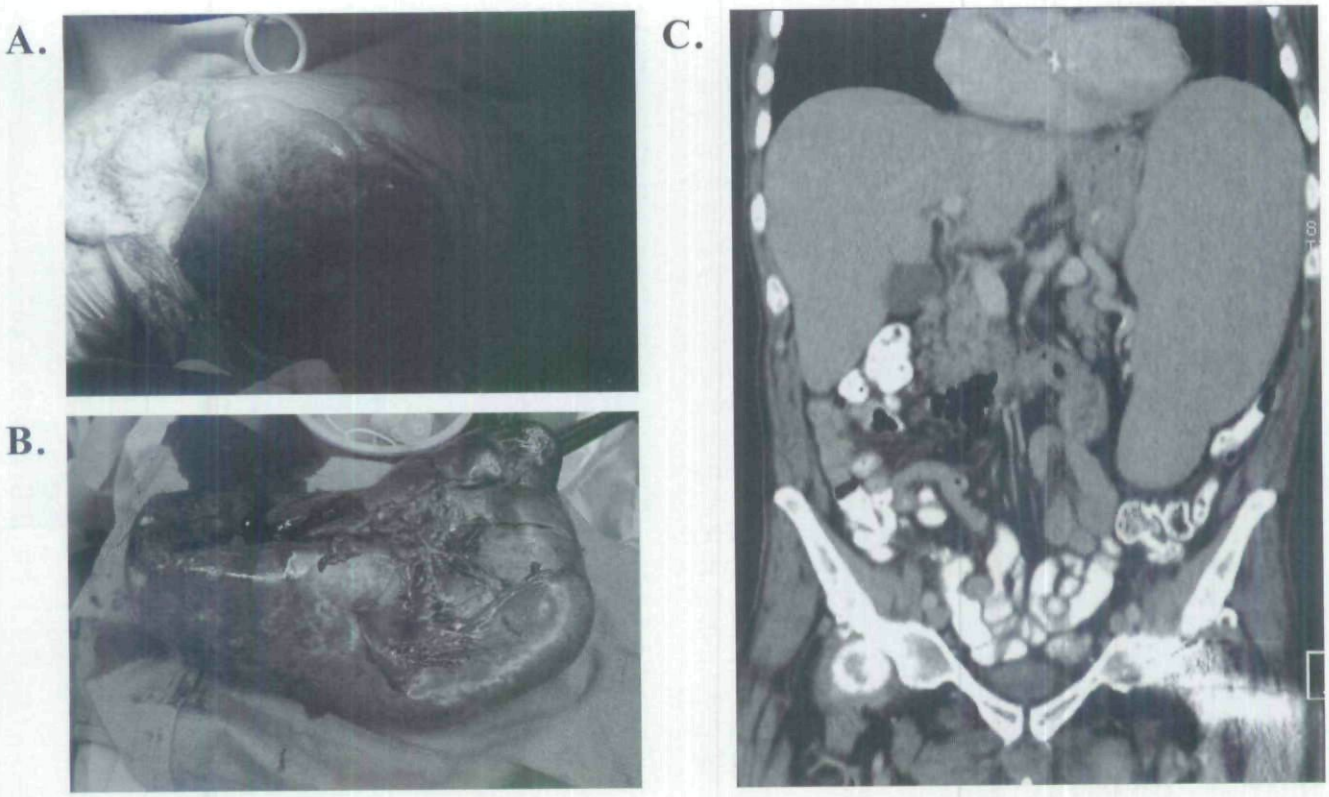

FIG. 1. Spleen involved with chronic myelogenous leukemia (CML). This case illustrates the marked degree of splenomegaly that may occur in patients with CML. Splenectomy was indicated in this case for relief of compressive symptoms. (A) After mobilization of the spleen, it was delivered through a left upper quadrant incision and then the splenectomy was completed (B). A preoperative computed tomography scan demonstrates the degree of splenomegaly and how this may lead to compressive symptoms (C).

less than 10 g/dL or platelet counts less than 50,000/L, splenectomy has been shown to improve long-term survival.[45]

Hairy Cell Leukemia

Hairy cell leukemia (HCL), formerly known as "surgical leukemia," is a rare, chronic lymphoid leukemia that generally affects the elderly with splenomegaly and pancytopenia. Neoplastic mononuclear cells with distinctive cytologic features are present in the peripheral blood and bone marrow. Although a minority of patients present with asymptomatic splenomegaly, most will require therapy to address manifestations of anemia, neutropenia, or thrombocytopenia. Historically, splenectomy played a definitive role in the treatment of patients with HCL.[46] At present, splenectomy is infrequently performed for HCL because interferon-α, and more recently, purine analogs have proven to be highly effective in the management of this type of leukemia.[47]

Primary and Metastatic Tumors

The spleen is a relatively infrequent site of metastases of nonhematologic malignancies, and this may be related to peculiarities of the splenic microcirculation or immunologic function.[48] Splenic tumors most commonly present with splenomegaly and diffuse parenchymal replacement may result in hematologic consequences. Moreover, a pathologic spleen is at risk for either spontaneous rupture or rupture with the slightest degree of external trauma, resulting in an intraabdominal catastrophe.

The most common primary tumors of the spleen are vascular in nature.[49] Benign primary vascular tumors of the spleen include hemangiomas and lymphangiomas. Both tumors are typically found incidentally. Hemangiomas are typically of the cavernous type and rarely rupture. On occasion, splenic hemangiomas are responsible for a consumptive coagulopathy, which may necessitate extirpation of the spleen because the process can be fatal.[50] Lymphangiomas are endothelial-lined lesions filled with proteinaceous material. Both hemangiomas and lymphangiomas may be single or multiple.[51] Littoral cell angiomas may present as single or multiple lesions.[52] Splenic hamartomas are well-circumscribed, nonencapsulated benign proliferations of normal splenic tissue elements.[48] Although most commonly an incidental finding at autopsy or on abdominal imaging, diffuse splenic hamartomas may result in hypersplenism. In addition, splenic hamartomas may be the cause of intraabdominal hemorrhage

after rupture.[53] Rarely, the spleen gives rise to lipomas[54] and angiomyolipomas.[55]

Hemangiosarcomas (Fig. 2) are the most common primary malignant tumor of the spleen and have received attention disproportionate to their incidence given the association with environmental factors such as vinyl chloride and thorium dioxide.[56] Splenic hemangiosarcomas may present with splenomegaly, anemia, pleural effusion, or spontaneous rupture. The prognosis is generally poor irrespective of the type of treatment rendered. Other sarcomas such as Kaposi's sarcoma arise within the spleen infrequently. When the spleen is the only site of disease or when splenic involvement by primary or metastatic sarcoma leads to symptoms, splenectomy would appear to be a reasonable option.

Various lymphoid processes may involve the spleen primarily. Although the spleen is more often a secondary site of involvement in Hodgkin's and non-Hodgkin's lymphoma, both may arise from the splenic white pulp. Primary lymphoma of the spleen (Fig. 3) may replace the organ diffusely or present as a multinodular process.[57] The spleen may also be affected by histiocytic tumors and angiofollicular lymphoid hyperplasia or Castleman's disease.[58]

The spleen may be involved by metastatic disease in up to 7 per cent of patients with malignant solid tumors.[48] Among the tumors that metastasize to the spleen, melanoma, adenocarcinoma of the breast, and lung cancer are most common. When the spleen is involved with metastatic disease, it is rarely the sole site of disease and therefore the role of splenectomy is generally reserved for palliation of splenomegaly or hypersplenism. Metastases to the spleen are usually an indicator of systemic disease and aggressive tumor biology, rendering splenectomy with curative intent generally inappropriate in these settings (Fig. 4).[59] Like with any tumor involving the spleen, rupture or abscess formation may occur and splenectomy may be required on these bases.

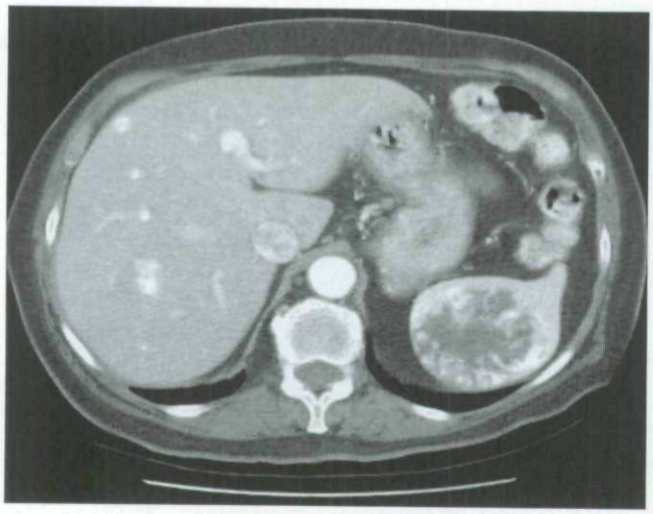

FIG. 2. Hemangiosarcoma of the spleen. Computed tomography scan of the abdomen with intravenous contrast demonstrates a mass within the spleen with areas of hypoattenuation and enhancement. The areas of enhancement are typical for vascular tumors such as hemangiosarcoma. The specimen measured approximately 8 cm in diameter and was completely resected.

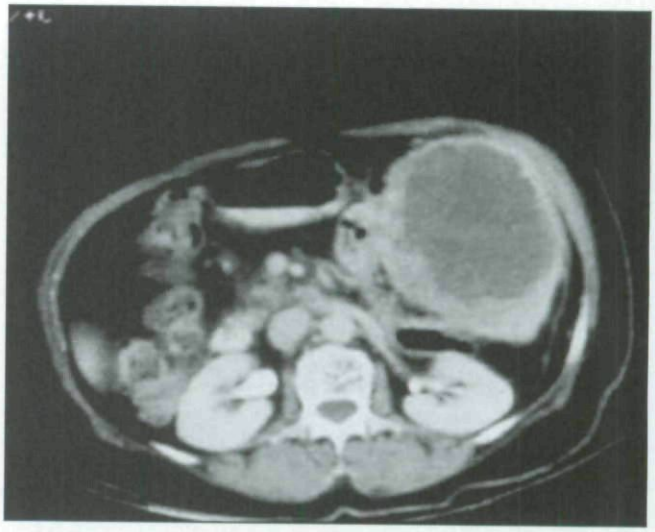

FIG. 3. Primary splenic lymphoma. The patient presented with symptoms related to splenomegaly and hypersplenism. This abdominal computed tomography scan with intravenous contrast demonstrated a low-attenuating lesion in the spleen. After splenectomy and a search for synchronous sites of disease, the diagnosis of primary splenic lymphoma was made.

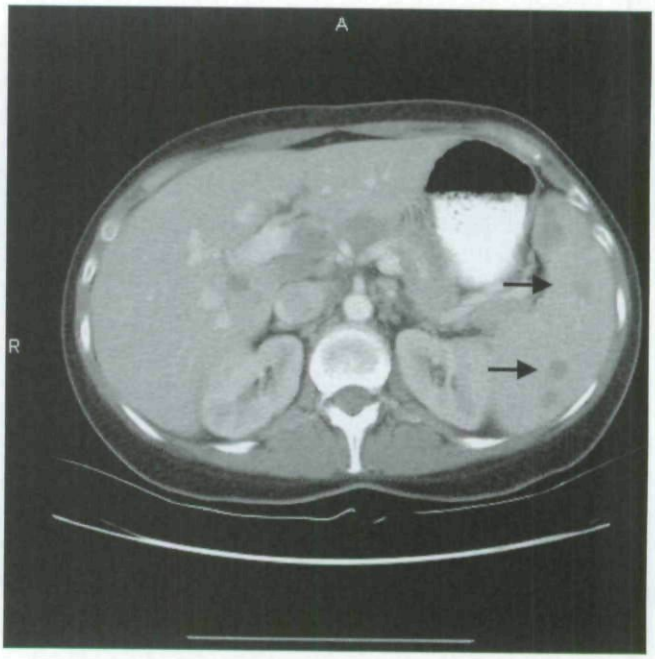

FIG. 4. Melanoma metastatic to the spleen. Several years after the excision of a cutaneous melanoma, this patient was found to have numerous low-attenuating lesions in the spleen and liver (arrows). These lesions were consistent with metastatic melanoma.

Benign Conditions Requiring Splenectomy

Gaucher's Disease

Gaucher's disease is an autosomal-recessive disorder in which glucocerebrosidase deficiency results in the systemic accumulation of glucocerebrosides, which may be accompanied by hepatosplenomegaly, anemia, thrombocytopenia, and skeletal manifestations. The spleen may be enlarged 60 to 70 times its normal size and 10 to 20 times its normal weight, and the degree of splenomegaly may correlate with disease progression.[60] Enzyme replacement therapy may result in hematologic improvement and reduction in organomegaly and bone pain for as long as 5 years.[61] Before enzyme replacement therapy, most patients with Gaucher's disease required splenectomy. Splenectomy is now reserved for persistent pancytopenias or pain, which may result from massive splenic expansion with associated infarcts. However, total splenectomy may promote accumulation of glucocerebrosides in other reticuloendothelial sites. Therefore, partial splenectomy is a reasonable option to limit the effects of hypersplenism and splenomegaly while minimizing the infectious and metabolic consequences.[62]

Wiskott-Aldrich Syndrome

Wiskott-Aldrich syndrome (WAS) is an X-linked immunodeficiency associated with autoimmune and inflammatory sequelae, including hemolytic anemia, thrombocytopenia, neutropenia, arthritis, vasculitis, and eczema.[63] Deranged natural killer T cell (NKT) function, which is known to possess immunoregulatory properties, may in part account for the autoimmune manifestations.[9] Bone marrow transplantation is the only definitive therapy for WAS but in some centers is reserved only for those with life-threatening complications.[64] Although the hematologic manifestations of WAS may respond to treatment with corticosteroids, immunosuppressive agents, or intravenous immunoglobulin, splenectomy is indicated for persistent thrombocytopenia.[63]

Chediak-Higashi Syndrome

Chediak-Higashi syndrome (CHS) is an autosomal-recessive immunodeficiency disorder involving defective leukocyte chemotaxis and phagocytosis. CHS may degenerate into an accelerated phase involving pancytopenia and cellular infiltration of the spleen.[65] Splenectomy may effectively address manifestations of hypersplenism when they are unresponsive to other modalities, including corticosteroids.

Splenic Cysts

Cystic lesions of the spleen may be divided into primary or true cysts and secondary or false cysts. True splenic cysts are parasitic, congenital, or neoplastic and typically have an epithelial lining. In contrast, false cysts lack a true epithelial lining and are most commonly a consequence of trauma. Splenic cysts may cause abdominal pain, become secondarily infected, or rupture. The appropriate management of splenic cysts depends on an understanding of their derivation and natural history.

Primary splenic cysts may originate as embryologic mesothelial inclusions[63] or represent a neoplastic process in which the squamous epithelial lining may be keratinized.[63] However, on a global basis, parasitic cysts are far more common than nonparasitic cysts of the spleen.[48] Although splenectomy may be necessary in the setting of excessively large cysts, splenic preservation is often possible. Cyst enucleation, partial cystectomy, and partial splenectomy have proven to be technically feasible. Splenic preservation may be possible in over 40 per cent of patients with echinococcal disease with recurrence rates comparable to those having undergone splenectomy.[66]

False cysts or pseudocysts of the spleen most commonly arise after trauma and account for the majority of nonparasitic splenic cysts.[67] Interestingly, only 30 per cent of such patients can recall a traumatic event. Splenic pseudocysts likely result from the formation of an inflammatory fibrous capsule surrounding the hematoma, which ultimately resorbs. A calcified rim is often present around the cyst (Fig. 5) and, in the ab-

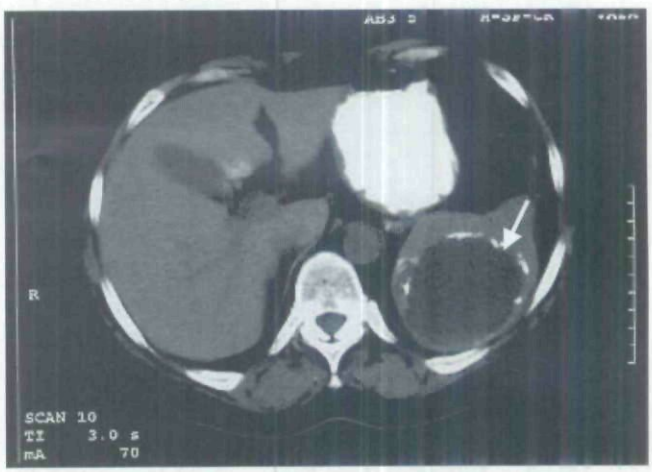

FIG. 5. Splenic pseudocyst. Several months after blunt abdominal trauma, this patient presented with left upper quadrant pain. A computed tomography scan of the abdomen demonstrating a large, well-defined cystic lesion of the spleen with a calcified rim (arrow). These imaging features are typical for a splenic pseudocyst.

sence of documented parasitic disease, is almost always indicative of a trauma. Small pseudocysts (<4 cm) tend to regress and should be observed in the absence of specific symptoms. Symptomatic pseudocysts or those greater than 5 cm should be treated surgically. If possible, preservation of a portion of the spleen should be attempted. In this regard, surgical options include cystectomy without splenectomy, partial splenectomy, or "decapsulization" of the cyst with or without omentopexy. Any of the aforementioned options may be approached traditionally or laparoscopically. It has been our experience that splenic pseudocysts >6 cm, especially those involving the medial portion of the spleen, have a tendency to recur when unroofed laparoscopically despite excising a large portion of the cyst wall. In our opinion, these pseudocysts are best managed by either partial splenic resection (Fig. 6). Occasionally, total splenectomy may be required (Fig. 7). Although percutaneous drainage of splenic pseudocysts has been described, the effectiveness of this approach is uncertain and the risk of secondarily infecting the lesion is not insignificant.

Splenic Abscesses

Perhaps owing to the potent immunologic capacity of resident splenic leukocytes,[9, 68] abscesses are rarely encountered in the spleen. The predominant manifestations are systemic such as leukocytosis and fever. Few patients present with localized symptoms. Splenic abscesses are unilocular in 65 per cent, multilocular in 8 per cent, and multiple in 27 per cent of cases.[69] The overall mortality rate is 13 per cent.[70] Like with other splenic lesions, abscesses may rupture with the potential for hemorrhage and disseminated peritonitis. Immunodeficiency is a common underlying factor and predisposes to fungal abscesses (Fig. 8). Other potential causes include endocarditis, intravenous drug abuse, pyogenic infections at distant sites, sickle cell anemia, and secondary infection of a traumatic pseudocyst.[71]

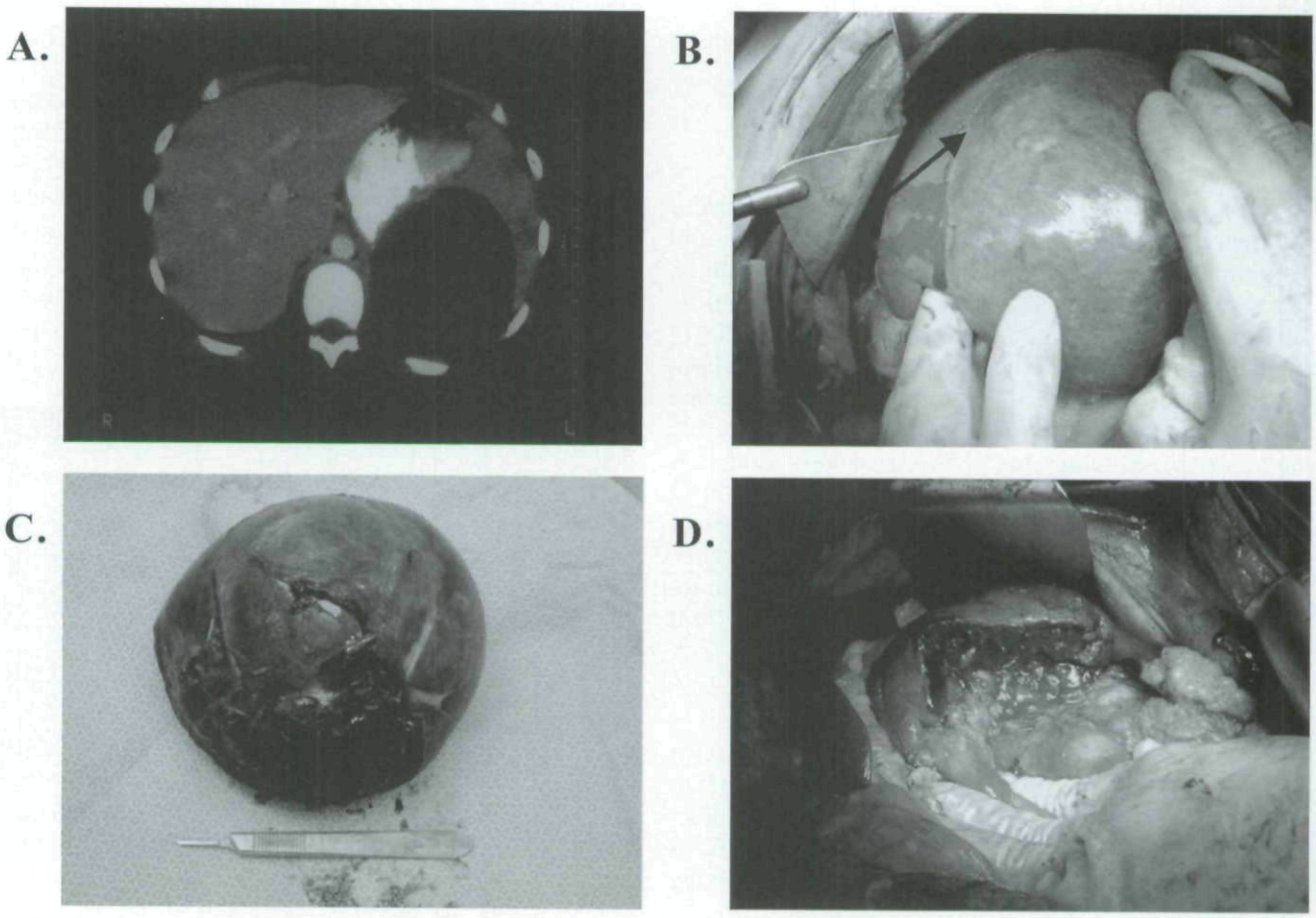

FIG. 6. Excision of a splenic pseudocyst. (A) Computed tomography scan of the abdomen demonstrating a large, well-defined cystic lesion of the spleen, which was found several weeks after blunt trauma. (B) The border between the pseudocyst and normal splenic parenchyma was identified (arrow). A cystectomy was performed, and the (C) intact pseudocyst and (D) residual spleen are demonstrated. Note that the greater omentum is generally conveniently situated for use in eliminating the cavity in the spleen after cyst excision.

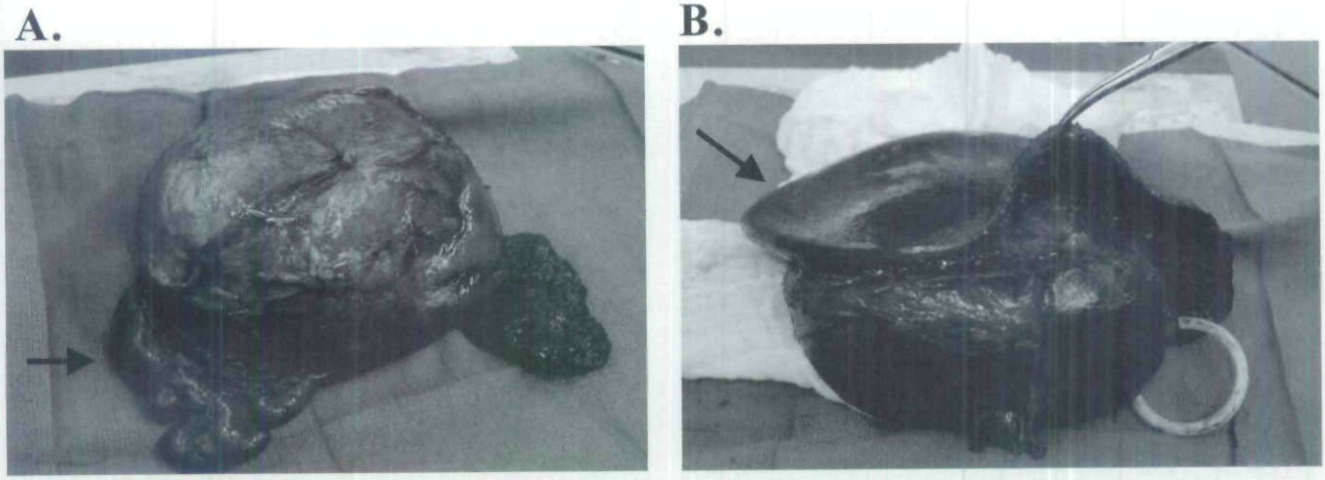

FIG. 7. Total splenectomy performed for pseudocyst. At times, splenic preservation is not possible given the size or location of a pseudocyst. In this case, splenectomy was performed for the treatment of this symptomatic pseudocyst. Note that the normal splenic parenchyma was markedly compressed (arrows) as a consequence of the pseudocyst (A and B).

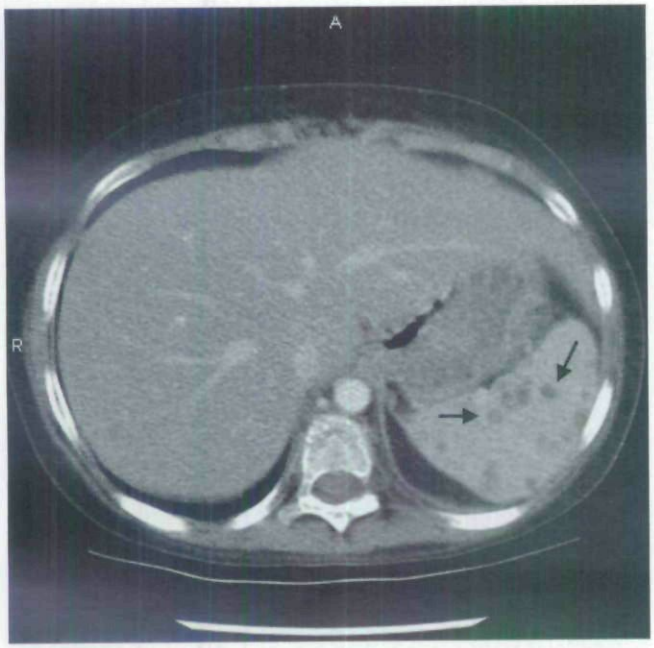

FIG. 8. Fungal abscesses of the spleen. Multiple low-attenuating lesions of the spleen representing abscesses resulting from *Candida albicans*. In this case, drainage was not possible as a result of the number of abscesses. The patient was treated with systemic antifungal agents and splenectomy was avoided.

Intervention, in some form, is mandatory for splenic abscesses because the mortality rate for untreated cases approaches 100 per cent. Initial management should be nonoperative, and image-guided percutaneous is particularly effective when the abscess is solitary and thick-walled.[71] If appropriate antibiotics have been administered in conjunction with percutaneous drainage in patients with unilocular abscesses and the clinical picture fails to improve within 48 hours, splenectomy should be undertaken without delay. Percutaneous drainage is less likely to be effective when a multilocular abscess is encountered. Under these conditions, splenectomy would appear to be the most effective definitive therapy.

Wandering Spleen and Splenic Torsion

Failure of the dorsal mesogastrium to fuse to the posterior abdominal wall may result in the absence of the spleen's normal peritoneal attachments. The lack of normal attachments such as the splenorenal and gastrosplenic ligaments predisposes the spleen to torsion and ischemia. Acquired factors such as the hormonal milieu of pregnancy may play a role as well.[72] Although most patients are asymptomatic, splenic torsion may manifest as recurrent bouts of abdominal pain. Persistent pain with a palpable, mobile mass suggests ischemia and possible infarction. The diagnosis may be reached by noting absence of intravenous contrast uptake within the spleen on computed tomography scanning. In the event of torsion with infarction, splenectomy is required.[73]

Trauma

Although splenectomy is often necessary after traumatic injury, nonoperative management of blunt splenic injury in the stable patient is currently the standard of care.[74] Spontaneous healing results in anatomic and functional restoration of the spleen.[1] Successful nonoperative management is also possible in patients with intrinsic splenic pathology. Eleven patients with HIV, acute leukemia, infectious mononucleosis, or sickle cell anemia were successfully managed without surgical intervention after splenic injury, demonstrating their ability to heal parenchymal disruption (Fig. 9).[75] However, in the setting of ongoing hemorrhage, hemodynamic instability, or con-

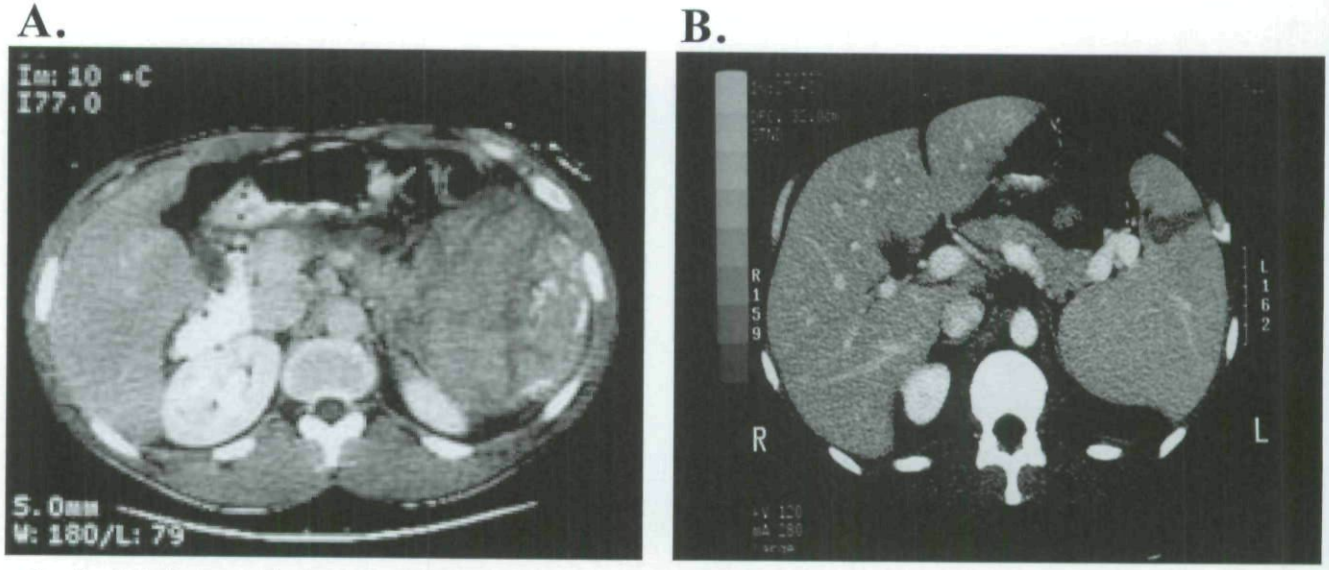

FIG. 9. Splenic rupture in the setting of HIV infection. The spleen undergoes pathologic changes in the setting of HIV infection. In this HIV-positive patient, a significant splenic injury was incurred after a motor vehicle accident. The splenic injury (A) was managed nonoperatively and a computed tomography scan 1 month after the injury reveals nearly complete healing.

comitant intraabdominal injury, splenectomy should be undertaken without unnecessary delay.[76] To achieve splenic preservation, a multidisciplinary approach may be necessary. Adjunctive splenic embolization may increase the chances for successful nonoperative management in appropriate patients.[77] When operative intervention is required, splenorrhaphy should be considered depending in the stability of the patient (Fig. 10).

Iatrogenic Injuries

Of note, up to 40 per cent of all splenectomies performed in the United States are a result of iatrogenic injuries caused during left hemicolectomies, antireflux procedures, and left nephrectomies.[78] With techniques described in this article, the overwhelming majority of these injuries can be managed without resorting splenectomy. Although preservation of splenic parenchyma should be attempted, splenectomy is the procedure of choice in the setting of excessive blood loss.

Surgical Therapy

Medical therapy may be inadequate or, at times, inappropriate in some patients with diseases involving the spleen. Patients may experience persistent abdominal pain, left shoulder pain, or early satiety. Massively

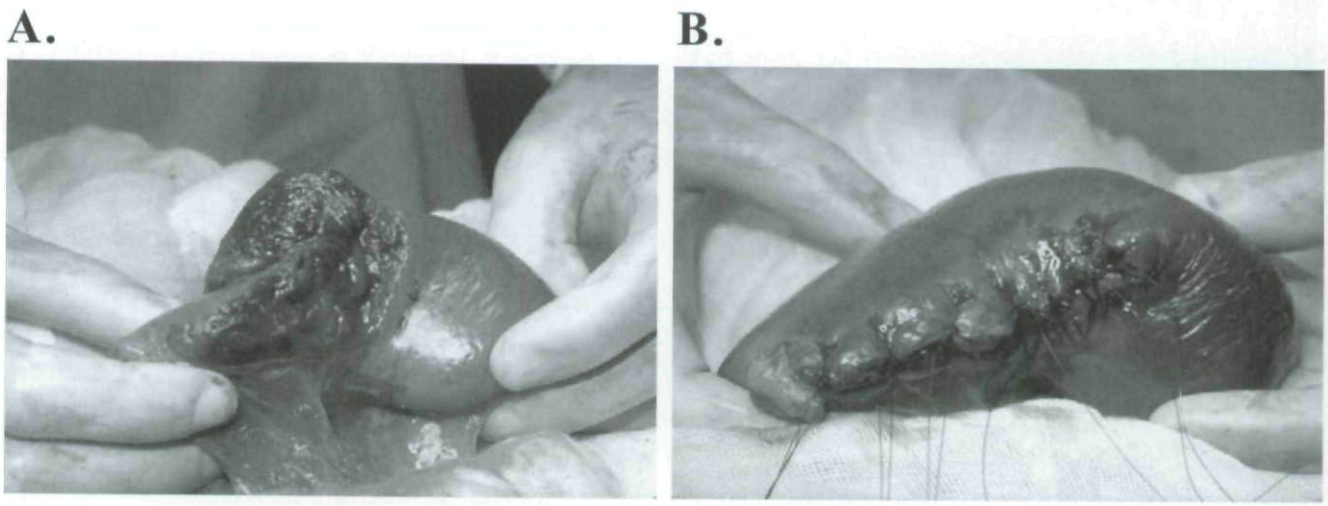

FIG. 10. Splenorrhaphy splenic preservation after traumatic injury (A) to the spleen is often possible and is desirable to avoid the risk of overwhelming postsplenectomy infection with its associated high mortality rate. In this patient, suture splenorrhaphy was performed with the edges of the injured splenic parenchyma reapproximated, whereas compression of the intervening tissue achieved hemostasis (B).

enlarged spleens may also cause an alteration of bowel habits or urinary frequency resulting from bladder compression. Nonoperative interventions may also fail to control anemia, thrombocytopenia, or neutropenia, leaving the patient susceptible to a variety of secondary complications. In some instances, splenectomy may also be necessary to reach a diagnosis such as in cases of idiopathic hypersplenism. As noted earlier, many of these patients harbor occult malignancy and therefore pathologic analysis of the splenic parenchyma is important when a cause for splenomegaly is not apparent. The importance of the aforementioned statement cannot be overemphasized, especially if a minimally invasive approach is used. Under these circumstances, the extraction site should be large enough so that adequate splenic parenchymal tissue is preserved for pathologic analysis.

Open Splenectomy

After the decision to perform splenectomy on a patient, the surgeon must ensure that the patient has received the appropriate immunizations and that hematologic deficiencies have been sufficiently corrected. Patients should be immunized against pneumococcus, *Haemophilus influenzae* type B, and group C meningococci.[79] Influenza vaccination may be considered as well. In addition, all patients should be prepared in anticipation of open splenectomy given the chance of conversion even if a laparoscopic approach is initially undertaken.

When performing open splenectomy (OS), adherence to sound principles of splenic surgery will maximize the chance of a successful outcome. Moreover, most of the concepts used in performing open splenectomy are applicable to the laparoscopic approach. The major pitfalls of splenectomy include hemorrhage, injury to the greater curvature of the stomach, pancreatic injury, failure to detect accessory spleens, and iatrogenic rupture of the spleen with subsequent implantation of splenic tissue within the peritoneal cavity. Ensuring complete hemostasis in the bed of the spleen at the conclusion of the operation is crucial. Areas deserving careful attention include the tail of the pancreas, the left adrenal gland, the posterior abdominal wall, and the left diaphragmatic surface. Diffuse oozing may require the administration of blood products, depending on the patient's underlying pathologic condition. To avoid pancreatic injury, the surgeon should clearly identify the pancreatic tail when managing the vasculature at the splenic hilum. In addition, the short gastric vessels must be defined and ligated with precision to avoid injury to the stomach and a potential gastric fistula.[80]

Early control and ligation of the arterial inflow is important not only to reduce the size of the spleen when it is enlarged, but it also allows for the safe transfusion of platelets without the fear that they will be rapidly consumed by the spleen. As the spleen decompresses and shrinks in size, further manipulation is facilitated and the risk of iatrogenic is significantly reduced. Moreover, maintaining the integrity of the splenic capsule is advisable for both oncologic and hemostatic reasons to minimize the chance of tumor dissemination or bleeding from the parenchyma.

Minimally Invasive Splenectomy

Laparoscopic splenectomy (LS) was initially described in 1991.[71] Because of a constellation of factors, including the advent of ultrasonic dissectors, improved optical technology, and use of endoscopic stapling devices, laparoscopic splenectomy is currently the preferred approach for benign splenic diseases.[71] The conversion rate for laparoscopic splenectomy performed for hematologic disease has been reported to be 5 per cent.[81] Although LS is associated with increased operative times, the duration of hospital stays are shorter and splenectomy-related morbidity is decreased.[82] Specifically, when splenectomy was performed for hematologic disease, the laparoscopic approach resulted in earlier initiation of oral feeding, earlier discharge, fewer blood transfusions, and a decreased analgesia requirement.[83]

Patients with malignant disease requiring splenectomy may have longer operative times and more blood loss during LS.[81] This is most likely related to the higher splenic volume typically present in patients with malignant disease in contrast to the benign processes such as ITP. Despite the increased operative time and blood loss, when LS is performed in the setting of splenomegaly, there were no statistically differences in conversion rates, time to discharge, or morbidity.[84] Splenomegaly cannot be considered an absolute contraindication to a minimally invasive approach but warrants careful patient selection and preoperative planning.[85] Hand-assisted laparoscopy may be of additional benefit when performing splenectomy in patients with splenomegaly and allow for removal of the intact organ when a histologic diagnosis is required.[86]

One criticism of the laparoscopic approach to splenectomy has been the lack of tactile feedback and perhaps an impaired ability to identify accessory spleens. The incidence of accessory spleens is approximately 15 per cent.[87] Failure to detect and ablate accessory splenic tissue may lead to treatment failure in cases in which the spleen is responsible for the destruction of platelets, erythrocytes, or leukocytes. These concerns, however, have not proven to be a significant impediment. Like in all of laparoscopic

surgery, lack of tactile sense is compensated for by experience. Furthermore, laparoscopy may instead facilitate detection of accessory splenic tissue because visualization is usually better than with an open approach. In a large meta-analysis, the rate of accessory spleen identification was similar among patients undergoing LS and OS.[82]

Splenic-Preserving Techniques

Partial splenectomy may be appropriate for treatment for certain benign conditions in which residual splenic tissue will not have undue hematologic or oncologic consequences. In most situations, preservation of sufficient normal splenic tissue lowers the risks of infectious complications. Between 30 per cent and 50 per cent of splenic tissue should be preserved along with an identifiable blood supply to preserve meaningful splenic function.[1] Subtotal splenectomy performed in children for hereditary spherocytosis can result in a prolonged decrease in hemolysis while offering the benefit of retained reticuloendothelial function in the splenic remnant.[88] As discussed earlier, splenic cysts have been treated by partial excision of the cyst wall or with "unroofing" procedures, and patients with Gaucher's disease may benefit from partial splenectomy. Partial cystectomy with omentopexy has been used in the management of hydatid disease[89] and traumatic pseudocysts have been effectively treated with subtotal splenectomy.[67] Approaches to splenic preservation in the setting of trauma include the use of suture splenorrhaphy, mesh splenorrhaphy, fibrin glue, and argon beam laser coagulation.[1]

Splenic Bed Drainage

Drainage of the splenic bed remains a controversial issue. The theoretic rationale for drainage of the splenic bed after splenectomy includes the removal of accumulated fluid, which could become a nidus for infection. Yet, it is uncertain if drainage of the splenic bed is of any significant benefit. Associated gastrointestinal injury and duration of drainage seem to be of greater significance in terms of postoperative morbidity than the presence or absence of drains.[90] If drains are to be used, then the closed suction variety such as a Jackson-Pratt should be used. To minimize infectious complication, drains should be removed as quickly as possible.

Postsplenectomy Complications

Early Morbidity

After splenectomy for hematologic conditions, the postoperative complication rate may reach 24 per cent. Patients having received corticosteroids are at highest risk for subsequent infectious complications.[14] In addition to commonly recognized postoperative complications such as wound infection, pneumonia, and sepsis, patients may develop a pancreatic or gastric fistula. When splenectomy is performed for hematologic disease, particular attention must be paid to the blood and platelet counts in the perioperative period.

Splenectomy may also be associated with an elevated risk for adverse cardiovascular events. Patients who undergo splenectomy for hereditary spherocytosis may experience a higher incidence of myocardial infarction, stroke,[91] and pulmonary hypertension.[92] In addition, splenectomy places patients at risk for other thromboembolic complications[75] such as splenic or portal vein thrombosis. Thrombotic prophylaxis with heparin products[93] and screening Doppler sonography[94] should be considered in high-risk patients. When screened with ultrasonography, portal or splenic vein thrombosis occurred in 55 per cent of patients after LS and 19 per cent after OS.[95] Furthermore, patients with fever or abdominal pain after splenectomy should be suspected of having portal and splenic vein thrombosis should be treated with anticoagulation therapy if this condition is documented.[94]

An additional clinical manifestation of splenectomy may be thrombocytosis. Theoretically, thrombocytosis after splenectomy may increase blood viscosity and create a more thrombogenic milieu. However, the relationship between postsplenectomy thrombocytosis and venous thrombosis is unclear.[96] The use of aspirin to treat postsplenectomy thrombocytosis must be considered on an individual basis taking into account the overall thrombotic diathesis, particularly the presence of an underlying myeloproliferative process. Most surgeons initiate antiplatelet or antithrombotic therapy at a platelet count greater than 750,00/mL.[97] Despite the potential for these complications, splenectomy can be performed safely in the vast majority of patients with benign and malignant disease who may benefit from removal of the spleen.

Late Morbidity

The immunologic effects of splenectomy include impaired responsiveness to new antigens, impaired phagocytic clearance of opsonized or unopsonized bacteria, and impaired production of the opsonin proteins tuftsin and properdin.[98] Therefore, patients having undergone splenectomy are at lifelong risk from bacterial sepsis.

Encapsulated bacteria such as *Streptococcus pneumoniae* are the most common pathogens involved in postsplenectomy sepsis.[99] The precise incidence of OPSI is not known because published reports vary considerably, which is in part the result of variations in

the study populations and definitions of OPSI. The annual incidence of OPSI has been reported to be as high as 0.23 per cent to 0.42 per cent[100] per year with a lifetime risk being 5 per cent.[98] In contrast, Cullingford reported the incidence of OPSI to be 0.04 per 100 person-years.[101] Although it is difficult to determine the precise incidence for OPSI, it is clear that its true occurrence has been often overstated.

The clinician must assess the individual patient's risk based on factors including the time interval from splenectomy, age, and underlying medical conditions. The risk of infection is highest in the first 2 years after splenectomy,[102] although it is unclear whether the risk of frank OPSI declines over time.[103] The risk of OPSI is elevated in children, in those with underlying hematologic or malignant processes, and those otherwise immunosuppressed.[103] Moreover, in patients with thalassemia major and sickle cell anemia, the incidence of infection and associated mortality is notably higher.[104] Less controversial is the lethal nature or OPSI. After the occurrence of OPSI, the mortality rates reported to range from 38 per cent to 69 per cent.[99] Therefore, the primary fear with OPSI may lie in its lethality rather than the frequency with which this complication occurs.

Several strategies to reduce the risk of OPSI have been used. Preservation of splenic tissue after trauma or utilization of splenic-sparing surgical techniques when possible should prevent OPSI when an adequate volume of parenchyma remains. Ideally, to maintain splenic immunologic function, at least 30 per cent of splenic parenchyma attached to an identifiable blood source should be preserved. Although autotransplanted splenic tissue has been shown to be both viable and functional, the true clinical impact of this procedure is uncertain[98] because the response to a specific bacterial antigenic challenge in humans is presently unknown. However, given its conceptual appeal and low risk of complications, autotransplantation of splenic tissue, if feasible, should be attempted.

If the entire spleen must be removed, the patient should be immunized with the Pneumovax vaccine against *S. pneumoniae*. Ideally, vaccinations should be given before splenectomy because the humoral response may be better with the spleen intact. Booster immunization should be given at 3- to 5-year intervals.[9] Vaccination against *Haemophilus influenzae* type b, *Neisseria meningitidis* type C, and influenza is generally recommended as well. Although prophylactic antibiotics should be given in the event of any dental or invasive medical procedure, routine antibiotic administration should be limited to 5 years in children and 2 years in adults after splenectomy.[105]

Any sign of infection in an asplenic individual must be considered a true medical emergency. The patient should receive immediate broad-spectrum intravenous antibiotic coverage subsequent to the withdrawal of blood samples for culture. Bacteremia can be demonstrated in nearly all cases of OPSI and bacteria are often present on a peripheral smear of the patient's blood.[99] Although intravenous immunoglobulin is theoretically appealing, evidence for its routine use is lacking.

Summary

The spleen is an important component of the immune and hematologic systems. When the spleen is responsible for or involved with pathologic processes, or when splenomegaly produces significant symptoms, operative therapy may be indicated. Given the potential complications of splenectomy, including OPSI, preservation of a critical mass of splenic parenchyma should be attempted when possible. In instances in which splenectomy is indicated, the laparoscopic approach may offer significant benefits. A sound understanding of the underlying pathophysiology of the process necessitating splenectomy and anticipation of the potential postsplenectomy complications will optimize the likelihood of successful clinical outcomes.

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