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E. J. Jindrich,[1] *M.D.*

Splenectomy and Sudden Death

Splenectomy has become a relatively common surgical procedure, most frequently performed subsequent to traumatic rupture, incidentally in the course of other surgical procedures, or in the staging or therapy of lymphomas. Occasionally it is a therapeutic modality in a hematologic disorder. Although initially considered to be associated with few serious sequelae, the recent medical literature contains numerous reports of fulminant death from bacteremia (usually *Streptococcus pneumoniae*) in splenectomized or hyposplenic patients. The following case reports exemplify some aspects of this clinical syndrome.

Case Histories

Case 1

A 53-year-old white man, in general good health, had a history of two previous surgical procedures for peptic ulcer disease. His spleen had apparently been removed in the course of one of the operations. Three days prior to admission he noted nonspecific illness characterized by nausea, vomiting, and abdominal discomfort which he treated with symptomatic medications. On the day of admission he suddenly became much worse symptomatically, and by the time he could be brought to the hospital he was comatose and in profound shock. His neck was slightly stiff, chest clear, abdomen silent but soft, and integument showed scattered petechiae, most common on the lower extremities. Blood pressure was 80 mm Hg with vasopressors, pulse 140/minute, arterial pH 7.09, Fibrindex® abnormal, prothrombin time 10.5%, hematocrit 40%, white blood count 10 400/mm^3 with 75% segmented neutrophils and 25% lymphocytes, and a random blood sugar of 13 mg/100 ml. Examination of the buffy coat revealed many gram-positive *Diplococcus pneumoniae* (Type V1 on culture). In spite of massive doses of Solu-Cortef®, Keflin® intravenously, kanamycin intramuscularly, penicillin intravenously, colistin intramuscularly, digoxin, vasopressors, and fluids, he died 2 h after admission with a final diagnosis of sepsis and disseminated intravascular coagulation.

Case 2

A 46-year-old black vocational nurse had enjoyed good health all of his life. He had no known diseases, and a medical workup in 1973 prior to his inclusion in a study control group revealed no abnormalities. Sickle-cell preparation and glucose-6-phosphate dehydrogenase were normal, and a serum electrophoresis showed a slight decrease in α_1, normal γ, and a slight increase in β-globulin. In December 1974, he was hospitalized in shock with a hematocrit of 18%, complaining of left upper quadrant abdominal pain,

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[1]Coroner, Marin County, San Rafael, Calif. 94903.

with no apparent antecedent trauma. Exploratory laparotomy revealed hemoperitoneum secondary to a capsular tear in a normal-sized spleen. Splenectomy was performed. Microscopic examination of the spleen revealed some hemosiderosis and plasmacytosis with Russell's bodies identified. Postoperative course was uneventful, and he returned to normal activities. Six months after the splenectomy he was hospitalized with an 8-h history of fever, shaking chills, and diaphoresis. Admission chest X-ray was within normal limits. His temperature was 104°F (40°C), his white blood cell count was 10 400/mm^3 with 71 segmented neutrophils and 24 bands, and examination of the buffy coat revealed many intra- and extra-cellular gram-positive cocci and diplococci (later proven to be Group-6 pneumococci). One gram of methicillin had been given on admission, and 4×10^6 units of penicillin was given intravenously with 2×10^6 units ordered every 2 h after identification of the apparent pneumococci. Vigorous supportive measures were instituted and continued. His condition continued to deteriorate, with increasing dyspnea (X-ray 2 h after the normal admission film showed "nickel" and "quarter"-sized bilateral nonsegmental patches and infiltrates) and large amounts of bloody diarrhea. Hematocrit was 45%; platelets, 57 000/mm^3; fibrinogen, 10 mg/100 ml; prothrombin time, less than 10%; and partial thromboplastin time, 150/37. He died 4 h after admission with a final diagnosis of fulminant pneumococcal septicemia with disseminated intravascular coagulation.

Case 3

A 31-year-old woman of Latin descent had undergone splenectomy for primary hypersplenism (characterized by easy bruising, petechiae of the legs, mild anemia, and persistently decreased white blood cell count and platelets) a few years prior to her death. At the time of splenectomy her bone marrow was described as being hypercellular with marked erythroid hyperplasia, numerous megakaryocytes, 6% plasma cells, and 7.5% eosinophils with markedly increased marrow iron. Serum immunoelectrophoresis revealed a moderate, diffuse increase in γM, γA, and γG. The spleen weighed 470 g and microscopically was characterized as consistent with congestive changes. Following splenectomy her clinical condition improved. On her last hospital visit she was seen by a physician for a two-day history of nausea, vomiting, muscle ache, and fever. It was stated that while at the hospital she became extremely dusky and blue. After she was examined, oral tetracycline was prescribed and she was discharged home. Upon arrival at home approximately 45 min after leaving the doctor's office she was again noted to be dusky, and she collapsed and was pronounced dead by an ambulance crew summoned by the family. The body was removed to the office of the local physician-coroner, and an autopsy was performed which revealed pulmonary and cerebral edema as well as petechiae of the skin. The death was certified as being due to primary myocarditis. Subsequent review of the microscopic slides by this author revealed no myocardial abnormalities. Cocci and diplococci were easily visualized in all tissues on the hematoxylin and eosin-stained materials, and the organisms stained positively with the Gram stain. The organisms were morphologically consistent with being pneumococci. There was no microscopic evidence of intravascular coagulation.

Case 4

A 37-year-old, divorced, white mother had a history of lupus erythematosus for 16 years. She had occasional episodes of pulmonary symptoms and had been on steroid medications for many years. Her anti-nuclear antibody test had remained persistently positive throughout her medical history. Five years prior to her death she had had a pro-

longed hospitalization for pneumococcal meningitis, followed by apparent complete recovery. There was one episode of generalized cutaneous rash treated successfully with high-dose steroids several years prior to her death. She had been asymptomatic on maintenance steroids until the evening prior to her death, when she complained of feeling intermittently hot and cold, sweating, having diarrhea, and heavy coughing. She was heard to be coughing frequently during the night, and was found dead on the floor next to the bed in the morning. The autopsy revealed a well-nourished woman with generalized cyanotic lividity not limited to dependent portions. The pleural and pericardial sacs were obliterated by fibrous adhesions. Vascular congestion of the lungs and liver was evident. The adrenal glands were markedly atrophied, the kidneys minimally scarred, and the brain edematous. The spleen was represented by a fibrotic tag of tissue weighing less than 5 g with no discernible parenchyma. The most striking microscopic findings were the atrophy and lipid depletion of the adrenals, the virtual absence of lymphocytes in the fibrotic spleen, and the numerous coccal bacteria (usually in pairs) in all organs easily visualized without special staining. There was a heavy growth of *Streptococcus pneumoniae* from the blood.

Discussion

The spleen plays a central role within the reticuloendothelial system by removing particulate matter and particulate antigens and with the production of antibodies. Splenectomy removes this particulate filter and results in an insufficient and delayed production of 19S antibodies during a primary immunologic response, and 7S antibodies in a secondary response [*1*]. Some investigators are of the opinion that the spleen produces specific pneumococcal opsonins [*2*]. Any deficiency of splenic function can be associated with an increased susceptibility to bacterial infection, often with a fulminant and fatal course. Although *Streptococcus pneumoniae* is responsible in the vast majority of bacterial infections, *Neisseria meningiditis, Haemophilus influenzae,* streptococci, staphylococci, *Escherichia coli, Klebsiella pneumoniae, Salmonella,* and *Pseudomonas aeruginosa* have also been implicated [*1,3,4*]. Fatal infections from *Plasmodium falciparum* and tic-borne protozoans of the genus *Babesia* have also been identified [*1*].

The exact incidence of infection in splenectomized individuals is uncertain. However, there is fairly general agreement that individuals with an underlying deficiency of reticuloendothelial function are at greatest risk. Fatalities have been reported in 15 to 20% of such patients [*5*], as have infection rates of up to 30% in splenectomized patients with thalassemia major [*6*]. Patients with lymphoma are at risk, in particular those with Hodgkin's disease who have a defect in cellular immunity [*7*]. Children under the age of 4 years also have an increased incidence of infection [*1,6*], particularly if the splenectomy was performed before the age of 1 year [*5*].

The incidence of fatal septicemia in persons splenectomized subsequent to trauma or incidentally is not well established, but definitely not insignificant. Recognition of the syndrome has resulted in an increasing number of case reports and series, and incidence estimates of between 2 and 9% have been made [*6,8*]. When fulminant pneumococcal sepsis does occur, however, the mortality rate may be 80% [*8*].

The mechanism of death from pneumococcal septicemia is at present unclear. Although cryptogenetic infection (no identifiable source infection) is uncommon in normal adults [*9*], an underlying infection is usually not identified in septic splenectomized persons. Symptoms tend to be nonspecific. The number of bacteria in the blood stream is extremely great, and they are frequently identified on routine blood smears or through microscopic examination of the blood buffy coat. They may be seen on tissue sections stained with hematoxylin and eosin or Gram's stain. It has been hypothesized that,

lacking a potent endotoxin, the great number of organisms is necessary to trigger a mechanism like disseminated intravascular coagulation [*10*], which results in death. Disseminated intravascular coagulation has been documented in many deaths, frequently in association with adrenal hemorrhage—the Waterhouse-Friderichsen syndrome [*5,7,10*]. It is of interest that pneumococcemia without asplenia is apparently not associated with the Waterhouse-Friderichsen syndrome [*10*]. Cutaneous purpura, especially of the head and trunk [*2,11*], has been observed and was present in two of the cases presented.

Summary

Four cases of fatal fulminant *Streptococcus pneumoniae* septicemia in asplenic individuals have been presented, demonstrating the relative lack of specificity of the symptoms and rapidity of the clinical course. Vigorous specific therapy was without apparent effect in two of the cases. No apparent reticuloendothelial deficiency prior to splenectomy was detected in two cases, and theoretically rather than clinically present in the others. One individual was hyposplenic secondary to splenic atrophy. The rapidity of the course and unexpected death will often bring such cases under the jurisdiction of the coroner or medical examiner, and medicolegal investigators should be alert for this syndrome.

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Marin County Coroner
Civic Center, Room 154
San Rafael, Calif. 94903