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Urgent Identification and Management of Postsplenectomy Sepsis

Urgent message: Asplenic individuals have a rate of severe infections two-to-three times higher than the general population. Postsplenectomy sepsis should be considered in patients with impaired splenic function who present with a fever.

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Case Presentation

A 45-year-old male presented to the urgent care with 18 days of sinus pain and congestion unresponsive to two courses of antibiotics, cefdinir and levofloxacin. Past surgical history revealed a splenectomy 20 years ago after a motor vehicle accident. Physical exam showed a temperature of 100.5°F and a heart rate of 114 BPM. Patient was well-appearing with normal heart and lung exams. He had mild frontal sinus tenderness.

Introduction

Individuals with impaired splenic function are at significant risk for severe infections leading to sepsis, with the risk being highest in the first 1-2 years postsplenectomy, but persisting lifelong.[1] Huebner and Milota opine that there is an opportunity for knowledge acquisition for primary care providers, who do not commonly see the devastating sequelae of missed diagnoses.[2]

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Condition Overview

The spleen is the largest collection of lymphoid tissue in the body and plays an important role in immune function, both in terms of innate immunity (ie, the body's natural, nonspecific defense mechanisms) and acquired immunity (immunity resulting from exposure to an agent).

The immune function of the spleen is to help clear encapsulated bacteria from the body, primarily *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b.[3,4] The spleen is also important for clearing intra-erythrocytic parasites like *Babesiosis* and *Plasmodium falciparum* (which causes malaria).[4]

Another important immune function of the spleen is to help produce IgM, which is important for the initial

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clearance of organisms from the body.[3,5] Consequently, asplenic individuals have a decreased response to polysaccharide vaccines and need more frequent boosters than the general population.[5,6] Asplenic individuals are more susceptible to severe infections, with a rate two-to-three times higher than the general population.[7]

Sepsis is defined as "life-threatening organ dysfunction caused by a dysregulated host response to infection."[8] *Postsplenectomy sepsis* is sepsis occurring any time after removal of the spleen.

The lifetime risk of postsplenectomy sepsis is about 5%. The risk for developing sepsis varies with patient population and depends on the individual's age, indication for splenectomy, and whether they have any additional ongoing immunosuppression. There is a higher risk if the splenectomy was due to a hematological disorder as opposed to trauma.[3] The greatest risk for developing postsplenectomy sepsis appears to be within the first 2 years after splenectomy, but this risk persists beyond that and likely lasts a lifetime.[3,6] The mortality rate for postsplenectomy sepsis ranges from 38% to 70%, even with adequate treatment.[3,5,6]

Keys To The Medical History And Physical Exam

Who Is at Risk?

Asplenia refers to complete loss of splenic function.

- Anatomical asplenia can be due to either a congenital condition or surgical removal, while functional asplenia occurs when diseases, such as sickle cell disease, cause the spleen to have decreased or absent function.
- Surgical asplenia following a trauma or for therapeutic purposes is the most common reason for asplenia.[1] There are approximately 25,000 splenectomies performed each year in the United States and the estimated number of asplenic individuals in the United States is around 1 million.[6]
- Congenital asplenia is rare.[6]

Hyposplenia is an acquired disorder associated with many different disease processes. The most common causes of hyposplenia are chronic graft vs host disease after stem cell transplant, celiac disease, and untreated HIV.[5] It is estimated that 50% of these patient populations have some degree of hyposplenia.[5,6]

Impaired splenic function in sickle cell disease begins manifesting at a very young age. Children under 3 years old are extremely susceptible to encapsulated bacteria, with risks 300–600 times higher than the general population's. The incidence of hyposplenia in celiac disease ranges from 33% to 76%. According to Di Sabatino, et al, the development of hyposplenia in this population appears to be related to gluten exposure prior to diagnosis. A gluten-free diet can sometimes restore splenic function—if there has not been irreversible loss of splenic tissue. Bone marrow transplantation is associated with hyposplenia 15%–40% of the time. The pathophysiology driving hyposplenia in these conditions is not well understood.[5]

While all patients with anatomic asplenia are at risk for severe infections, it is not as easy to determine the risk in patients with functional asplenia and hyposplenia because their splenic function is so variable.

The best way to determine splenic function has not been established. The gold standard for assessing splenic function is to count pitted erythrocytes; however, because of the specific equipment needed for this, it is rarely used in clinical practice. Most commonly, detection of Howell Jolly bodies on peripheral blood smear is used, but the sensitivity and specificity of this have been questioned, especially in milder forms of hyposplenia. Because of the difficulty in assessing splenic function, patients with functional asplenia and hyposplenia are typically treated like patients with anatomic asplenia when they present with signs and symptoms of a severe illness or fever.[5]

Clinical Features

Postsplenectomy sepsis often presents as a mild flu-like illness with fever, chills, sore throat, headache, muscle aches, vomiting, and/or diarrhea that can be hard to distinguish from other disease processes.[3] Fever in an asplenic patient should be taken seriously, as it could be the first sign of an infection that could rapidly progress to sepsis. Asplenic patients presenting without a fever, but who appear toxic, should also be treated very aggressively.[6] It is also important to remember that sepsis can present with a low body temperature, typically defined as less than 36°C.[8]

The most common foci of sepsis in asplenic individuals are the respiratory tract, abdominal cavity, and central nervous system; however, much of the time no focus is found.[9] While a healthy individual with a functioning spleen may take days to decline, asplenic patients can deteriorate within hours.[6] There is a high incidence of shock, hypoglycemia, acidosis, electrolyte abnormalities, respiratory distress, and disseminated intravascular coagulation in the asplenic patient population.[3]

Diagnostics and Initial Treatment

Individuals with impaired splenic function who present

Table 1. Vaccination Recommendations[1,6]

Organism	Primary Vaccinations		Boosters
	Initial	*8 weeks later*	
Pneumococcus	PCV13 (conjugate)	PPSV23 (polysaccharide)	PPSV23 booster every 5 years
Haemophilus influenzae type b	Conjugate Hib		None
Meningococcus	Conjugate ACWY	2nd dose of conjugate ACWY	Booster every 5 years
	Recombinant B+	2nd dose of recombinant B+	None
Influenza	Influenza vaccine		Annually

with fever and/or severe illness should be transferred to the emergency department for further evaluation.[2]

Early administration of broad-spectrum antibiotics is the most important action to decrease mortality from postsplenectomy sepsis.[3,4] Early goal-directed therapy including fluid resuscitation, vasopressor management, and airway management, in addition to early empiric antibiotics, has the potential to reduce mortality from postsplenectomy sepsis by 30% to 60%.[3]

Preventing Infection

Studies have demonstrated poor compliance among healthcare providers with the recommendations and guidelines for asplenic patients, especially in the outpatient setting.[1,2] Asplenia and hyposplenia are often overlooked as causes of immunocompromise, which places patients at risk for developing severe infections and subsequent sepsis. There are three main categories of recommendations that focus on prevention of postsplenectomy sepsis: patient education, vaccination, and empiric antibiotics.

Patient Education

Patients who have impaired splenic function should be informed about their lifelong increased risk of infection and educated about the signs and symptoms of infection and sepsis, as this education has been shown to reduce incidence.[1,4,10] A 2004 study by El-Alfy and El-Sayed demonstrated rates of postsplenectomy sepsis to be 1.4% among patients deemed to have good knowledge about their condition, versus 16.5% among patients who had poor knowledge.[10]

Patients should also be informed about the risk of animal bites and traveling overseas, as these increase the risk of severe infection in asplenic and hyposplenic patients. Dog bites in asplenic individuals can be associated with sepsis from *Capnocytophaga canimorsus*. Patients with impaired splenic function are also at increased risk of developing a severe malarial infection, so malaria prophylaxis is very important if patients are traveling to endemic areas. Most sources recommend patients with impaired splenic function seek expert consultation prior to traveling.[1] Patients without a functioning spleen are also at risk for severe tick-borne illnesses, including *Babesiosis*, necessitating that patients be counseled on how to avoid tick bites.[4]

Vaccination

There are three vaccines that target infections asplenic patients are especially prone to: pneumococcal, Hib, and meningococcal (see **Table 1**). The timing of vaccination will depend on whether the splenectomy is elective or emergent. There is some evidence to suggest that administration of the vaccines in the 2 weeks prior to or the 2 weeks after splenectomy can impair the body's immune response.[6] If the splenectomy is elective, patients should start the vaccine series at least 2 weeks prior to the procedure[1]; if the splenectomy is emergent, the series will typically not be initiated until at least 2 weeks after the splenectomy.[6]

There are two vaccines recommended to protect against *Pneumococcus*: Prevnar 13 (conjugate vaccine) and Pneumovax 23 (polysaccharide vaccine). Current recommendations are to start with the conjugate vaccine (Prevnar 13) and give the polysaccharide vaccine (Pneumovax 23) 8 weeks later. This sequence improves antibody concentrations because asplenic individuals have a decreased immune response to polysaccharide vaccines.[4,6] The polysaccharide vaccine should be re-administered every 5 years because antibody concentrations decline in asplenic individuals over this time period.[11] The Hib vaccine is recommended in patients who did not previously receive it as a child.[6]

There are two vaccines recommended for protection against *Meningococcus*: Conjugate ACWY and Recombinant B+. Both require two doses separated by 8 weeks. The conjugate vaccine should be re-administered every 5 years while the recombinant vaccine does not require

any boosters. It is also recommended for patients to get a yearly influenza vaccine, as influenza infection can predispose them to secondary bacterial infections with *Streptococcus pneumonia* and *Staphylococcus aureus*.[1]

"It is not uncommon for patients who do not have a primary care provider to seek care in the urgent care setting, so implementing these prevention strategies may fall solely on the urgent care provider."

Empiric Antibiotics

All asplenic individuals should have a supply of antibiotics to take empirically if they develop signs of infection and cannot get to a medical facility in a timely manner, to prevent the development of clinical sepsis.[6] Patients should be educated to go to a medical facility for evaluation if they develop fever, malaise, chills, or other constitutional symptoms. If they cannot get to a medical facility that can administer parenteral antibiotics within 2 hours, they should take a dose of the antibiotic they have on hand. All guidelines recommend empiric antibiotics in these cases, and patients should receive empiric antibiotics whether or not they are already receiving prophylactic antibiotics (discussed below). The chosen antibiotic should target encapsulated organisms, as these are the most common culprits in postsplenectomy sepsis. The most common regimens are amoxicillin or amoxicillin/clavulanic acid and, alternatively, levofloxacin or moxifloxacin if the patient has a penicillin allergy.[1,6]

A more controversial topic is the concept of prophylactic antibiotics, which are taken on a daily basis to prevent infection. Some sources recommend lifelong antibiotic prophylaxis in everyone with impaired splenic function, but the general consensus seems to be that only certain populations require long-term prophylaxis, including the first 3 years postsplenectomy, children under 5 years old, and anyone who has survived an episode of postsplenectomy sepsis.[1,2,6] The standard regimen for prophylactic antibiotics is penicillin because it is inexpensive, well-tolerated, and effective against encapsulated bacteria.[4]

Conclusion

Patients with impaired splenic function are commonly encountered in the urgent care setting, and the immunosuppressive nature of this disease is often overlooked. The warning signs for impending sepsis may be subtle in this patient population, so it is important to be especially cognizant of abnormal vital signs like fever and tachycardia. It is also imperative to be aware of the conditions that predispose individuals to impaired splenic function, like sickle cell disease, celiac disease, HIV, and stem cell transplantation, because many patients with impaired splenic function are unaware of their condition. The management and disposition differ for individuals with impaired splenic function compared to otherwise healthy individuals.

The three most important aspects of preventing postsplenectomy sepsis are patient education, vaccination, and the use of empiric antibiotics. It is not uncommon for patients who do not have a primary care provider to seek care in the urgent care setting, so implementing these prevention strategies may fall solely on the urgent care provider.

Case Resolution

The case presented at the beginning of this article concerns a patient who is clearly at risk for developing postsplenectomy sepsis. Red flags are that he had already completed two rounds of oral antibiotics without improvement and the fact that he is febrile and tachycardic. This patient was transported to the emergency department, then admitted to the progressive care unit for 5 days. He received IV antibiotics and his symptoms gradually started to improve, but no focus of infection was found. He was discharged home on PO antibiotics. ■

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