Overwhelming Pneumococcal Sepsis in a Patient with Splenic Hypoplasia

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A 58-year-old female was admitted due to severe sepsis and multi-organ failure with a fulminant purpuric rash. Meropenem, vancomycin and levofloxacin were administered, although no focus of infection was detected. However, computed tomography revealed a profoundly hypoplastic spleen, and a blood smear detected Howell-Jolly bodies. Blood cultures grew *Streptococcus pneumoniae* (serotype 22F) three hours after admission. The patient was finally diagnosed as overwhelming pneumococcal sepsis with hyposplenism precipitated by splenic hypoplasia. Clinicians should pay attention to the splenic size and Howell-Jolly bodies in cases of sepsis of unknown origin.

Keywords: *Streptococcus pneumoniae*, splenic hypoplasia, Howell-Jolly bodies, purpura fulminans, Pneumovax® 23, 23-valent pneumococcal polysaccharide vaccine

CASE REPORT

A 58-year-old female was admitted to Yokohama Municipal Citizen’s Hospital due to severe sepsis, and multi-organ failure in April 2013. She developed general fatigue, diarrhea and a high-grade fever of 42°C on the day before hospitalization. On the day of admission, the patient also developed dyspnea. She had a past surgical history of osteosarcoma at the age of 23 years and breast cancer at the age of 49 years requiring a mastectomy and axillary lymphadenectomy, followed by adjuvant chemotherapy and hormone therapy for five years. She had not been previously vaccinated with the 23-valent pneumococcal polysaccharide vaccine (PPSV23).

In the emergency room, her vital signs were as follows: blood pressure was 99/73 mmHg, heart rate was 100 beats/min, respiratory rate was 45 breaths/min, body temperature was 33.3°C and Glasgow Coma Scale was E3V4M6 (total 13/15).

Physical examination revealed purpura on her face and extremities (Figure 1), whereas other system examinations were unrevealing. Despite a whole body computed tomography (CT) scan, urine Gram staining, and rapid diagnostic testing (group A streptococcus, *Streptococcus pneumoniae*, and Influenza) from the patient’s throat, it was not possible to detect the...
evidence of infection. Laboratory studies were compatible with a systemic inflammatory response syndrome and multiple organ failure as follows: white blood cell (WBC) count 2,600/µL (neutrophils 77%, lymphocytes 23%) (reference range WBC 3500–9000/µL, neutrophils 43–69%, lymphocytes 23–48%), platelet count 20,000/µL (reference range 130,000–370,000/µL), aspartate aminotransferase 1,123 IU/L (reference range 8–37 IU/L), alanine transaminase 211 IU/L (reference range 4–44 IU/L), alkaline phosphatase 293 IU/L (reference range 104–338 IU/L), serum creatinine 3.66 mg/dL (reference range 0.2–0.9 mg/dL), blood urea nitrogen 38.3 mg/dL (reference range 8.0–21.0 mg/dL), immunoglobulin G 489 mg/dL (reference range 640–1800 mg/dL), fibrinogen 430.2 µg/mL (reference range <10 µg/mL), respectively. Using CT scan images, we detected no other abnormalities other than a significantly hypoplastic spleen (Figure 2). The volume of the patient’s spleen, as calculated by SYNAPSE VINCENT (FUJIFILM, Tokyo, Japan) with CT images, was approximately 27.5 ml (normal range for splenic size in Japanese was described in Discussion). In addition, Howell-Jolly bodies were detected in a blood smear. Overwhelming bacterial sepsis with encapsulated bacteria secondary to splenic hypoplasia was strongly suspected. Although no focus was detected, we administered meropenem 2 g, vancomycin 500 mg, and levofloxacin 500 mg, in addition to fluid resuscitation. On admission to the Intensive Care Unit, the Acute Physiology and Chronic Health Evaluation II (APACHE II) score was 54 points, the Sequential Organ Failure Assessment (SOFA) score was 16 points, and the predictive mortality rate was calculated at 98.9% based on the former score. Her blood cultures were positive for Gram-positive diplococci that were eventually typed as Streptococcus pneumoniae, just three hours after admission. Although intensive therapy including mechanical ventilation, continuous hemodialfiltration, vasopressor drugs, and blood transfusion were rapidly instituted, her general condition rapidly worsened, and within eight hours after admission she died in the ICU. A postmortem was not performed because the consent from the patient’s family had not been obtained.

Further microbiological results revealed that the serotype of S. pneumoniae was 22F, the PPSV23 covers. Moreover, the bacterium had a mutated pbp2x gene rendering it intermediate-penicillin resistant. However the bacterial strain was found to be susceptible to all the antibiotics that were administered.

**DISCUSSION**

Asplenia and hyposplenism are risk factors for developing overwhelming pneumococcal sepsis. The spleen has an important role in prevention against bacterial infection, particularly encapsulated organisms (S. pneumoniae, Haemophilus influenzae and Neisseria...
The spleen is an organ that acts as an endothelial filtration system with main properties involving phagocytosis, and the production of opsonins. Asplenic and hyposplenic patients, these functions are thought to be deficient and this is believed to be the reason for severe infection from encapsulated bacteria. This condition occurs mostly in children and is somewhat rare in adults. Most of the cases of overwhelming pneumococcal sepsis in adults have been reported in the post-splenectomy period. Few reports on the relationship between splenic hypoplasia and sepsis from encapsulated organisms have been published. In Japan, Yahagi et al, summarized 11 previously published adult Japanese cases. In a review of the literature, these cases had sudden symptoms including nausea, fever, abdominal pain, and diarrhea, and were referred to hospitals within several hours to two days from the time of onset. The clinical characteristics of our patient were compatible with the summary. However, Kubo et al, described the controversy in respect of whether splenic hypoplasia is also a risk factor for overwhelming pneumococcal sepsis. Firstly, there are no reports in the literature about congenital diseases causing splenic hypoplasia. Secondly, aging might result in atrophy of the spleen. Thirdly, the spleen might change in size when responding to excessive stress or increased adrenalin levels. Harris et al, reported an average volume of the spleen for Japanese persons. Among persons of 51 to 60 years of age, the spleen size averaged 119.3 ± 74.0 ml, whereas the spleen size was larger among younger persons (20 to 30 years of age; 171.0 ± 57.8 ml, 31 to 40 years of age; 132.4 ± 56.7 ml). Although we could not clarify whether our patient’s splenic hypoplasia was congenital, CT images obtained in 2005 also revealed splenic hypotrophy. In addition, Nakagawa et al, clarified the relationship between Howell-Jolly bodies and splenic hypoplasia. Of 149 participants in whom Howell-Jolly bodies were detected, 20 cases had hypoplastic spleens (mean volume: 44.2 ml; range: 12.9 to 124.4 ml; age range 33 to 95 years). Howell-Jolly bodies, which are an indicator of hyposplenism, were present in our patient’s blood smear and support a deficit of splenic function due to hypoplasia. Three points for the prevention of overwhelming sepsis are vaccination, antibiotic prophylaxis, and awareness of hyposplenism. In Cherif’s report, 28% of splenectomized patients with hematological diseases were classified as poor responders to PPSV23. Conversely, in a retrospective population-based cohort study concerning the efficacy of PPSV23 for asplenic patients, the mortality rate for a pneumococcal vaccine cohort was less than that of a cohort without pneumococcal vaccination (28.44/1000 person-years versus 45.78/1000 person-years, adjusted Hazard Ratio = 1.07, 95% Confidence Interval 0.70–1.65) although it was not statistically significant. PPSV23 administration might have altered our patient’s eventual clinical outcome. Australian guidelines which are one of the most detailed and newest guidelines concerning the management of asplenic and hyposplenic patients, recommends antibiotic prophylaxis in combination with vaccination against encapsulated bacteria. However, the duration of prophylaxis being unclear, adherence to taking daily medications, and the acquisition of drug-resistant bacteria are current unresolved problems. For prevention, the most important point is the physician’s and the patient’s awareness of a hyposplenism. Asplenia and splenic hypoplasia detected by CT or ultrasonography by chance, present opportunities to search for Howell-Jolly bodies. If hyposplenism is confirmed, physicians must consider preventive measures and warn the patient about the risk of overwhelming sepsis.

CONCLUSION
We have reported a case of overwhelming pneumococcal sepsis with splenic hypoplasia as evidenced by CT scan evaluation and the presence of Howell-Jolly bodies by blood smear. Through this case and a review of the literature, we consider that splenic hypoplasia is a potential risk factor for overwhelming pneumococcal sepsis. Clinicians should carefully check splenic size and check for the presence of Howell-Jolly bodies on blood smears in patients with sepsis of unknown origin. The administration of the PPSV23 must be strongly considered for hyposplenic patients due to splenic hypoplasia.
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Conflicts of interest
None.

References