Case Report

Overwhelming postsplenectomy infection

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ABSTRACT. This report aims to deepen the understanding of the pathogenesis, diagnosis, clinical characteristics, and treatment of overwhelming postsplenectomy infection (OPSI). A patient treated at Taihe Hospital for tuberculous OPSI is described, and relevant literature is reviewed. Broad-spectrum antibiotics, suppression of the systemic inflammatory reaction, and anti-shock measures were the keys to the successful treatment of this condition. OPSI is a life-threatening condition and has a high mortality rate. Early diagnosis, use of anti-inflammatory glucocorticoids, and administration of high-dose gamma globulin and ulinastatin for the treatment of OPSI may improve outcomes.

Key words: Splenectomy; Overwhelming infection; Retrospective study
INTRODUCTION

Overwhelming postsplenectomy infection (OPSI) is an uncommon disease that is rarely seen in general hospitals (Morgan and Tomich, 2012). Therefore, errors in the diagnosis of OPSI often occur. Tuberculous OPSI is an even rarer condition, and few retrospective studies have reported on it (Polák et al., 2012). To deepen understanding of the pathogenesis, diagnosis, clinical characteristics, and treatment of OPSI, we report here on the diagnosis, disease progression, salvage, and treatment in the intensive care unit of a patient with tuberculous OPSI at Taihe Hospital.

CASE REPORT

A 39-year-old man was emergently hospitalized 2 h after the sudden onset of shivering, hyperpyrexia (temperature 40.1°C), headache, and projectile vomiting. The patient also complained of lightheadedness, pharyngeal discomfort, and malaise a day before, and he had self-administered “Gankang” tablets (cold medicine) without effect.

The patient had undergone a splenectomy after a traumatic liver rupture 2 years before. He had no history of hypertension, diabetes, or contagious diseases, such as hepatitis or tuberculosis. He worked as a designer in a construction company and had no known history of exposure to any toxic chemical or stimulant. Furthermore, he denied use of tobacco, alcohol, and illicit drugs. The patient lived with his wife and child and owned a pet dog. He gave no history of recent travel or contact with ill individuals.

On admission, the patient was conscious, with a moderately distressed face. His vital signs included temperature 39.6°C, heart rate 110 beats/min, respiratory rate 32 breaths/min, blood pressure 85/50 mmHg, and oxygen saturation 86%. He exhibited cyanotic lips and fingertips and noticeable pharyngeal congestion, but without tonsillar swelling or secretions. No heart murmur or pulmonary dry/moist rales were heard. Abdominal examination was unremarkable. Discrete hemorrhagic maculopapules were sporadically distributed over the patient’s entire body. The patient had normal orientation but was slow to respond. He had a tonic neck (2 fingers), and positive Brudzinski’s and Kernig’s signs.

The patient’s white blood cell count was 3.9 x 10^9/L (78% neutrophils) with a hemoglobin level of 130 g/L and platelet count of 69 x 10^9/L. Chest X-ray was normal. Coagulation indices were as follows: prothrombin time 15.6 s (International Sensitivity Index 1.52), activated partial thromboplastin time 76.3 s, fibrinogen 12 g/L, D-dimer positive, and blood sedimentation 55 mm/h. Peripheral blood smears showed mature neutrophils, no immature bone marrow cells, and a reduced number of platelets. Blood gas results were as follows: pH 7.325, PCO₂ 27.4 mmHg, PO₂ 66.5 mmHg, HCO₃, 23.5 mM, and base excess -4.5 mM. The patient’s hepatic and renal functions were basically normal. Chest and abdominal computed tomography (CT) revealed no pulmonary abnormalities but showed small volumes of hemorrhage from the adrenal glands bilaterally. On lumbar puncture, cerebrospinal fluid (CSF) showed a pressure of 260 cm H₂O, with 0.68 g/L protein, 4.0 mM glucose, 100 mM chloride, and positive acid-fast stain.

The patient was diagnosed with tuberculous OPSI accompanied by multiple organ failure, including disseminated intravascular coagulation (DIC) and circulatory and respiratory failure.

On day 1 after hospitalization, the patient received dual-channel oxygen inhalation, fluid replacement, and vasopressors for treatment of shock, and low-dose heparin and fresh...
plasma transfusion for DIC. After the CSF results were obtained, the patient was started on combination therapy for tuberculosis with isoniazid, rifampicin, ethambutol, and amikacin. The patient’s blood pressure was 90/60 mmHg after resuscitation. On day 2, the patient’s body temperature remained elevated, his dyspnea did not improve, his BP failed to normalize, his DIC worsened, and he became oliguric. Accordingly, 100 mg hydrocortisone was administered every 6 h. On day 3, the patient’s body temperature returned to a normal level, dyspnea noticeably lessened, BP normalized, and blood coagulation function slightly improved. The combination therapy for tuberculosis was continued for 1 week, and the patient’s condition further improved. Hemogram, blood coagulation function, and chest and abdominal CT scans revealed no abnormalities. After leaving the hospital, the patient received continuous treatment for tuberculosis and recovered after 1 year of treatment. Extrapulmonary tuberculosis did not occur during the treatment.

**DISCUSSION**

OPSII is diagnosed based on the following criteria: 1) history of total splenectomy, 2) typical symptoms of sudden systemic infection, 3) dermatorrhagia and DIC, 4) positive bacterial blood culture or smear examination, 5) no specific loci of surgical infection, and 6) hemorrhage from bilateral adrenal glands and internal organs (Zuo et al., 2005).

Our patient was diagnosed with tuberculous OPSI for the following reasons: First, the patient was young and healthy without a history of chronic illness. The disease occurred 2 years after splenectomy, which is an onset time consistent with that of OPSI. Second, the disease had a sudden onset and fast progression, manifested initially as symptoms of an upper respiratory tract infection, followed soon afterward by sudden, severe toxic shock and then DIC. Third, CSF acid-fast staining was positive. Fourth, the patient was hemorrhaging from both adrenal glands. All these features basically met the diagnostic criteria for OPSI.

The spleen, which contains a small amount of hematopoietic stem cells, is the largest immune organ in the body. In the wall of the splenic sinusoids are micropores that filter off bacteria for removal by macrophages. The spleen contains a large amount of immune competent cells, such as macrophages, T- and B-lymphocytes, natural killer cells, and dendritic cells. Furthermore, the spleen produces opsonins, complements, and endogenous cytotoxic factors. Therefore, total splenectomy leads to a decrease in immunity, including a decrease in the functions and numbers of T- and B-lymphocytes, decrease in serum immunoglobulin M, filtration dysfunctions of microporous cells and Howell-Towelly’s globules, decrease in the concentrations of blood properdin and opsonin, and reduction of Tuftsin (Cameron et al., 2011). Normally, the phagocytosis of pneumococci requires the spleen to provide opsonizing antibodies. Thus, splenectomy causes a decrease in phagocytosis. Under such condition, virulent bacteria can abundantly proliferate in the blood to cause septicemia, leading to a severe systemic inflammatory reaction syndrome, such as septic shock, internal environmental disturbance, DIC, respiratory distress syndrome, and, ultimately, OPSI (Cameron et al., 2011). Although the pathogenesis of OPSI remains unclear, it has been proved that splenectomy delays the removal of endotoxins (causing their accumulation in tissues), increases lipopolysaccharide binding protein mRNA expression, and increases the sensitivity of endotoxin-activating cells; these effects consequently induce the generation of a large number of inflammatory factors, leading to an uncontrolled systemic inflammatory reaction, thereby resulting in serious organ damage (Xu et al., 2011). In addition, tumor necrosis factor alpha induces nitric oxide synthase
to release abundant nitric oxide, which may also constitute part of the pathogenesis of OPSI.

OPSI has a fast, overwhelming onset. It first manifests as a slight upper respiratory tract infection and then progresses to hyperpyrexia, headache, shivering, jaundice, anuria, coma, and septic shock. In the early stages of OPSI, DIC, multiple organ dysfunction syndrome, and acute respiratory distress syndrome occur. Patients present with acute respiratory distress; adrenal hemorrhage; hepatic, renal, cardiac, and pulmonary dysfunctions; hyperkalemia; severe metabolic acidosis; and serious disturbances of fluid and electrolytes; death often occurs within 48-72 h. Conventional antibiotic treatment has no effect on OPSI (Chihara et al., 2010). Blood cultures can show the number of bacterial colonies as >10^6/mL, which is approximately 10,000 times higher than the colony count in common septicemia. Our patient was diagnosed with tuberculous OPSI, an even rarer condition than OPSI from other causes. Normally, CSF acid-fast staining has a very low positive rate; for example, no positive CSF acid-fast staining was observed among 83 patients with tuberculous meningitis (Ho et al., 2013). However, in our patient, CSF acid-fast staining was positive, which suggests a large number of acid-fast bacilli and is in line with the characteristics of OPSI bacterial infection.

The primary pathogenic bacteria of OPSI are pneumococci, meningococci, and *Haemophilus influenzae*; streptococci, *Escherichia coli*, and other bacterial species may also be causative (Coignard-Biehler et al., 2008). The incidence of OPSI varies according to the reason for the antecedent splenectomy; OPSI incidence after traumatic splenectomy is 3.4%, whereas its incidence after pathological splenectomy is as high as 12.1% (Coignard-Biehler et al., 2008). Furthermore, OPSI is most closely correlated with malignant diseases (plus chemotherapy, 5.63%), followed by advanced schistosomiasis and other types of hepatic cirrhosis (3.68%), hematologic diseases (3.13%), and traumas (5.63%); it is not correlated with intraoperative accidental traumas, wandering spleen, splenic cyst, or splenic abscess (Coignard-Biehler et al., 2008). The risk of OPSI also correlates with age at the time of splenectomy and is high in children, particularly in those less than 2 years old.

OPSI is primarily treated with integrated therapy, which includes low-dose antibiotics, reinforced supportive treatment, anti-shock measures, fluid replacement, and correction of electrolyte disturbances and acidosis. However, none of these interventions has a high success rate, and OPSI is still very difficult to cure. Therefore, prevention becomes the key point in the treatment of OPSI (Coignard-Biehler et al., 2011).

Tuberculosis has a high incidence worldwide. It is also one of the most common causes of nonidiopathic adrenocortical hypofunction. However, it seldom involves the adrenal cortex. In our patient, CT scanning showed bilateral adrenal hemorrhage, a condition that frequently occurs in patients taking anticoagulants and sometimes in those with meningococcus or pseudomonas sepsis, and which can lead to adrenal crisis. When neither vasopressors nor volume resuscitation achieves a satisfactory effect in patients at risk for adrenal hypofunction during significant stress or infection or in those with promoting risk factors (e.g., acquired immune deficiency syndrome, tuberculosis, anticoagulant administration, and metastatic carcinoma) who present with symptoms of shock, acute adrenocortical insufficiency should be taken into consideration. A large dose of intravenous isotonic saline solution should be administered to these patients along with high-dose glucocorticoids (normally, 100 mg hydrocortisone every 6 h) (Coignard-Biehler et al., 2011). In addition, the treatment of the patient’s primary disease is very important. After patients’ pathogenetic conditions become stable, the dosage of glucocorticoid is reduced to an oral maintenance level. The successful treatment of tuberculous OPSI in our patient indicates that an early diagnosis and directed therapies (i.e.,
anti-pathogenic bacteria, anti-inflammation, anti-shock, and anti-DIC) based on the understanding of the pathogenesis of OPSI, along with internal environmental stabilization, are of great significance.

The basic method for preventing OPSI is to avoid unnecessary total splenectomies and to individualize treatment approaches for splenic injuries and neoplasms according to different conditions (Jones et al., 2010). Patients who have undergone total splenectomies should have frequent follow-ups. Furthermore, preventive measures should be adopted as follows: First, antibiotics should be used for at least 18 months to 2 years to prevent infections. Second, multivalent vaccines should be administered for the generation of active immunity, which has certain value for preventing OPSI, although whether this measure is effective for patients with asplenia remains to be explored (Jones et al., 2010). In view of the case of tuberculous OPSI in this report, whether bacillus Calmette-Guerin vaccine should be readministered and whether revaccination has an effect need further exploration. Third, education for patients with asplenia should be strengthened—guidance should be given for appropriate participation in outdoor activities, and exposure to cold temperatures should be prevented as much as possible. Once fever and influenza-like symptoms occur, prompt medical evaluation is needed.

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REFERENCES


