Case of Invasive Streptococcus Dysgalactiae Infection Presenting as Infective Endocarditis with Multiple Brain Embolisms

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Summary
A 65-year-old Japanese man complaining of general malaise and presenting with high fever was admitted to our hospital. He had untreated diabetes and hepatocellular carcinoma with liver cirrhosis. Overall findings of the patient indicated sepsis. Two blood cultures were positive for Streptococcus dysgalactiae, a group C or G Streptococcus. Transthoracic and transesophageal echocardiography revealed vegetations on the aortic and mitral valves. Although antimicrobial therapy with aminobenzyl penicillin was effective for controlling infection, multiple cerebral embolisms occurred in the clinical course of the disease. Primary care doctors should consider invasive Streptococcus dysgalactiae infections when treating elderly patients with underlying diseases, and Streptococcus dysgalactiae should be included in the list of microorganisms considered to cause endocarditis in such patients.

Key words: Vegetation, Antimicrobial therapy, Echocardiography

In 1996, Streptococcus dysgalactiae subsp. equisimilis (SDSE) was proposed as a new taxon involved in human streptococcal infections. SDSE has Lancefield group C or G antigens and exhibits strong beta-hemolysis. The spectrum of SDSE diseases ranges from pharyngitis, tonsillitis, and skin and soft-tissue infections, such as wound infections and cellulitis, to life-threatening necrotizing fasciitis and streptococcal toxic shock syndrome. SDSE infections typically occur among elderly patients with underlying malignancies or diabetes, and cellulitis is the most common clinical manifestation in SDSE bacteremia. Invasive SDSE infections are currently being increasingly observed worldwide. However, SDSE is a rare cause of infective endocarditis (IE), whereas oral streptococci, Streptococcus bovis group, and staphylococci are common causative microorganism of IE. In this paper, we report the case of an elderly man with native valve IE caused by Streptococcus dysgalactiae infection that was complicated by cerebral embolisms.

Case Report
A 65-year-old Japanese man was admitted to the emergency department of our institution complaining of general malaise and weakness. A few days earlier, he felt sick and was anorexic. Five years before admission, he underwent amputation of his right thumb because of cellulitis and osteomyelitis caused by methicillin-susceptible Staphylococcus aureus. He was diagnosed with diabetes at this point but discontinued his prescribed medical therapy shortly after diagnosis. He smoked five cigarettes a day and consumed 20 units of alcohol each week. Upon admission, his body temperature was 38.9°C, heart rate was 120 beats/minute, blood pressure was 109/61 mmHg, respiratory rate was 48 breaths/minute, and oxygen saturation was 96% while breathing ambient air. Neurological findings were normal. A cardiac examination revealed normal S1 and S2 sounds with grade 2 systolic murmurs at the apex. Laboratory testing revealed elevated white blood cell count (9,800 cells/μL), creatine kinase (4,853 IU/L), total bilirubin (2.0 mg/dL), aspartate aminotransferase (137 IU/L), lactate dehydrogenase (551 IU/L), gamma-glutamyl transpeptidase (1,508 IU/L), C-reactive protein (25.1 mg/dL), creatinine (1.84 mg/dL), plasma glucose (239 mg/dL), and glycated hemoglobin A1c (9.1%). The platelet count was 56,000 cells/μL. Electrocardiography revealed sinus rhythm and complete right bundle branch block at a rate of 129 beats/minute. Chest X-ray revealed no pulmonary congestion. Overall findings indicated sepsis, a life-threatening organ dysfunction caused by infection (Sequential Organ Failure Assessment Score: 8). Two sets of blood cultures were obtained. Antimicrobial therapy with meropenem (1 g/day) was immediately initiated. Contrast-enhanced abdominal computed tomography revealed a nodular lesion (15 mm in size) in the anterior segment of the liver in the background of cirrhosis. However, the focus of infection was not identified. Two blood cultures were positive for Streptococcus dysgalactiae (Mi-
transesophageal echocardiography revealing cord-like vegetation on the aortic valve (A) and irregular border vegetation on the mitral valve (B).

Figure 2. Brain magnetic resonance images with diffusion-weighted imaging showing multiple acute embolisms in left posterior lobe (A) and bilateral front-parietal lobe (B).

croscan Walkaway 40 Plus system, Beckman Coulter, Tokyo, Japan). The susceptibility of the strains to aminobenzyl penicillin and penicillin G was excellent [minimal inhibitory concentrations (MICs), < 0.12 and < 0.03 μg/mL, respectively]. Therefore, the antimicrobial treatment was switched from meropenem to aminobenzyl penicillin. The patient’s conditions improved, and his fever was resolved on day 5 following admission. Transthoracic echocardiography (TTE) was performed on day 7 for suspected IE and revealed vegetation on the non-coronary cusp of the aortic valve. TTE also revealed mitral annular calcification with mild mitral regurgitation and mild aortic valve sclerosis without aortic regurgitation. The patient was then referred to our department for further examinations and treatment. Transesophageal echocardiography (TEE) revealed vegetations on the aortic valve and on the posterior leaflet of the mitral valve (Figure 1A, B). The vegetation on the aortic valve was cord-like, 20 mm in length and that on the mitral valve had an irregular border, 10 × 5 mm in size. Both vegetations were mobile. Valve surgery for the prevention of embolism was proposed, but the patient rejected the surgery. On day 16, the patient complained of inaccuracy of vision, and right visual field defect was observed on neurological examination. Magnetic resonance imaging with diffusion-weighted imaging demonstrated multiple acute embolisms in the left posterior lobe, right cerebellar hemisphere, and bilateral front-parietal lobe (Figure 2A, B). The patient was observed closely and continued to receive antimicrobial treatment. Subsequent examinations using TTE and TEE revealed decreased size of the vegetations. Mitral regurgitation did not deteriorate, and annular abscesses were not detected. The patient did not develop heart failure, and his visual impairment marginally improved. After rehabilitation for several weeks, he was discharged on day 68 and continued to receive oral antimicrobial treatment in our outpatient clinic. He was followed-up on an outpatient basis for 34 months, and no clinical or echocardiographic signs of recurring endocarditis were noted.

Discussion

In this report, we describe a case of IE caused by Streptococcus dysgalactiae, which is an uncommon cause of IE.5-10 Streptococcus dysgalactiae can be classified into five distinct subtypes, and human disease is most fre-
quently associated with *Streptococcus dysgalactiae* subsp. *equisimilis* (SDSE), Lancefield serogroup C or G.

Although our laboratory system could not identify the subspecies of *Streptococcus dysgalactiae*, SDSE was the most probable causative microorganism in the present patient. SDSE is a common colonizer of the pharynx, skin, gastrointestinal tract, and female genital tract and is a member of the normal human flora. It can cause wound infection, cellulitis, life-threatening necrotizing fasciitis, pneumonia, arthritis, osteomyelitis, meningitis, endocarditis, and sepsis. SDSE infections generally occur among elderly patients with underlying malignancies or diabetes.

The present patient also had several underlying diseases, such as untreated diabetes, liver cirrhosis, and malignancy. Recently, invasive SDSE infections have been increasingly recognized worldwide. Although IE is a manifestation of invasive SDSE infection, SDSE is a rare cause of IE, whereas oral streptococci, *Streptococcus bovis* group and staphylococci are common causative microorganisms of IE.

Takahashi, et al. have reported the incidence and clinical characteristics of SDSE infection and demonstrated that IE accounted for only 4 (1.7%) of the 231 cases of SDSE invasive infection. Moreover, the clinical characteristics of SDSE endocarditis are rapid and aggressive and include acute onset of illness, large vegetations, presence of embolic complications in 50% of cases, and a high mortality rate. Therefore, SDSE endocarditis may pose a significant challenge in aging populations, although SDSE endocarditis has accounted for a minority of IE.

In general, thromboembolic events complicate the course of IE in 20%-50% of patients. The incidence of embolic events is the highest during the first week following the initiation of antimicrobial therapy. Patients with vegetations of > 10 mm in length are at higher risk of embolism, and this risk is even higher in patients with larger (> 15 mm) and mobile vegetations, particularly in staphylococcal IE affecting the mitral valve. Although the present patient was undergoing appropriate antimicrobial therapy, cerebral embolisms occurred in the clinical course of the disease. Because the size and mobility of the vegetations are the most potent independent predictors of a new embolic event, the present patient appeared to be at high risk for embolic events. Moreover, it is suggested that IE caused by *Streptococcus dysgalactiae* may be a risk factor for embolic complications.

The indications for and optimal timing of surgery of left-sided native valve IE are debatable. The European Society of Cardiology guidelines for IE suggest that surgical intervention should be considered in the following cases: (1) presence of heart failure, (2) uncontrolled infection, and (3) an increased risk of embolism. These guidelines recommend that early surgery should be considered in patients with large (> 15 mm) isolated vegetations on the aortic or mitral valve. However, the operative risk should be weighed against any benefit, and decisions regarding early surgery are often difficult and specific for an individual patient. Oppgaard, et al. reported that the 30-day mortality rate for SDSE endocarditis was 22%, and one of three patients who underwent valve replacement surgery died following surgery, although the number of cases was small. It is regrettable that this patient suffered complicated cerebral embolisms during the course of antimicrobial treatment. However, antimicrobial treatment controlled the infection and prevented the patient from developing heart failure despite poor clinical conditions. The present case report suggests the importance of initiating appropriate antimicrobial treatment on one hand, as well as the difficulty of making decisions regarding early surgery on the other hand in patients with IE caused by SDSE.

In conclusion, primary care doctors should consider invasive *Streptococcus dysgalactiae* infections when treating elderly patients with underlying diseases, and *Streptococcus dysgalactiae* should be included in the list of microorganisms considered to cause endocarditis in such patients. The selection of appropriate antimicrobial agents based on microbiologic findings is essential for controlling *Streptococcus dysgalactiae* endocarditis. The prevention and elimination of embolic events is a challenge in patients with IE caused by SDSE, as well as that caused by other microorganisms.

Disclosures

Conflicts of interest: None declared.

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