

CASE REPORT

Invasive infection due to *Streptococcus dysgalactiae* subspecies *equisimilis* causing endocarditis and ventriculitis: A case report

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Abstract

We aim to raise awareness of the role of *Streptococcus dysgalactiae* subsp. *equisimilis* (SDSE) in causing endovascular and central nervous system infections, and to promote recognition of SDSE as a pathogen that may cause serious invasive infections.

KEYWORDS

infective endocarditis, septic shock, *Streptococcus dysgalactiae* subspecies *equisimilis*, ventriculitis

1 | INTRODUCTION

An 82-year-old man presented with septic shock with *Streptococcus dysgalactiae* subsp. *equisimilis* (SDSE) on blood culture, which caused infectious endocarditis and pyogenic ventriculitis. We aim to raise awareness of the role of SDSE in causing endovascular and central nervous system infections.

Streptococcus dysgalactiae subsp. *equisimilis* belongs to Lancefield groups C and G, and a normal human commensal, colonizing the skin, pharynx, gastrointestinal tract, and female genital tract. Although SDSE has recently been recognized to cause life-threatening infections such as necrotizing fasciitis and toxic shock syndrome resembling its clinical picture with *Streptococcus pyogenes*,¹ it is a rare cause of infective endocarditis (IE) and central nervous system infection. To the best of our knowledge, this is the first report of SDSE simultaneously causing IE and ventriculitis. We aim to raise awareness of its role as a causative pathogen of endovascular and central nervous

system infections, and promote its recognition as a virulent pathogen that may cause serious invasive infections.

2 | CASE PRESENTATION

An 82-year-old man with a history of stroke, polycythemia vera, chronic atrial fibrillation, and lung cancer visited a nearby general hospital with a mild decrease in his level of consciousness which had a gradual onset. He was admitted due to an elevated C-reactive protein level of unknown origin and worsening renal function. After 2 days of hospitalization, he was transferred to the emergency department at our hospital because of fever and worsening mental status. On the initial physical examination, he was disoriented with a Glasgow Coma Scale (GCS) score of 5 (E3V1M1), a body temperature of 38.6°C, blood pressure of 98/80 mm Hg, pulse rate of 136 beats/min, respiratory rate of 27 breaths/min, and oxygen saturation of 98% with a 4 L/min oxygen

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TABLE 1 Laboratory results on admission

Variables	Reference range	Results
Arterial blood gas analysis (4 L/min oxygen mask)		
pH	7.35–7.45	7.25
PaCO ₂ (mmHg)	35.0–45.0	39.2
PaO ₂ (mmHg)	–	78.5
HCO ₃ [−] (mmol/L)	22.0–28.0	16.8
Lactate (mmol/L)	0.4–2.2	3.1
Complete blood cell count		
White blood cells (/μl)	3300–8600	15,700
Red blood cells (×10 ⁴ /μl)	405–585	516
Hemoglobin (g/dl)	13.7–16.8	15.0
Platelets (×10 ⁴ /μl)	13.0–35.0	5.4
Blood biochemistry		
Total protein (g/dl)	6.6–8.1	5.7
Albumin (g/dl)	4.1–5.1	2.2
Urea nitrogen (mg/dl)	8.0–20.0	98.4
Creatinine (mg/dl)	0.65–1.07	2.30
Total bilirubin (mg/dl)	0.40–1.50	1.42
Aspartate aminotransferase (U/L)	13–30	71
Alanine aminotransferase (U/L)	10–42	50
Lactate dehydrogenase (U/L)	124–222	322
Glucose (mg/dl)	73–109	123
C-reactive protein (mg/dl)	0.00–0.14	34.71
Blood coagulation		
Prothrombin time (%)	75.0–120.0	62.1
Activated partial thrombin time (s)	24.0–39.0	39.0
Fibrin/fibrinogen degradatoin products (μg/ml)	<5.0	107.4
Cerebrospinal fluid analysis		
Leukocytes (cells/μl)	0–5	157
Polymorphonuclear cells (cells/μl)	–	125
Mononuclear cells (cells/μl)	–	32
Protein (g/L)	10.0–40.0	283.8
Glucose (mg/dl)	50.0–75.0	15.0

mask. There was systolic murmur on auscultation of the chest and nuchal rigidity, but no other findings of note, including no skin lesions. His initial arterial blood gas analysis showed a metabolic acidosis with an elevated anion gap (Table 1). Laboratory results showed elevated levels of inflammatory markers (white blood cell count: 15,700°cells/μl, and C-reactive protein: 34.7°mg/dl), thrombocytopenia (54,000°/μl), and elevated creatinine

level of 2.3°mg/dl. His laboratory results are shown in Table 1. He was admitted to the intensive care unit and his condition continued to worsen, warranting fluid resuscitation, vasopressor support, and mechanical ventilation, indicating septic shock with a Sequential Organ Failure Assessment score of 14. Both transthoracic and transesophageal echocardiograms revealed a 13-mm vegetation on the mitral valve (Figure 1) with moderate mitral valve regurgitation. Cerebrospinal fluid (CSF) analysis showed leukocytes, 157°cells/μl with 80% of neutrophils, protein 2.8°g/L, and glucose 15°mg/dl, indicating pyogenic meningitis.

In addition to resuscitative therapy for septic shock, empiric antibiotic treatment was initiated with cefepime, vancomycin, and ampicillin for both IE and pyogenic meningitis. The preliminary report on blood culture in progress suggested growth of streptococci with hemolysis, and so clindamycin was added to his antibiotic regimen. The antibiotic was switched to ampicillin after SDSE was isolated from the initial blood cultures. The CSF culture was negative. The SDSE isolate was susceptible to penicillin, showing a minimum inhibitory concentration of <0.03°μg/ml. The use of an aminoglycoside was for the streptococcal IE was contraindicated because he had acute renal failure requiring renal replacement therapy.

As his neurological state did not fully recover with a GCS score of E3VtM4, we performed brain magnetic resonance imaging (MRI) on day 14. The MRI showed debris inside the lateral ventricles, which indicated acute ventriculitis (Figure 2). Although the interpretation of the pleocytosis in the CSF analysis was initially pyogenic meningitis, additional MRI findings indicated pyogenic ventriculitis. Because of the diagnosis of IE and pyogenic ventriculitis, antibiotic treatment was continued for a total of 6 weeks. The vegetation on the mitral valve resolved without worsening regurgitation and did not necessitate valve replacement. Eventually, the vegetation of the mitral valve resolved, leaving residual thickening of the mitral valve without clinically significant regurgitation. Although we did not perform follow-up brain MRI, his neurological state gradually recovered to GCS of E4VtM6. However, he was unable to walk, and his poor cognitive function required that he be transferred to a nursing facility. His clinical course is summarized in Figure 3.

3 | DISCUSSION

Streptococcus dysgalactiae subsp. *equisimilis* was formerly considered to be a low virulence pathogen than its virulence to *S. pyogenes*. However, recent molecular and clinical features suggest that SDSE shares similar virulence factors to *S. pyogenes* and may also follow a

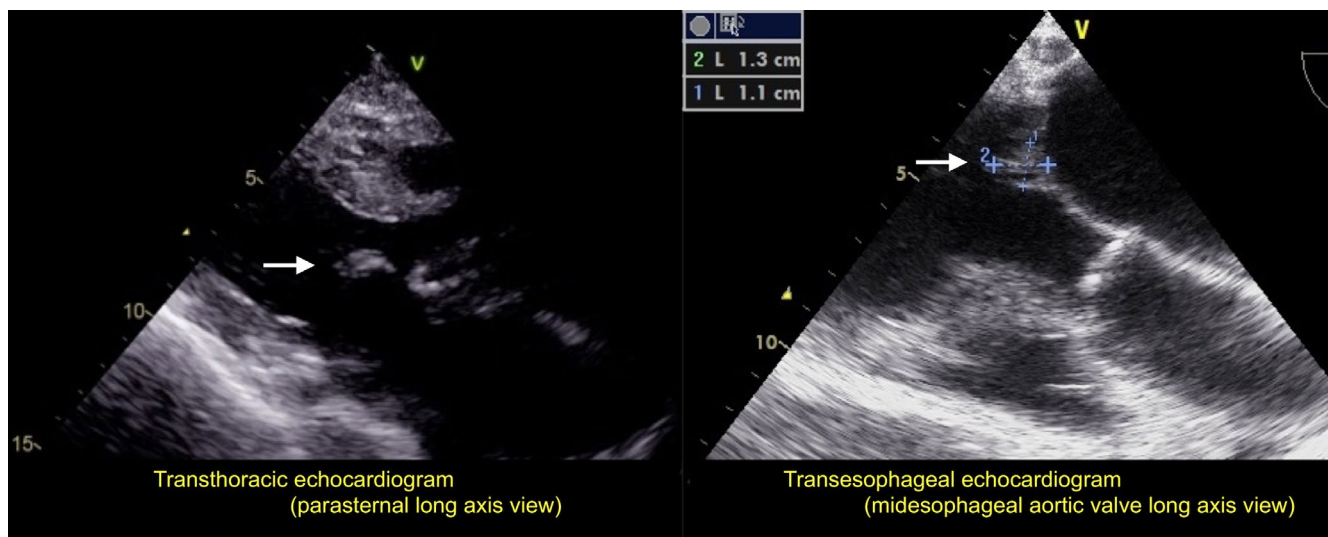


FIGURE 1 Transthoracic (left) and transesophageal (right) echocardiogram showing a 13-mm vegetation at the mitral valve (white arrow)

life-threatening clinical course.² Accumulation of clinical reports on SDSE indicates a wide spectrum of clinical manifestations, ranging from mild forms such as cellulitis and pharyngitis to life-threatening manifestations including bacteremia, necrotizing fasciitis, and toxic shock syndrome. Elderly patients with underlying comorbidities such as diabetes mellitus, malignancy, cardiovascular disease, and liver cirrhosis are more prone to invasive forms with poor outcomes,^{1–3} indicating that the disease is challenging for clinicians and warrants a multidisciplinary treatment strategy.

According to current guidelines, SDSE is considered to be a rare causative pathogen of IE; however, a recent report concluded that IE occurred in 6% of patients with group C and G streptococci bacteremia,⁴ showing that the risk of endocarditis is not negligible when SDSE is positive in blood cultures. Endocarditis involving the native valve^{5,6} and prosthetic valve⁷ has been reported, as well as cardiac device-related endocarditis.⁸ Apart from endocarditis, endovascular infections such as aortic root abscess⁹ and infected aneurysm⁶ have been reported, which may indicate that the bacteria adhere to endovascular systems. Clinicians should be well prepared and acknowledge that SDSE bacteremia warrants investigations for IE as well as other endovascular complications.

Pyogenic ventriculitis is often associated with complications of brain surgery, ventricular shunts, and drains, whereas reports on community-acquired pyogenic ventriculitis are limited. In the published literature, only a few cases were caused by *Neisseria meningitidis*,¹⁰ *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Peptostreptococcus* spp., *Streptococcus intermedius*, and *Listeria monocytogenes* have been described as causing primary pyogenic

ventriculitis.¹¹ Diagnosis of pyogenic ventriculitis is made using cerebrospinal fluid analysis and imaging studies. Because CT has low sensitivity, MRI is preferred for the diagnosis of ventriculitis. MRI findings such as ventricular debris, hydrocephalus, periventricular hyperintense signals, and ependymal enhancement are specific features for diagnosing ventriculitis. As meningitis and ventriculitis share similar clinical and laboratory findings, MRI is not routinely performed in patients with pleocytosis and a positive CSF culture, ventriculitis could be misdiagnosed and treated as meningitis. Gronthoud *et al.*¹¹ also noted that the lack of a clear definition of ventriculitis makes it difficult to conclude whether primary pyogenic ventriculitis is a rare or underdiagnosed infection.

Our patient developed IE of the mitral valve and pyogenic ventriculitis. One of the complications of left-sided IE is neurological complications¹² due to septic embolism. Clinical manifestations may include ischemic stroke, cerebral hemorrhage, brain abscess, meningitis, and mycotic aneurysms; however, ventriculitis is not a common neurological complication of IE^{13,14} and rarely described as a complication of endocarditis. Therefore, in our case, we speculate that endocarditis and pyogenic ventriculitis developed through the hematogenous spread of SDSE, rather than ventriculitis that developed secondary to endocarditis. However, we could not identify the focal entity of SDSE bacteremia.

Penicillin or beta-lactams are the antibiotic treatments of choice for SDSE. As combination with clindamycin to inhibit protein synthesis is generally indicated for the treatment of invasive *S. pyogenes* infections, published literature also reports combined antibiotic treatment including clindamycin for invasive SDSE infection.⁶ Guidelines

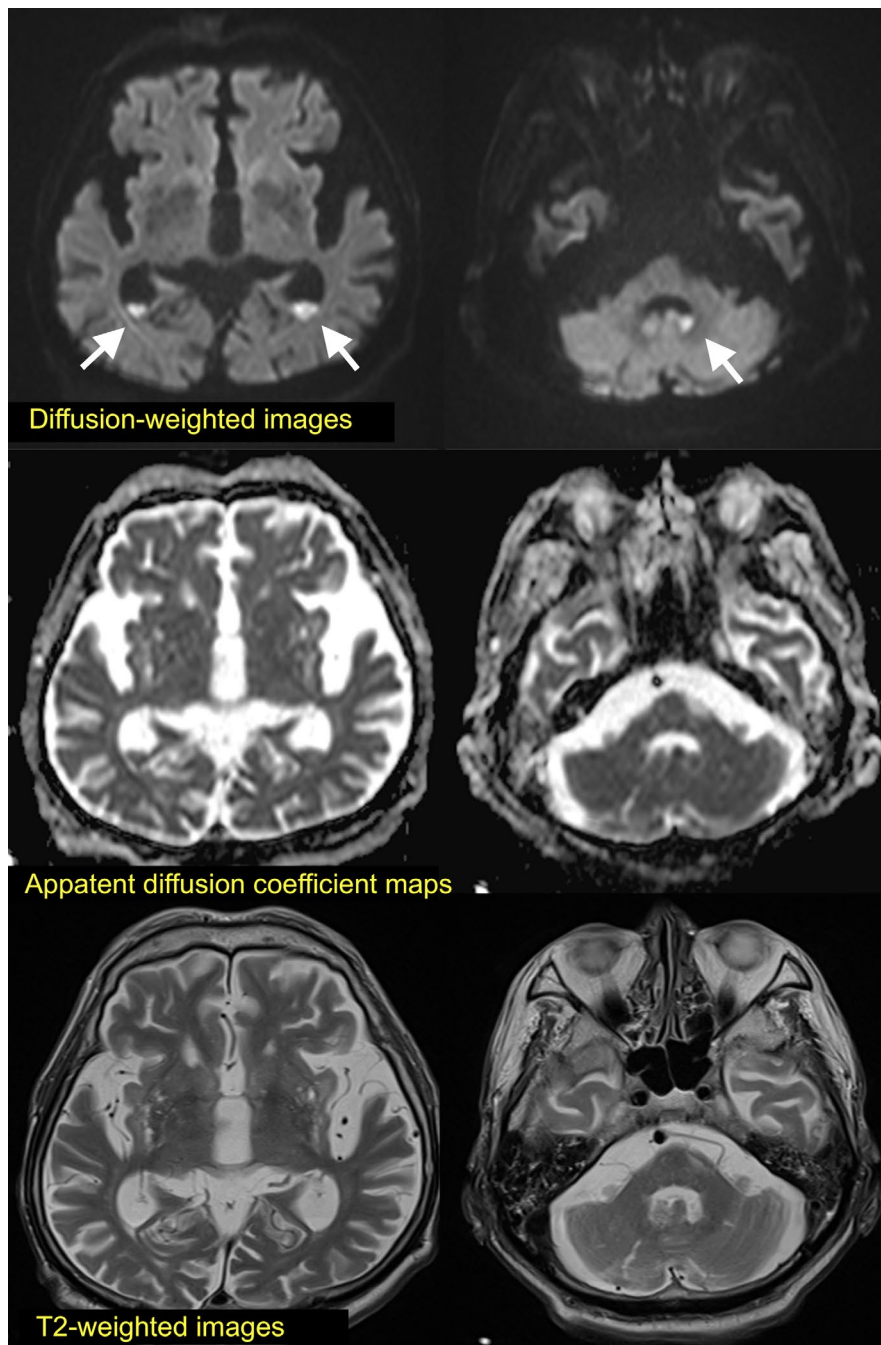


FIGURE 2 Brain magnetic resonance imaging showing accumulation of debris inside the lateral ventricles (white arrow)

are available on the treatment of streptococcal endocarditis including optimal antibiotic regimen, treatment duration, and indication for surgical intervention.^{15,16} They recommend the addition of gentamicin to penicillin or ceftriaxone for the first 2 weeks of 4–6 weeks of treatment, as well as consultation with experts to guide treatment strategies for IE caused by beta-hemolytic streptococci. Although there are detailed guidelines for the management of nosocomial ventricular infections,¹⁷ there are no recommendations for community-acquired pyogenic ventriculitis. Case reports suggest that the antibiotic regimen and dosage should be selected according to that of bacterial meningitis but that treatment should be continued for

6–12 weeks, according to the recommendations for brain abscesses.^{10,18,19} Some patients require ventricular drainage.¹¹ Considering the longer treatment duration required and the possibility of requiring ventricular drainage, it is important to consider the diagnosis of ventriculitis and to consider performing additional neuroimaging studies if ventriculitis is suspected.

In conclusion, we hope that our case report raises the level of awareness among clinicians that SDSE can cause invasive infections in several organ systems, including the endovascular and central nervous systems as were affected in our case. From a clinical and an epidemiological perspective, it is important to consider these

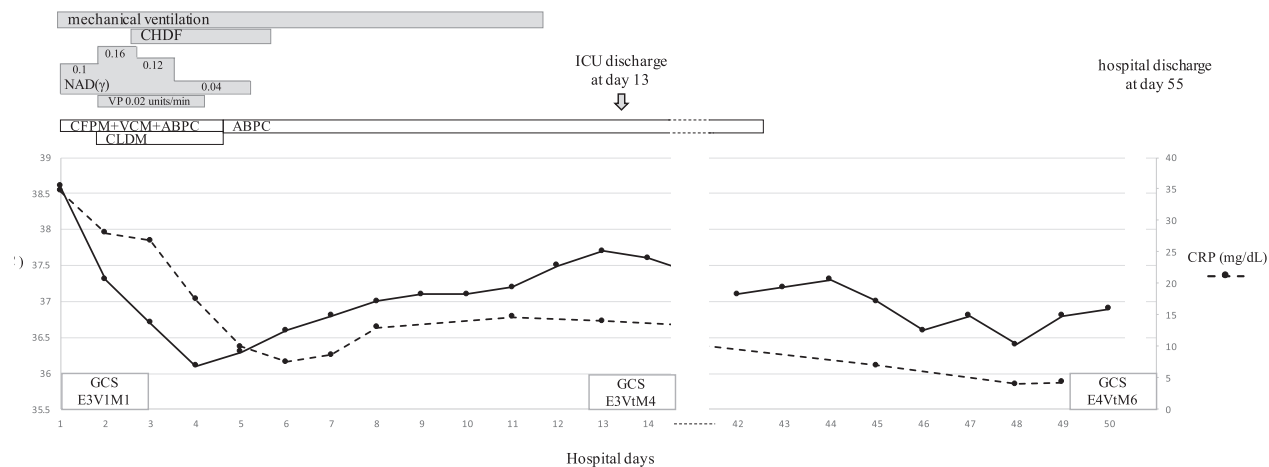


FIGURE 3 Summary of the patient's clinical course and treatment. ABPC, ampicillin; CFPM, cefepime; CHDF, continuous hemodiafiltration; CLDM, clindamycin; CRP, C-reactive protein; GCS, Glasgow coma scale; ICU, intensive care unit; NAD, noradrenaline; Temp, temperature; VCM, vancomycin; VP, vasopressin.

complications and to consider performing additional investigations and treatment strategies if SDSE infection is diagnosed.

ACKNOWLEDGEMENTS

We would like to thank Editage for English language editing.

CONFLICTS OF INTEREST

None of the authors have any conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

MH involved in the treatment and clinical management decision-making of the patient, obtained consent for the publication, and wrote draft manuscript. KN, KI, and SN interpreted clinical data and critically revised the manuscript for important intellectual content. KS and YH involved in the treatment and clinical management decision-making of the patient and critically revised the manuscript.

CONSENT

Consent could not be obtained from the patient because of his clinical condition. The patient's family provided consent for the case presentation and images to be published.

DATA AVAILABILITY STATEMENT

The data that support the findings from this study are available from the corresponding author upon reasonable request.

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How to cite this article: Hikone M, Nagai K, Inoue K, Noji S, Sugiyama K, Hamabe Y. Invasive infection due to *Streptococcus dysgalactiae* subspecies *equisimilis* causing endocarditis and ventriculitis: A case report. *Clin Case Rep*. 2021;9:e04638. <https://doi.org/10.1002/ccr3.4638>