

Infective endocarditis due to a rare pathogen, *Streptococcus constellatus*, in a patient with gingivitis: A case report and review of the literature

Research Article

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Abstract: A 78-year-old Japanese man with a 5-day history of fever (~38°C) and decreased appetite was admitted to our hospital. Transesophageal echocardiography revealed aortic valve vegetation. *Streptococcus constellatus* was detected from a blood culture. An antibiotic sensitive to this strain was administered for 6 weeks, and the patient has been well for 6 months without any sign of relapse. A review of all documented cases of infective endocarditis due to *S. constellatus* revealed nonspecific initial symptoms, especially coughing, and complications of abscess formation and septic embolisation. Clinicians should carefully consider the choice of antibiotic agents in the treatment of infective endocarditis due to *S. constellatus*, because penicillin-resistant strains have been documented in some cases.

Keywords: Infective endocarditis • *Streptococcus constellatus* • Clinical features • Rare pathogenesis

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1. Introduction

Infective endocarditis (IE) is a serious infectious disease with a high mortality rate [1,2]. Gram-positive cocci, such as *Streptococcus* spp. and *Staphylococcus* spp., are mainly responsible for IE [3]. Among the *Streptococcus* spp., Streptococci viridans are the main cause of IE [3]. However, 1 group of *S. viridans*, the *S. milleri* group, which includes *S. constellatus*, *S. anginosus*, and *S. intermedius*, rarely cause IE; among these, *S. anginosus* is predominant [4]. *S. constellatus* is a very rare pathogen of IE; there are only 10 case reports in the literature [5-14]. The clinical features of IE due to *S. constellatus* remain unclear.

Here, we report a case of IE due to *S. constellatus* in a patient with gingivitis. We also review previously published reports and discuss the clinical features of IE due to *S. constellatus*.

2. Case

A 78-year-old Japanese man with a 5-day history of fever (~38°C) and appetite loss was admitted to our hospital. The patient also had a 2-week history of intermittent headaches. The patient was previously diagnosed with prostatic carcinoma at the age of 71 years; a radical operation was carried out at that time, and there was no evidence of relapse. The patient was also diagnosed with moderate aortic regurgitation at the age of 78 years, and follow-up examinations were planned every 6 months. Upon admission to our hospital, the patient's temperature was 36.7°C, heart rate was 112/min (regular), and consciousness was clear. A grade IV/VI diastolic heart murmur was most evident at the left sternal border. Oral findings showed chronic gingivitis. Chest/abdominal radiographs and brain computed tomography (CT) upon admission revealed normal findings. Blood testing showed a white blood cell (WBC) count of 18,700/ μ L and C-reactive protein (CRP) level of 14.48 mg/dL; however, there were no other significant findings indicating

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the focus of infection. Blood was collected twice after admission and before the administration of antibiotic agents, for culturing. Daily intravenous ceftriaxone (2 g) was then administered starting on the day of admission. Subsequently, the patient's fever diminished rapidly after the initial administration of the antibiotic, and his WBC count and CRP level gradually declined.

After admission, transthoracic echocardiography and transesophageal echocardiography (TEE) revealed moderate aortic regurgitation and a 7.5×2.8 -mm vegetation on the non-coronary cusp of the aortic valve (Figure 1). Brain magnetic resonance imaging (MRI) showed normal findings. A chest/abdominal enhanced CT scan also showed normal findings. Blood cultures revealed penicillin-sensitive *S. constellatus* (minimum inhibitory concentration [MIC] < 0.125 µg/mL). Therefore, the patient was diagnosed with IE due to *S. constellatus* and chronic gingivitis.



Figure 1. Transesophageal echocardiography revealed an area of vegetation on the noncoronary cusp of the aortic valve.
Ao, aorta; LA, left atrium; LV, left ventricle

Five days after admission, we changed the antibiotic agent from ceftriaxone to penicillin G (4 million units every 4 h). We then changed the antibiotic agent from penicillin G to ampicillin (2 g every 6 h) because vasculitis occurred as an adverse effect of penicillin G. After the administration of penicillin G and ampicillin, the patient's symptoms continued to improve gradually. His WBC count and CRP level also continued to decrease. Six weeks after the initiation of treatment, the size of the vegetation was reduced on TEE, and no embolic infarction was observed. Antibiotic administration was terminated 6 weeks after the initiation of treatment. This patient has been well for 6 months without any sign of relapse.

3. Discussion

Streptococcus constellatus is recognised as a rare pathogen of IE. Only 10 cases are reported in the literature [5–14]. It is reported that *S. constellatus* is not readily associated with the heart valves, which may explain why *S. constellatus* rarely causes IE [15,16]. We reviewed the clinical features of IE due to previously documented *S. constellatus* infection (Table 1).

With regard to initial symptoms, it was seen that fever was common, as 97% of all IE cases presented with fever. Malaise and endurance fatigue are also common, which occur in 90% of IE patients [17]. Seven of 11 cases (63.6%) of IE due to *S. constellatus*, including the present case, had a fever on admission, and 4 of 11 (36.7%) had fatigue. However, patients with IE due to *S. constellatus* tended to present with a variety of nonspecific symptoms, among which, coughing was the most prevalent (4/11 cases [36.4%]). Coughing is thought to be an uncommon symptom, although there are no reports showing the prevalence of coughing as one of the initial symptoms of IE. Moreover, coughing may be a significant initial symptom in cases of IE due to *S. constellatus*. Coughing may be a symptom of pulmonary septic embolisation, because 2 cases were complicated with septic pulmonary embolisation among all 4 cases.

IE tends to exhibit a variety of complications. Cardiac complications such as heart failure and perivalvular abscesses are the most common and occurred in one-third to one-half of patients in a previously documented case series [18]. In contrast, metastatic abscesses rarely develop in the kidneys, spleen, brain, or soft tissues in the setting of IE, although the frequency of metastatic abscesses in IE remains unknown. However, 4 of 11 patients (36.4%) with IE due to *S. constellatus* developed abscesses. This shows that *S. constellatus* has a strong ability to invade tissue, which is a major feature of this strain [16]. In addition, 7 of 11 cases (63.6%) exhibited evidence of septic embolisation. Embolisation is known to be one of the common complications of IE, and a previous study reports a 30.4% complication rate of septic emboli [19]. These results indicate *S. constellatus* infection tends to be complicated with a high frequency of septic embolisation, possibly because *S. constellatus* has thrombin-like activity [16].

Gingivitis is thought to be a risk factor of IE, particularly due to oral microflora [20]. Although only 2 cases including the present one had gingivitis among all 11 cases, the detection of gingivitis is not usually carried out in all cases of IE. Gingivitis may be found in some cases of IE due to *S. constellatus*. This pathogen does not have much affinity for the heart valves, which potentially helps avoid the development of IE [15,16]. However, gingivitis may provide an environment for bacterial growth.

Table 1. Review of the literature, including the present case.

Citation	Age (y)	Gender	Symptoms	Focus	Background	Complications	Embolitic site	Antibiotic agents	Operation	Outcome	PenG-resistant
5	2	Female	Fever	Unknown	Multiple congenital anomalies	None	None	PenG + Streptomycin, Clinda	-	Cured	+
6	74	Male	Fever, Cough, Fatigue, Weight loss	Mitral valve	Hypertension	None	None	Unknown	-	Cured	-
7	70	Female	Hemiparesis, Urinary incontinence, Depressed	Mitral valve	Breast Ca	MR	Brain	Vanco + Gentamicin, PenG	-	Death	-
8	41	Male	Fever, Cough, Malaise	Tricuspid valve	Unknown	Liver abscess	Lung	PenG + Gentamicin	-	Death	-
9	61	Male	Fever, Fatigue	Aortic prosthetic valve	AS, MR, Af, Gingivitis	Mediastinal abscess	Spleen, Kidney	PenG + Gentamicin	-	Cured	-
10	25	Male	Headache, Blurred vision	Aortic valve	Unknown	Mycotic aneurysm	Brain	PenG	+	Cured	-
11	72	Female	Backache	Mitral valve	Unknown	AMI, MR	Coronary artery	PenG + Gentamicin	+	Cured	-
12	35	Male	Fever, Fatigue, Cough, Night sweating	Aortic valve	Unknown	None	None	PenG + Gentamicin, Cefotaxime	+	Cured	+
13	26	Male	Fever, Myalgia, Cough, Emesis, Weight loss	Tricuspid valve	Injection drug user	Intramuscular abscess	Lung	Vanco + PIP-TZ, PenG + Gentamicin, Ceftriaxone + Gentamicin	-	Cured	-
14	79	Male	Unknown	Aortic mitral valve	Unknown	None	Spleen	PenG + Gentamicin, Cefotaxime	+	Cured	+
Our case	78	Male	Fever, Headache, Appetite loss	Aortic valve	AR, Gingivitis, Prostatic Ca	None	None	Ceftriaxone, PenG, AMP	-	Cured	-

Ca, carcinoma; AS, aortic stenosis; MR, mitral regurgitation; Af, atrial fibrillation; AR, aortic regurgitation; AMI, acute myocardial infarction; PenG, penicillin G; Clinda, clindamycin; Vanco, vancomycin; PIP-TZ, piperacillin-tazobactam; AMP, ampicillin

Gram-positive cocci such as *Streptococcus* spp. and *Staphylococcus* spp. are mainly responsible for IE [3]. Choosing antibiotic agents for IE depends on the antibiotic sensitivities of pathogens. Penicillin and gentamicin are the usual treatment agents for IE due to oral streptococci including *S. constellatus*. In cases of IE due to oral streptococci highly sensitive to penicillin (MIC < 0.125 µg/mL), monotherapy with parenteral penicillin is recommended as a suitable treatment [21]. In the present case, *S. constellatus* was highly sensitive to penicillin G; therefore, we chose monotherapy with penicillin G or ampicillin. In particular, *S. constellatus* was 100% highly sensitive to penicillin G (MIC < 0.125 µg/mL) in our hospital (i.e. in all 23 samples including this case cultured from January 2010 to December 2012). Furthermore, penicillin is a suitable treatment agent for IE due to *S. constellatus*, even as an empiric therapy. However, in 3 previous cases, *S. constellatus* was resistant to penicillin. Therefore, we should consider the possibility of penicillin-resistant strains, especially in treatment-resistant cases.

4. Conclusions

We presented a case of IE due to *S. constellatus*. A review of all documented cases including the present one indicates IE due to *S. constellatus* tends to produce nonspecific initial symptoms, especially coughing, and is complicated by abscess formations and septic embolisation. The choice of antibiotic agent for the treatment of IE due to *S. constellatus* should be given special attention, because penicillin-resistant strains have been documented in some cases.

Conflict of interest

None declared.

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