



Incidental detection of *Corynebacterium jeikeium* endocarditis via regular blood examination in an afebrile hemodialysis patient

Nanako Oshiro¹ · Kentro Kohagura² · Ryo Zamami^{1,2} · Kumiko Omine¹ · Yoshitsugu Sunagawa¹ · Hirona Taira¹ · Kojiro Kinjo^{1,2} · Takuto Nakamura¹ · Takanori Kinjo¹ · Masanobu Yamazato¹ · Akio Ishida¹ · Yusuke Ohya¹

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Abstract

Herein, we describe a rare case of *Corynebacterium jeikeium* endocarditis that silently progressed in a 65-year-old man undergoing hemodialysis. Because routine monthly blood examination revealed high C-reactive protein levels, blood cultures were collected, although he had no symptom and was afebrile. After 2 days, a Gram-positive rod was detected in one set of the blood culture. Furthermore, transthoracic echocardiography revealed new aortic regurgitation (AR) and vegetations, and, therefore, infective endocarditis was suspected. Transesophageal echocardiography showed vegetations with a maximum diameter of 8 mm on his aortic valve, with some valve destruction. *C. jeikeium* was identified in three sets of blood cultures. Administration of daptomycin was started because he had vancomycin allergy. Judging from the high risk of embolization due to vegetations, emergency aortic valve replacement was performed on the second day. *C. jeikeium* was detected in a resected cardiac valve specimen and blood. This case emphasizes that physicians should always consider the possibility of infective endocarditis even in hemodialysis patients without any symptoms.

Keywords *Corynebacterium jeikeium* · Hemodialysis · Infective endocarditis · Afebrile · C-reactive protein

Introduction

Because of frequent intravascular access, the risk of infective endocarditis (IE) in hemodialysis (HD) patients is significantly higher than that in the general population. A 1-year IE French survey showed that the incidence of IE in HD patients is 50–60 times higher than the overall incidence of IE [1]. However, atypical presentation of infection is not rare among hemodialysis patients. A previous study of IE revealed that fever is less commonly observed in hemodialysis patients (45–70%) than in individuals in the general population (80–90%) [2]. Hence, physicians might underdiagnose IE, eventually delaying the diagnosis in these patients. This could cause high mortality and poor prognosis

in IE patients of this group. Therefore, early diagnosis of IE in HD patients is very important.

Corynebacterium jeikeium is an aerobic Gram-positive rod bacterium present in the skin flora. Therefore, the isolation of *C. jeikeium* in blood cultures is not considered to be clinically significant and is overlooked as contaminant skin flora. However, several studies have focused on the clinical significance of this organism and have described its relationship with IE. In a case series of 129 patients with *Corynebacterium* endocarditis, those with *C. jeikeium* infections were more likely to require valve replacement [3]. In addition, a previous study reported that hemodialysis was identified as an associated comorbidity of *C. jeikeium* IE [3]. However, information regarding the occurrence of *C. jeikeium* IE in hemodialysis patients is limited.

Herein, we describe a rare case of *C. jeikeium* endocarditis that silently progressed in the native aortic valve of a patient undergoing hemodialysis.

✉ Kentro Kohagura
kohagura@med.u-ryukyuu.ac.jp

¹ Department of Cardiovascular Medicine, Nephrology and Neurology, Faculty of Medicine, University of the Ryukyus, 207 Uehara, Nishihara-cho, Okinawa 903-0215, Japan

² Dialysis Unit, University of the Ryukyus Hospital, 207 Uehara, Nishihara-cho, Okinawa 903-0215, Japan

Case report

A 65-year-old man had been undergoing hemodialysis for the past 20 years because of end-stage renal failure due to glycogen storage disease type I, and had no history of valvular disease. He previously had a rash allergy of vancomycin and meropenem. The patient underwent routine blood examination every month. Previous blood examination revealed that the C-reactive protein (CRP) level was 1 mg/dL; however, the subsequent blood examination incidentally revealed that the CRP level had significantly increased to 10 mg/dL. The patient was afebrile and did not complain of any symptoms. Two sets of blood cultures were collected. After 2 days, a Gram-positive rod was isolated from one set of the blood cultures, and the patient was admitted to the hospital.

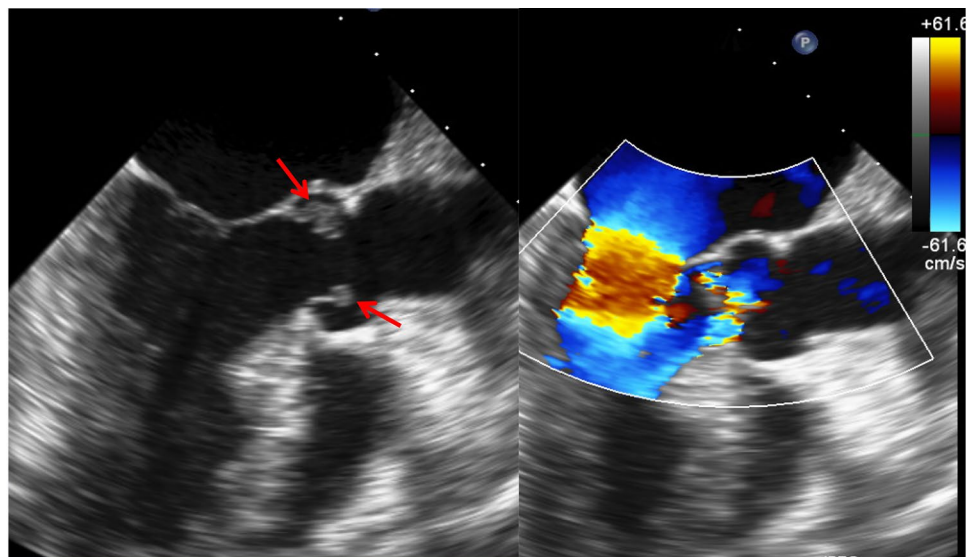
Upon admission, his height was 148 cm, weight was 37.4 kg, and body mass index was 17 kg/m². Physical examination revealed body temperature of 36.3°C, blood pressure of 128/54 mmHg, and pulse rate was regular at 84 beats/min. Chest examination revealed normal vesicular breath sounds and a regular cardiac sound with no adventitious sounds. Any findings indicative of peripheral embolism or heart failure were not observed. Laboratory examination revealed the following: hemoglobin level, 8.6 g/dL, white blood cell count, 7.3×10^3 /mL with 85.4% neutrophils; serum creatinine level 7.28 mg/dL; blood urea level, 83 mg/dL; serum sodium level, 133 mEq/L; potassium level, 4.1 mEq/L; chloride level, 99 mEq/L; total bilirubin level 0.1 mg/dL; aspartate aminotransferase level, 34 IU/L; alanine aminotransferase level, 21 IU/L; γ -glutamyl transpeptidase level, 229 IU/L; alkaline phosphatase level, 429 IU/L; lactate dehydrogenase level,

125 IU/L; creatine phosphokinase level, 12 IU/L; and procalcitonin level, 30.7 ng/mL. An electrocardiogram did not show changes compared to previous studies and chest radiography revealed no evidence of cardiomegaly or pulmonary edema. Retinal findings revealed the absence of Roth spots or endophthalmitis.

Transthoracic echocardiography, revealed new-onset aortic regurgitation (AR) and aortic valve vegetation (Fig. 1). Contrast-enhanced computed tomography and magnetic resonance imaging did not reveal any findings indicative of peripheral embolism. Finally, *C. jeikeium* was identified in three sets of blood cultures, and the patient's preoperative clinical condition fulfilled the Duke criteria for the diagnosis of IE (two major criteria). The patient was diagnosed with IE, and treatment with daptomycin (300 mg intravenously three times a week following dialysis) was initiated. He did not present with heart failure under strict volume control during dialysis. Transesophageal echocardiography revealed moderate AR and an 8 × 6 mm vegetation attached to the noncoronary cusp (NCC) and 3 × 3 mm vegetation attached to the right coronary cusp (RCC), with aortic valve destruction. The presence of this large vegetation was a risk factor for embolization due to atheroma. Therefore, the patient underwent emergency aortic valve replacement on the second day of hospitalization.

During surgery, vegetations were found on the RCC and NCC, and valvular perforation was observed in the NCC (Fig. 2). Histopathologic examination of the resected vegetation revealed an acute inflammatory change which was consistent with active IE. Moreover, *C. jeikeium* was isolated from the resected vegetation after surgery. Based on the results obtained after surgery, the Duke criteria were met and a definitive diagnosis of *C. jeikeium* native aortic valve IE was made. After surgery, treatment with rifampicin

Fig. 1 Transesophageal echocardiography views of the aortic valve: **a** long-axis image. Vegetations in the noncoronary cusp and right coronary cusp are shown (arrow). **b** Aortic regurgitation appeared in long-axis color views



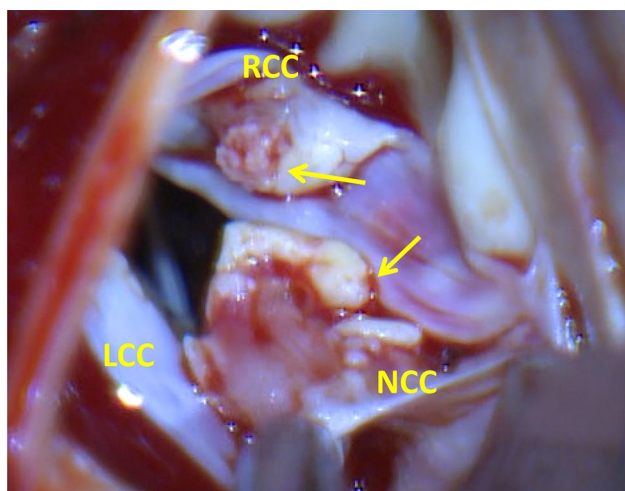


Fig. 2 Intraoperatively, vegetations are observed in the right coronary and noncoronary cusps as shown by transesophageal echocardiography (arrow)

(300 mg orally once daily), which was sensitive to the causative bacteria was also initiated. The patient received antibiotic therapy using daptomycin for 6 weeks. After surgery, the patient recovered, and no recurrence was noted.

Discussion

The occurrence of atypical presentation of IE is not rare among hemodialysis patients.

Herein, we report a rare case of *C. jeikeium* native aortic valve endocarditis that was incidentally diagnosed during regular blood examination. The clinical course of the patient indicated two important possibilities: *C. jeikeium* may cause IE, and may silently progress without apparent clinical signs or symptoms.

Corynebacterium species are aerobic Gram-positive rod bacteria that are well-recognized components of the skin flora and are considered to cause minimal problems in people with normal immunity. Therefore, the isolation of *C.*

jeikeium in blood cultures is not considered to be clinically significant and is overlooked as contaminant skin flora. However, in recent years, it has been reported that *Corynebacterium* species exhibit pathogenicity against immunocompromised hosts. Infantidou et al. have reported indications that increase the clinical significance of coryneform bacteria isolated from blood cultures, in patients with nosocomial risk factors including those undergoing hemodialysis [4]. Furthermore, *C. jeikeium*, a type of *Corynebacterium* species, cause IE. Notably, the mortality rate of *C. jeikeium* IE is as high as 33% [2]. Hemodialysis is reported to be an associated comorbidity of *C. jeikeium*, which is observed in approximately one-quarter of *C. jeikeium* IE cases.

The silent course of the disease was the highlight of the present case. Most patients with *C. jeikeium* endocarditis present with systemic symptoms such as fever and dyspnea. In addition, the diagnosis of most patients (46%) with *C. jeikeium* IE takes 1–3 months, and the condition follows a subacute course [2]. Three cases of confirmed *C. jeikeium* endocarditis were previously reported in HD patients. Table 1 summarizes these cases. All patients had left-sided native valve endocarditis, and it has been suggested that *C. jeikeium* may cause endocarditis in HD patients without a history of cardiac surgery. Notably, our patient was completely afebrile at presentation. This is not rare among hemodialysis patients. For example, fever is less commonly observed in hemodialysis patients (45–70%) than in individuals in the general population (80–90%), probably due to uremia-related impaired cellular host defense [1]. Moreover, it was also reported that among adult chronic HD patients with bacteremia, the serum albumin level, a predictor of nutritional status, was lower in the afebrile group than in the febrile group [5]. Low level of serum albumin and body mass index suggested malnutrition in our case. Furthermore, glycogen storage disease type I, which caused renal failure in this patient, also could cause immunodeficiency [6]. Thus, malnutrition and the comorbidity might be associated with the asymptomatic IE.

Although elevated CRP levels were only abnormal findings in this case, CRP levels are reportedly elevated in a

Table 1 Summary of *C. jeikeium* endocarditis reported cases in HD patients

Patient	References	Age/sex	Valve	Site	Co-morbidity/condition	Fever	outcome
1	Bookani [9]	56/F	Native	AV	Alcoholic, liver transplant, Hepatorenal syndrome, Dialysis catheter and central lines	NA	Recovery
2	Vanbosterhaut [10]	54/M	Native	MV	ESRD as a result of abuse of analgesics	+	Recovery
3	Clarke [11]	53/F	Native	MV	Focal segmental glomerulosclerosis(FSGS), AV graft	+	Recovery
4 (our case)		65/M	Native	AV	Glycogen storage disease type I	–	Recovery

AV aortic valve, ESRD end-stage renal disease, HD hemodialysis, MV mitral valve

considerable proportion of HD patients without any apparent reason [7]. Therefore, physicians might not always suspect bacteremia even if patients have elevated CRP levels. Sasaki et al. have reported the “use of the BAC-HD score,” which is a clinical predictive score including CRP level for bacteremia in hemodialysis patients [8]. In this case, the patient had CRP level > 10 mg/dL, ALP level > 360 U/L, and no prior antibiotic use within 1 week; therefore, the patient’s BAC-HD score was 3. Considering that dialysis patients are at a high risk of developing bacteremia due to frequent intravascular access, regular assessment of CRP levels facilitate the early diagnosis of IE.

The modified Duke criteria are generally applied when diagnosing IE. However, to diagnose *C. jeikeium* endocarditis is challenging, because the organisms growing in blood culture are often considered to be skin contaminants. In our case, when *C. jeikeium* was isolated from the blood culture, we initially associated it with contamination. But, our patient did fulfill the required criteria and was considered to be a definitely case before surgery. Finally, histopathological examination of the resected valve revealed that the patient had active infection. Moreover, both blood cultures and the resected valve specimens were positive for *C. jeikeium* resulting in the definite diagnosis of *C. jeikeium* endocarditis.

Antibiotic therapy and surgical debridement are essential for the treatment of *C. jeikeium* endocarditis. Several *Corynebacterium* species, including *C. jeikeium*, are resistant to various antimicrobial agents, such as ampicillin, cephalothin, cefuroxime, and imipenem [9]. A recent report has shown that for species intrinsically resistant to multiple antimicrobials such as *C. jeikeium*, vancomycin or teicoplanin might be the first and only choice for antimicrobial therapy [9]. In fact, in a previous study, most patients with *C. jeikeium* IE were treated with multiple antibacterial agents, mainly vancomycin, for 6 weeks [9]. Because our patient was allergic to vancomycin, we administered daptomycin as empirical treatment, and after antimicrobial susceptibility testing result was obtained, we added rifampicin as multiple therapy. Surgical resection is required in 62% of *C. jeikeium* IE cases [2]. Our patient had vegetation that was as large as 10 mm. Previous studies have shown that patients with vegetations larger than 10 mm are at high risk of embolism. Cerebral infarction can substantially exacerbate patient’s ADL, even if it is not directly life threatening. A randomized study conducted in 2012 on patients with left heart autologous valve IE with a vegetation larger than 10 mm has reported that the total mortality rate after early surgery for large vegetations did not differ. However, the combined endpoints (total mortality rate, incidence of embolism, and IE recurrence) were significantly better in the early intervention group than in the non-surgical treatment group. Therefore, we decided to perform cardiac surgery on our patient.

In conclusion, our patient presented with a clinically rare case of *C. jeikeium* native valve endocarditis. He did not present with any clinical symptoms and the infection silently and latently progressed until it was incidentally found. Considering that dialysis patients are at a high risk of developing bacteremia, regular assessment of CRP levels may help in the early diagnosis of hidden bacteremia in hemodialysis patients. In our case, early diagnosis by blood culturing resulted in the initiation of appropriate antibacterial drug treatment and early intervention of surgical treatment, which may have greatly contributed to saving the life of the patient without any serious complications.

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Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interests.

Ethical approval All procedures performed in this case report were in accordance with the ethical standards of the institutional committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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