Native Valve Endocarditis due to *Corynebacterium striatum* confirmed by 16S Ribosomal RNA Sequencing: A Case Report and Literature Review

Hyo-Lim Hong¹, Hwi-In Koh¹, and A-Jin Lee²

¹Department of Internal Medicine; and ²Department of Laboratory Medicine, Catholic University of Daegu School of Medicine, Daegu, Korea

*Corynebacterium* species are non-fermentous Gram-positive bacilli that are normal flora of human skin and mucous membranes and are commonly isolated in clinical specimens. Non-*diphtheriae* *Corynebacterium* are regarded as contaminants when found in blood culture. Currently, *Corynebacterium striatum* is considered one of the emerging nosocomial agents implicated in endocarditis and serious infections. We report a case of native-valve infective endocarditis caused by *C. striatum*, which was misidentified by automated identification system but identified accurately by 16S ribosomal RNA sequencing, in a 55-year-old male patient. The patient had two mobile vegetations on his mitral valve, both of which had high embolic risk. Through surgical valve replacement and an antibiotic regimen, the patient recovered completely. In unusual clinical scenarios, *C. striatum* should not be simply dismissed as a contaminant when isolated from clinical specimens. The possibility of *C. striatum* infection should be considered even in an immunocompetent patient, and we suggest a genotypic assay, such as 16S rRNA sequencing, to confirm species identity.

**Key Words:** *Corynebacterium*; Endocarditis; RNA, Ribosomal, 16S

**Introduction**

*Corynebacterium* species are non-spore-forming aerobic Gram-positive bacilli that are spread widely in the environment and constitute part of the normal flora on skin and mucosa in humans [1, 2]. In a hospital setting, non-*diphtheriae* *Corynebacterium* are commonly considered contaminants when found in blood cultures because of their low virulence. Recently, there have been increasingly frequent reports of infection by non-*diphtheriae* *Corynebacterium* in immunocompromised patients who were hospitalized or in immunocompetent patients who had implanted medical devices. *Corynebacterium striatum* is a commonly-isolated corynebacteria in the clinical microbiology laboratory, although confirmed infections from sterile sites are relatively rare [3]. *C. striatum* can cause pulmonary abscess, meningitis, septic ar-
Infective endocarditis due to *Corynebacterium striatum*

The aid of molecular diagnostic methods, especially the 16S rRNA and rpoB gene sequencing, has greatly improved the ability to detect *C. striatum* in clinical specimen [5, 6]. Here, we report a case of native-valve endocarditis caused by *C. striatum*, which was accurately identified by 16S ribosomal RNA sequencing in a non-immunocompromised patient.

**Case Report**

A 55-year-old man with no significant medical history was transferred to our hospital with a 14-day history of fever and lethargy. Over the previous 5 weeks, he had been treated for traumatic subdural hemorrhage after a car accident. Two weeks prior to transfer, a high fever suddenly developed and persisted despite administration of broad-spectrum antibiotics including ceftriaxone, piperacillin-tazobactam, or meropenem in combination with moxifloxacin. There was a healing abrasion on his hand after the car accident, but there were no stigmata of endocarditis. He had no indwelling medical device and no medical history of allergy.

On admission to our hospital, his blood pressure was 150/100 mmHg, pulse rate was regular at 100 beats per minute, and temperature was 38.0°C. He was slightly drowsy and confused but exhibited no neurologic deformity. Heart sounds were regular without murmur, and breathing sounds were normal.

His white blood cell count was 7,400/mm³ with 79.4% neutrophils. Laboratory data were as follows: hemoglobin, 11.2 g/dL; platelets, 251,000/mm³; C-reactive protein, 79.7 mg/dL; procalcitonin 0.18 ng/mL; and erythrocyte sedimentation rate, 52 mm/h. Electrolyte levels and kidney and liver function tests were normal.

Electrocardiogram showed normal sinus rhythm. Computed tomography (CT) of the chest showed pulmonary emphysema, and abdominal CT was normal. Brain CT revealed a small, chronic subdural hematoma on the left frontal convexity.

The patient initially received 2 g ceftazidime intravenously every 8 hours in combination with oral metronidazole (500 mg every 8 hours). On the third day of admission, 2 separate sets of blood cultures were positive for Gram-positive cocci. After the second set of blood cultures, intravenous vancomycin (1 g every 12 h) was added empirically. On the sixth day, *Kocuria kristinae* was identified in both blood cultures using the Vitek 2 system (bioMérieux, Marcy-l’Etoile, France) in the absence of definitive laboratory guidelines for determining the antibiotic susceptibility. While the initial blood culture was regarded as contaminated, when the same pathogen was isolated from the consecutive blood culture, we determined that *K. kristinae* might be the true pathogen. At this time, initial empiric cefazidime and metronidazole were discontinued and intravenous vancomycin was maintained. Because *K. kristinae* is not a common infective endocarditis pathogen, we also performed 16S rRNA sequencing analysis to confirm the identification of the pathogen in the blood isolates. The universal eubacterial primers RU1 (5’-TTGGAGAGTTTGATCCTGGCTC-3’) and RU2 (GGACTACCAGGTATCTAA-3’) were used. The 16S rRNA gene sequence (766 bp) was blasted with NCBI Blast website http://blast.ncbi.nlm.nih.gov/Blast.cgi. The sequence was 99.00% identical to that of *C. striatum* was identified (GenBank accession number JF342700.1). Transthoracic echocardiography showed 2 mobile oscillating masses at the tip of the mitral valve leaflet. Transesophageal echocardiography revealed 2 hypermobile echogenic masses on the anterior and posterior mitral valve leaflets, 10 mm and 8 mm, respectively (Fig. 1). There was no involvement of either the subvalvular structure or paravalvular structure. There was no evidence of any metastatic lesions at other sites.

Thus, the patient was diagnosed with *C. striatum* infective endocarditis not *K. kristinae* infective endocarditis. After vancomycin was administrated, the fever subsided dramatically. Because of the high embolic risk, mitral valve replacement was performed. Interestingly, *K. kristinae*, which was found in the blood cultures, was also cultured from mitral valve vegetation.

![Figure 1. Transesophageal echocardiogram findings. Large, hypermobile vegetations were attached to the middle scallop of the anterior (arrowhead) and posterior mitral valve leaflets (arrow), 10 mm and 8 mm, respectively. Vegetation on the posterior mitral valve leaflet showed a 7 mm lineal mobile structure, which indicates a high embolic risk.](image)

LA, left atrium; LV, left ventricle; Ao, aorta.
tion despite administration of vancomycin for 14 days. The patient completed 6 weeks of intravenous vancomycin for prosthetic valve endocarditis. At a follow-up over one year later, the patient remained free of infection.

Discussion

Non-diphtheriae Corynebacterium are commonly isolated from clinical specimens but are typically considered contaminants. In addition to C. diphtheriae, Corynebacterium are considered organisms that are normal inhabitants of human skin and respiratory tract [1-3, 7]. Also, with the use of molecular diagnostic methods, the taxonomy of Corynebacterium species has changed and has been reclassified from earlier defined taxa in recent years [1]. There is an increased frequency of reported non-diphtheriae Corynebacterium infections, particularly as a cause of nosocomial infection in hospitalized and immunocompromised patients, though these pathogens are widely distributed in the environment and mucous membranes of humans. Common nosocomial pathogens include Corynebacterium amycolatum, Corynebacterium jeikeium, Corynebacterium urealyticum, and C. striatum [8].

C. striatum is widely distributed in the environment, especially in hospital settings associated with nosocomial infection. It colonizes on the skin and mucous membranes of normal hosts and hospitalized patients, and disruption of its integument may lead to bacteremia and subsequent septic complications in either immunocompromised patients or patients with medical devices [3, 7, 9]. In addition, while C. striatum is frequently isolated in polymicrobial infections, its degree of pathogenicity is unclear, and differentiation of colonization from pathogen-causing infection has been difficult [3]. This organism can cause pneumonia, empyema, meningitis, septic arthritis, vertebral osteomyelitis, and endocarditis [2-4]. C. striatum is an uncommon cause of infective endocarditis. An English language literature search in Medline revealed 22 previously reported cases of endocarditis due to C. striatum (Table 1). The majority of cases (82%, 18/22) are native valve endocarditis. More than half of cases are hospital-acquired infection, and 11 cases (50%) are associated with medical devices, including 4 cases of prosthetic valve, 3 cases of pacemaker lead, 3 cases of vascular access for hemodialysis, and 1 case of ventriculo-atrial shunt. Valve replacements are performed in one quarter of the cases and overall mortality approaches 27%. In our case, the patient had recently experienced a long-term hospital stay and had a scar from an abrasion received during a traffic accident, but had not required a central venous catheter.

One interesting finding is that C. striatum can be misidentified as K. kristinae using automated systems (bioMérieux Vitek 2 GP card). Identification of the genus Corynebacterium to species level is usually based on biochemical tests. Though API Coryne system is a useful tool for identifying Corynebacterium species in the clinical laboratory, this may not incorporate all of the tests necessary for the identification of every Corynebacterium species. In recent years, the introduction of molecular methods, especially 16S rRNA gene and rpoB gene sequencing, has improved the ability to identification of Corynebacterium species [5, 6, 10]. In our case, the causative organism was misidentified as K. kristinae by the commercial identification kit but was confirmed as C. striatum by 16S rRNA sequence analysis. There is a previous similar case report of misidentification of C. striatum as K. kristinae using the commercial identification kit [11]. In literature review, there are only 3 cases of infective endocarditis caused by C. striatum identified by 16S rRNA sequencing [10, 12, 13]. Clinically, when organisms such as C. striatum or K. kristinae are identified from subsequent blood cultures in unusual clinical scenarios, we suggest a genotypic assay, such as 16S rRNA, to confirm species identity. Additionally, 16S rRNA sequencing of resected endocardial specimen is useful tool for verifying the causative agent [14, 15]. Bosshard et al. [14] suggested that the sensitivity, specificity, and positive and negative predictive values of 16S rRNA sequencing were 94%, 100%, 100%, and 90%, for cases of native valve endocarditis. In our case, unfortunately, 16S rRNA sequencing on vegetation acquired in the operative field was not performed. However, because organisms detected from blood and vegetation were both misidentified as K. kristinae using the commercial identification kit, the microorganisms in the vegetation might be C. striatum. Despite the excellent specificity of 16S rRNA sequencing, clinicians have to be aware of the interpretation of a positive result within clinical context; even several months after completion of successful therapy for endocarditis, 16S rRNA sequencing results may still be positive [14].

Antibiotic-susceptibility data of C. striatum is scarce. However, C. striatum may be susceptible to vancomycin but resistant to penicillin, ciprofloxacin, erythromycin, rifampin, and tetracycline; it has variable susceptibility to other β-lactams and aminoglycosides [2]. Recently, the emergence of multidrug-resistant strains acting as nosocomial pathogens was reported in long-term hospitalized patients with underlying disease, and the most effective antibiotic was vancomycin [3, 7, 9].
### Table 1. Reported cases of infective endocarditis caused by *Corynebacterium striatum*

| Year of publication | Age | Sex | Underlying disease                                                                 | Prosthetic valve | Other medical device | Nosocomial risk factors | Affected valve | Echocardiography | Surgery | Antibiotic (s) administered | Survival |
|---------------------|-----|-----|------------------------------------------------------------------------------------|------------------|----------------------|------------------------|---------------|------------------|---------|-----------------------------|----------|
| 1990                | 76  | M   | None                                                                               | N                | N                    | N                      | Aortic         | Echocardiography   | N       | Ampicillin, gentamicin      | N        |
| 1994                | 54  | M   | None                                                                               | N                | N                    | N                      | Aortic         | TTE, TEE         | AVR     | Penicillin, gentamicin; vancomycin | Y        |
| 1996                | 73  | M   | Pacemaker (6 yr ago)                                                               | N                | Y                    | Y                      | Tricuspid      | TEE              | Electrode lead removal | Vancomycin | Y        |
| 1996                | 24  | M   | Congenital hydrocephalus, Ventriculo-atrial shunt state (age of 2 m) Sacral bedsore | N                | Y                    | Y                      | Pulmonary      | TTE, TEE         | N       | Amoxicillin, netilmicin, teicoplanin | Y        |
| 2002                | 68  | M   | Mitral regurgitation, DM, CHF                                                      | N                | N                    | N                      | Mitral         | TTE, TEE         | N       | Vancomycin; penicillin      | Y        |
| 2002                | 62  | F   | AVR (a few years ago)                                                              | Y                | N                    | N                      | Aortic         | TEE              | N       | Vancomycin                | Y        |
| 2002                | 69  | F   | ESRD via prosthetic arteriovenous fistula, ANCA-positive vasculitis                | N                | Y                    | Y                      | Mitral         | TEE              | MVR     | Vancomycin, rifampin        | N        |
| 2002                | 50  | M   | Surgery for mycotic aneurysm (2 m ago)                                             | N                | Y                    | Y                      | Aortic         | TEE              | AVR     | Vancomycin, gentamicin, doxycycline | Y        |
| 2002                | 72  | F   | AVR state (52 d ago), DM, IHD                                                      | Y                | N                    | Y                      | Mitral         | TTE              | N       | Vancomycin, gentamicin      | N        |
| 2005                | 72  | F   | MVR state (1990), culture-negative endocarditis (18 m ago), ANCA positive vasculitis, ARF on HD | Y                | Maybe HD catheter    | Y                      | Mitral         | TEE              | N       | Vancomycin, rifampin        | Y        |
| 2005                | 61  | F   | Cutaneous lupus, IHD                                                               | N                | N                    | N                      | Mitral         | TEE              | N       | Vancomycin, gentamicin      | Y        |
| 2005                | 46  | F   | ESRD, graft-related infection                                                      | N                | Y                    | Y                      | Tricuspid      | TEE              | N       | Linezolid, daptomycin, rifampin | Y        |
| 2006                | 68  | M   | AVR (3 yr ago), MVR (1 yr ago), CHE, AF, CVA                                      | Y                | N                    | N                      | Mitral         | TTE              | N       | Vancomycin                | Y        |
| 2006                | 69  | F   | Endometrial cancer                                                                | N                | N                    | Y                      | Mitral         | TEE              | MVR     | Vancomycin                | Y        |
| 2006                | 77  | F   | None                                                                               | N                | N                    | N                      | Mitral         | Echocardiography   | N       | Medical                    | Y        |
| Year of publication | Age | Sex | Underlying disease | Prosthetic valve | Other medical device | Nosocomial risk factors | Affected valve | Echocardiography | Surgery | Antibiotic(s) administered | Survival |
|---------------------|-----|-----|-------------------|-----------------|---------------------|------------------------|--------------|-----------------|---------|-------------------------|----------|
| 2007                | 62  | M   | CRF, AF           | N               | N                   | Y                      | Aortic        | TEE             | AVR     | Vancomycin              | Y        |
| 2008                | 83  | M   | Metastatic prostate cancer | N       | N                   | N                      | Mitral        | TEE             | N       | Vancomycin, rifampin, penicillin, gentamicin, daptomycin | N        |
| 2008                | 73  | F   | CHF, CRE, DM      | N               | N                   | Y                      | Mitral        | TTE, TEE       | N       | Vancomycin              | Y        |
| 2009                | 71  | M   | DM                | N               | N                   | Y                      | Mitral        | TEE             | N       | Vancomycin              | N        |
| 2010                | 71  | F   | Pacemaker (2 m ago) | N           | Y                   | Y                      | Pacemaker lead| TTE             | Device removal | Daptomycin | Y        |
| 2012                | 56  | M   | DM, ESRD          | N               | N                   | Y                      | Mitral        | TEE             | MVR     | Daptomycin; telavanciAn | N        |
| 2013                | 78  | M   | Pacemaker (6 m ago), DM, CRF | N         | Y                   | N                      | Tricuspid     | TTE             | Electrode lead removal | Daptomycin | Y        |

TTE, transthoracic echocardiography; TEE, transesophageal echocardiography; AVR, aortic valve replacement; yr, years; m, months; DM, diabetes mellitus; CHF, congestive heart failure; ESRD, end-stage renal disease; ANCA, anti-neutrophil cytoplasmic antibody; d, days; IHD, ischemic heart disease; MVR, mitral valve replacement; HD, hemodialysis; ARF, acute renal failure; AF, atrial fibrillation; CVA, cerebrovascular accident; CRF, chronic renal failure.
13, 16]. There are no definitive laboratory guidelines for determining the antibiotic susceptibility of coryneform bacteria, and in our case, susceptibility testing was not available. We treated the patient with vancomycin, which was reported as the most active antibiotic against corynebacteria in the literature, and clinical response was good. Defervescence was achieved after 3 days of vancomycin treatment. In a literature review of *C. striatum* endocarditis, there were more cases treated with medical therapy alone than with valve replacement (Table 1). In our case, we performed mitral valve replacement therapy due to high embolic risk. Interestingly, resected vegetation was culture-positive despite 14 days of vancomycin treatment, so we administered antibiotics for another 4 weeks after valve resection. This bacterial persistence might be associated with multidrug resistance or a high tolerance to antibiotic-induced killing in *C. striatum*. According to Yoo et al. [16], we need awareness of the emergence of multidrug-resistant *C. striatum* in Korea; however, further investigation is required.

Because *Corynebacterium* species are usually considered to be contaminants and are not routinely identified to the species level, *C. striatum* infection rates are probably underestimated. In unusual clinical scenarios, blood cultures positive for *Corynebacterium* species or *K. kristinae*, as determined by a commercial automatic culture system, should not be overlooked. The possibility of *C. striatum* infective endocarditis should be considered even in a patient without structural heart disease or prosthetic valves, and the genotypic assay, such as 16S rRNA sequence analysis, may be very useful.

**Conflicts of Interest**

No conflicts of interest.

**ORCID**

Hwi-In Koh  http://orcid.org/0000-0003-0238-3415

A-Jin Lee  http://orcid.org/0000-0001-7504-0881

Hwi-In Koh  http://orcid.org/0000-0003-2147-1381

**References**

1. Funke G, von Graevenitz A, Claridge JE 3rd, Bernard KA. Clinical microbiology of coryneform bacteria. Clin Microbiol Rev 1997;10:125-59.
2. Rufael DW, Cohn SE. Native valve endocarditis due to *Corynebacterium striatum*: case report and review. Clin Infect Dis 1994;19:1054-61.
3. Lee PP, Ferguson DA Jr, Sarubbi FA. *Corynebacterium striatum*: an underappreciated community and nosocomial pathogen. J Infect 2005;50:338-43.
4. Boltin D, Katzir M, Bugoslavsky V, Yalashvili I, Brosh-Nissimov T, Fried M, Elkayam O. *Corynebacterium striatum*: a classic pathogen eluding diagnosis. Eur J Intern Med 2009;20:e49-52.
5. Yang HS, Kim YJ, Cho SY, Shin E, Lee HJ. Central venous catheter-related bloodstream infection by *Corynebacterium striatum* identified by 16S rRNA and *rpoB* gene sequencing. Ann Lab Med 2015;35:548-50.
6. Khamis A, Raoul D, La Scola B. Comparison between *rpoB* and 16S rRNA gene sequencing for molecular identification of 168 clinical isolates of *Corynebacterium*. J Clin Microbiol 2005;43:1934-6.
7. Weiss K, Labbé AC, Lavenderière M. *Corynebacterium striatum* meningitis: case report and review of an increasingly important *Corynebacterium* species. Clin Infect Dis 1996;23:1246-8.
8. Riegel P, Ruimy R, Christen R, Monteil H. Species identities and antimicrobial susceptibilities of corynebacteria isolated from various clinical sources. Eur J Clin Microbiol Infect Dis 1996;15:657-62.
9. Kim R, Reboli AC. Principles and practice of infectious diseases. 8th ed. New York: Elsevier Saunders; 2015:2373-82.
10. Elshibly S, Xu J, Millar BC, Armstrong C, Moore JE. Molecular diagnosis of native mitral valve endocarditis due to *Corynebacterium striatum*. Br J Biomed Sci 2006;63:181-4.
11. Iaria C, Stassi G, Costa GB, Biundo C, Gerace E, Noto A, Spinella SG, David A, Cascio A. Outbreak of multi-resistant *Corynebacterium striatum* infection in an Italian general intensive care unit. J Hosp Infect 2007;67:102-4.
12. Tran TT, Jaijakul S, Lewis CT, Díaz L, Panesso D, Kaplan HB, Murray BE, Wanger A, Arias CA. Native valve endocarditis caused by *Corynebacterium striatum* with heterogeneous high-level daptomycin resistance: collateral damage from daptomycin therapy? Antimicrob Agents Chemother 2012;56:3461-4.
13. Oliva A, Belvisi V, Iannetta M, Andreoni C, Mascellino MT, Lichtner M, Vullo V, Mastroianii CM. Pacemaker lead endocarditis due to multidrug-resistant *Corynebacterium striatum* detected with sonication of the device. J Clin Microbiol 2010;48:4669-71.
14. Bosshard PP, Kronenberg A, Zbinden R, Ruef C, Bottger EC, Alteweg M. Etiologic diagnosis of infective endocarditis due to...
tis by broad-range polymerase chain reaction: a 3-year experience. Clin Infect Dis 2003;37:167-72.
15. Ha YE, Ryu SY, Ko KS, Joo EJ, Park SY, Kim HA, Lim MH, Kang CI, Chung DR, Song JH, Park PW, Peck KR. Native valve infective endocarditis due to *Staphylococcus lugdunensis* confirmed by 16S ribosomal RNA sequencing. Infect Chemother 2011;43:372-6.
16. Yoo G, Kim J, Uh Y, Lee HG, Hwang GY, Yoon KJ. Multi-drug-resistant *Corynebacterium striatum* bacteremia: first case in Korea. Ann Lab Med 2015;35:472-3.