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Case Report

Corynebacterium jeikeium bacteremia in a hemodialyzed patient

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SUMMARY

Corynebacterium jeikeium, frequently encountered in clinical specimens, is part of the normal skin flora. Nevertheless, a few cases of *C. jeikeium* bacteremia followed by severe clinical manifestations have been reported. *C. jeikeium* has been reported to cause endocarditis, septicemia, meningitis, pneumonia and osteomyelitis, along with soft tissue and trauma infections. Herein we describe a case of *C. jeikeium* bacteremia in Greece. The isolation of a coryneform bacterium from a clinical specimen should not immediately be considered a superinfection by the skin flora. Clinical and laboratory investigations are essential in order to evaluate such cases before applying appropriate treatment. On the other hand, the association of coryneform bacteria and disease should be critically investigated, with a thorough identification of the strain, ideally beyond the classical methods, at a specialized center.

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1. Introduction

Corynebacterium jeikeium (*C. jeikeium*) is a Gram-positive, aerobic bacterium commonly located on the surface of the skin, constituting a part of the normal flora and not causing disease. However, in some rare cases, *C. jeikeium* bacteremia is responsible for extremely severe clinical manifestations, which might result to death, if left untreated. We describe a molecularly confirmed case of a *C. jeikeium* bacteremia in Greece.

2. Case report

A 67-year-old female patient, who had been undergoing hemodialysis for the last two years, was admitted to the hospital for a scheduled session, with a 2-day fever, fatigue, malaise and weakness. A permanent, single lumen subclavian venous catheter was being used for the hemodialysis; she also had a urinary bladder catheter because of chronic interstitial cystitis (for the last 4 months). During hemodialysis, the patient had a fever (39 °C) and chills. Cultures of urine and blood (20 ml from one site (peripheral vein) for an anaerobic and an aerobic bottle) were taken prior to initiating antimicrobial therapy. Vancomycin (VAN; 1 g intravenously once daily) plus amikacin (AMK; 500 mg intravenously once daily) were initially started by the renal service (empirical treatment). The patient was transferred to the internal medicine department of the hospital. Upon transfer, intravenous levofloxacin (LEV; 500 mg every 12 h) was administered for the first day, followed by oral LEV (250 mg every 12 h) for the next 2 days. One day after admission, the patient became afebrile. Hematological investigations revealed a white blood cell count of 13.5×10^9/l, a hemoglobin level of 12.7 g/dl, and a hematocrit of 38.3%. Urea was elevated at 36.414 mmol/l (reference range 3.570–17.850 mmol/l), while creatinine levels reached 486.2 μmol/l (reference range 53–97 μmol/l). C-reactive protein was 55 mg/l. The urine culture and anaerobic blood culture were negative, while a Gram-positive coryneform bacterium was isolated from the aerobic blood culture. This positive result was not disregarded as a contaminant.

On day 5 after admission, the patient developed another feverish episode with the temperature reaching 38 °C, along with rigors. Urine and blood cultures were collected during the hemodialysis session (20 ml blood from the subclavian venous catheter for an anaerobic and an aerobic bottle). The urine and anaerobic blood cultures were both negative. The same Gram-positive coryneform bacterium was isolated from the aerobic

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Table 1
Biochemical characteristics and other traits of the isolated bacterium

Biochemical characteristic/other trait	Result
Fermentation/oxidation (F/O)	O
Lipophilic	+
Nitrate reduction	–
Urease	–
Esculin hydrolysis	–
Acid production/glucose	+
Acid production/sucrose	–
Acid production/mannitol	–
Acid production/xylose	–
CAMP test	–
Fructose	–
Anaerobic growth	–

Table 2
Antimicrobial susceptibility pattern of *Corynebacterium jeikeium*

Antimicrobial agent	MIC (mg/l)	S/R	Breakpoint (mg/l)
Ampicillin (AMP)	>32	R	1
Cefotaxime (CTX)	>32	R	1
Chloramphenicol (CHL)	128	R	8
Ciprofloxacin (CIP)	>32	R	1
Clindamycin (CLI)	>256	R	0.5
Erythromycin (ERY)	>256	R	0.5
Gentamicin (GEN)	>256	R	1
Linezolid (LZD)	1	S	4
Moxifloxacin (MXF)	16	R	1
Penicillin (PEN)	>32	R	0.125
Rifampin (RIF)	0.016	S	1
Teicoplanin (TEC)	2	S	4
Tetracycline (TET)	16	R	1
Vancomycin (VAN)	2	S	4

S, sensitive; R, resistant.

blood culture. VAN was administered (1 g intravenously once daily) simultaneously with rifampin (RIF; 600 mg orally every 12 h) for 3 weeks. One day after VAN administration, her temperature again fell to within the normal range and the patient has remained afebrile and in good clinical condition ever since. In a scheduled hemodialysis session 3 weeks after the second feverish episode, the urine and blood cultures (20 ml from one site (peripheral vein) for an anaerobic and an aerobic bottle) were negative.

Blood cultures were incubated in a Bactec 9050 analyzer (Becton Dickinson, NJ USA). Positive blood cultures were inoculated onto Colombia agar plates (Becton Dickinson) supplemented with 5% sheep blood (SBA). The plates were incubated at 37 °C in a 5% CO_2 enriched atmosphere. Primary identification of the two strains, performed according to Gram stain and morphology of colonies along with a set of biochemical properties, revealed *C. jeikeium* (Table 1).[1,2] After 24 h of growth, colonies were small (0.5–1 mm), entire, low convex, grayish-white and non-hemolytic. Gram stain revealed pleomorphic, occasionally club-shaped, Gram-positive rods, arranged in V forms or palisades. The strains were further characterized with the RapID CB plus system (Rymel) as *C. jeikeium*.

DNA was extracted from cultured microorganisms using the Qiagen DNA extraction kit (Qiagen, Hilden, Germany). A PCR that amplifies nearly the full-length of the 16S ribosomal DNA (rDNA) using the primer set fD1–rP2 was applied, and a PCR product of approximately 1500 bp was obtained.[3] The strain was sent to a specialized center (Dr Guido Funke, Department of Medical Microbiology and Hygiene, Gärtner & Colleagues Laboratories, Weingarten, Germany), where the full 16S rDNA sequence (>1400 bp) was established, confirming that the microorganism was *C. jeikeium*, being almost identical to *C. jeikeium* strain K411 (fully sequenced genome).

Although the isolated strain was multi-resistant to several antibiotics, it was susceptible to glycopeptides (VAN, teicoplanin (TEC)), linezolid (LZD) and RIF (Table 2). Molecular identification was conducted for both isolates and they were found to be identical.

3. Discussion

Unusual cases of coryneform bacteria causing endocarditis (*Corynebacterium striatum*,[4] *Corynebacterium amicolatum*[5]) and septicemia[6] (*Corynebacterium macginleyi*), retrospectively, have recently been reported. We have described a molecularly confirmed case of a *C. jeikeium* bacteremia in Greece.

Since positive results were obtained from both blood cultures (from the peripheral vein and from the hemodialysis catheter), it could not be determined if the infection was due to the presence of the subclavian venous catheter (line infection). The catheter was necessary for hemodialysis, hence it was not removed. Therapeutic application of the proper antibiotic scheme led to the successful treatment of this *C. jeikeium*-induced bacteremia.

C. jeikeium is considered a bacterium of the normal skin flora. It is especially encountered in hospitalized patients, while it has also been isolated from the broad hospital environment.[7] *C. jeikeium* is one of the most frequent Gram-positive coryneform bacteria isolated from clinical specimens.[2] The clinical spectrum of manifestations attributed to *C. jeikeium* is wide. It has been reported to cause endocarditis (particularly after surgical interventions), bacteremia, septicemia, meningitis, pneumonia, osteomyelitis or infectious arthritis after total hip arthroplasty replacement plus skin, soft tissue, and trauma infections.[8–13] A case of endocarditis due to *C. jeikeium* in a Greek patient with acute myelogenous leukemia has been described.[14] In that case, the result was based on two blood culture sets, along with a culture taken from the skin lesion; however it was not confirmed by molecular methods. Furthermore, *C. jeikeium*-attributed sepsis after administration of 8-methoxypsoralen for the treatment of a cutaneous T-cell lymphoma has been reported.[15] Several cases of bacteremia caused by *Corynebacterium spp* in patients with central venous catheters have been described. Colonization of the venous catheter by *Corynebacterium spp* frequently co-exists with the aforementioned bacteremia in such cases.[16,17]

C. jeikeium is resistant to a variety of antimicrobial agents. Resistance is considered chromosome-mediated and not plasmid-mediated.[18] The bacterium is characteristically resistant to penicillin, aminoglycosides and cephalosporins, it is sensitive to glycopeptides and pristinamycin, while its sensitivity to erythromycin, tetracycline, rifampin and to quinolones varies.[7,9,19–25] Although *C. jeikeium* is a significant opportunistic pathogen, its presence in the hospital environment is probably the most clinically important aspect of the natural history of this organism. This is because there is recent evidence that drug resistance genes may have transferred from corynebacteria to a *Propionibacterium sp* clinical isolate. Thus, the high incidence of multiple drug-resistant *C. jeikeium* suggests that this organism may be an important environmental reservoir of drug resistance genes.[26] *C. jeikeium* is the most frequently recovered medically significant corynebacterial species in intensive care facilities.[26]

The evaluation of the clinical significance of the isolation of a Corynebacterium strain from clinical specimens is not always easy. This is partly due to the fact that corynebacteria constitute part of the normal skin flora. Thus, their isolation might be attributed to poor techniques during sample collection. In such cases, there is not bacteremia, but the presence of the aforementioned bacterium in the skin. However, there are cases where there is indeed bacteremia of coryneform bacteria and positive

Table 3
Indications that increase the clinical significance of coryneform bacteria isolated from blood cultures—underlying diseases and risk factors

Underling disease	Source
Neoplastic disease; immunosuppressed patients	Wang et al. 2001,[27] Van der Lelie et al. 1995,[10] Ross et al. 2001,[28] Mookadam et al. 2006[13]
Cirrhosis	Bhayani et al. 2009[32]
Brain infarction; cerebrovascular disorders; subarachnoid hemorrhage; spinal injury; multiple sclerosis	Otsuka et al. 2006[33]
Diabetes	Otsuka et al. 2006[33]
Pneumonia	Otsuka et al. 2006[33]
Acute myocardial infarction	Otsuka et al. 2006[33]
Risk factors	Source
Prosthetic material (catheters, cardiac valves, cerebrospinal fluid shunt)	Keren et al. 1988,[29] Rozdzinski et al. 1991,[30] Akan et al. 2002,[31] Mookadam et al. 2006[13]
Prolonged neutropenia	Rozdzinski et al. 1991[30]
Treatment with multiple antibiotics	Rozdzinski et al. 1991[30]
Extended hospitalization	Umeh et al. 2004[15]
Disruption of skin integuments; anal fistula	Brown 1995,[34] Otsuka et al. 2006[33]
Clinical and/or echocardiographic evidence of infective endocarditis	Mookadam et al. 2006[13]
Hemodialysis	Mookadam et al. 2006[13]
Adult male or postmenopausal female	Van der Lelie et al. 1995[10]

blood cultures should not be disregarded in these cases. Such positive cultures should be evaluated, according to specific criteria. In these cases, further testing (more blood cultures obtained, identification to species level) and follow-up of the patients are necessary. In particular, concomitant and underlying diseases, along with various risk factors, increase the clinical importance of coryneform bacteria isolated from blood cultures (Table 3).[1,10,13,27–34] Other indications of clinical significance, according to the experience of our center, include multiple blood cultures positive for the same coryneform bacteria, absence of isolation of other pathogenic microorganisms, symptoms and signs compatible with bacteremia, and negative blood cultures or recession of the febrile disease after applying appropriate treatment according to the antibiogram. In the aforementioned cases, the strains of the isolated coryneform bacteria should be identified, combined with an antibiogram in order to determine the proper treatment.

The clinical correlation between the isolation of *C. jeikeium* strains and the feverish disease in our patient is based on the following evidence: (1) The bacterium was isolated from a normally sterile body site (blood); (2) the same bacterium was isolated from more than one specimen (subclavian venous catheter and peripheral vein); (3) the identification process revealed the same microbial strain in both feverish episodes of the patient; (4) no other pathogenic microorganism was isolated; (5) the negativity of blood cultures and the final recession of the febrile disease were accomplished after initiating appropriate antimicrobial treatment, according to an antibiogram. Risk factors for a *C. jeikeium*-related bacteremia in our patient were the presence of a central venous catheter and the hemodialysis sessions, along with her post-menopausal status.[10,13]

In conclusion, timely therapeutic intervention with the proper antibiotic scheme can lead to the successful treatment of *C. jeikeium*-induced bacteremia, without removal of the central venous catheter.[27] Isolation of a coryneform bacterium from a clinical specimen has to be critically evaluated and followed by a thorough identification of the strain, ideally beyond the classical methods, at a specialized center.

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