IDCases 23 (2021) e01046

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcr

Case report

Brevibacteria tibial osteomyelitis

Yehuda Eidensohn[a], Abraham Wei[b], Michael Sirkin[c], Lisa L. Dever[b,*]

[a] Department of Medicine, Rutgers New Jersey Medical School, Newark, NJ, United States
[b] Division of Infectious Diseases, Department of Medicine, Rutgers New Jersey Medical School, Newark, NJ, United States
[c] Department of Orthopaedics, Rutgers New Jersey Medical School, Newark, NJ, United States

ARTICLE INFO

Article history:
Received 22 December 2020
Received in revised form 8 January 2021
Accepted 9 January 2021

Keywords:
Brevibacterium
Osteomyelitis
Tibial infection
Implanted hardware

ABSTRACT

Brevibacteria are Gram-positive rods found in human skin flora and dairy products. Although generally not considered human pathogens, case reports have implicated *Brevibacterium* species as rare causes of bacteremia, endocarditis, peritonitis, and osteomyelitis. We report a case of *Brevibacterium* tibial osteomyelitis in an immunocompetent individual with implanted hardware and highlight the challenge of identifying the organism and recognizing it as a potential pathogen.

Introduction

Brevibacteria are Gram-positive rods that appear as diphtheroid rods in cultures for the first 24 h and then transition to coccoid or coccobacillary morphology [1]. They are found in raw milk and contribute to the taste and scent of cheese. They are normal human skin flora and are thought to contribute to foot odor. We report a case of tibial osteomyelitis associated with implanted hardware in an immunocompetent adult due to this organism.

Case presentation

A 40-year-old man with a history of extensive lower extremity trauma two years prior requiring left leg open reduction and internal fixation presented to the emergency department with left ankle pain and serous drainage for two months. He had been treated previously with oral cephalexin with no response. He was afebrile and his vital signs were within normal limits. Physical examination was remarkable only for a 0.5 cm open wound over the left medial malleolus. There was no drainage, erythema or swelling noted. Laboratory studies were performed including complete blood count, complete metabolic panel, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and procalcitonin. All were within normal limits. Plain radiograph of the left ankle showed a healed fracture of the distal tibia with intact plate and screws. There were no acute changes. He was discharged with wound care instructions.

In outpatient follow-up one week later, he was found to have expansion of the left ankle wound with profuse serous drainage concerning for underlying osteomyelitis. He underwent incision and drainage of the left distal tibia. Surgical exploration revealed a purulent sinus tract from the skin to the implanted plate and screws. All hardware was removed. Four operative cultures were obtained; two from the wound, one from deep ankle tissue, and one from the periosteum. Post-operatively, he received empiric intravenous (IV) vancomycin 1250 mg every 8 h, cefepime 2 g every 8 h and metronidazole 500 mg every 8 h. Routine laboratory studies were normal with the exception of an elevated CRP that trended from 24 to 3 mg/L and ESR that trended from 9 to 17 mm/hour during the course of his hospitalization. Blood and urine cultures were negative. Two wound cultures and one tissue culture grew coryneform Gram-positive rods initially identified as *Corynebacterium* species. Two days later, the isolate was confirmed to be *Brevibacterium* species via biochemical testing (Analytical Profile Index Coryne, bioMerieux, Marcy-l'Etoile, France), but was unable to be identified to the species level.

The patient had decreased pain and improved wound healing following surgery. Due to subtherapeutic vancomycin levels despite aggressive dosing, he was changed to IV daptomycin 10 mg/kg (750 mg) every 24 h. He was discharged home to complete a five-week course of therapy. The susceptibility of the *Brevibacterium* species was not known at the time of discharge. Agar disc diffusion susceptibility testing was not available at the time due to a nationwide shortage of Mueller-Hinton agar during the coronavirus pandemic. The isolate was sent to an external laboratory for susceptibility testing.

* Corresponding author at: Division of Infectious Diseases, Department of Medicine, Rutgers New Jersey Medical School, Newark, NJ, 07103, United States.
E-mail address: deverll@njms.rutgers.edu (L.L. Dever).

http://dx.doi.org/10.1016/j.idcr.2021.e01046

Susceptibility results returned two weeks later. The isolate was susceptible to erythromycin (MIC < 0.50 μg/mL), gentamicin (MIC < 1.0 μg/mL), penicillin (MIC 0.12 μg/mL), rifampin (MIC < 1.0 μg/mL), tetracycline (MIC < 1.0 μg/mL), and vancomycin (MIC < 2.0 μg/mL).

Three weeks following surgery, the patient's left tibial wound was healing and sutures were removed. After 5 weeks of IV daptomycin he was transitioned to oral amoxicillin 500 mg every 8 h for a planned 4 week-course of therapy. Six weeks post-operatively, his surgical wound was well healed with no tenderness or erythema, and ESR and CRP levels were normal.

Discussion

The genus *Brevibacterium* includes many species but only nine have been isolated from humans: *B. linens, B. iodinum, B. epidermidis, B. casei, B. mcbrellneri, B. otitidis, B. paucivorans, B. massiliense* and *B. sanguinis. Brevibacterium* species were thought to be apathogenic until 1991, when the first case of sepsis due to *B. epidermidis* central line-associated blood stream infection was reported by McCaughey [2]. Since that time, at least 18 total case reports have implicated *Brevibacterium* species in human disease (Table 1) [3–21]. *B. casei* is the most frequent species isolated from clinical specimens [1]. The most common infection has been bacteremia (n = 10), with the rest of cases being peritonitis, pericarditis, endocarditis, brain abscess, and osteomyelitis.

Reported patient characteristics vary widely. Five patients were immunocompromised; two had acquired immunodeficiency syndrome (AIDS) and three were receiving chemotherapy for cancer. Others had a history of cancer, or had other systemic diseases including Zollinger-Ellison, aplastic anemia, pulmonary hypertension, heart failure or methylmalonic acidemia. Presence of foreign material or central venous catheters (CVC) were common. Most cases of bacteremia were associated with CVC. The patient with peritonitis was receiving continuous ambulatory peritoneal dialysis, and the patient with endocarditis had prosthetic valves. The cases of *Brevibacterium* brain abscess and osteomyelitis occurred in immunocompetent healthy patients with no apparent predisposition [2,20].

A theme of these case reports is the challenge of recognizing the organism is not a skin contaminant and correctly identifying it. This often requires extensive biochemical testing or sending

Table 1
Summary of *Brevibacterium* species Infection Case Reports.

Author/Year	Age	Comorbidities	Foreign Material	Type of Infection	*Brevibacterium* species	Antibiotic Therapy	Identification Technique	Outcome
McCaughey 1991 [2]	40 years	Zollinger-Ellison	Central catheter	Bacteremia	*B. epidermidis***	Erythromycin	Reference laboratory	Recovered
Neumeister 1993 [3]	4 weeks	None	None	Osteomyelitis	Not specified	Cefazolin Oxacillin	Fatty acid analysis	Recovered
Lina 1994 [4]	19 years	Acute lymphocytic leukemia	Not reported	Bacteremia	Not specified	Tetracycline Amikacin	API Coryne System and biochemical tests	Recovered
Reinert 1995 [5]	25 years	Testicular choriocarcinoma	Central catheter	Bacteremia	*B. casei*	Piperacillin Teicoplanin	Carbohydrate assimilation*	Recovered
Kaukoranta-Tolvanen 1995 [6]	46 years	Hodgkins lymphoma	Central catheter	Bacteremia	Not specified	Cephalexin	API Coryne System and biochemical tests	Not reported
Castaglona 1996 [7]	Not reported	Neuroblastoma	Central catheter	Bacteremia	*B. casei*	Not reported	Reference laboratory	Not reported
Antoniou 1997 [8]	69 years	Not reported	Peritoneal catheter	Peritonitis	*B. iodinum*	Cefuroxime Ciprofloxacin	API Coryne System and biochemical tests	Recovered
Brazzola 2000 [9]	18 years	HIV infection	Implanted central catheter	Bacteremia	*B. casei*	Ciprofloxacin	API Coryne System	Recovered
Wauters 2000 [10]	73 years	Peritoneal dialysis	Peritoneal catheter	Peritonitis	*B. otitidis*	Cefazolin Gentamicin	Fatty acid analysis and rRNA analysis	Recovered
Ogunc 2002 [11]	60 years	Chronic lymphocytic leukemia	None	Bacteremia	Not specified	Vancomycin	Reference laboratory*	Recovered
Janda 2002 [12]	34 years	AIDS	Central catheter	Bacteremia	*B. casei*	Vancomycin	API Coryne System	Recovered
Dass 2002 [13]	No reported	No reported	Prosthetic heart valve	Endocarditis	Not specified	Vancomycin Gentamicin Azithromycin	Not reported	Recovered
Cannon 2004 [14]	78 years	Cancer	None	Pericarditis	*B. casei*	Vancomycin	Not reported	Recovered
Vecten 2006 [15]	4 years	Methylmalonic acidemia	Gastric tube	Bacteremia	*B. massilense*	Ofloxacin	16s rRNA analysis	Recovered
Ulrich 2006 [16]	62 years	Pulmonary hypertension	Central catheter	Bacteremia	Not specified	Vancomycin Moxifloxacin	Biochemical testing	Recovered
Kumar 2011 [17]	31 years	None	None	Brain abscess	*B. casei*	Cefotaxime Amoxicillin	Biochemical testing and genetic sequencing	Recovered
Bal 2015 [18]	6 years	Acute lymphocytic leukemia	Central catheter	Bacteremia	*B. casei*	Vancomycin Piperacillin-tazobactam	MALDI-TOF	Recovered
Magi 2018 [19]	48 years	Breast cancer	Implanted central catheter	Bacteremia	*B. casei*	Teicoplanin Linezolid	MALDI-TOF	Recovered
Asai 2019 [20]	94 years	Heart failure, diabetes mellitus	No	Bacteremia	*B. paucivorans*	Meropenem Tetracycline	MALDI-TOF	Died from candida sepsis
Joshi 2020 [21]	6 years	Aplastic anemia	Central catheter	Bacteremia	*B. casei*	Meropenem Amikacin	MALDI-TOF	Recovered

Abbreviations: MALDI-TOF: Matrix assisted laser desorption ionization time of flight.
API Coryne system is licensed by Bio-Merieux.
* Isolate was misidentified by API Coryne system.
** This identification is questioned by Funke et al. [1].

isolates to a reference laboratory for identification. Simple mass spectrometry is not adequate for identification. Earlier identification techniques such as the API Coryne System (bioMérieux, USA), were reported having discrepancies or errors in identification [10,18]. Other adjunctive tests include 16s rRNA analysis, fatty acid analysis with gas chromatography, and degradation of casein, tyrosine, and xanthine. Matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) using spectra of bacterial peptides is the most reliable newer modality of identification, but is not yet widely available in microbiology laboratories.

Antimicrobial susceptibility testing is also a challenge. Techniques most commonly reported are Etest and agar disc diffusion, with only a few successful instances of automated microdilution testing. Even when a MIC value is obtained, no standard breakpoints exist for *Brevibacterium*. The most commonly used breakpoints were proposed by Funke in 1996 [22]. More recent reports used the Clinical and Laboratory Standards Institute's recently established breakpoints for *Corynebacterium* [23]. Isolates are universally sensitive to the glycopeptides with occasional beta-lactam resistance. These are consistent with early work by Funke, and are why the most common empiric therapy has been vancomycin or teicoplanin [22]. We chose to use daptomycin in our patient due to the inability to achieve therapeutic levels of vancomycin despite every 8-h dosing.

Conclusion

Brevibacteria can cause serious infections even in immunocompetent individuals, especially in the presence of CVC or implanted hardware. The presence of implanted hardware was likely a predisposing factor in our patient. Our case highlights the need for greater awareness of the potential pathogenicity of *Brevibacterium* species, especially in patients with implanted material, and the possibility of misidentification as apathogenic coryneform bacteria.

Funding

None.

Consent

The patient provided verbal and written consent for publication.

Ethical approval

N/A.

Author contribution

Yehuda Eidensohn: Care of patient, writing and editing of manuscript.

Abraham Wei: Care of the patient, editing of manuscript.

Michael Sirkin: Care of patient and review of manuscript.

Lisa L. Dever: Care of patient, writing, editing, submitting and revising manuscript.

Declaration of Competing Interest

The authors report no declarations of interest.

References

[1] Funke G, von Graevenitz A, Clarridge JE, Bernard KA. Clinical microbiology of coryneform bacteria. Clin Microbiol Rev 1997;10(1):125–59, doi:http://dx.doi.org/10.1128/CMR.10.1.125-159.1997.

[2] McCaughey C, Damani NN. Central venous line infection caused by Brevibacterium epidermidis. J Inf 1991;23:211–2.

[3] Neumeister B, Mandel T, Gruner E, Pfyffer GE. Brevibacterium species as a cause of osteomyelitis in a neonate. Infection 1993;21(3):177–8, doi:http://dx.doi.org/10.1007/BF01710543.

[4] Lina B, Carlotti A, Lesaint V, Devaux Y, Freney J, Fleurette J. Persistent bacteremia due to Brevibacterium species in an immunocompromised patient. Clin Infect Dis 1994;18:487–8, doi:http://dx.doi.org/10.1093/clinids/18.3.487.

[5] Reinert RR, Schnitzler N, Haase G, Luttticken R, Fabry U, Schaal KP, et al. Recurrent bacteremia due to Brevibacterium casei in an immunocompromised patient. Eur J Clin Microbiol Infect Dis 1995;14:1082–5, doi:http://dx.doi.org/10.1007/BF01590943.

[6] Kaukoranta-Tolvanen SS, Sivonen A, Kostiala AA, Hormila P, Vaara M. Bacteremia caused by Brevibacterium species in an immunocompromised patient. Eur J Clin Microbiol Infect Dis 1995;14:801–4, doi:http://dx.doi.org/10.1007/BF01690997.

[7] Castagnola E, Conte M, Venzano P, Garaventa A, Viscoli C, Pescetto L, et al. Broviac catheter-related bacteremias due to unusual pathogens in children with cancer: case reports with literature review. J Infect 1997;34:215–8, doi:http://dx.doi.org/10.1016/s0163-4453(97)94199-2.

[8] Antoniou S, Dimitriadis A, Polydorou F, Malaka E. Brevibacterium iodum peritonitis associated with acute urticaria in a CAPD patient. Perit Dial Int 1997;17:614–5.

[9] Brazzola P, Zbinden R, Rudin C, Schaad UB, Heininger U. Brevibacterium casei sepsis in an 18-year-old female with AIDS. J Clin Microbiol 2000;38:3513–4, doi:http://dx.doi.org/10.1128/JCM.38.9.3513-3514.2000.

[10] Wauters G, Van Bosterhaut B, Avesani V, Cuvelier R, Charlier J, Janssens M, et al. Peritonitis due to Brevibacterium otitidis in a patient undergoing continuous ambulatory peritoneal dialysis. J Clin Microbiol 2000;38:4292–3, doi:http://dx.doi.org/10.1128/JCM.38.11.4292-4293.2000.

[11] Ogunc D, Gultekin M, Colak D, Timurajaoglu A, Ongut G, Mutlu G, et al. Bacteremia caused by Brevibacterium species in a patient with chronic lymphocytic leukemia. Haematologia 2002;32:151–3, doi:http://dx.doi.org/10.1163/156855902320387998.

[12] Janda WM, Tipirneni P, Novak RM. Brevibacterium casei bacteremia and line sepsis in a patient with AIDS. J Infect 2003;46:61–4, doi:http://dx.doi.org/10.1053/jinf.2002.1076.

[13] Dass KN, Smith MA, Gill VJ, Glodstein SA, Lucey DR. Brevibacterium endocarditis: a first report. Clin Infect Dis 2002;35:e20–21, doi:http://dx.doi.org/10.1086/340984.

[14] Cannon JP, Spandoni SL, Pesh-Iman S, Johnson S. Pericardial infection caused by Brevibacterium casei. Clin Microbiol Infect 2005;11(2):164–5, doi:http://dx.doi.org/10.1111/j.1469-0691.2004.01050.x.

[15] Vecten M, Gouriet F, Cano A, Raoult D. Brevibacterium massiliense bacteremia. IDCases 2016;7:25–6, doi:http://dx.doi.org/10.1016/j.idcr.2016.11.010.

[16] Ulrich S, Zbinden R, Pagano M, Fischler M, Speich R. Central venous catheter infection with Brevibacterium sp. in an immunocompetent woman: case report and review of the literature. Infection 2006;34(2):103–6, doi:http://dx.doi.org/10.1007/s15010-006-5027-6.

[17] Kumar VA, Augustine D, Panikar D, Nandakumar A, Dinesh KR, Karim S, et al. Brevibacterium casei as a cause of brain abscess in an immunocompetent patient. J Clin Microbiol 2011;49(12):4374–6, doi:http://dx.doi.org/10.1128/JCM.01086-11.

[18] Bal ZS, Sen S, Karapinar DY, Aydemir S, Vardar F. The first reported catheter-related Brevibacterium casei bloodstream infection in a child with acute leukemia and review of the literature. Braz J Infect Dis 2015;19(2):213–5, doi:http://dx.doi.org/10.1016/j.bjid.2014.09.011.

[19] Magi M, Migliorini L, Sansoni A, Cusi MG. Brevibacterium casei bacteraemia in a port-a-cath carrier patient: a case report. Infez Med 2018;26(3):263–5.

[20] Asai N, Suematsu H, Yamada A, Watanabe H, Nishiyama N, Sakanashi D, et al. Brevibacterium paucivorans bacteremia: case report and review of the literature. BMC Infect Dis 2019;19(1):344, doi:http://dx.doi.org/10.1186/s12879-019-3962-y.

[21] Joshi S, Misra R, Kirolikar S, Mushrif S. Catheter-related Brevibacterium casei bloodstream infection in a child with aplastic anaemia. Indian J Med Microbiol 2020;38(2):226–8, doi:http://dx.doi.org/10.4103/ijmm.IJMM_20_292.

[22] Funke G, Pünter V, von Graevenitz A. Antimicrobial susceptibility patterns of some recently established coryneform bacteria. Antimicrob Agents Chemother 1996;40(12):2874–8, doi:http://dx.doi.org/10.1128/AAC.40.12.2874.

[23] Clinical and Laboratory Standards Institute. Methods for antimicrobial dilution and disk susceptibility testing for infrequently isolated or fastidious bacteria; CLSI guideline M45. 3rd ed. 2015 Wayne, PA.ce:bibliography-sec>