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Case report

The first reported catheter-related *Brevibacterium casei* bloodstream infection in a child with acute leukemia and review of the literature



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ABSTRACT

Brevibacterium spp. are catalase-positive, non-spore-forming, non motile, aerobic Gram-positive rods that were considered apathogenic until a few reports of infections in immunocompromised patients had been published. To the best of our knowledge, this is the first report of *B. casei* catheter-related bloodstream infection in a child with acute leukemia. We aim to enhance the awareness of pediatric hematology and infectious disease specialists about this pathogen and review of the literature.

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Introduction

Since the first description of the genus *Brevibacterium* in 1953 by Breed,¹ it had been rarely reported as a cause of catheter related bloodstream infection (CRBSI). This microorganism was considered apathogenic until a few reports of infections in immunocompromised patients were published. Coryneform bacteria are aerobically growing Gram-positive rods with distinctive irregular morphology on staining. Taxonomically, they are a heterogeneous group consisting of various genera, includ-

ing the genus *Corynebacterium* and the genus *Brevibacterium*. *Brevibacteria* are nonmotile, nonfastidious, chemoorganotrophic, obligately aerobic, rod-shaped, halotolerant ($\geq 6.5\%$ NaCl), and catalase positive.² In nature, *Brevibacterium* contributes notably to the aroma and color (orange pigment) of surface-ripened cheese. The organism can also be found in raw milk, human skin, and animal sources. Presently, the genus *Brevibacterium* consists of 45 different species, of which only ten, namely, *B. linens*, *B. casei*, *B. epidermidis*, *B. iodinum*, *B. mcbrellneri*, *B. otitidis*, *B. paucivorans*, *B. sanguinis*, *B. mas-siliense*, *B. avium* have been isolated from clinical samples.³

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B. casei is the most frequently isolated *Brevibacterium* species from otherwise sterile human sites.³ In English literature among the eight patients with *B. Casei* catheter-related bacteremia reported, three were pediatric patients.⁴⁻¹¹ This is the first case of *B. casei* CRBSI in a child with acute leukemia.

Case report

A 6-year-old male child with standard-risk group B-cell acute lymphoblastic leukemia (ALL) was being treated according to BFM-2002, in the maintenance phase of a chemotherapeutic regimen that included methotrexate and 6-mercaptopurine was admitted to our hospital complaining of small grouped maculopapular lesions on an erythematous base. The papules rapidly turned into vesicles, then into pustules in the lumbar area. The patient received intravenous acyclovir for herpes zoster infection. He developed fever on the fifth day of hospitalization and his whole blood cell count revealed pancytopenia; he was then put on piperacillin-tazobactam (75 mg/kg every 8 h) empirically according to febrile neutropenia guidelines. Intravenous vancomycin (15 mg/kg every 6 h) was added because the patient had a history of coagulase-negative staphylococcus CRBSI. The complete blood cell count (CBC) at the time of fever included a white blood cell count of $1930 \text{ mm}^3/\mu\text{L}$ (reference range, $[4-10.2] \times 10^3 \text{ mm}^3/\mu\text{L}$), hemoglobin of 7.24 g/dL (reference range, 11-16 g/dL), and a platelet count of $85 \times 10^3 \text{ mm}^3/\mu\text{L}$ (reference range, $[150-400] \times 10^3 \text{ mm}^3/\mu\text{L}$), absolute neutrophil count of $387 \text{ mm}^3/\mu\text{L}$ (reference range, $[1.5-6] \times 10^3 \text{ mm}^3/\mu\text{L}$). C-reactive protein was 6.1 mg/dL. A complete metabolic panel turned out normal, with no evidence of liver or renal dysfunction. The patient was febrile with an ill appearance but maintained normal blood pressure and normal mental status, and there was no concern for sepsis. All three blood cultures collected following fever turned out positive with the same coryneform bacteria *Brevibacterium casei*. Antimicrobial susceptibility testing revealed that the organism was susceptible to vancomycin and fever resolved after 24 h of antibiotic therapy and was not switched.

Two follow-up blood cultures were collected in the subsequent week of incubation. These cultures came back negative. The patient finally defervesced 10 days after starting therapy.

Positive blood cultures that were collected through the Hickmann catheter suggested that the portal of entry of the organisms was related to compromised mucosal integrity secondary to the indwelling central line.

Catheter removal was not required and bacteremia due to the same pathogen for more than six months has not recurred.

Microbiology

The organism was recovered in the BacT/Alert system (bioMérieux, France) from both the aerobic and anaerobic bottles of all three blood culture sets. On Gram-stained smears from the culture bottles, the organisms appeared as Gram-positive, club-shaped, slightly curved rods, and some coccal forms were also present. Colonies on sheep blood and choco-

late agars were gray-white, smooth, non-hemolytic, and had a pungent cheese-like odor.

Presumptive identification of *Brevibacterium* spp was made and the isolate was further identified by VITEK MS (bioMérieux, France). Vitek-MS that is using Matrix assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS) technology which is a new technology for species identification based on the protein composition of microbial cells. The most prominent advantages are the quick turnaround time and its low cost to access a quality database of reference spectra, including *Brevibacteria*.¹² The isolate was tested for antibiotic sensitivity on Muller Hinton agar by Kirby Bauer disc diffusion technique using standard methods. The strain was sensitive to all antibiotics tested, i.e. penicillin, cephalothin, cefotaxime, gentamicin, erythromycin, ciprofloxacin, and vancomycin as per Clinical and Laboratory Standards Institute (CLSI) guidelines. CLSI for interpreting susceptibility results are based on the recommendations that apply to *Corynebacterium* species.¹³

Discussion

The most common organisms isolated from pediatric CRBSI are coagulase-negative staphylococci (CNS) and *Staphylococcus aureus*. Gram-negative bacilli, *Candida* spp., and enterococci can be isolated, especially in neonates.¹⁴ *Brevibacteria* are catalase-positive, non-spore-forming, nonmotile, aerobic Gram-positive rods. They can be found in raw milk and surface-ripened cheese as well as on human skin and in animal sources. *Brevibacterium* spp. are very rare pathogens. Therefore, they were not considered human pathogens until case reports have been published.⁴⁻¹¹

The first pediatric patient reported in the literature had a diagnosis of neuroblastoma and was non-neutropenic at the time of *B. casei* septicemia, the catheter was removed but antibiotic therapy was not reported.⁶ Reinert et al.⁴ reported on a 25-year-old boy with a diagnosis of testicular choriocarcinoma; while he was receiving chemotherapy he developed pancytopenia and fever, and the hemoculture revealed *B. casei*. The reported patient was treated with piperacillin and teicoplanin for the first 10 days, and in the subsequent 10 days he was on piperacillin and tobramycin. He relapsed two weeks after therapy was stopped. Brazzola et al.⁷ reported on an 18-year-old girl with AIDS, who developed persisting fever and dehydration and had a port-a-cath. Hemoculture and port-a-cath culture both revealed *B. casei* and the patient was treated with ciprofloxacin for 14 days and the port-a-cath was removed. She had no relapses. Janda et al.⁸ reported on a 34-year-old man with AIDS, who had persisting fever and pancytopenia. The culture from Hickmann catheter and hemoculture both revealed *B. casei*. The patient was given vancomycin for eight days and the catheter was removed. He had no relapses. Ulrich et al.⁹ reported on a 62-year-old man, who was treated with continuous-intravenous iloprost via non-tunneled central venous catheter (CVC) for severe pulmonary hypertension. The patient developed fever, chills, cough and dyspnea, and the culture from peripheral vein and CVC both revealed *B. casei*. He was treated with vancomycin for 10 days and moxifloxacin for the subsequent 21 days; the catheter was

removed, no recurrence occurred. Our patient had Hickmann catheter, he was treated with vancomycin for 10 days but the catheter was not removed. He had no relapses after *B. casei* septicemia on the following six months.

Conclusion

Brevibacterium spp. was not considered human pathogens until few cases were published in the literature. All reported cases treated with combination of various antibiotics, especially glycopeptides and quinolones, and catheter removal. The recent patient was treated with vancomycin, the catheter was not removed because of ongoing chemotherapy, no recurrence occurred in the following six months. Patients with indwelling central venous catheters are at high risk of acquiring bloodstream infections. A variety of unusual pathogens may be encountered, especially in immunocompromised patients. Among these, *Brevibacterium* spp. are rarely found and can be confused with apathogenic corynebacteria. Physicians treating patients with cytotoxic chemotherapeutic regimens should be aware of this bacterial genus as a potential cause of invasive infection.

Conflicts of interest

The authors declare no conflicts of interest.

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