Central Venous Catheter Infection with *Brevibacterium* sp. in an Immunocompetent Woman: Case Report and Review of the Literature

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Abstract
Brevibacterium spp. were considered apathogenic until a few reports of infections in immunocompromised patients were published. Herein, we present a case of a catheter-related septicemia with *Brevibacterium casei* in an immunocompetent patient receiving continuous iloprost infusion for pulmonary arterial hypertension and review the clinical presentation of this mainly emerging opportunistic pathogen.

Infection 2006; 34: 103–106
DOI 10.1007/s15010-006-5027-6

Introduction

Patients with indwelling foreign material bear considerable risk of acquiring bloodstream infections. Among a wide range of causative agents, Brevibacterium spp. are rarely found and were considered apathogenic until a few reports of clinically relevant infections with Brevibacterium spp. were reported mainly in immunocompromised patients [1]. Herein, we report a case of a central venous catheter (CVC) related blood stream infection with Brevibacterium casei in an immunocompetent patient and review the literature with emphasis on the clinical presentation of this emerging, mainly opportunistic pathogen.

Case Report

A 62-year-old violinist with severe pulmonary hypertension who was being treated with continuous intravenous iloprost via a non-tunneled central venous catheter (CVC) presented with flu-like symptoms, productive cough and chills at our outpatient clinic. She was afebrile and routine blood analyses including C-reactive protein (CRP) were normal. Pulmonary infection was suspected and antibiotic therapy with moxifloxacin 400 mg twice daily was prescribed empirically for 5 days. But the patient's general condition failed to recover, although remaining afebrile. Slightly elevated neutrophils (8.2×10^3/ml) and CRP (8 mg/dl) were found as the only pathologic blood value and chest X-ray was without infiltrates. When she developed fever and chills several weeks after her first symptoms, the patient was hospitalized. Her body temperature was 38.4 °C (101.12 °F), heart rate 78 beats/min, blood pressure 159/60 mmHg, respiratory rate 24 breaths/min and the arterial oxygen saturation 85% while breathing ambient air. The lungs were clear on auscultation, a middle-loud systolic heart murmur was heard as previous. There was no erythema, pus or tenderness at the site of the CVC insertion. Blood for culture was obtained from two separate peripheral venipuncture sites. CRP had increased to 38 mg/dl; neutrophil count had normalized. Antibiotic therapy with moxifloxacin 400 mg twice daily was restarted empirically. Body temperature and CRP rapidly normalized.

Growth of Brevibacterium sp. was reported in both of the aerobic blood cultures. Antibiotic therapy was changed to intravenous vancomycin (1 g twice daily) and the CVC was changed. The same Brevibacterium sp. was cultured on the CVC that was removed, and the bacteria were further specified as Brevibacterium casei. CVC-associated septicemia with B. casei was diagnosed. After 10 days of intravenous vancomycin, antibiotic therapy was switched to oral moxifloxacin 400 mg twice daily for another 20 days according to microbiological sensitivity testing. During this time, the patient recovered consistently. None of the following monthly surveillance blood cultures revealed *B. casei* and up to 6 months later, the patient remained without further infectious complications.

Microbiology

The patient's isolates of both the peripheral blood samples and CVC tip showed gram-positive short coryneform rods forming whitish gray colonies with a distinctive cheese-like smell typical of *Brevibacterium* sp. Their identity was confirmed by conventional tests, i.e., production of methanethiol and hydrolysis of casein and tyrosine [2]. The isolate was identified as *B. casei* by use of carbohydrate

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Received: March 8, 2005 • Revision accepted: May 10, 2005

assimilation tests as previously described [2]. were 0.75 mg/ml and 0.19 mg/l, respectively. Interpretative breakpoints are not available for coryneform bacteria, but our results of decreased susceptibilities to beta-lactams are in line with the data of *Funke* et al. [3]. We assume from the clinical improvement of our patient that the isolate was susceptible to vancomycin and moxifloxacin.

Table 1
Clinical pictures of infections with *Brevibacterium species*.

Reference	Type of Infection	*Brevibacterium* species	Main underlying disease	Clinical symptoms	Indwelling foreign material	Symptom onset to treatment	Time to recurrence (days)	Treatment regimen(s)
McCaughey [13]	Septicemia	*Epidermidis*	Zollinger–Ellison Syndrome	Weight loss, postprandial vomiting, fever, slight erythema around CVC[a]	CVC[a]	≅ 15 days	No	Erythromycin
Lina [14]	Septicemia	Not specified	Lymphoblastic lymphoma	Fever, diplopia, retroocular pain	CVC[a]	> 23 days	28	Teicoplanin and amikacin 20 days, Teicoplanin 21 days
Reinert [10]	Septicemia	*Casei*	Testicular Chorion-carcinoma	High fever, pancytopenia	CVC[a]	Few days	13	Piperacillin and teicoplanin 10 days, piperacillin and tobramycin 10 days
Kaukoranta-Tolvanen [12]	Septicemia	*Casei*	Non-Hodgkin's Lymphoma	Initially high, recurrent fever, tachycardia, CRP[b] up to 42 mg/dl, pancytopenia	CVC[a]	≅ 18 days	16	Not mentioned
Castagnola [1]	Septicemia	*Casei*	Neuro-blastoma	Fever, neutrophil count above 1,000/cm^3	CVC[a]	Not mentioned	No	Not mentioned
Antoniou [18]	Peritonitis	*Iodinum*	CAPD[c]	Fever, abdominal pain and tenderness, urticaria, pruritus, CRP[b] 17.2 mg/dl	CAPD[c] - Catheter	Rapid onset	No	Intraperitoneal cefuroxime 375 mg/exchange 2 days, than ciprofloxacin 50 mg/exchange 6 days
Wauters [17]	Peritonitis	*Otitidis*	CAPD[c] due to nephro-sclerosis	Moderate abdominal pain, subfebril body temperature, effluent with 160 white blood cells/mm^3 (46% PMN[d])	CAPD[c] - Catheter	Several days	No	Intraperitoneal cefazolin and gentamicin
Brazzola [11]	Septicemia	*Casei*	AIDS[e]	Persisting fever, dehydration	Port-à-Cath	> 10 days	No	Ciprofloxacin 14 days
Ogunc [15]	Septicemia	Not specified	Chronic lymphatic leucemia	High fever, slight leucocytosis (with 85% lymphocytes)	Not mentioned	Not reported	No	Not mentioned
Janda [4]	Septicemia	*Casei*	AIDS[e]	Weight loss, dysphagia, odynophagia, fatigue for 1 month, fever, pancytopenia	CVC[a]	≅ 30 days	No	Vancomycin 8 days

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Table 1 **(continued)**

Reference	Type of Infection	*Brevibacterium* species	Main underlying disease	Clinical symptoms	Indwelling foreign material	Symptom onset to treatment	Time to recurrence (days)	Treatment regimen(s)
Dass [16]	Endocarditis	*Otitidis*	Prosthetic mitral and aortic valve replacement	Fever and chills for 4 days, malaise, loss of appetite, fatigue	Prosthetic valve	4 days	No	Vancomycin 6 weeks and gentamicin 2 weeks
Our patient	Septicemia	*Casei*	Continuous iv-iloprost in pulmonary hypertension	Fever, chills, fatigue, cough, dyspnea previous 1–2 month, CRP[b] max 36 mg/dl	CVC[a]	> 1 months	No	Vancomycin 10 days followed by moxifloxacin 21 days

[a] Central venous catheter; [b] C-reactive protein; [c] continuous ambulatory peritoneal dialysis; [d] polymorph nuclear neutrophils; [e] acquired immunodeficiency syndrome

Discussion

Brevibacterium spp. are gram-positive, irregular, rod-shaped, non-acid-fast bacteria which resemble corynebacteria. At the present time, ten species are classified in this genus: *B. linens, B. iodinum, B. epidermidis, B. casei, B. mcbrellneri, B. otitidis, B. avium, B. paucivorans, B. luteolum and B. sanguinis* [4–7]. The main habitat of *Brevibacterium* sp. are dairy products, where the bacteria contribute to the aroma and color. They are also found on human skin surfaces, genital hair and otorrhea [6, 8, 9].

Brevibacterium spp. had not been considered as human pathogens until about a decade ago. Since then, a few cases have been reported with *Brevibacterium* spp. causing disease in humans [1, 4, 10–18] (Table 1). Symptomatic bacteremia with *Brevibacterium* spp. are almost exclusively described in immunocompromised patients [1, 4, 10–12, 14, 15], two of them infected with HIV type 1 [4, 11], the others induced by treatment of malignant disease [10, 12, 14, 15]. All but one had an indwelling CVC as an additional risk factor [1, 4, 10–14]. Only three patients with *Brevibacterium* sp. bacteremia [13, 16] were not conventionally immunocompromised but suffered from severe disease. All of these three, seven of the eight immunocompromised patients with bacteremia and the two patients with peritonitis [17, 18] had indwelling foreign material (CVC [1, 4, 10–14], prosthetic mitral and aortic valve [16], or continuous ambulatory peritoneal dialysis catheter [17, 18]) as risk factors for infection.

The clinical presentation of *Brevibacterium* sp. infection varied with the underlying disease (Table 1). All patients presented with elevated body temperature, some of the patients with chills; most patients had additional unspecific symptoms such as weakness, general discomfort, weight loss and reduced appetite. Exacerbation of symptoms related to underlying disease was also observed (gastrointestinal discomfort in CPAP patients, dyspnea and cough in our patient with pulmonary hypertension). Moderately elevated CRP-levels were reported in only three patients (our patient [12, 18]). Only the patient with lymphocytic leukemia presented with leukocytosis. Although it is comprehensible that elevation of inflammatory markers (CRP, leukocytes) were only moderate or absent in this predominantly immunocompromised patient, *Brevibacterium* spp. seem to only mildly activate the immune response in their hosts; the CRP in our immunocompetent patient was only slightly elevated. The time from onset of symptoms to diagnosis and therapy varied between rapid onset with fever and chills, and lingering disease with unspecific symptoms for up to 2 months. Recurrence was reported in about a quarter of the patients (Table 1).

Indwelling foreign material can be a risk factor of catheter-related bloodstream infections (CR-BSI). Beside common causative pathogens, a variety of unusual pathogens may also be encountered, particularly in immunocompro-mised patients [19]. The observation of *Brevibacterium* sp. in blood cultures of patients with corresponding clinical symptoms is new and adds this species to the list of unusual pathogens. Accordingly, apart from *in vitro* susceptibility tests [20], little is known about the preferable antibiotic therapy and its required duration *in vivo*. Vancomycin was the therapeutic agent most frequently reported for around 8 days in septicemia and up to 6 weeks in endocarditis. Others used other glycopeptides (teicoplanin), penicillin-derivates (piperacillin) or chinolones (ciprofloxacin, moxifloxacin) or combinations. The choice and duration of therapy will strongly depend on clinical symptoms, site of infection and underlying disease.

We present this case report as patients suffering from infections caused by *Brevibacterium* sp. may present with sparse and often unrecognized symptoms, possibly related to the underlying disease. Underestimation of these unspecific but relevant clinical symptoms and misinterpretation as apathogenic organisms may considerably delay diagnosis and treatment of this emerging, mainly opportunistic pathogen. Therefore, it is important to sensitize physicians and microbiologists to this environmental pathogenic

microorganism possibly severely affecting profoundly ill patients.

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