Brevibacterium Endocarditis: A First Report

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There are few case reports of infections caused by Brevibacterium species, and there have been no previously reported cases of endocarditis caused by any of the 6 known species of Brevibacterium. We report the first case of Brevibacterium endocarditis (caused by Brevibacterium otitidis) in a patient with prosthetic heart valves. The patient responded to 6 weeks of treatment with vancomycin and 2 weeks with gentamicin, and she has been receiving long-term maintenance therapy with oral azithromycin.

The genus of Brevibacterium, formerly known as “Centers for Disease Control and Prevention coryneform groups B-1 and B-3” [1], consists of nonmotile, nonhemolytic, gram-positive rods that require detailed biochemical or nucleic acid analyses for accurate species identification [2]. The organisms colonize human skin and are found in dairy products, particularly cheese. There are only a few case reports about infections caused by these organisms, and, to our knowledge, no cases of endocarditis due to any species of Brevibacterium have yet been reported. This report is the first description of a case of Brevibacterium otitidis endocarditis.

Case report. A 68-year-old woman, who had prosthetic mitral and aortic valve replacement performed in 1996 because of rheumatic heart disease, was admitted to the hospital in July 2001 with a complaint of fever and chills of 4 days’ duration. She also noted having malaise, loss of appetite, and fatigue during this same period, but she did not complain of shortness of breath, chest pain, or paroxysmal nocturnal dyspnea. The findings of her physical examination were remarkable for normal prosthetic heart valve sounds, but there were no murmurs or rub and no peripheral stigmata of endocarditis. There was no splenomegaly. The findings of the remainder of her physical examination were unremarkable, including the examinations of neurological, respiratory, abdominal, and musculoskeletal systems.

Laboratory studies performed at admission to the hospital yielded the following values: WBC count, \(5.6 \times 10^9 \) cells/L (67% neutrophils, 25% lymphocytes, 7% monocytes, and 1% eosinophils); hemoglobin, 11 g/dL; hematocrit, 32%; and platelet count, \(276 \times 10^9 \) platelets/L. Renal function and hepatic enzyme levels were normal. Six blood samples (4 from a referring hospital and 2 from our institution) were obtained for culture before antibiotic treatment was initiated. All 6 blood cultures yielded organisms that were initially identified as diphtheroids. Isolates from each hospital were sent to the Microbiology Service laboratory of the National Institutes of Health (Bethesda, MD) for further identification. This included additional biochemical testing and 16S rRNA sequence analysis. Both hospital isolates were confirmed to be the same organism, which was identified as B. otitidis. We were unable to visualize the prosthetic valves adequately using transthoracic echocardiography; therefore, transesophageal echocardiography was performed, which revealed multiple vegetations, the largest of which was 1.2 cm in diameter and was located on the mitral valve.

The patient was treated with vancomycin (1 g iv b.i.d.) for 6 weeks and also gentamicin (80 mg iv b.i.d.) for the first 2 weeks. At a cardiothoracic surgery consultation, pharmacologic treatment alone was advised because of the increased surgical risk resulting from prior cardiac surgery. After discharge from the hospital, the patient completed her intravenous regimen of antibiotics, and she then began receiving azithromycin (250 mg orally q.d.). She has remained clinically stable for >11 months.

Our patient continued to receive oral anticoagulation with warfarin (Coumadin; DuPont Pharma), which was initiated in 1996 at the time of her mitral and aortic valve replacements. Because she was not a surgical candidate, and because there are no prior reports of Brevibacterium endocarditis, we arbitrarily decided to treat her with long-term oral azithromycin therapy for her prosthetic valve endocarditis. Azithromycin was chosen to avoid the complex drug interactions that can be seen with warfarin and with an alternative oral antibiotic regimen of rifampin-ciprofloxacin that we had considered. These particular antibiotic choices were considered because of the results of in vitro antibiotic-susceptibility testing. Antibiotic-susceptibility data were determined using the Microscan gram-positive...
Discussion. Brevibacterium species, which may resemble corynebacteria or diphtheroids, are frequently considered contaminants, even when found in blood cultures or other potentially clinically significant specimens. It is only recently that these organisms have been recognized as causes of significant diseases, such as bacteremia [3–5], peritonitis [6, 7], osteomyelitis [8], and white piedra [9]. Of the 6 known species of Brevibacterium (Brevibacterium casei, Brevibacterium epidermidis, B. otitidis, Brevibacterium iodinum, Brevibacterium linens, and Brevibacterium mcbrellneri), B. casei is the most common to be found in clinical specimens. B. otitidis was first described in 1996 by Pascual et al. [10] in 2 patients with ear infections. The only other case report was published in 2000 by Wauters et al. [6], which described a patient receiving continuous ambulatory peritoneal dialysis who had peritonitis due to B. otitidis.

Brevibacterium species can be differentiated from other coryneform bacteria by testing a wide array of biochemical reactions. These biochemical profiles can now be obtained by the use of commercially available multitest panels designed to test and identify various species of clinically encountered Gram-positive rods. Our patient’s isolates were identified as Brevibacterium species by use of the rapID CB Plus System (Innovative Diagnostic Systems), but the system could not determine the exact species. The presence of mesodiaminopimelic acid in the peptidoglycan layer of the cell wall of Brevibacterium species and strong, rapid methane-thiol production are helpful in confirming the identification of this genus, but these tests are not readily available in a clinical laboratory setting.

Once the genus has been determined to be Brevibacterium, species identification can be done by means of examination of colony morphology, additional biochemical testing, and 16S rRNA sequence analysis, if available. The smooth, yellowish colony morphology of B. otitidis, along with a positive pyrrolidone-peptidase reaction, help to distinguish this species from B. mcbrellneri, and a lack of ability to assimilate carbohydrates (such as D-arabinose and mannitol) differentiates it from B. casei and B. epidermidis [10]. On the basis of colony morphology and biochemical reactions, our isolate most closely resembled B. otitidis. The 16S rRNA sequence analysis was used to help confirm the species identification. Sequence analysis revealed that the isolate was most highly related (≥99%) to 2 strains of B. otitidis in the GenBank database.

Conclusions. Brevibacterium organisms, once thought to be strictly nonpathogenic, can cause clinically significant disease. Our case is, to our knowledge, the first reported case of endocarditis due to any species of Brevibacterium. In addition, this case is only the fourth reported case of infection caused by B. otitidis. There have been very few previously reported cases of Brevibacterium infection and none of Brevibacterium endocarditis that could help guide our choices for antibiotic therapy. No National Committee for Clinical Laboratory Standards criteria for antibiotic susceptibility are available for Brevibacterium species. Therefore, our empiric selection of antibiotics included those with low MICs and a relatively low risk of drug interaction with warfarin. The combination of vancomycin plus gentamicin proved to be successful in the absence of surgical intervention, as evidenced by clinical improvement and the lack of further positive blood cultures. Long-term maintenance therapy with azithromycin is ongoing, and the patient has remained clinically stable for >11 months.

References