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CASE REPORT

Pediococcus acidilactici Endocarditis Successfully Treated with Daptomycin

Peter C. Iwen,[a] Cezarina Mindru,[b] Andre C. Kalil,[a,b] and Diana F. Florescu[a,b]

Department of Pathology and Microbiology[a] and Department of Internal Medicine,[b] Section of Infectious Diseases, University of Nebraska Medical Center, Omaha, Nebraska, USA

This report describes the first case of persistent bacteremia with endocarditis caused by *Pediococcus acidilactici* in a 32-year-old male with a history of short gut syndrome following a small bowel transplant. The results showed the utility of sequencing the intergenic spacer region for species identification and successful treatment using daptomycin.

CASE REPORT

A 32-year-old male with a history of short gut syndrome following a small bowel transplant 1 year prior with severe rejection requiring explantation 3 weeks after transplant presented with fever (102°F), rigors, and dyspnea of 3 days' duration. His medical history included multiple abdominal surgeries, hepatosteatosis, and diabetes mellitus. He was total parenteral nutrition (TPN) dependent due to short bowel syndrome, with a history of multiple bacterial and fungal line infections. He denied any use of intravenous drugs. The review of systems was positive for dry cough, palpitations, and diffuse myalgias. On the physical examination, the patient was febrile (101.8°F) and his lungs were clear, with no heart murmur, conjunctival hemorrhage, splinter hemorrhages, Janeway lesions, or Osler nodules noted. The laboratory data showed a normal white blood cell count and differential, anemia (hemoglobin of 8.2 g/dl), and mild thrombocytopenia (114,000 cells/microliter). A chest X-ray performed upon admission showed bilateral patchy opacities. He was started on empirical treatment with vancomycin, piperacillin-tazobactam, and micafungin for a suspected line infection. A computer tomography (CT) scan of the chest with intravenous contrast showed multiple bilateral lung nodules suggestive for septic emboli. A transesophageal echocardiogram (TEE) exam showed a subcentimeter vegetation on the mitral valve, as well as a small patent foramen ovale with right to left shunt. He remained febrile during the following 4 days despite broad-spectrum antibiotics. Six sets of blood cultures (standard aerobic and anaerobic media [Bactec System, BD Diagnostics, Franklin Lakes, NJ]) drawn from the central line and peripherally over the next 5 days of hospitalization were Gram stain positive for Gram-positive cocci in clusters after 24 to 27 h of incubation at 37°C. The catheter tip culture following removal (day 5 of hospitalization) also was positive for a nonhemolytic, catalase-negative, Gram-positive coccus in clusters. Subsequent biochemical analysis showed all isolates to be negative for the production of pyrrolidonyl arylamidase (PYR test), positive for the production of leucine aminopeptidase and for the ability to grow in 6.5% NaCl, and resistant to vancomycin for a presumptive identification of the blood culture and catheter tip isolates as a *Pediococcus* species. At the time of positive blood cultures, micafungin and vancomycin were discontinued and the patient was on only piperacillin-tazobactam. The patient met the Duke criteria for infectious endocarditis. Given the persistent low-grade fever on the appropriate antibiotic therapy, as well as persistent positive blood cultures, the clinical decision was made to switch the antibiotic regimen on day 7 of hospitalization to daptomycin (6 mg/kg/day) which led to fever resolution and clearance of the bacteremia. Overall, the patient was bacteremic for a total of 8 days. A repeat TEE 18 days after initial exam (day 11 of daptomycin) showed resolution of the vegetation. The pulmonary nodules disappeared at 1 month on the follow-up CT scan of the chest. Although the planned length of daptomycin therapy was 42 days, the patient was readmitted after 39 days of therapy with fever and subsequently diagnosed with a methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia. The MRSA strain was susceptible to both daptomycin (MIC = 0.5 μg/ml) and vancomycin (MIC = 1 μg/ml). Subsequently, daptomycin was discontinued on day 39 of therapy and the patient began treatment with vancomycin (for 2 weeks) after the removal of the central line and placement of a new line. The patient did not have recurrent *Pediococcus* infection detected at a 1-year follow-up. To identify the *Pediococcus* to the species level, a blood culture isolate was subsequently evaluated using a molecular method as described by Florescu et al. to amplify the intergenic spacer region located between the 16S and 23S rRNA genes (5). Following sequencing of a 565-bp product and analysis using the GenBank (National Center for Biotechnology Information, Washington, DC) advanced Basic Local Alignment Search Tool (BLAST) consensus method, the isolate showed a >99.5% similarity to five strains of *Pediococcus acidilactici* (AF405364, AF405363, AF405355, AF405368, and AF405380) available within the database (search performed on 5 October 2011). The next closest species for which a sequence alignment involved at least 93% query coverage was a *Pediococcus pentosaceus* strain (CP000422) at 96.2% similarity to the case isolate. The original type strain for *P. acidilactici*, ATCC 33316^T, which had been previously reclassified in the GenBank database as *P. pentosaceus* (AF405369), showed only a 95.7% similarity to the case isolate. The neotype strain for *P. acidilactici* has been designated DSM 20284 (8, 12). Currently, this strain does not have an intergenic

Received 31 August 2011 **Returned for modification** 27 September 2011
Accepted 20 December 2011
Published ahead of print 28 December 2011
Address correspondence to Peter C. Iwen, piwen@unmc.edu.

doi:10.1128/JCM.05648-11

spacer (IGS) sequence available in the GenBank database for sequence comparison.

Susceptibility testing on the case isolate was performed, and the results were interpreted using methods described in the Clinical and Laboratory Standards Institute (CLSI) document M45-A2 (4). The results of testing showed the isolate to be susceptible to penicillin (MIC, 0.25 μg/ml) and nonsusceptible to meropenem (MIC, 2.0 μg/ml, using the interpretive standards as described for imipenem). The Etest method (bioMérieux, Durham, NC) described by Huang et al. was used to test the isolate for susceptibility to daptomycin, with the standards listed in the CLSI document M100-S21 for *Enterococcus* species used for interpretation of results (3, 7). Huang et al. evaluated the daptomycin Etest method with the standardized microdilution method (7). They showed good correlation indicating the clinical usefulness of the Etest method for daptomycin susceptibility testing of unusual Gram-positive bacteria. Thirteen *Pediococcus* species were evaluated, with the MIC for daptomycin ranging from 0.032 to 2 μg/ml (7). The results of testing our case isolate showed susceptibility to daptomycin at an MIC of 0.75 μg/ml.

Pediococcus species are infrequent causes of diseases and classified as aerobic, catalase-negative, vancomycin-resistant, Gram-positive cocci (1). Due to similar phenotypic characteristics, species within this genus may be misidentified as viridans group streptococci, which were observed as a problem in many of the cases described in the literature (9). Fifteen valid *Pediococcus* species are recognized, most of them associated with plants and foods, although they are frequent colonizers of humans (J. P. Euzeby: List of Prokaryotic Names with Standing in Nomenclature, http://www.bacterio.cict.fr/p/pediococcus.html) (11). *Pediococcus acidilactici* and *Pediococcus pentosaceus* are the most common species associated with opportunistic infections affecting compromised hosts. Two reviews are available in the literature that report on rare cases of bacteremia in humans caused by *Pediococcus* species (9, 10). The clinical significance of infection caused by these bacteria in most of the reported cases, however, is not clear, since a majority describe the detection of *Pediococcus* species in only a single positive blood culture. Suh reports on four cases of persistent bacteremia where *P. acidilactici* was detected in multiple blood cultures (10). These cases represented three males and one female with a median age of 52 years (range, 29 to 67). Each of these patients had underlying predisposing conditions (two with cancer undergoing chemotherapy treatment [adenocarcinoma and acute myelogenous leukemia], one case of cutaneous Recklinghausen's disease, and one case of acute appendicitis with abdominal complications). All were treated prior to diagnosis of a *Pediococcus* bacteremia with multiple antimicrobial agents that included vancomycin. For three of the cases, vancomycin was replaced by another antimicrobial at the time of detection of *P. acidilactici* in blood cultures (one switched to daptomycin, one to penicillin plus tobramycin, and one to imipenem plus clindamycin). One patient with a concomitant *Staphylococcus epidermidis*, *Enterococcus faecalis*, *Escherichia coli*, and *Pseudomonas aeruginosa* bacteremia was maintained on vancomycin with the addition of imipenem and fosfomycin. Although endocarditis was suggested in some of these cases due to the persistence of bacteremia, no echocardiogram results were made available to confirm this finding (10). The present case showed many similarities to these four reported cases of persistent bacteremia such as a middle-aged male with an immunosuppressive underlying disease (short bowel syndrome with small bowel transplant), a polymicrobial bacteremia (concurrent with MRSA), and prior therapy with vancomycin. Our case represents only the second time that daptomycin was successfully used in therapy and the first time this drug was used to treat a confirmed case of endocarditis (10). Finally, this present case is only the second time that molecular sequencing was performed to verify the species identification (6). Most of the previous cases used a series of biochemical tests to provide a species identification. However, atypical biochemical reactions have been seen within the *Pediococcus* species which did not allow for phenotypic characterization to identify all *Pediococcus* strains isolated from human clinical specimens (2). To overcome this, molecular sequencing has been considered (6). Heinz et al. sequenced both the full-length 16S rRNA gene and the D-lactate dehydrogenase gene and was able to show a 99% similarity to the *P. acidilactici* type strain (DSM 20284) in the GenBank database, with the next closest identification to the *P. pentosaceus* type strain at 72.7% (6). We sequenced the intergenic spacer (IGS) region target within the rRNA gene complex, which also was able to give reliable results using comparison analysis in the GenBank database. Our findings, along with the report by Heinz et al., showed the reliability of using genomic sequencing to identify *P. acidilactici*. In conclusion, this report presents the first case of endocarditis caused by *P. acidilactici* and showed the utility of molecular sequencing using the IGS region for species identification and successful treatment with daptomycin.

Nucleotide sequence accession number. A sequence of the case isolate has been deposited into the GenBank database under accession no. JN801158.

ACKNOWLEDGMENTS

We thank Ashley Calhoon for the preparation of the manuscript.

We report no conflict of interest.

Roles of each author: Diana Florescu, Cezarina Mindru, Peter Iwen, and Andre Kalil were responsible for writing and conclusions.

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