Lactobacillus paracasei Continuous Ambulatory Peritoneal Dialysis-Related Peritonitis and Review of the Literature

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We describe the first case of continuous ambulatory peritoneal dialysis (CAPD)-related peritonitis due to *Lactobacillus paracasei*. It occurred in a 65-year-old patient with recurrent episodes of peritonitis while he was receiving a prolonged course of intraperitoneal vancomycin. *L. paracasei* should be considered in the differential diagnosis of pathogens in CAPD-related peritonitis, especially in patients receiving prolonged vancomycin or glycopeptide treatment.

CASE REPORT

A 65-year-old diabetic male with end-stage renal disease commenced continuous ambulatory peritoneal dialysis (CAPD) in March 1999. In July 2001, he first reported abdominal discomfort and cloudy dialysate but no fever. Physical examination demonstrated a benign abdomen with a normal-appearing catheter exit site. Peritoneal fluid dialysate was hazy in appearance (white blood cell [WBC] count of 2,040/ μ l, with 96% segmented neutrophils). Therapy with intraperitoneal aztreonam and vancomycin was initiated. Peritoneal fluid culture grew methicillin-resistant *Staphylococcus haemolyticus*. The patient finished a 2-week course of vancomycin with good results. Shortly thereafter (at the end of August 2001), he developed another episode of CAPD-related peritonitis (peritoneal fluid WBC count of 500/ μ l, with 90% segmented neutrophils). This time, the peritoneal fluid Gram stain showed gram-positive cocci in chains and the culture grew alpha-hemolytic streptococcus species, not enterococcus species. He was given an additional 4 weeks of intraperitoneal vancomycin, during which his abdominal complaints and peritoneal fluid pleocytosis worsened (WBC count increased to 3,200/ μ l, with 80% segmented neutrophils, 5% lymphocytes, and 15% monocytes). Peritoneal fluid cultures during this period revealed diphtheroids and alpha-hemolytic streptococcus species, not enterococcus species. Due to nonclearing of the peritoneal dialysate and ongoing abdominal discomfort, vancomycin was stopped and he received oral levofloxacin and intraperitoneal ceftriaxone, with mild improvement. In early October 2001, the peritoneal fluid analysis showed a WBC count of 784/ μ l (97% segmented neutrophils and 3% monocytes), and culture grew methicillin-resistant *Staphylococcus simulans*; he was restarted on intraperitoneal vancomycin and continued oral levofloxacin. Two weeks later, on 18 October 2001, the peritoneal fluid analysis revealed a WBC count of 126/ μ l, with 21% segmented neutrophils, 16% lymphocytes, 61% monocytes, and 2% eosinophils, and culture grew a *Lactobacillus* species, later identified

as *Lactobacillus paracasei*. Antibiotics were stopped at that point, with the assumption that the mild cloudy dialysate effluent represented chemical peritonitis. However, he continued to have abdominal discomfort and started becoming hypotensive. Intraperitoneal vancomycin and aztreonam were started. He was later admitted to the hospital. Repeat peritoneal fluid analysis (9 November 2001) revealed a WBC count of 325/ μ l (21% segmented neutrophils, 16% lymphocytes, 61% monocytes, and 2% eosinophils), and the peritoneal fluid culture on three consecutive occasions yielded pure growth of *L. paracasei*. This organism was resistant to vancomycin, which had a MIC of ≥ 256 μ g/ml by the Epsilometer (Etest) system (AB Biodisk, Solna, Sweden). The MICs of erythromycin, penicillin, levofloxacin, linezolid, and ceftriaxone were 0.047, 0.50, 0.75, 1.0, and ≥ 32 μ g/ml, respectively. Vancomycin was discontinued, and the patient was treated with intraperitoneal penicillin G and oral levofloxacin with good results (the patient became asymptomatic, and peritoneal fluid analysis and cultures were normal and sterile, respectively). Because of multiple episodes of CAPD-related peritonitis, the patient elected to change to hemodialysis and underwent placement of the arteriovenous fistula. One month later, he had another episode of *S. haemolyticus* CAPD-related peritonitis (WBC count of 234/ μ l, with 99% segmented neutrophils) for which he received another course of intraperitoneal vancomycin. Ten days later, peritoneal fluid culture again yielded *L. paracasei*. Intraperitoneal penicillin and gentamicin were administered, and the peritoneal dialysis catheter was removed. His arteriovenous access was mature by now, and he commenced hemodialysis treatment and has had no further episodes of peritonitis. Nine months later, he is doing well on hemodialysis. He has gained his lost lean muscle mass, and his serum albumin has improved.

Microbiological identification. The isolates were catalase-negative, gram-positive rods with a tendency to chain and grew equally well in both air supplemented with CO₂ and an anaerobic atmosphere at 35°C on routine media. Better growth was obtained on Columbia colistin-nalidixic acid-agar than on chocolate medium. These characteristics put the strain into the

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Lactobacillus genus. Because identification of species within the genus is extremely difficult using conventional methods, and because the various *Lactobacillus* spp. have been shown to have different disease associations, 16S rRNA gene sequence identification was performed using the MicroSeq 500 gene kit (Applied Biosystems, Foster City, Calif.) and the model 3100 genetic analyzer (Hitachi, Tokyo, Japan) in accordance with the manufacturer's specifications. Approximately 500 bp in both forward and reverse sense were sequenced for each isolate. Test strain sequences were compared against the MicroSeq 16S rRNA gene sequence database. The database contains sequences from 1,297 different species (1,187 type strains), including 20 type strains from the genus *Lactobacillus*. Sequence data matched the type strain of *L. paracasei*.

Discussion. *Lactobacillus* spp. are gram-positive, nonmotile, nonsporulating, facultative anaerobes. They can form long slender rods or short coccoid rods, which may appear as cocci on a Gram stain (4, 7, 9). Moreover, they can often form chains and can be mistaken for *Streptococcus* spp. (4). We suspect that our patient (based on the Gram stain morphology of the peritoneal fluid isolates from August and September 2001) manifested *Lactobacillus* infection 2 months before the actual isolation of this organism from the peritoneal fluid. Previous reports have indicated that the variable Gram stain morphology and the slow and minimal growth of lactobacilli on the common media, coupled with their anaerobic requirements, can lead in many instances to their misidentification in clinical material (4).

Peritonitis is a common problem in patients with end-stage renal disease treated by CAPD. The most common organisms are usually the skin flora such as coagulase-negative staphylococci, especially *Staphylococcus epidermidis*, and intraperitoneal vancomycin is considered first-line treatment (8). Lactobacilli are part of the normal flora of the mouth, colon, and female genital tract but are not commonly found on the skin (1, 3, 4, 6). There have been only four cases of CAPD-related *Lactobacillus* peritonitis (3, 5, 7, 9). Schleifer et al. were the first to report a case of *Lactobacillus* CAPD-related peritonitis (9). The patient had five prior episodes of peritonitis and had received a 2-week course of intraperitoneal vancomycin before developing *Lactobacillus acidophilus* peritonitis. Rao et al. described a patient with CAPD-related peritonitis with *Enterobacter aerogenes* and *Lactobacillus casei* subsp. *rhamnosus* (5). There was no mention of prior history of CAPD-related peritonitis or vancomycin therapy. The patient died within several days from cardiac arrest related to gastrointestinal bleeding but not related to peritonitis. Sanyal et al. reported a patient who had seven prior episodes of CAPD-related peritonitis in 2 years and had received a prolonged course of vancomycin before developing *Lactobacillus rhamnosus* CAPD-related peritonitis (7, 8). The isolate was initially misidentified as *Enterococcus avium*, emphasizing the difficulties in identification of *Lactobacillus* spp. The fourth case was a 57-year-old man who had received teicoplanin for coagulase-negative staphylococcus CAPD-related peritonitis (3). Two months later, he developed *L. rhamnosus* CAPD-related peritonitis. It is very likely that the treatment for recurrent peritonitis with intraperitoneal vancomycin or glycopeptide has provided selection pressure for emergence of organisms such as *Lactobacillus* species that

are intrinsically resistant to vancomycin (7). Our patient denied any unusual dietary habits or hygienic practices that would have allowed infection to occur via skin route. We hypothesize that treatment with prolonged vancomycin allowed for proliferation of lactobacilli in the gut with subsequent translocation across the bowel wall into the peritoneal cavity.

Our review suggests that *L. paracasei*, *L. casei*, and *L. rhamnosus* are closely genetically related and cause similar diseases. In fact, because they are similar and were not identified by 16S ribosomal DNA sequence analysis, they could indeed be the same. This is in contrast to *L. gasseri*, *L. amylovorus*, and *L. acidophilus*, which are not closely related and are found more frequently in the normal genitourinary tract (J. Claridge III and K. Hulten, Abstr. 102nd Gen. Meet. Am. Soc. Microbiol. 2002, abstr. C-310, p. 155, 2002).

Treatment of infections with *Lactobacillus* spp. should be guided by the clinical presentation and susceptibility results (1, 6). There have been variable sensitivities reported in the literature, so it is advisable to test these organisms against a wide range of antibiotics (1, 2, 6). They are uniformly resistant to vancomycin but sensitive to penicillin as well as clindamycin and erythromycin, which was the case with our patient (1, 6). Previous successful treatment for *Lactobacillus* spp. CAPD-related peritonitis included combinations of ampicillin with gentamicin and rifampin with erythromycin, as well as rifampin and imipenem alone (3, 5, 7, 9). In general, active agents include penicillin, imipenem, aminoglycosides, clindamycin, erythromycin, and chloramphenicol (1). For serious infections, such as endocarditis, combination therapy (penicillin and an aminoglycoside) is advisable (1). Additionally, removal of the foreign body (e.g., catheter) may be necessary for cure, which was evident in our patient, who relapsed even after he received the appropriate antibiotic therapy.

Conclusion. We document the first case of *L. paracasei* CAPD-related peritonitis. This case should increase clinicians' awareness of the possibility of a *Lactobacillus* species in patients with CAPD-related peritonitis. *Lactobacillus* spp. can be difficult to identify, usually occur in patients with recurrent peritonitis, and are inherently resistant to vancomycin. Prior vancomycin or glycopeptide use is a common denominator.

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