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We describe the first two cases of continuous ambulatory peritoneal dialysis-related peritonitis associated with Lancefield group G beta-hemolytic streptococci in the literature. Both patients presented with abdominal pain and turbid dialysis effluent with or without fever. Both had concomitant gastrointestinal tract disturbance. Both did not respond to intraperitoneal cefazolin and tobramycin and required removal of the Tenckhoff catheters.

CASE REPORTS

Case 1. A 38-year-old Chinese woman was admitted to the hospital in November 2003 because of abdominal pain and cloudy dialysate effluent for 1 day. She had a history of end stage renal disease as a result of hypertensive nephrosclerosis, for which continuous ambulatory peritoneal dialysis (CAPD) had commenced 6 years ago. She had an episode of Pseudomonas aeruginosa peritonitis in 1999, which required removal and reinsertion of the Tenckhoff catheter. She had 3 days of constipation prior to the development of abdominal pain and cloudy dialysate effluent. On admission, she was afebrile with generalized abdominal tenderness and turbid dialysate effluent. The hemoglobin was 7.2 g/dl; the total white cell count was 17.2 \times 10^9/liter, with a neutrophil count of 15.0 \times 10^9/liter, a lymphocyte count of 0.7 \times 10^9/liter, a monocyte count of 1.3 \times 10^9/liter, and an eosinophil count of 0.2 \times 10^9/liter; and the platelet count was 376 \times 10^9/liter. The serum urea and creatinine levels were 26.2 mmol/liter and 1,110 \mu mol/liter, respectively, with normal levels of liver enzymes except an elevated alkaline phosphatase level of 164 U/liter. The total leukocyte count of the dialysis fluid was 5,432 \times 10^6/liter. A Gram stain of the dialysate effluent after centrifugation revealed only numerous leukocytes; no microorganisms were seen. Intrapерitoneal cefazolin and tobramycin were started for empirical treatment of CAPD peritonitis.

Culture of the dialysate effluent obtained on admission yielded pure growth of a gram-positive coccus in chains. It appeared on horse blood agar as beta-hemolytic, white, smooth colonies 1 mm in diameter after incubation at 37°C in 5% CO_2 for 24 h. It did not grow on MacConkey agar. The isolate was catalase negative. Lancefield serogrouping with Streptex (Murex Biotech Ltd., Dartford, United Kingdom) revealed that it was group G. It was identified as \textit{Streptococcus dysgalactiae} by the Vitek GPI system (bioMerieux Vitek, Hazelwood, Mo.) with >99% confidence. 16S rRNA gene sequencing, using primers and the protocol described in our previous publication (16) and \textit{Streptococcus pyogenes} (ATCC 19615) as the control, showed that it was \textit{S. dysgalactiae} subsp. \textit{equisimilis}. The isolate was sensitive to penicillin, erythromycin, clindamycin, and vancomycin.

The patient did not respond to cefazolin and tobramycin, which were stopped on day 4, and intraperitoneal vancomycin and amikacin were commenced. As the response was still unsatisfactory after another 4 days, intravenous ceftazidime and amikacin were commenced and the Tenckhoff catheter was removed. The two sets of blood cultures taken on admission were negative for bacteria after 7 days of incubation. The patient received 2 weeks of intravenous ceftazidime and amikacin. Due to the presence of extensive peritoneal adhesions, the patient was subsequently put on long-term hemodialysis.

Case 2. A 41-year-old Chinese man was admitted to the hospital in December 2003 because of fever, chills, rigor, abdominal pain, watery diarrhea (10 times per day), and cloudy dialysate effluent for 1 day. He had end stage renal disease of unknown etiology, for which CAPD had commenced 18 years ago. He had had a cadaveric renal transplant in 1991, complicated by acute graft rejection on day 6 after transplant, with graft kidney nephrectomy in 1997. He also had secondary hyperparathyroidism with total parathyroidectomy and left forearm autotransplantation in 2000. On admission, he had a temperature of 39°C with generalized abdominal tenderness and turbid dialysate effluent. The hemoglobin was 10.6 g/dl; the total white cell count was 5.4 \times 10^9/liter, with a neutrophil count of 4.2 \times 10^9/liter, a lymphocyte count of 0.6 \times 10^9/liter, a monocyte count of 0.0 \times 10^9/liter, an eosinophil count of 0.6 \times 10^9/liter, and a basophil count of 0.0 \times 10^9/liter; and the platelet count was 191 \times 10^9/liter. The serum urea and creatinine levels were 28.5 mmol/liter and 1,106 \mu mol/liter, respectively, with normal levels of liver enzymes. The total leukocyte count of the dialysate fluid was 5,432 \times 10^6/liter. A Gram stain of the dialysate effluent after centrifugation revealed only numerous leukocytes; no microorganisms were seen. Intrapерitoneal cefazolin and tobramycin were started for empirical treatment of CAPD peritonitis.

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Culture of the dialysis effluent obtained on admission yielded two organisms. The first was a gram-positive coccus in chains that appeared on horse blood agar as beta-hemolytic, white, smooth colonies 1 mm in diameter after incubation at 37°C in 5% CO₂ for 24 h. It did not grow on MacConkey agar. The isolate was catalase negative. Lancefield serogrouping with Streptex (Murex Biotech Ltd.) revealed that it was group G. It was identified as S. dysgalactiae by the Vitek GPI system (bioMerieux Vitek) with ≥99% confidence. 16S rRNA gene sequencing showed that it was S. dysgalactiae subsp. equisimilis. The isolate was sensitive to penicillin, erythromycin, clindamycin, and vancomycin. The second one was a gram-negative strictly anaerobic bacillus. It appeared on horse blood agar as nonhemolytic, smooth, gray colonies 1 mm in diameter after incubation at 37°C in an anaerobic environment for 24 h. It was identified as Bacteroides fragilis by the Vitek ANI system (bioMerieux Vitek) with ≥99% confidence.

The patient did not respond to cefazolin and tobramycin, which were stopped on day 4, and intraperitoneal vancomycin and amikacin were commenced. As the response was still unsatisfactory after another 4 days, intravenous penicillin was commenced and the Tenckhoff catheter was removed. The two sets of blood cultures taken on admission (Bactee 9240; Becton Dickinson) were negative for bacteria after 7 days of incubation. Stool for aerobic culture, Clostridium difficile culture and cytotoxin detection, and parasitic ovum and cyst examination performed on admission were all negative. The patient received 2 weeks of intravenous penicillin. Due to the discovery of a carcinoma in the sigmoid colon with carcinomatosis and peritoneal metastasis 1 month after the episode of CAPD-related peritonitis, the patient was put on long-term hemodialysis.

Lancefield groups A, B, C, and G are the major groups of beta-hemolytic streptococci causing infections in humans (8, 14, 16, 19). Although it has been shown in various studies that group G beta-hemolytic streptococci are the commonest cause of beta-hemolytic bacteremia in some parts of the world (12, 16), relatively little is known about the other diseases caused by group G beta-hemolytic streptococci versus those caused by group A or group B beta-hemolytic streptococci. In our recent study, we showed that 52, 26, and 12% of patients with group G beta-hemolytic streptococcal bacteremia had primary bacteraemia, cellulitis, and bed sore or wound infection, respectively, and that the remaining 10% had infective endocarditis, pneumonia, abscess, and septic arthritis (16).

The most common pathogens associated with peritonitis in patients with CAPD are the gram-positive bacteria, which constitute 60 to 80% of all isolates. These include coagulase-negative staphylococci, Staphylococcus aureus, and diphtheroids, which are essentially part of the normal skin flora. The reason for their predominance as causative agents in CAPD-related peritonitis presumably is associated with the portal of entry along the Tenckhoff catheter in situ. Gram-negative bacteria are much less frequently isolated, with members of the Enterobacteriaceae and Pseudomonas species being the most commonly involved. Less frequently seen are Acinetobacter species, anaerobic bacteria, Mycobacterium species, and Candida albicans. Recently, we have reported cases of CAPD-related peritonitis caused by pathogens rarely associated with this condition (7, 15, 18). For CAPD-related peritonitis associated with Streptococcus and Enterococcus species, these bacteria account for about 10 to 15% of the total number of cases (5, 6, 9). Most of these cases were associated with Enterococcus faecalis or viridans group streptococci. On the other hand, as of January 2004, only 12 cases of CAPD-related peritonitis caused by beta-hemolytic streptococci have been reported in the English literature (1–6, 10, 11; T. P. Officer, J. Black, C. Rotellar, J. F. Winchester, and T. A. Rakowski, Letter, Am. J. Med. 87:487, 1989; D. Pagniez, A. Fruchart, and P. Dequiedt, Letter, Nephron 71:480, 1995; A. M. Yinnon, V. Jain, and C. R. Magnusson, Letter, Perit. Dial. Int. 13:241, 1993). None of them was caused by group G beta-hemolytic streptococci. In this article, we describe the first two cases of CAPD-related peritonitis associated with group G beta-hemolytic streptococci in the literature.

Compared to CAPD-related peritonitis caused by other gram-positive bacteria, such as coagulase-negative staphylococci, S. aureus, diphtheroids, enterococci, and viridans group streptococci, CAPD-related peritonitis associated with beta-hemolytic streptococci seems to be more difficult to treat. Including the present 2 cases, 14 cases of CAPD-related peritonitis caused by beta-hemolytic streptococci have been reported in the English literature (Table 1) (1–6, 10, 11; Officer et al., letter; Pagniez et al., letter; Yinnon et al., letter). Overall, 7 (58%) of the 12 cases with information available had bacteremia (cases 1, 6, and 9), required removal of the Tenckhoff catheter (cases 2, 6, 13, and 14), and/or died (cases 1 and 8). Early removal of Tenckhoff catheters should be considered in patients with CAPD-related peritonitis associated with beta-hemolytic streptococci.

The route of transmission in the present two cases of CAPD-related peritonitis caused by group G beta-hemolytic streptococci could be due to direct contamination of the connection device or bacterial translocation through the gastrointestinal tract. CAPD-related peritonitis has been reported to be associated with other bacteria that reside in the gastrointestinal tract and those that cause diarrhea (13, 18; W. Al-Wali, R. Baillod, J. M. T. Hamilton-Miller, and W. Brumfitt, Letter, Lancet ii:457, 1988). For some patients, it was obvious that they acquired their infections through direct contamination of the catheters (13; Al-Wali et al., letter). On the other hand, the other patients, especially those with histories of diarrhea, probably acquired the infection through the oral route. In these patients, the bacteria could have reached the peritoneal cavity by translocation across the intestinal wall into the peritoneal cavity or direct contamination of the connection device by the hands of patients that were contaminated with the bacteria. Both of our two patients with group G beta-hemolytic streptococcal CAPD-related peritonitis had concomitant gastrointestinal tract disturbance, and one also had colonic carcinoma and had B. fragilis recovered from the peritoneal dialysate. In fact, in a lot of the patients with group G beta-hemolytic streptococcal primary bacteremia, the gastrointestinal tract was believed to be the source of the group G beta-hemolytic streptococci (16). Furthermore, in one of our bacteremic patients infected with erythromycin-resistant group G beta-hemolytic streptococci, the erythromycin resistance methylase
<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Reference or source</th>
<th>Sex/age (yr)</th>
<th>Underlying diseases other than end stage renal failure</th>
<th>Lancefield grouping (species, if available)</th>
<th>Presence of bacteremia</th>
<th>Other bacteria recovered in peritoneal dialysate</th>
<th>Antibiotic treatment</th>
<th>Removal of Tenckhoff catheter</th>
<th>Outcome</th>
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<td>NM</td>
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<td>B</td>
<td>Yes</td>
<td>NM</td>
<td>NM</td>
<td>NM</td>
<td>Died</td>
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<tr>
<td>2</td>
<td>F/38</td>
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<td>None</td>
<td>A</td>
<td>No</td>
<td>None</td>
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<td>NM</td>
<td>Amyloidosis</td>
<td>NM</td>
<td>NM</td>
<td>NM</td>
<td>i.p. vancomycin</td>
<td>NM</td>
<td>Remission</td>
</tr>
<tr>
<td>4</td>
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<td>Remission</td>
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<tr>
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<td>7</td>
<td>M/52</td>
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<td>B (S. agalactiae)</td>
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<td>i.p. vancomycin and gentamicin</td>
<td>No</td>
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<tr>
<td>8</td>
<td>LB</td>
<td>M/63</td>
<td>HIV infection, diabetes mellitus, acute gastroenteritis caused by Cryptosporidium and Salmonella</td>
<td>A (S. pyogenes)</td>
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<td>Secondary hyperparathyroidism with total parathyroidectomy and autotransplantation</td>
<td>G (S. dysgalactiae)</td>
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<td>None</td>
<td>None</td>
<td>i.p. cefazolin and tobramycin, i.p. vancomycin and amikacin, i.v. penicillin</td>
<td>Yes</td>
<td>Remission</td>
</tr>
</tbody>
</table>

*NM, not mentioned.
1 i.v., intravenous; i.m., intramuscular; i.p., intraperitoneal.
1 LA, officer et al., letter; LB, Yinnon et al., letter; LC, Pagniez et al., letter.
1 HIV, human immunodeficiency virus.
1 Salmonella enterica serovar Paratyphi B.
gene (erm) was probably acquired by horizontal gene transfer of the erm gene from other bacteria in the gastrointestinal tract (17). Therefore, the origin of the group G beta-hemolytic streptococci in the present two cases was probably the gastrointestinal tract, although the portal of entry in them remains elusive.

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REFERENCES


