2015

Successful treatment of peritoneal dialysis catheter-related polymicrobial peritonitis involving Clostridium difficile, a case report and review of the literature

S. Bharti
Northwell Health

P. Malhotra
Hofstra Northwell School of Medicine

S. Juretschko
Hofstra Northwell School of Medicine

JCM
Journals.ASM.org

Successful Treatment of Peritoneal Dialysis Catheter-Related Polymicrobial Peritonitis Involving *Clostridium difficile*

Sheena Bharti,[a]* Prashant Malhotra,[a] Stefan Juretschko[b]

Department of Infectious Diseases[a] and Department of Microbiology,[b] Hoftstra North Shore-LIJ School of Medicine, Manhasset, New York, USA

***Clostridium difficile* is one of the most common nosocomial pathogens and the cause of pseudomembranous colitis in cases of prior antimicrobial exposure. Extraintestinal manifestations of *C. difficile* are uncommon and rarely reported. We report the first successfully treated case of catheter-related *C. difficile* peritonitis in a patient undergoing peritoneal dialysis.**

CASE REPORT

A 72-year-old man was admitted to the hospital with shortness of breath and abdominal pain for 2 days. His past medical history was significant for congestive heart failure, hypertension, and type II diabetes with end-stage nephropathy requiring continuous ambulatory peritoneal dialysis (CAPD). A peritoneal catheter had been in place for the past 2.5 years.

Upon admission, the patient was afebrile (temperature, 36.7°C), his blood pressure was 115/62 mm Hg, and his pulse was 59/min. His abdomen was diffusely tender to palpation, with signs of peritonitis, but the peritoneal catheter site was unremarkable. Laboratory findings included a hemoglobin level of 11.8 g/dl, total leukocyte count of 12.0×10^6/liter (79.5% neutrophils), and creatinine level of 12.69 mg/dl. Examination of the peritoneal dialysis (PD) fluid revealed a white blood cell (WBC) count of 16,000 cells/μl with a 93% neutrophil predominance.

One hundred milliliters of PD fluid was transferred into two 50-ml conical tubes and centrifuged for 30 min at 3,000 rpm. After the supernatant had been discarded, 3 ml of the resuspended sediment from each tube was used for inoculation in a Plus Aerobic/F blood culture bottle and a Plus Anaerobic/F blood culture bottle (Bactec, Becton Dickinson, Sparks, MD). All blood culture bottles were incubated in the Bactec 9240 blood culture system at 35°C for 5 days. Positive blood culture bottles were plated on 5% sheep blood agar, chocolate agar, and Columbia naladixic acid (CAN) agar and incubated at 35°C at 5% CO_2 for 5 days. In addition, CDC agar was set up under anaerobic conditions at 35°C, and thioglycolate broth (enriched) was used to facilitate growth of anaerobes. All prepared media were purchased from BD BBL (Becton Dickinson, Sparks, MD).

All 8 blood culture sets containing concentrated peritoneal dialysis fluid samples from 8 different specimens turned positive within 1 to 4 days. *Escherichia coli*, *Bacterioides fragilis* group, *Candida albicans*, and *Clostridium difficile* were identified by matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) with a Vitek mass spectrometer (bioMérieux, Durham, NC), and automated susceptibility testing for *Escherichia coli* with MicroScan WalkAway Plus (Beckman Coulter, Inc., Brea, CA) was performed. *E. coli* was isolated from 3/8 aerobic bottles and 4/8 anaerobic bottles. *B. fragilis* was isolated from 2/8 aerobic bottles and 3/8 anaerobic bottles. *C. albicans* was isolated from 2/8 aerobic bottles, and *C. difficile* was isolated from 3/8 anaerobic bottles.

For further identification of the anaerobic bacteria, the RapID ANA II system (Remel, Lenexa, KS) was used. The isolates of *C. difficile* grew as small gray to yellow-white colonies with a Gram-variable rod appearance on CDC agar after initial growth in thioglycolate broth. The RapID ANA II system and MALDI-TOF MS identified the isolates as *C. difficile* with 99.92% and 99.9% confidence values (CV), respectively. Identification was confirmed by positive tests for glutamate dehydrogenase (GDH) and toxin B by antigen testing and molecular identification of the specimen and a dilution from the isolate using the C. Diff Quik Chek Complete (Alere, Orlando, FL) and BD Max CDiff assay (Becton Dickinson, Sparks, MD).

The patient was empirically started on intravenous piperacillin-tazobactam (3.375 mg every 12 h) and intraperitoneal (i.p.) ceftazidime (500 mg every 24 h). Upon identification of the isolates, intravenous fluconazole (100 mg every 24 h) was added. Blood cultures yielded no growth, and intravenous piperacillin-tazobactam was later discontinued. Although the patient's abdominal pain improved and leukocytosis resolved, his PD fluid cultures remained positive with growth of *E. coli*, *B. fragilis*, and *C. albicans* on hospital days 1 to 3 and *C. difficile* on hospital days 5 to 7. Computed tomography (CT) of the abdomen/pelvis was obtained to evaluate for abdominal perforation but was unremarkable.

Intraperitoneal ceftazidime was discontinued after identification of the organisms, and intravenous ertapenem was initiated for improved anaerobic coverage. On hospital day 7, because of persistent growth with *Clostridium difficile*, the PD catheter was removed, and the patient improved clinically. Eventually, he was transitioned to oral antibiotics with cefuroxime (500 mg twice daily), metronidazole (500 mg three times daily), and fluconazole (100 mg daily) for an additional 14 days and then discharged.

Received 24 July 2015 **Returned for modification** 3 September 2015
Accepted 15 September 2015

Accepted manuscript posted online 16 September 2015

Citation Bharti S, Malhotra P, Juretschko S. 2015. Successful treatment of peritoneal dialysis catheter-related polymicrobial peritonitis involving *Clostridium difficile*. J Clin Microbiol 53:3945–3946. doi:10.1128/JCM.02021-15.

Editor: A. B. Onderdonk

Address correspondence to Sheena Bharti, sbharti@nshs.edu.

* Present address: Sheena Bharti, Division of Infectious Diseases, Hofstra North Shore-LIJ School of Medicine, Manhasset, New York, USA.

P.M. and S.J. contributed equally to this article.

At outpatient follow-up 2 weeks later, clinical improvement was noted, and the patient remained asymptomatic after finishing the course of antimicrobials.

Peritonitis has been the main complication associated with peritoneal dialysis and has caused significant morbidity and mortality (1, 2). The majority of peritonitis cases (50%) are attributed to Gram-positive organisms—typically coagulase-negative staphylococci, *Staphylococci aureus*, and *Enterococcus* (3). A smaller percentage (15%) are due to Gram-negative organisms such as *E. coli* and *Bacteroides*, and 4% of cases are mixed Gram-positive and -negative infections. Culture-negative etiology accounts for 20% of cases (3).

We report the first known successfully treated PD catheter-related *C. difficile* peritonitis case. Similar to our case, Laroche et al. had earlier reported isolation of *C. difficile* in the PD fluid of a patient who also had polymicrobial peritonitis (4). In that case, despite catheter removal and appropriate antibiotics, the patient developed septic shock and died.

C. difficile is known for causing intestinal infections but is seldom found in extraintestinal locations (5). *C. difficile* toxin is known to have a profound effect on colonic mucosa but is thought to have minimal pathogenic ability outside the gastrointestinal tract (6). The extraintestinal *C. difficile* infections described have included bacteremia, abdomino-pelvic infections, wound infections with bone and joint involvement, pulmonary effusions, empyemas, and extra-abdominal abscesses (7). *C. difficile* is isolated alone in only a small percentage of cases and is typically found in polymicrobial infections, where it may play a role in enhancing the virulence of other pathogens (6).

Because *C. difficile* is a fastidious anaerobe and is often isolated with other microbes, its isolation often is difficult and challenging and emphasizes the need for sensitive microbiologic detection methods (8, 9). In distinction from intestinal infections, where the diagnostic criteria are well defined, the significance of isolation of *C. difficile* from extraintestinal sites can sometimes be unclear. Initially, our patient exhibited polymicrobial growth in dialysis fluid cultures on hospital days 1 to 4 with isolation of *E. coli*, *B. fragilis*, and *C. albicans*, but as he experienced persistent abdominal symptoms, he was found to have single isolation of *C. difficile* on 3 different specimens on hospital days 5 to 7, which suggests that the isolate was indeed pathogenic.

Gupta et al. have described association of previous antimicrobial exposure and underlying comorbidities such as malignancy, renal disease, trauma, or surgery with extraintestinal *C. difficile* infections (9). Our patient had multiple comorbidities predisposing him to infection, including congestive heart failure, diabetes, hypertension, and end-stage renal disease.

Although this association exists, in another review by Bedimo and Weinstein, at least one-third of cases of extraintestinal *C. difficile* infections had no predisposing factors (10).

Most studies propose that *C. difficile* enters the bloodstream or abdominal compartment after mucosal wall breakdown or penetration (10). As a result, direct spread can occur from the intestine or from transient bacteremia causing infection at distant locations (7). However, infections without gastrointestinal pathology can occur in up to 27% of cases (10). Diarrhea was found in approximately 32 to 52% of cases (8–10). Since our patient lacked a history of diarrhea, bacteremia, recent intestinal surgery, or perforation, we think that he may have acquired the *C. difficile* infection environmentally or was colonized with it, and a microperforation that was not visible on imaging may have caused his infection.

There are no specific guidelines for the treatment of extraintestinal *C. difficile* infections. *C. difficile* isolates in most cases are susceptible to metronidazole and piperacillin-tazobactam. Vancomycin is also frequently used in both parenteral and oral forms (9). In one case of primary *C. difficile* peritonitis, successful treatment was rapidly achieved with intravenous metronidazole (500 mg intravenous every 8 h) after treatment failure on imipenem-cilastatin (11). Metronidazole (500 mg oral every 8 h) for a 10-day course also worked effectively in a patient with culture-negative peritoneal dialysis-related peritonitis secondary to *C. difficile* colitis (12). Our patient was treated successfully with a 14-day course of oral metronidazole (500 mg oral every 8 h) in addition to antibiotics directed to cover other microorganisms. Although our patient had a favorable outcome, mortality rates from these infections can be high, ranging from 25 to 37% (8–10).

Our case demonstrated that effective combination antimicrobial therapy using metronidazole and catheter removal can successfully cure *C. difficile* catheter-related peritonitis. Further studies may be needed to define the optimal treatment approach for the management of extraintestinal *C. difficile* infections.

REFERENCES

1. **Ballinger AE, Palmer SC, Wiggins KJ, Craig JC, Johnson DW, Cross NB, Strippoli GF.** 2014. Treatment for peritoneal dialysis-associated peritonitis. Cochrane Database Syst Rev **4:**CD005284. http://dx.doi.org/10.1002/14651858.CD005284.pub3.
2. **Barretti P, Doles JV, Pinotti DG, El Dib RP.** 2015. Evidence-based medicine: an update on treatments for peritoneal dialysis-related peritonitis. World J Nephrol **4:**287–294. http://dx.doi.org/10.5527/wjn.v4.i2.287.
3. **Port FK, Held PJ, Nolph KD, Turenne MN, Wolfe RA.** 1992. Risk of peritonitis and technique failure by CAPD connection technique: a national study. Kidney Int **42:**967–974. http://dx.doi.org/10.1038/ki.1992.375.
4. **Laroche MC, Alfa MJ, Harding GK.** 1997. Isolation of toxigenic Clostridium difficile from dialysate fluid in a fatal case of chronic ambulatory peritoneal dialysis-related peritonitis. Clin Infect Dis **25:**1248. http://dx.doi.org/10.1086/516960.
5. **Levett PN.** 1986. Clostridium difficile in habitats other than the human gastro-intestinal tract. J Infect **12:**253–263. http://dx.doi.org/10.1016/S0163-4453(86)94294-5.
6. **Brook I, Walker RI.** 1986. Pathogenicity of Clostridium species with other bacteria in mixed infections. J Infect **13:**245–253. http://dx.doi.org/10.1016/S0163-4453(86)91190-4.
7. **Jacobs A, Barnard K, Fishel R, Gradon JD.** 2001. Extracolonic manifestations of Clostridium difficile infections. Presentation of 2 cases and review of the literature. Medicine (Baltimore) **80:**88–101.
8. **Mattila E, Arkkila P, Mattila PS, Tarkka E, Tissari P, Anttila VJ.** 2013. Extraintestinal Clostridium difficile infections. Clin Infect Dis **57:**e148–e153. http://dx.doi.org/10.1093/cid/cit392.
9. **Gupta A, Patel R, Baddour LM, Pardi DS, Khanna S.** 2014. Extraintestinal Clostridium difficile infections: a single-center experience. Mayo Clin Proc **89:**1525–1536. http://dx.doi.org/10.1016/j.mayocp.2014.07.012.
10. **Bedimo R, Weinstein J.** 2003. Recurrent extraintestinal Clostridium difficile infection. Am J Med **114:**770–771. http://dx.doi.org/10.1016/S0002-9343(03)00184-0.
11. **de Leeuw P, de Mot H, Dugernier T, Wautelet J, Bohy E, Delmee M.** 1990. Primary infection of ascitic fluid with Clostridium difficile. J Infect **21:**77–80. http://dx.doi.org/10.1016/0163-4453(90)90715-K.
12. **Arikan T, Unal A, Kocyigit I, Yurci A, Oymak O.** 2014. Peritoneal dialysis-related peritonitis triggered by Clostridium difficile-associated colitis. Perit Dial Int **34:**139–140. http://dx.doi.org/10.3747/pdi.2012.00177.