Repeated *Burkholderia cepacia* Peritonitis in a Patient Undergoing Continuous Ambulatory Peritoneal Dialysis

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ABSTRACT

Burkholderia cepacia (B cepacia) *is a rare opportunistic pathogen in continuous ambulatory peritoneal dialysis (CAPD) peritonitis. We describe the first case of repeated* B cepacia *CAPD peritonitis, occurring in an outpatient environment, treated with antimicrobial medication without peritoneal catheter removal.* B cepacia *may lead to repeat infection, therefore, we should insist on catheter removal during each peritonitis episode.*

Keywords: *Burkholderia cepacia,* continuous ambulatory peritoneal dialysis, peritonitis

Peritonitis Repetida Causada por *Burkholderia cepacia* en un Paciente Sometido a Diálisis Peritoneal Ambulatoria Continua

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RESUMEN

Burkholderia cepacia (B cepacia) *es un patógeno oportunista raro en la peritonitis de la diálisis peritoneal ambulatoria continua (DPAC). Describimos el primer caso de peritonitis repetida de DPAC por* B cepacia, *que se presenta en un ambiente ambulatorio, en un paciente tratado con medicamentos antimicrobianos sin retirada del catéter peritoneal.* B cepacia *puede llevar a que se repita la infección. Por lo tanto, debemos insistir en retirar el catéter durante cada episodio de peritonitis.*

Palabras claves: *Burkholderia cepacia,* diálisis peritoneal ambulatoria continua, peritonitis

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INTRODUCTION

Continuous ambulatory peritoneal dialysis (CAPD) is a required method for treating patients with end-stage renal disease (ESRD). Consequently, peritonitis represents the leading complication on peritoneal dialysis (PD) and greatly affects morbidity and mortality in these patients; 1–6 % of all episodes result in death (1). It also remains a major cause of patients discontinuing PD and switching to haemodialysis.

Microbiologic evaluation showed that almost two-thirds of peritonitis episodes cultured positive. Gram-positive organisms are responsible for most of the cases. Gram-negative rods are less commonly isolated from peritoneal effluent than gram-positive one. However, gram-negative peritonitis is usually complicated to treat due to its high resistance to many antimicrobial agents. Gram-negative peritonitis requires a long-term hospitalization and considerably increases the cost of healthcare (2).

Burkholderia cepacia (B cepacia) is a gram-negative, aerobic, glucose nonfermentative bacillus, from the family of *Pseudomonadaceae*. These ubiquitous bacteria may be acquired through the soil, water, plants, contaminated disinfectants and medical instruments (3–5). Detailed epidemiologic and microbiologic evaluations have shown that it can survive with minimal nutritional requirements in accordance with its biological characteristics (6). As an opportunistic pathogen, it may cause infection in patients with defective immunity, especially patients with cystic fibrosis (CF) and chronic granulomatous diseases (CGD). Likewise, as an opportunistic agent, bacteria mostly infect patients in intensive care units [ICU] (7).

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B cepacia infection in CAPD patients has only scarcely been reported and not included in an overview of possible pathogens. To the authors' knowledge, this is the first reported case of repeated peritonitis due to *B cepacia* in a patient undergoing CAPD.

CASE REPORT

A 60-year old man presented to the nephrology department with turbid peritoneal effluent, bloating and widespread abdominal pain, nausea and vomiting. The patient was subfebrile (38.2 ˚C). He reported previous history of insulin-treated Type 2 diabetes mellitus for 23 years, and high blood pressure for 12 years. He has been a long-time smoker. Continuous ambulatory peritoneal dialysis therapy was started 26 months before the present event and dialysis treatment consisted of four 1.5-L exchanges of dialysate.

Clinical manifestations and the results of the laboratory evaluation revealed the presence of acute peritonitis. His white blood cells (WBC) count was 6.3 x 10^9/L with 72.8% polymorphonuclear cells, C-reactive protein (CRP) 34.1 mg/L, ferritin level 585.9 μg/L, while peritoneal effluent contained 2020 leukocytes/mL (normally contains less than 100 leukocytes/mL). At the beginning of treatment, peritoneal effluent was sampled for microbiological examination and the patient received empiric antibiotic therapy, based on the local protocol treatment for CAPD peritonitis (cefuroxime 750 mg administered three times per day and gentamicin 40 mg in the overnight exchange, intraperitoneally). On the fourth day of hospitalization, peritoneal effluent culture was positive for *B cepacia,* sensitive to ceftriaxone, cefuroxime, ceftazimide, cefepime, ciprofloxacin, imipenem, meropenem, ertapenem, gentamicin, amikacin, cotrimoxazole and doxycycline and resistant to ampicillin and amoxicillin. According to the antibiogram results, therapy was switched to ceftazidime (750 mg three times per day) along with amikacin (500 mg per day) intraperitoneally (serum levels 4–6 mcg/mL). On the eighth day of hospitalization, symptoms ceased and the number of peritoneal leukocytes decreased (20 leukocytes/mL). Negative culture results were found in the fluid after clinical improvement and the patient was discharged on the thirteenth day with recommendations to take cotrimoxazole for the next ten days (960 mg orally per day).

Seven months after the described episode, the patient was admitted to the hospital with cloudy peritoneal effluent and the same symptoms as we previously mentioned. This time his body temperature was 36.8 ˚C, WBC was 5.1 x 10^9/L with 70.9% polymorphonuclears, CRP 79.6 mg/L and ferritin level 649.5 μg/L. Peritoneal effluent contained 4000 leukocytes/mL. *B cepacia* was identified from the effluent, sensitive to cotrimoxasole, amikacin, cefepime, ciprofloxacin, imipenem, meropene, doripenem and doxycycline, and resistant to ampicillin, amoxicillin, ceftriaxone, cefuroxime and gentamicin. He refused CAPD catheter removal. The initial empiric therapy was changed to cotrimoxazole (480 mg three times per day) and amikacin (500 mg per day), intraperitoneally. By the ninth day of hospitalization, the peritoneal effluent was clear and contained 80 leukocytes/mL. After 14 days of hospitalization, clinical improvement was achieved and the patient received outpatient therapy (cotrimoxazole 960 mg orally per day for one week).

DISCUSSION

We have described the first case of *B cepacia* CAPD peritonitis in our thirty-year centre experience. With the exception of CF and CGD patients, most reported *B cepacia* infections involved nosocomial outbreaks among immunocompromised and/or severely ill patients (8). In our case, *B cepacia* peritonitis appeared in outpatient conditions. Seven months after the first episode, another one emerged with the same bacteria. Predisposing factors that contribute to patient immunosuppression are multi-year diabetes mellitus, chronic renal failure and long-time tobacco consumption.

Continuous ambulatory peritoneal dialysis procedure requires everyday multiple hand washing as well as the use of hand antiseptics during the exchange. At the time of peritonitis outbreak, the patient had used 0.6% chlorhexidine – digluconate antiseptic solution on the alcohol basis (not registered by the National Medicines and Medical Devices Agency). A combination of alcohol effect and the persistence of chlorhexidine would seem to provide a desirable antiseptic combination (9). However, previous studies have shown that unopened bottles of 0.5% aqueous solution chlorhexidine were a source of *B cepacia* infection. In addition, 2.5% chlorhexidine solutions for dialysis machines disinfection were the source of *B cepacia* outbreak (10, 11). We did not isolate *B cepacia* from the hand antiseptic. However, we recommended that he change the disinfectant sprayer; we could not for sure confirm if he complied with our recommendations until the second peritonitis episode outbreak.

B cepacia is widespread in nature and present in moist soil, plant rhizospheres and agriculture products. The patient lived in a rural environment and had daily contact with the soil and plants. Searching for the source of infection, we have analysed weather conditions and discovered it was a rainy time (April and November) when both episodes occurred. We speculate that soil could be one of the potential sources of *B cepacia* contamination.

B cepacia infections are particularly difficult to treat and often require prolonged therapy with two combined antibiotics. Cotrimoxazole has been a drug of choice, whereas ceftazidime, meropenem and piperacillin, in combination with other antimicrobial agents are alternative options for *B cepacia* infections (12). According to the *in vitro* antimicrobial susceptibility patterns, the patient was treated with ceftazidime and amikacin in the first episode, while cotrimoxazole in combination with amikacin was used in the second episode. Although intrinsic resistance to polycationic peptides, including aminoglycoside antibiotics, characterizes *B cepacia,* isolated strain was sensitive to amikacin. However, an inappropriate treatment of peritonitis appears to increase the risk of

another episode outbreak. Increasing risk of repeating or relapsing peritonitis could be a result of depressed intraperitoneal immune response or of inadequate effluent exchange technique. In addition, we emphasize the importance of proper patient re-education/retraining after every single peritonitis episode, which represents a regular protocol in our centre.

The International Society of Peritoneal Dialysis (ISPD) recommends removal of peritoneal catheter (PC) if there is no improvement after five days on appropriate antibiotic therapy [refractory peritonitis] (13). The primary goal of catheter removal should be peritonitis prevention and peritoneal membrane protection (14). In the first episode, since clinical condition improved, we did not consider the possibility of removing the PC. In the second episode, despite the good therapeutic response, we recommended PC removal, but the patient categorically refused. Presence of *B cepacia* biofilm within catheter may be one of the possible explanations for repeat infection. We speculate that catheter biofilm was not properly treated with antibiotics during the first episode, which provoked another one. This fact, nevertheless to the described potential sources of contamination in the first episode, could be a significant reason for the second episode outbreak. Hence, we highlight the need of further investigations into the role of biofilm in repeated episodes.

B cepacia rarely causes peritonitis in CAPD patients. Physicians should be aware of the possibility of uncommon bacterial peritonitis, especially in vulnerable patients and those in rural and poor socio-economic conditions. *B cepacia* may lead to repeat infection, therefore, we have to insist on catheter removal during each peritonitis episode. The available clinical data of *B cepacia* CAPD peritonitis are not sufficient. More studies are necessary, especially in extrapulmonary clinical cases, in order to specify the most appropriate treatment for *B cepacia* infection.

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