PERITONEAL DIALYSIS-RELATED PERITONITIS WITH *ACINETOBACTER BAUMANNII*: A REVIEW OF SEVEN CASES

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Peritonitis is still known as an important complication of continuous ambulatory peritoneal dialysis (CAPD). Multi-drug resistant (MDR) *Acinetobacter baumannii* is an increasing problem worldwide. Moreover, the increasing reports of carbapenem-resistant *A. baumannii* strains is common. Although peritoneal dialysis-related peritonitis with MDR *A. baumannii* is rarely reported, infection with this organism always results in serious peritonitis and increases the possibility of dropout or mortality. Here, we present 7 cases of peritonitis caused by *A. baumannii* species. Among those 7 cases, 2 involved MDR *A. baumannii*, and 1 involved a carbapenem-resistant strain. All the MDR bacterial infections failed treatment. We also review the literature about *Acinetobacter* peritonitis and current treatment protocols.

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KEY WORDS: Peritonitis; *Acinetobacter baumannii*; multi-drug resistance; peritonitis treatment.

Acinetobacter baumannii, a gram-negative bacterium, has been identified as a significant cause of antibiotic-resistant infections and has emerged as one of the most troublesome pathogens for health care institutions (1). Multidrug resistant (MDR) *A. baumannii* is a growing problem worldwide, and reports of carbapenem-resistant *A. baumannii* strains are common. Some *A. baumannii* strains have been found to be resistant to all known antibiotics (2).

Although MDR *A. baumannii* is rarely reported in association with peritonitis in peritoneal dialysis (PD) patients, when this organism is present, it results in serious infection and increases the possibility of dropout or mortality (3–5). Here, we present 7 cases

of peritonitis caused by *A. baumannii*. Of those cases, 2 involved MDR *A. baumannii*, and 1 was caused by a carbapenem-resistant strain. Refractory peritonitis in 3 patients resulted in prolonged hospitalization, the need for catheter removal, and finally PD dropout and a switch to hemodialysis. The other 4 patients were cured and continued PD therapy. *Acinetobacter* peritonitis and its treatment process are particularly concerning.

CASE DESCRIPTIONS

Over a period of 3 years (2009 – 2011), we diagnosed 7 cases of peritonitis attributed to *A. baumannii* in patients receiving PD. Susceptibility to various classes of antibiotics was tested using the disk diffusion technique. The procedure for peritoneal effluent culture followed International Society for Peritoneal Dialysis recommendations (6).

Of the 7 episodes, 2 were polymicrobial in nature (Table 1). Of the 7 patients, 3 dropped out from PD and switched to hemodialysis, and 1 of the hemodialysis patients died from a cerebral hemorrhage a year later. The other 4 patients were cured and continued PD therapy (Table 2). In all 3 drop-out cases, the infections were attributed to resistant organisms: in 2 patients the organism was MDR *A. baumannii*, and in 1 (patient 5), the strain was carbapenem-resistant *A. baumannii*. Resistance to amikacin was found in only 1 of the 4 patients that were cured (Table 1).

Of the 7 cases, 5 occurred in the patient's first year of PD (Table 2). Only 1 patient (patient 5) had experienced a previous peritonitis episode: that episode had occurred 20 days earlier, and the diagnosis was peritonitis attributed to *A. lwoffii*. Antibiotic treatment for 2 weeks was effective, and the white blood cell counts in peritoneal effluent were normal. However, a week later, the patient experienced diarrhea and abdominal pain. Culture of the peritoneal effluent showed *A. baumannii* that was resistant to many antibiotics, including imipenem (Table 1).

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TABLE 1
Characteristics of Peritoneal Effluent Cultures in Seven Peritoneal Dialysis Patients

Patient ID	Age (years)	Sex (M/F)	Organisms	Antimicrobial patterns for <i>A. baumannii</i>		Antibiotics used		Time to WBCs < 100/ μ L (days)	Duration of treatment (days)	Catheter withdrawal
				Sensitivity	Resistance	Type	Route			
1	41	M	<i>Acinetobacter baumannii</i> , then <i>Pseudomonas aeruginosa</i>	AMP-sulbactam, AK, CAZ, CTX-CIP, FEP, GM, IPM-LEV, PIP, SMZ, TIC/k-clav, TOB	Intermediate resistance: AZT, CTRX	Amikacin and ceftazidime Imipenem-cilastatin	IP IP	10	20	Yes
2	28	M	<i>A. baumannii</i>	AMP-sulbactam, AK, CTRX, CAZ, CTX, IPM, PIP, SMZ, TIC/k-clav, TOB	Intermediate resistance: AZT, FEP, GM Resistant: CIP, LEV	Amikacin and ceftazidime Imipenem-cilastatin	IP IP	—	10	Yes
3	64	M	<i>A. baumannii</i>	AMP-sulbactam, AZT, CTRX, CAZ, CTX, CIP, FEP, LEV, PIP, TOB, TIC/k-clav, IPM	Resistant: AK	Cefoxitin Levofloxacin	IP IV	4	14	No
4	39	F	<i>A. baumannii</i>	AMP-sulbactam, AK, CTRX, CAZ, CTX, CIP, FEP, GM, IPM, LEV, PIP, SMZ, TIC/k-clav, TOB		Ceftazidime	IP	Discharged	5	No
5	54	F	<i>A. baumannii</i>	AK, CIP, GM, LEV, TIC/k-clav, TOB	Resistant: AMP-sulbactam, CTRX, CAZ, CTX, FEP, IPM, PIP, SMZ	Ciprofloxacin	IV	—	7	Yes
6	41	F	<i>A. baumannii</i>	AMP-sulbactam, AK, CTRX, CAZ, CTX, CIP, FEP, GM, LEV, PIP, SMZ, TIC/k-clav, TOB, IPM		Vancomycin and ceftazidime Imipenem-cilastatin (for a WBC count rising to 19571/ μ L) Amikacin Levofloxacin	IP IP IP PO	6	19	No
7	39	F	<i>A. baumannii</i> and <i>Staphylococcus epidermidis</i>	AMP-sulbactam, AK, CTRX, CAZ, CTX, CIP, FEP, GM, LEV, PIP, SMZ, TIC/k-clav, TOB, IPM		Vancomycin and ceftazidime	IP	7	17	No

M/F = male/female; WBCs = white blood cells; AMP = ampicillin; AK = amikacin; CAZ = ceftazidime; CTX = cefotaxime; CIP = ciprofloxacin; FEP = cefepime; GM = gentamicin; IPM = imipenem; LEV = levofloxacin; PIP = piperacillin; SMZ = trimethoprim-sulfamethoxazole; TIC/k clav = ticarcillin-clavulanic acid; TOB = tobramycin; AZT = aztreonam; CTRX = ceftriaxone; IP = intra-peritoneal; IV = intravenous; PO = oral.

TABLE 2
Clinical Data for Seven Patients with *A. baumannii* Peritoneal Dialysis (PD)-Related Peritonitis

Pt ID	Date of peritonitis	Type of PD	Duration of PD (months)	Previous episodes	Signs	Analytical tests	Catheter removed	Outcome
1	12 Jun 2009	CAPD	9	No	Fever, abdominal pain, cloudy fluid	Hb: 83 g/L, A: 32.1 g/L, PA: 325 g/L, K: 4.03 mmol/L	Yes	Hemodialysis, patient died 1 year later
2	15 Jun 2009	CAPD	7	No	Diarrhea, cloudy fluid	Hb: 73 g/L, A: 23 g/L, PA: 282 g/L, K: 3.15 mmol/L	Yes	Hemodialysis
3	16 Jul 2010	CAPD	15	No	Abdominal pain, cloudy fluid	Hb: 136 g/L, A: 33.1 g/L, PA: 291 g/L, K: 3.3 mmol/L	No	Cured
4	11 Oct 2010	CAPD	4	No	Diarrhea, abdominal pain, cloudy fluid	Hb: 99 g/L, A: 26.1 g/L, PA: 184 g/L, K: 5.2 mmol/L	No	Cured
5	10 Jan 2011	CAPD	58	Yes (<i>A. lwoffii</i>)	Diarrhea, abdominal pain, cloudy fluid	Hb: 108 g/L, A: 23.6 g/L, PA: 439 g/L, K: 3.0 mmol/L	Yes	Hemodialysis
6	1 Sep 2011	CAPD	1	No	Diarrhea, abdominal pain, cloudy fluid	Hb: 95 g/L, A: 26.1 g/L, PA: 260 g/L, K: 4.9 mmol/L	No	Cured
7	16 Sep 2011	CAPD	5	No	Abdominal pain, cloudy fluid	Hb: 63 g/L, A: 15.5 g/L, PA: 121 g/L, K: 2.66 mmol/L	No	Cured

Pt = patient; CAPD = continuous ambulatory peritoneal dialysis; Hb = hemoglobin; A = albumin; PA = prealbumin; K = potassium.

All the cases of *A. baumannii* infection were community-acquired (Table 2). All patients but 1 (patient 3) were anemic. Serum albumin was below 30 g/L except in 2 patients (patients 1 and 3). All 7 patients had cloudy peritoneal effluent, and abdominal pain was frequent. Diarrhea occurred in 4 cases. Only 1 patient had a fever (Table 2).

During the course of antibiotics in the 4 patients who were cured, white blood cell counts in peritoneal effluent started to decline after 4 days of therapy. However, 1 patient (patient 4) refused to accept continuous therapy and was discharged without any drugs on the 5th day of antibiotic administration. The other 3 cured patients continued treatment for at least 14 days (Table 2).

The patient infected with carbapenem-resistant *A. baumannii* (patient 5) had previously been infected with *A. lwoffii*. She also had anemia, hypoproteinemia, and a low body mass index of 16.87. We didn't think that this patient would be able to survive the recurrent infection, and so her catheter was removed the day the bacterial infection was identified. She was given ciprofloxacin intravenously for 7 days to cure the infection.

DISCUSSION

The outcome of PD-related peritonitis greatly depends on the infecting micro-organism. Gram-positive cocci are still the causative organisms in most cases of peritonitis. *Acinetobacter* species are seldom involved in PD-related peritonitis, but when they are, delivering effective therapy is difficult (7,8).

When we reviewed PD-related peritonitis cases over a period of 3 years, we found that 72.4% were the result of gram-positive cocci; only 7.6% were attributed to *Acinetobacter* species. Among the *Acinetobacter* infections, 87.5% were caused by *A. baumannii*. Other research showed that the most common *Acinetobacter* species was *A. baumannii* and that resistance to numerous drugs in this organism has become a public health problem (1,9). Imipenem and meropenem have traditionally been the antimicrobials most effective against *A. baumannii* (10), but reports of carbapenem-resistant *A. baumannii* strains are becoming common.

Standardized terminology to describe drug-resistant bacteria was proposed by a group of international experts and published in *Clinical Microbiology and Infection* (11).

Criteria for classifying *Acinetobacter* species as MDR, extensively drug-resistant (XDR), or pan-drug-resistant (PDR) were described as follows: "MDR was defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories, XDR was defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories ... and PDR was defined as non-susceptibility to all agents in all antimicrobial categories" (11, p. 268). According to those criteria, 2 of the 7 cases of peritonitis in our study (patients 2 and 5) were caused by MDR *A. baumannii*. In 1 of the 2 cases, the bacterium was resistant to carbapenem. Both cases were treated to no effect, and the catheter was ultimately removed.

In our study, 3 *A. baumannii* peritonitis episodes resulted in PD dropout, and 4 patients were cured. Of the 3 patients who switched to hemodialysis, 1 died of a cerebral hemorrhage (not from infection). All patients who failed to respond to antibiotics were infected with antibiotic-resistant bacilli. We found 1 specimen resistant to carbapenem. The case in which the bacterium was found to be resistant to amikacin suggests that prompted antibiotic resistance in *A. baumannii* may be a key factor in refractory peritonitis. Solak *et al.* (5) reported that a patient with *A. baumannii* peritonitis that was sensitive only to aminoglycosides and tigecycline died of refractory septic shock. Another 2 patients were administered antibiotic therapy and recovered from non-MDR *A. baumannii* infection (3,4).

Galvao *et al.* (12) surveyed 23 episodes of *Acinetobacter* peritonitis, more than half of which occurred in the patient's first year of PD. In our study, 5 of 7 patients were infected their first year of PD. In all of the patients except patient 5, the *Acinetobacter* infection was their first episode of peritonitis. In the study by Galvao and colleagues, *Acinetobacter* accounted for a second peritonitis episode in 6 patients. Interestingly, the incidence of *Acinetobacter* peritonitis in that study increased significantly in the first 2 – 3 months after a prior episode of peritonitis (12). In our study, 1 episode of *Acinetobacter* infection occurred at day 20 after a preceding infection.

The clinical features and outcomes of PD-related peritonitis caused by co-infection with *Acinetobacter* species and other pathogens have rarely been reported. We had 1 patient with co-infection: in patient 7, the peritoneal effluent culture was positive for both *A. baumannii* and *Staphylococcus epidermidis*. That patient was cured, which suggests that co-infection with other bacteria may be not a refractory factor in *A. baumannii* peritonitis. In addition, patient 1 experienced 2 peritonitis episodes during the study, but a sample was not cultured between

the two episodes. In that patient, the peritoneal effluent again turned cloudy 20 days into the antibiotic course, and a culture from the removed catheter was positive for *Pseudomonas aeruginosa*.

Many factors promote peritonitis in PD patients: age (60 years and older), anemia (hemoglobin: <70 g/L), hypoalbuminemia (serum albumin: <30 g/L or, in some research, <35 g/L), hypokalemia (serum potassium: <3.5 mmol/L), diverticulosis, and diabetes, among others (13). In our study, 6 of 7 patients had anemia; the hemoglobin concentration in 1 patient was below 70 g/L. All patients had hypoalbuminemia, and 5 patients had albumin concentrations below 30 g/L. Of our 7 patients, 4 had hypokalemia, and 2 had diabetes. The age of the patients varied from 28 years to 64 years (only 1 patient was more than 60 years of age). Whether the patients had diverticulosis was unknown, because colonoscopies and barium enema examinations were not performed. In a few cases, we presumed that *A. baumannii* and other frequent bacterial infections were co-equal predisposing factors for peritonitis in PD patients, but hypoalbuminemia was probably more important.

CONCLUSIONS

A. baumannii appears to be rapidly developing resistance to multiple antimicrobials, resulting in serious infections and, when treatment is ineffective, high mortality. Our study found 1 specimen of *A. baumannii* with carbapenem resistance. Perhaps PDR *A. baumannii* will be the next threat to PD patients. To lower the peritonitis rate, predisposing factors such as malnutrition, anemia, and hypokalemia should be immediately and adequately corrected. Educating patients and caregivers on good hygiene and fluid exchange procedures will also be helpful.

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DISCLOSURES

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