

Peritonitis from facultative anaerobic gram-negative bacilli likely due to translocation of bacteria from gut in a patient undergoing peritoneal dialysis

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Abstract

The peritonitis caused by gram-negative organisms is a serious complication encountered in patients undergoing peritoneal dialysis, often causing high morbidity and mortality. There has been recognition of peritonitis caused by uncommon organisms because of improved microbiological detection techniques. The healthcare providers involved in the management of these patients should be very vigilant. We report a rare case of peritonitis caused by *Citrobacter freundii*. A 42-year-old male on peritoneal dialysis for five years presented with abdominal pain and cloudy effluent. The peritoneal fluid analysis was consistent with peritonitis, and peritoneal fluid culture grew *Citrobacter freundii*. The patient was treated with two courses of double antibiotic coverage with intraperitoneal ceftazidime and oral ciprofloxacin, which failed to resolve the infection and hence resulted in the removal of the peritoneal dialysis catheter and dialysis modality change.

Introduction

Gram-negative organism peritonitis is a severe complication encountered in patients undergoing peritoneal dialysis, often causing high morbidity and mortality. The healthcare providers involved in the care of patients undergoing peritoneal dialysis should recognize that unusual organisms could cause peritonitis. We report the case of a 42-year-old male on peritoneal dialysis

presenting with *Citrobacter freundii* peritonitis.

Citrobacter freundii (*C. freundii*) is a motile, facultative anaerobe, non-sporing gram-negative bacilli colonize in the gastrointestinal tract of humans and other animals. It is also found in water, soil, and food.¹ Werkman and Gillen discovered genus *Citrobacter* in 1932 and the organism uses citrate a sole carbon source for the energy source and hence derives its name.² *C. freundii* is hydrogen sulfide positive, indole negative, adonitol negative, and malonate negative in character.³ Peritonitis from gram-negative organisms frequently results in hospitalization, catheter loss, dialysis modality change, and mortality. These infections are hard to treat because of biofilm formation, which makes them less susceptible to antibiotics.

Case Report

A 42-year-old male on peritoneal dialysis presented with abdominal pain and cloudy effluent of one-day duration. The patient denied any fever and denied any in advent breach in the technique while making peritoneal dialysis connections. Moreover, the patient denied history of diarrhea or constipation. The patient has been on peritoneal dialysis for five years and had no prior history of peritonitis. Past medical history was signification for diabetes, hypertension, hyperlipidemia, hyperparathyroidism, end-stage renal disease on peritoneal dialysis. Home medications included metoprolol 100 milligrams (mg) twice a day, nifedipine 60 mg extended-release daily, atorvastatin 80 mg daily, sevelamer 2400 mg three times a day with meals, calcitriol 0.5 micrograms (mcg) daily, gabapentin 100 mg daily at bedtime, cinacalcet 30 mg daily, insulin glargine 15 units daily, insulin sliding scale.

The vital signs on presentation were the temperature of 36.4 Celsius, pulse rate of 84 beats per minute, respiratory rate of 16 breath per minute, blood pressure of 158/95 mm Hg. Physical examination revealed abdominal tenderness with a peritoneal dialysis catheter in the right lower quadrant. There was no exit site drainage or redness along the tunnel and the rest of the physical examination was nonsignificant.

Laboratory analysis showed white blood count 10300 mm³, hemoglobin 11.2 gm/dl, platelet count 22300 mm³, sodium 138 mmol/l, potassium 4.5 mmol/l, bicarbonate 22 mmol/l, blood urea nitrogen 58 mg/dl, creatinine 11.6 mg/dl, albumin 3.3 g/dl. The peritoneal fluid effluent revealed peritoneal fluid white blood cells (WBC)

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1837 cells/ul with 85% predominant neutrophils. Peritoneal fluid gram stain revealed >100 WBC, and no organisms were seen. The patient was started on empiric treatment for peritonitis with intraperitoneal vancomycin and ceftazidime. Later on, peritoneal fluid culture grew *Citrobacter freundii* in both aerobic and anaerobic bottles. The sensitivities of *Citrobacter freundii* were listed in Table 1 done by VITEK 2 method.

The patient was treated with double antibiotic coverage of intraperitoneal ceftazidime and oral ciprofloxacin for three weeks. The repeat peritoneal fluid cultures after finishing the antibiotic course yielded heavy growth of *C. freundii* again. The sensitivities of *Citrobacter freundii* are listed in Table 2 done. Another three weeks course

of double antibiotic treatment (intraperitoneal ceftazidime and intravenous imipenem) was given, which failed to clear the organism. The symptoms resolved when peritoneal dialysis catheter was removed after failing two double antibiotic courses. Subsequently, he did not require a further course of antibiotics. The dialysis modality of the patient was then switched to hemodialysis and the patient continues to be hemodialysis dependent after two years of follow up.

Discussion

C. freundii belongs to the *Enterobacteriaceae* family, which accounts for more than 10% of cases of peritonitis. *Serratia*, *Pseudomonas/Providencia*, *indole positive Proteus/Acinetobacter/Morganella*, *Citrobacter*, *Enterobacter*, and *Hafnia* group of organisms (SPICE) are associated with peritonitis with high mortality, and morbidity.⁴ *Citrobacter* has low virulence and accounts for 4.8% of all *Enterobacteriaceae* peritonitis.⁵

C. freundii and *C. koseri* are the most pathogenic strains and cause seventy percent of human infections among the *Citrobacter* genus. Other medically important species in *Citrobacter* are *C. amalonaticus*, *C. farmeri*, *C. braakii*, *C. werkmanii*, and *C. sedlakii*.⁶ *Citrobacter* is the rare cause of peritonitis, and *C. freundii* is the common species involved, frequently

leads to peritoneal dialysis catheter removal despite repeated courses of double antibiotic coverage.⁴ Dialysis patients are prone to have gastrointestinal colonization from

gram-negative bacteria, particularly *Citrobacter* compared to the general population. *Citrobacter* peritonitis tends to be polymicrobial in 10-15% episodes com-

Table 1. Sensitivities of *Citrobacter freundii*, isolated in our patient with peritonitis.

Antibiotic	Minimum inhibitory concentration	Sensitivity result
Cefazolin	≥64 mcg/ml	Resistant
Cefepime	≤1 mcg/ml	Sensitive
Ceftazidime	≤1 mcg/ml	Sensitive
Ceftriaxone	≤1 mcg/ml	Sensitive
Ciprofloxacin	0.5 mcg/ml	Sensitive
Gentamicin	≥16 mcg/ml	Resistant
Imipenem	2 mcg/ml	Sensitive

Table 2. Sensitivities of *Citrobacter freundii* during antibiotic treatment.

Antibiotic	Minimum inhibitory concentration	Sensitivity result
Cefazolin	≥64 mcg/ml	Resistant
Cefepime	≤1 mcg/ml	Sensitive
Ceftazidime	≤1 mcg/ml	Sensitive
Ceftriaxone	≤1 mcg/ml	Sensitive
Ciprofloxacin	1 mcg/ml	Intermediate
Gentamicin	≥16 mcg/ml	Resistant
Imipenem	1 mcg/ml	Sensitive
Levofloxacin	4 mcg/ml	Intermediate
Tobramycin	8 mcg/ml	Resistant
Trimethoprim/Sulfamethoxazole	≥320 mcg/ml	Resistant
Piperacillin-tazobactam	16 mcg/ml	Sensitive

Table 3. Summary all the cases listed as *Citrobacter freundii* peritonitis with patients on dialysis as per PubMed review of literature.

Author	Year	Age/ Gender	Duration (months)	Duration Mode	Dialysis association	Polymicrobial culture	Dialysate	Treatment salvage	Catheter	Outcome
Dervisoglu <i>et al.</i> ⁸	2008	33/F	96		CAPD	No	Positive	Intravenous Meropenem Intraperitoneal Gentamicin	No	Infection resolved and patient was switched to HD
Farinha <i>et al.</i> ⁹	2013	65/M	NA		NA	No	Positive	IV Ceftazidime IV piperacillin-tazobactam IV Gentamicin	No	Patient died for peritonitis before completion of antibiotic course and PD catheter removal
Kusaba <i>et al.</i> ¹⁰	2012	66/M	12		NA	Yes Enterococcus Stenotrophomonas Maltophilia	Positive	Intraperitoneal Ceftazidime Intravenous Vancomycin Intravenous Ciprofloxacin	No	Infection resolved and patient was switched to HD
Oh <i>et al.</i> ¹¹	2015	34/F	48		CAPD	Yes Candida Tropicalis	Positive	Intravenous Gentamicin	No	Infection resolved and patient was switched to HD
Kataria <i>et al.</i> ⁴	2015	76/M	6		CCPD	No	Positive	Oral ciprofloxacin and Intraperitoneal Gentamicin	Yes	Infection resolved with antibiotics

CAPD, continuous ambulatory peritoneal dialysis; CCPD, continuous cyclic peritoneal dialysis; NIPD, nocturnal intermittent peritoneal dialysis; HD, hemodialysis; NA, not available.

pared to 13-30% episodes in other infections.⁷ We summarized all the cases listed as *C. freundii* peritonitis on literature review from PubMed in Table 3.⁸⁻¹⁴

The patients who are at risk of developing infections from *Citrobacter* are elderly, immunocompromised, debilitated, and have multiple comorbidities.² Invasive genitourinary procedures increase the risk of colonization and infection by this organism.² The mode of transmission in peritonitis could be from microbial transmural migration from the gastrointestinal tract by their colonization accounting for 45% compared to 5-10% from other organisms.^{12,13} It is associated with constipation and/ or diarrhea in 46% of episodes in a case series.⁷ It is implicated in causing bacteremia, septicemia, superficial skin infections, brain abscess, meningitis, and urinary tract infections.^{2,4} *Citrobacter* is typically isolated using standard microbiological techniques using Mueller Hinton agar by the standard disc diffusion method recommended by the Clinical and Laboratory Standards Institute (CLSI).¹⁴ The genus *Citrobacter* can be identified by culture of the blood or body fluid and most of them ferment glucose with the production of gas and exclusively utilize citrate as a carbon source. Species differentiation is done by biochemical tests, DNA hybridization, and Vitek GNI+ card.

ISPD (International Society of peritoneal dialysis) 2016 guidelines recommends treating SPICE organisms for three weeks with double antibiotic coverage as per sensitivities.¹⁵ There is a high level of resistance to ampicillin and first-generation cephalosporin in a bacterial strain of *C. freundii* attributed to ampC gene as in our patient.⁴ The organisms are often sensitive to quinolones, aminoglycosides, and carbapenems. However, in our patient, *Citrobacter freundii* was resistant to aminoglycosides from the beginning and developed intermediate sensitivity to fluoroquinolones. The mortality rate associated with *Citrobacter* peritonitis is 18%.⁷ The dialysis modality was switched in 89% of

surviving patients with *Citrobacter* peritonitis over twelve months follow up.

Conclusions

This case highlights that rare organisms like *Citrobacter freundii* can cause peritonitis likely due to the translocation of bacteria from the gut. There has been increased identification of peritonitis from SPICE organisms due to recent advances in microbiological techniques. Double antibiotic treatment is required for SPICE organisms as per ISPD.

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