**Case Report**

**Clostridium perfringens Bacteremia in a Peritoneal Dialysis Patient: Clinical Implications**

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**Abstract**

Clostridial species bacteremia rarely occurs in general population. Usually hosts with organic gastrointestinal lesion or immunocompromised background are more likely to contract this disease. We present a case of *Clostridium perfringens* bacteremia in an end-stage renal disease patient undergoing peritoneal dialysis, without other underlying disease. The role of uremia and associated dialytic therapy in mediating this infrequent infection among the end-stage renal disease population was discussed, with relevant reports provided. Our patient also displayed infrequent manifestation of *Clostridium perfringens* sepsis and severe anemia. Several potential mechanisms were also suggested. According to the current finding, it is then imperative for us to reconsider end-stage renal disease as an immunocompromised background.

**KEY WORDS:** anemia, *Clostridium perfringens*, peritoneal dialysis, sepsis

**Introduction**

*Clostridium perfringens*, previously known as *Clostridium welchii*, is a Gram positive, saprophytic anaerobic organism widely distributed in the ambient environment (1). Besides this ubiquitous inhabitation, *Clostridium perfringens* also colonizes in gastrointestinal tract of various animals, including human. Risk factors of acquiring *Clostridium perfringens* infection include malignancy, especially hematologic ones, and other immunosuppressive status (2, 3). Patients with uremia have traditionally been regarded as “secondarily immunocompromised”, and the renal replacement therapy per se also contributes to host immunodysregulatory process (4-6). Herein we report a case of long-term peritoneal dialysis patients developing spontaneous *Clostridium perfringens* septicemia, and discuss the current evidence linking peritoneal dialysis patients to this infrequent infection.

**Case Report**

A 72-year-old woman presenting with days of conscious disturbance was brought to our emergency department. Her past medical experience included chronic kidney disease of unknown origin, prompting her to start hemodialysis a decade ago, an episode of uncomplicated gallstone, and major depression undergoing psychiatric clinical treatment. Her dialysis modality was switched to peritoneal dialysis owing to exhaustion of vascular access one year ago. Her peritoneal dialysis Kt/V was 1.85 one month before the current episode without residual renal function, and her serum albumin level was 3.6 g/dL. She was found to have diminished facial expression and drowsy appearance in recent days, and was confined to bed most of the time with little oral intake. Several times of watery diarrhea without bloody or mucus component also occurred for one day, without abdominal discomfort. Her family members brought her to our emergency department, and elevated body temperature (38°C) with hypotension (blood pressure 77/42 mmHg) was detected. Fluid resuscitation commenced immediately, and serial blood test yielded severe normocytic anemia (hemoglobin [Hb] 4.8 g/dL), mild transaminase elevation (alanine transaminase [ALT])...
48 U/L) and hyperlactatemia (lactate 5.2 mmol/L) (Fig. 1). Hepatitis B and C markers were negative from her medical record. Septic shock with multiorgan dysfunction syndrome was impressed, and we started early-goal directed therapy judiciously according to her body volume status (7). Empirical antibiotic with Cefepime along with component therapy was provided. A comprehensive search for infection focus was carried out, including chest roentgenography and abdominal computed tomography (CT), but both were unrevealing (Figs. 2, 3). There were no tenderness over exit site or tunnel area of her Tenckhoff catheter, and microscopic examination of dialysate fluid showed leukocyte count: 0 cells/mm³. Stool analysis was negative for pus cells. She was admitted to intensive care unit (ICU) for further management.

A lumbar puncture in ICU was also negative for leukocyte, and the amount of cerebrospinal fluid protein was normal. Her consciousness still fluctuated with intermittent disorientation of time and place. Blood culture subsequently grew *Clostridium perfringens*, while other body fluid cultures were all negative. Cefepime was de-escalated to Ceftazidime and Clindamycin, and her consciousness level gradually returned after days of ICU stay. Her blood pressure also stabilized after the use of vasoactive agents was discontinued. Anemia also resolved with component therapy (Fig. 1). She was discharged after a complete 2-week course of antibiotics.

**Discussion**

*Clostridium* species infection in human usually manifests with severe soft tissue infection (especially muscle) and gas gangrene formation, with sources of wound contamination, septic abortion or intra-abdominal sepsis (8, 9). It is estimated that clostridial bacteremia occurred with a 0.1-2.0% prevalence within all positive blood culture specimens, among which *Clostridium perfringens* was the most common pathogen identified (20-50%) (9). Traditionally, clostridial

![Fig. 2. Initial chest X-ray showed no obvious pulmonary consolidation patch or pleural effusion bilaterally.](image)

![Fig. 3. Abdominal CT without contrast enhancement showed an intact gallbladder without obvious gallstone or cholecystitis presence. Hepatic parenchyma was also unremarkable.](image)
bacteremia carries a cutaneous or frank gastrointestinal (GI) origin, and is often part of the polymicrobial septicemic processes. In a moderate-size community population, Rechner et al. reported that clostridial species came from a prominent gastrointestinal focus in 50% of cases, with colon constituting the most frequent source (~25%) (9). Shah and coworkers also reached similar conclusion in a single-center setting, with gastrointestinal malignancy as a common host background (10). Other potential foci such as positive culture from environmental contamination or other gas-forming visceral infection have also been reported (11, 12).

On the contrary, spontaneous clostridial bacteremia, that is, bacteremia without an identifiable source, has been put forth as another clinical entity relatively distinct from the traditionally held view of frank GI-related one. Spontaneous episodes usually occur in immunocompromised hosts such as patients with diabetes mellitus, liver cirrhosis and malignancies (12, 13). Clinicians managing patients with this type of clostridial bacteremia often have to regard it as a marker of “relative host immunodeficiency”, thus taking steps to investigate whether such host factor exists or not. In addition, the decision about the length of empirical antibiotics also depends upon the origin of clostridial species and host defense. Such differentiation is consequently useful both in the issues of diagnosis and treatment. Our patient, with neither identifiable frank GI lesions both from history and radiologic studies nor traumatic skin or mucosal breaching, is compatible with acquiring the latter type of clostridial infection. She had several times of diarrhea preceding this admission, and though not inflammatory, might contribute somewhat to the clostridial bactereemic process through mucosal breakage. This finding hence supports the view that uremia and the accompanying dialysis process provide the immunocompromised background, which is a prerequisite for clostridial appearance. GI complications also occur commonly in uremic patients undergoing dialysis. Uremic platelet dysfunction and heightened risk of vascular ectasia in GI tracts will undoubtedly lead to more frequent GI bleeding and mucosal sloughing, while GI symptoms are also prone to be more common in uremic population (14). These also pave the way toward higher likelihood of developing clostridial bacteremia, whether spontaneous or with frank GI lesion. Indeed, Leal et al. found in their study from a large population-based survey for 6 years that hemodialysis was associated with a 200-fold higher risk of contracting clostridial bacteremia, a number far higher than that conferred by malignancy (odds ratio 40) (15).

Clostridium perfringens, as mentioned previously, is the most commonly identified clostridial species in human infection. Fujita et al. performed a single-center retrospective study of patients with Clostridium perfringens bacteremia, and found that Clostridium perfringens is most commonly associated with hepatobiliary lesion and immunosuppressive conditions (16). This is different from the epide- miological findings from population-based clostridial species bacteremia, but their number of cases is too small to allow for a definite comparison. Manifestations of Clostridium perfringens infection include food poisoning, necrotizing soft tissue gangrene, visceral abscess, septic venous thrombosis and rarely pleuropulmonary infection (1, 17). Our patient initially presented with severe anemia (Hb 4.8), which is not a typical sign of Clostridium perfringens infection. Clostridium perfringens has been reported to cause bone marrow involvement (18). Even more rarely, Clostridium perfringens causes a dramatic and massive intravascular hemolysis through production of exotoxin, specifically, alpha-hemolysin (19). Since we did not check the hemolytic profile including indirect bilirubin or haptoglobin or reticulocyte production index during the event, we cannot confirm whether hemolysis has occurred or not. It is thus likely that our patient might suffer from GI bleeding, bone marrow involvement, or rarely hemolysis during spontaneous clostridial bacteremia with severe anemia.

The outcome of clostridial bacteremia is frequently grave, with reported mortality as high as 50%, with or without appropriate antibiotic coverage (9, 11, 12). The more important factors determining patient survival are host susceptibility, such as presence of cirrhosis, or disease presentation, especially initial hemodynamic status (9, 12). Although our patient did have initial circulatory failure, she only had a background of uremic status, without previously established adverse prognosis factors such as diabetes mellitus or cirrhosis, thus explaining partially her fair prognosis. However, a timely recognition of the presence of septic shock and prompt protocol-based management may also contribute.

Our patient is not the first case of Clostridium perfringens infection in peritoneal dialysis patients (20), but is among the very few cases of developing spontaneous clostridial bacteremia in the peritoneal dialysis population. Clostridium perfringens infection has been previously reported to cause peritonitis in peritoneal dialysis patients without identifiable GI lesion (20, 21), another with asymptomatic emphy- sematous cholecystitis (22), and in a hemodialysis patient with arteriovenous graft infection with cellulites (23). In light of these reports, the spectrum of Clostridium perfringens infection in dialysis population ranges from spontaneous or secondary peritonitis to vascular access infection. However, spontaneous bacteremia is still a rare encounter.
In conclusion, we present a case of end-stage renal disease patient undergoing peritoneal dialysis developing spontaneous *Clostridium perfringens* bacteremia with initial septic shock and severe anemia, but successfully resuscitated. This case exemplifies the role of uremia in modulating host immunity, and also raises an issue of some infrequent manifestations of *Clostridium perfringens* infection.

References