Bacillus subtilis-associated abdominal catastrophe in a Japanese patient with peritoneal dialysis-related peritonitis

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**NEPHROLOGY & UROLOGY | CASE REPORT**

*Bacillus subtilis*-associated abdominal catastrophe in a Japanese patient with peritoneal dialysis-related peritonitis

Sae Aratani¹, Yuta Nakagawa¹, Yuichiro Sumi¹ and Yukinao Sakai¹

**Abstract:** Abdominal catastrophe in patients with peritoneal dialysis (PD) is a condition in which visceral injury may cause leakage of enteric microorganisms into the peritoneal cavity, resulting in peritonitis. A 50-year-old Japanese male, who had been on PD for 5 years, was diagnosed with PD-related peritonitis. The initial peritoneal fluid culture detected *Bacillus subtilis* and Enterococcus faecalis. Antibiotic treatment was immediately initiated. Abdominal computed tomography (CT) revealed a pelvic abscess and ileus without mechanical obstruction. We consulted with surgeons regarding surgical intervention. Since mechanical obstruction or perforation was not detected in the initial abdominal CT, abscess drainage was recommended. However, the fever recurred. Abdominal CT performed for the seventh time identified a fistula between the sigmoid colon and pelvic cavity. Surgical removal of the colon was performed. Herein, we elucidate a very rare case of *Bacillus subtilis*-associated abdominal catastrophe and discuss the clinically important aspects of it.

**Subjects:** Medicine; Infectious Diseases; Nephrology

**Keywords:** abdominal catastrophe; peritoneal dialysis; peritoneal dialysis-related peritonitis; *Bacillus subtilis*

**ABOUT THE AUTHOR**

The Department of Nephrology at the Nippon Medical School is playing a central role in the treatment of patients with various kidney diseases, including end-stage kidney disease (ESKD). Peritoneal dialysis (PD) is one of the modalities for renal replacement therapy of ESKD patients. Although the prevalence of PD has recently been declining in Japan, we constantly manage no less than 100 patients with PD. We are responsible for not only the medical management, but also the operation for PD catheter insertion. Importantly, we have been engaging in clinical studies related to PD, such as the association of adipocytokines with peritoneal function, investigation of more beneficial dialysate compositions, and evaluation of predictive factors for heart failure in patients with PD. We have presented our case study in the Japanese Society for Peritoneal Dialysis conference. We believe our work will contribute to the better clinical management of PD.

**PUBLIC INTEREST STATEMENT**

Peritoneal dialysis (PD) is one of the modalities for renal replacement therapy of end-stage kidney disease patients. PD-related peritonitis remains the most serious complication in patients undergoing PD. *Bacillus subtilis* (*B. subtilis*) is a gram-positive rod-shaped bacterium and ubiquitously found in the environment. It has been regarded as non-pathogenic for humans. This report illustrates abdominal catastrophe in PD-related peritonitis, in which *B. subtilis* was confirmed as a very rare causative microorganism. To our knowledge, this is the first report of *B. subtilis*-associated PD-related peritonitis. Importantly, we emphasize that it is essential for nephrologists to be more aware of abdominal catastrophe in PD-related peritonitis, and to cooperate with surgeons to improve the clinical care and outcomes for PD patients. We feel our manuscript will be of special interest to the readers of Cogent Medicine.
1. Introduction
Peritoneal dialysis (PD)-related peritonitis remains the most serious complication in patients undergoing PD and contributes to morbidity, increased risk of hospitalization, and permanent transfer to hemodialysis (Bieber & Mehrotra, 2019). The prognosis is more likely to depend on the underlying etiology rather than the specific microorganisms isolated (Faber & Yee, 2006). Abdominal catastrophe is defined as peritonitis from a visceral source with striking morbidity and mortality (Newman et al., 2001). Surgical intervention is required for both diagnosis and treatment. However, the correct diagnosis and timely surgical intervention remain challenging. There may be several reasons for this. First, the suspicion of abdominal catastrophe is low even among nephrologists. In addition, its initial manifestation is not significantly different from PD-related peritonitis with other etiologies (Kern et al., 2002). Moreover, the antecedents of enteric injury are unpredictable.

_Bacillus subtilis_ is a gram-positive rod-shaped bacterium, which is ubiquitously found in the environment, and may occasionally contaminate food, thereby causing food poisoning (Sinnela et al., 2019). It has been regarded as non-pathogenic for humans. Therefore, the contribution of _B. subtilis_ to the development of PD-related peritonitis has still been unclear.

Herein, we report abdominal catastrophe in a patient with PD-related peritonitis, in which _B. subtilis_ was revealed as an etiological agent. To our knowledge, this is the first report of _B. subtilis_-associated PD-related peritonitis.

2. Case
A 50-year-old Japanese man complaining of severe abdominal pain and fever was brought to our hospital. Twelve days prior to the admission, the patient had started developing symptoms. The

### Table 1. Blood analysis on admission

| Blood analysis | WBC | RBC | Hb  | Ht  | Plt | PT-INR | APTT | AST  | ALT  | γGTP | T-Bil | LDH  | Total-Chol | LDL-Chol | HDL-Chol | TG   |
|---------------|-----|-----|-----|-----|-----|-------|------|------|------|------|-------|------|------------|----------|----------|------|
| WBC           | 6600/μL | 3980000/μL | 10.1 g/dL | 48.7 % | 275000/μL | 1.18 Sec | 38.9 | 10 IU/L | 14 IU/L | 43 IU/L | 0.15 mg/dL | 148 IU/L | 144 mg/dL | 54 mg/dL | 115 mg/dL |
| TP            | 4.8 g/dL | 1.7 g/dL | 29.6 mg/dL | 79.1 mg/dL | 12.71 mg/dL | β2-microglobulin | 32.4 mg/dL | 133 mEq/L | 4.5 mEq/L | 87 mEq/L | 4.4 mg/dL | HbA1c | 5.0 % | HIV |
| Alb           | 1.7 g/dL | 29.6 mg/dL | 79.1 mg/dL | 12.71 mg/dL | β2-microglobulin | 32.4 mg/dL | 133 mEq/L | 4.5 mEq/L | 87 mEq/L | 4.4 mg/dL | HbA1c | 5.0 % | HIV |
| CRP           | 29.6 mg/dL | 79.1 mg/dL | 12.71 mg/dL | β2-microglobulin | 32.4 mg/dL | 133 mEq/L | 4.5 mEq/L | 87 mEq/L | 4.4 mg/dL | HbA1c | 5.0 % | HIV |
| BUN           | 79.1 mg/dL | 12.71 mg/dL | β2-microglobulin | 32.4 mg/dL | 133 mEq/L | 4.5 mEq/L | 87 mEq/L | 4.4 mg/dL | HbA1c | 5.0 % | HIV |
| Cr            | 12.71 mg/dL | β2-microglobulin | 32.4 mg/dL | 133 mEq/L | 4.5 mEq/L | 87 mEq/L | 4.4 mg/dL | HbA1c | 5.0 % | HIV |
| Na            | 133 mEq/L | 4.5 mEq/L | 87 mEq/L | 4.4 mg/dL | HbA1c | 5.0 % | HIV |
| K             | 4.5 mEq/L | 87 mEq/L | 4.4 mg/dL | HbA1c | 5.0 % | HIV |
| Cl            | 87 mEq/L | 4.4 mg/dL | HbA1c | 5.0 % | HIV |
| Ca            | 9.6 mg/dL | 4.4 mg/dL | HbA1c | 5.0 % | HIV |
| P             | 7.9 mg/dL | 4.4 mg/dL | HbA1c | 5.0 % | HIV |
| UA            | 4.4 mg/dL | HbA1c | 5.0 % | HIV |
| HbA1c         | 5.0 % | HIV |
| HIV           | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |

Alb, albumin; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Cr, creatinine; CRP, C-reactive protein; GTP, guanosine triphosphate; Hb, hemoglobin; HbA1c, hemoglobin A1c; HBS-Ag, hepatitis B surface antigen; HCV-Ab, hepatitis C virus antibody; HDL-C, high-density lipoprotein cholesterol; HIV, human immunodeficiency virus; Ht, hematocrit; LDH, lactate dehydrogenase; LDL-C, low-density lipoprotein cholesterol; Plt, platelet; PT-INR, prothrombin time–International normalized ratio; RBC, red blood cell; T-Bil, total bilirubin; TC, total cholesterol; TG, triglyceride; TP, total protein; UA, uric acid; WBC, white blood cell.
Symptoms were getting worse and subsequently led to nausea and vomiting. The patient had been on continuous ambulatory PD for 5 years. The patient’s past medical history included colonic diverticulosis.

On admission, the patient’s temperature was 37.7°C and blood pressure was 120/90 mm Hg. The abdominal examination revealed a decrease in bowel sounds and tenderness in the lower abdominal area.

The laboratory test revealed white blood cell count of 6600/µL, hemoglobin level of 10.1 g/dL, and serum C-reactive protein level of 29 mg/dL. Blood analysis showed BUN level of 79.1 g/dL and Cr level of 12.71 mg/dL (Table 1). The initial abdominal computed tomography (CT) revealed ileus without mechanical obstruction and pelvic abscess (Figure 1). Analysis of the peritoneal effluent revealed a white blood cell count of 2006/µL with 99% of cells to be neutrophils. The blood culture and peritoneal effluent culture were obtained.

Figure 1. Clinical course. According to the results of peritoneal fluid culture, antibiotic treatment was immediately switched to vancomycin (VCM). In addition, drainage and concomitant administration of piperacillin/tazobactam (PIPC/TAZ) were also performed for the pelvic abscess. Peritoneal effluent culture further revealed the presence of Candida spp., which required administration of fluconazole (FLCZ). PD catheter was removed on day 33 of hospitalization, and antibiotic and antifungal treatment were continued until Day 50. However, the fever recurred. The seventh abdominal CT identified a fistula between the sigmoid colon and pelvic cavity, necessitating a surgical intervention. The patient was transferred to maintenance hemodialysis and discharged on Day 112 with colostomy.

AV fistula, arteriovenous fistula; CAG, coronary angiography; CCU, coronary care unit; CEZ, cefazolin; CHDF, continuous hemofiltration; CT, computed tomography; CRP, C-reactive protein; FLCZ, fluconazole; GM, gentamicin; IP, intraperitoneal; IV, intravenous; MCFG, micafungin; MEPM, meropenem; PD, peritoneal dialysis; PIPC/TAZ, piperacillin/tazobactam; S/A, Sulbactam/Ampicillin; and VCM, vancomycin.
According to the initial evaluation, the patient was diagnosed with PD-related peritonitis. Empirical antibiotic therapy that included intraperitoneal administration of gentamycin and intravenous administration of cefazolin was initiated. Subsequently, peritoneal effluent culture revealed the presence of *B. subtilis* and *Enterococcus faecalis*. Antibiogram was examined (Table 2). Based on the results, the intraperitoneal administration of vancomycin was immediately administered. We also added intravenous administration of piperacillin/tazobactam for pelvic abscess. At the same time, we consulted the surgeons for the recommendation of surgical intervention for the pelvic abscess and ileus. Since mechanical obstruction or perforation was not detected in the initial abdominal CT, abscess drainage was recommended and performed (Figure 2). On Day 12 of hospitalization, peritoneal effluent culture further revealed the presence of *Candida* spp. Therefore, we administered intravenous fluconazole. We repeatedly performed abdominal CT to evaluate visceral injury, which showed no abdominal perforation. Since *Candida* spp. were identified, PD catheter removal was considered. Ideally, the PD catheter should have been removed immediately after the diagnosis of fungal peritonitis.

However, on Day 17 of hospitalization, the patient complained of dyspnea. The ECG showed ST elevation in the precordial lead. The patient was moved to the cardiac care unit and subjected to

**Table 2. Antibiogram**

|               | *Bacillus subtilis* | *Enterococcus faecalis* |
|---------------|---------------------|-------------------------|
| Vancomycin    | S                   | S                       |
| Sulbactam/Ampicillin | S                 | S                       |
| Panipenem    | S                   | S                       |
| Cefmezazole   | S                   | N                       |
| Ceftazidime   | S                   | N                       |
| Levofloxacin  | R                   | R                       |
| Fosfomycin    | I                   | S                       |

I, intermitted; N, not assessed; R, resistant; and S, Sensitive.

Figure 2. Abdominal CT. Initial abdominal computed tomography (CT) revealed an ileus without mechanical obstruction (white arrow heads in Figure 2(a)). However, a visceral injury was not identified. It also showed a pelvic abscess (white arrow in Figure 2(a) and white head in Figure 2(b)). The seventh abdominal CT detected a fistula between the sigmoid colon and pelvic cavity (black arrow head in Figure 2(c)).
urgent coronary angiography (CAG). The CAG revealed neither obstruction nor stenosis. The patient was diagnosed with Takotsubo cardiomyopathy. Intravenous nitrogen was administered and non-invasive positive pressure ventilation and continuous hemodiafiltration (CHDF) were introduced. The patient’s general condition did not allow him to undergo the surgical operation; therefore, after discharge from the cardiac care unit, the PD catheter was removed and the patient was switched to maintenance hemodialysis. Until Day 50 of hospitalization, antibiotic treatment was continued. However, blood analysis again showed an increase in serum CRP on Day 61. Therefore, abdominal CT was performed for the seventh time, which identified the fistula between the sigmoid colon and pelvic abscess (Figure 2). We again consulted the surgeons, and the colon was surgically removed on Day 67. The arteriovenous fistula was created and the patient was discharged on Day 112 with maintenance hemodialysis and colostomy.

3. Discussion
Abdominal catastrophe in PD-related peritonitis is a condition in which visceral injury may cause leakage of enteric organisms into the peritoneal cavity, resulting in peritonitis. It has remained a serious concern with high mortality rate of approximately 50% (Faber & Yee, 2006; Harwell et al., 1997; Newman et al., 2001). Although timely diagnosis and surgical intervention of abdominal catastrophe are critical, it has still remained challenging even among nephrologists. In this report, we propose several important aspects, which not only nephrologists but also surgeons need to be aware of.

Importantly, abdominal catastrophe can be caused by a polymicrobial infection. Usually, about 30–65% cases of PD-related peritonitis are caused by gram-positive bacteria, 20-30% by gram-negative bacteria, and 2.6–10% by polymicrobial communities (Andy Tang et al., 2019; Barraclough et al., 2010; Whitty et al., 2017). Among gram-positive bacteria, coagulase-negative Staphylococcus was the most common cause of PD-related peritonitis (Whitty et al., 2017). In contrast, when multiple microorganisms are present, especially gram-negative bacteria or fungi, there is a high possibility of gastrointestinal pathogenesis. It was reported that patients with gram-negative bacteria or fungi showed 66-fold higher prevalence of visceral injury compared to patients with gram-positive bacteria (Kern et al., 2002). In the present case, multiple organisms, including B. subtilis, were identified by PD effluent culture. B. subtilis is a gram-positive bacterium and considered non-pathogenic to humans, and there have been no reports of PD-related peritonitis. However, some serious B. subtilis-induced infectious diseases have been reported (Farrar, 1963). A study has previously shown B. subtilis bacteremia with gastrointestinal tract complications, such as ileus, colon perforation, and peritonitis (Hashimoto et al., 2017). Notably, it was reinforced that B. subtilis had adapted to life within the human gastrointestinal tract (Hong et al., 2009). Therefore, we propose that the detection of polymicrobial species, including even those of rare microorganisms, such as B. subtilis, should raise a strong suspicion of abdominal catastrophe. Although there has not been established treatment for B. subtilis, antimicrobial susceptibility results were helpful for clinical management. According to the previous reports, B. subtilis is susceptible to some antibiotics, including ampicillin, gentamycin, cefazolin, ceftriaxone, and vancomycin (Hashimoto et al., 2017; Tsonis et al., 2018). In the present case, the antibiogram revealed that B. subtilis was susceptible to vancomycin, subbactam/ampicillin, panipenem, cefmetazole, and ceftazidime. According to the MIC analysis, B. subtilis was the most sensitive to vancomycin. Therefore, vancomycin was chosen as a definitive treatment against infections caused by both B. subtilis and Enterococcus faecalis.

In addition, the sensitivity and specificity of common imaging evaluation are less reliable in patients with PD. For example, the clinical significance of pneumoperitoneum is controversial in PD patients. Usually, pneumoperitoneum is a sign of viscus perforation. However, it can be seen in PD-related peritonitis without perforation (Chen, 2012), or it can also appear to be low unless a large amount of air is present. In the present case, initial abdominal CT could not detect the signs of visceral perforation despite the presence of abscess in the pelvic cavity. We repeatedly performed abdominal CT, and it took seven attempts to finally detect the fistula between sigmoid colon and pelvic cavity. We suggest
that even negative findings in abdominal CT may be unreliable. Other complementary examinations, such as contrast enema, colonoscopy, and exploratory laparotomy should be carried out.

Further, cooperating with nephrologists and surgeons is very important to improve the clinical outcome of PD-related peritonitis. There has been a paucity of evidence regarding the surgical management of complications arising from PD (Ratajczak et al., 2017). In other words, even experienced surgeons may have little knowledge and experience with abdominal catastrophe in patients with PD-related peritonitis. Faber et al. demonstrated several cases in which definitive surgery had been delayed at most 3 weeks in PD patients with visceral rupture (Faber & Yee, 2006). In addition, as seen in the present case, imaging evaluations may mislead the surgeons, making them reluctant to explore surgical interventions. We emphasize that not only nephrologists but also surgeons must be aware of the low reliability of CT to correctly diagnose the disease.

Therefore, nephrologists who suspect an abdominal catastrophe are highly responsible for consulting surgeons, sharing unique characteristics of PD patients, and discussing the timely surgical intervention. We strongly emphasize that the cooperation between nephrologists and surgeons is necessary, and no delay in surgical intervention is warranted.

4. Conclusion
We present the first case of B. subtilis-associated abdominal catastrophe in PD-related peritonitis. It is essential for nephrologists to be more aware of abdominal catastrophe in PD-related peritonitis, and to cooperate with surgeons to improve the clinical care and outcomes for PD patients.

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Disclosure statement
The authors report no conflict of interest.

Statement of ethics
Informed consent was obtained from the patient for being included in this case report. The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Cover Image
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References
Andy Tang, S. O., Carolisyna, Y. I., Sakura, D., Yeo, S. T., & Koh, K. H. (2019). Demographic characteristics and outcomes of continuous ambulatory peritoneal dialysis related peritonitis in Miri General Hospital, Malaysia. The Medical Journal of Malaysia, 74(4), 270–274.

Barroclough, K., Howley, C. M., McDonald, S. P., Brown, F. G., Rosman, J. B., Wiggins, K. J., ... Johnson, D. W. (2010). Polymicrobial peritonitis in peritoneal dialysis patients in Australia: Predictors, treatment, and outcomes. American Journal of Kidney Diseases, 55(1), 121–131. https://doi.org/10.1053/j.ajkd.2009.08.020

Bieber, S., & Mehrotra, R. (2019). Peritoneal dialysis access associated infections. Advances in Chronic Kidney Disease, 26(1), 23–29. https://doi.org/10.1053.j.ackd.2018.09.002

Chen, Y. C. (2012). Peritoneal dialysis-related peritonitis with klebsiella pneumonoperitoneum mimicking viscous perforation. Peritoneal Dialysis International: Journal of the International Society for Peritoneal Dialysis, 32(5), 575–577. https://doi.org/10.3747/pdi.011.00304

Faber, M. D., & Yee, J. (2006). Diagnosis and management of enteric disease and abdominal catastrophe in peritoneal dialysis patients with peritonitis. Advances in Chronic Kidney Disease, 13(3), 271–279. https://doi.org/10.1053/j.ackd.2006.04.001

Farrar, W. E., Jr. (1963). Serious infections due to “non-pathogenic” organisms of the genus Bacillus. Review of their status as pathogens. The American Journal of Medicine, 34(1), 134–141. https://doi.org/10.1016/0002-9343(63)90047-0

Harwell, C. M., Newman, L. N., Cocho, C. P., Mulligan, D. C., Schulak, J. A., & Friedlander, M. A. (1997). Abdominal catastrophe: Visceral injury as a cause of peritonitis in patients treated by peritoneal dialysis. Peritoneal Dialysis International: Journal of the International Society for Peritoneal Dialysis, 17(6), 586–594. https://doi.org/10.1177/089686089701700611

Hashimoto, T., Hayokawa, K., Mezaki, K., Kutsuna, S., Takeshita, N., Yamamoto, K., ... Ohmagari, N. (2017). Bacteremia due to bacillus subtilis: A case report and clinical evaluation of 10 cases. Kansenshogaku Zasshi, 91(2), 151–154. https://doi.org/10.11150/kansenshogakuuzasshi.91.151
Hong, H. A., Khaneja, R., Tam, N. M., Cazzato, A., Tan, S., Urdaci, M., Brisson, A., Gasbarrini, A., Barnes, I., & Cutting, S. M. (2009). Bacillus subtilis isolated from the human gastrointestinal tract. Research in Microbiology, 160(2), 134–143. https://doi.org/10.1016/j.resmic.2008.11.002

Kern, E. O., Newman, L. N., Cacho, C. P., Schulak, J. A., & Weiss, M. F. (2002). Abdominal catastrophe revisited: The risk and outcome of enteric peritoneal contamination. Peritoneal Dialysis International: Journal of the International Society for Peritoneal Dialysis, 22(3), 323–334. https://doi.org/10.1177/089686080202200305

Newman, L. N., Cacho, C. P., Schulak, J. A., & Weiss, M. F. (2001). Abdominal catastrophe: Definition and proposal for a new approach. Advances in Peritoneal Dialysis. Conference on Peritoneal Dialysis, 17, 93–97. https://www.researchgate.net/publication/11835695

Ratajczak, A., Lange-Ratajczak, M., Bobkiewicz, A., & Studniarek, A. (2017). Surgical management of complications with peritoneal dialysis. Seminars in Dialysis, 30(1), 63–68. https://doi.org/10.1111/sdi.12538

Sinnela, M. T., Park, Y. K., Lee, J. H., Jeong, K. C., Kim, Y. W., Hwang, H. J., & Mah, J. H. (2019). Effects of calcium and manganese on sporulation of Bacillus Species involved in food poisoning and spoilage. Foods, 8(4), 119. https://doi.org/10.3390/foods8040119

Tsonis, I., Karamani, L., Xaplanteri, P., Kolonitsiou, F., Zampakis, P., Gatzounis, G., Marangos, M., & Assimakopoulos, S. F. (2018). Spontaneous cerebral abscess due to Bacillus subtilis in an immunocompetent male patient: A case report and review of literature. World Journal of Clinical Cases, 6(16), 1169–1174. https://doi.org/10.12998/wjcc.v6.i16.1169

Whitty, R., Bargman, J. M., Kiss, A., Dresser, L., & Lui, P. (2017). Residual Kidney Function and Peritoneal Dialysis–Associated Peritonitis Treatment Outcomes. Clinical Journal of the American Society of Nephrology, 12(12), 2016–2022. https://doi.org/10.2215/cjn.00630117