Case report

Presumptive complicating *Clostridium paraputrificum* bacteremia as a presenting manifestation in a patient with undiagnosed ulcerative colitis followed by acute colonic pseudo-obstruction

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ABSTRACT

*Clostridium paraputrificum* is a member of the commensal flora of the gastrointestinal tract and skin. Despite being linked with cases of severe invasive infection, this organism is an uncommon pathogen in humans. Here, we report a case of undiagnosed ulcerative colitis in which the presentation was one of presumptive complicating *C. paraputrificum* bacteremia and, later, acute colonic pseudo-obstruction. The patient was an elderly male with prostate cancer who was admitted in a state of shock secondary to suspected septicemia from an abdominal source. Only one of two sets of anaerobic blood cultures were positive for *C. paraputrificum*. Endoscopic and pathological investigations revealed proctitis consistent with ulcerative colitis. The patient’s abdominal manifestations worsened, and abdominal imaging demonstrated *de novo* massive colonic dilatation without any apparent mechanical obstruction. We speculated that *C. paraputrificum* bacteremia caused by undiagnosed ulcerative colitis had created ideal conditions for acute colonic pseudo-obstruction. This case demonstrates that *C. paraputrificum* bacteremia can be associated with latent severe gastrointestinal pathologies, indicating the need to investigate any abdominal source of infection, even if only a single blood culture is positive.

Introduction

Infections with anaerobic organisms are uncommon and pose a diagnostic challenge. Bacteria that comprise the commensal flora of the skin are often considered contaminants when present in blood cultures, especially if only a single blood culture is positive. However, in rare cases, this may indicate true bacteremia causing severe infection [1–3]. *Clostridium* species are anaerobic Gram-positive bacilli, many of which may become pathogenic and cause of a broad range of invasive infections in humans. Some of these may result in soft tissue, bloodstream, and gas-forming infections that can be potentially life-threatening [4]. The portals of entry for this organism can be the gastrointestinal tract (42.9%), unknown (35.7%), or the skin (16.7%) [5]. *Clostridium paraputrificum*, which is an infrequently isolated *Clostridium* species, is usually present in soil, human skin, and animal and human feces, and infection can be acquired in the setting of defective integrity of the bowel mucosa or skin. Infections with *C. paraputrificum* are rare, and the etiology varies.

Multiple clinical presentations have been described in the literature. It has been known to affect adults and newborns, presenting as bacteremia, necrotizing enterocolitis, septic arthritis, or cyst formation [6].

Acute colonic pseudo-obstruction (ACPO) is characterized by sudden, massive dilation of the large intestine in the absence of any evident mechanical etiology [7]. Several risk factors for the development of ACPO have been identified, including critical illness, recent surgical procedures, metabolic imbalance, and nonoperative trauma [8]. Here we report an informative case in which *C. paraputrificum* grown from a single positive blood culture served as a clue to undiagnosed ulcerative colitis later complicated by ACPO.

Case presentation

A 77-year-old man was brought to our emergency department because of abrupt onset of impaired consciousness and hypotension. He had been aware of intermittent mild lower abdominal discomfort

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associated with a small amount of bloody, loose stools occurring two to four times per day for 5 days prior to admission. He had a 2-year history of prostate cancer in complete remission that had been well controlled with Bicalutamide. He also had long-standing hypertension, hyperlipidemia, hyperuricemia, and lumbar spinal stenosis. On arrival, the patient’s general condition was poor, with a Glasgow score (GCS) of 10 (E2, V3, M5). In addition, the limbs were cold and moist. His vital signs included body temperature 35.6 °C; pulse rate 42 bpm with regular rhythm; blood pressure 65/36 mmHg; respiration rate 28 breaths/min; and oxygen saturation 95 % (2 L/min of oxygen). On physical examination, the patient had mild abdominal tenderness with normal bowel sounds. The findings of other physical examinations were normal. Initial blood tests showed normal white blood cell (neutrophils, 49.9 %) and platelet counts, and the hemoglobin level was within the normal range. The results of additional laboratory tests, including the serum levels of C-reactive protein (CRP) and procalcitonin, liver function tests, clotting screen, and arterial blood gases, were within the normal ranges. However, the levels of serum creatinine (Cr; 1.28 mg/dL [normal range: 0.36–1.06 mg/dL]) and lactic acid 31.5 mg/dL (normal range: 4.0–20.0 mg/dL) were elevated. The level of hemoglobin Alc (National Glycohemoglobin Standardization Program, NGSP) was slightly elevated at 6.3 % (normal range, 4.6–6.2 %). Echocardiography and abdominal ultrasound demonstrated no abnormalities. Non-contrast-enhanced whole-body computed tomography (CT) revealed mild edematous swelling of the small-intestinal wall thought to be enterocolitis, but no marked free air or ascites was noted. He was transferred to the medical intensive care unit for septic shock secondary to a suspected complicating intra-abdominal infection, and a large volume of intravenous crystalloid solution was administered with noradrenaline to maintain the blood pressure. Meropenem was initiated promptly as empiric antibiotic coverage for severe sepsis. On day 3 of hospitalization, the patient’s state of consciousness gradually improved, and vital signs became normalized except for a spike in body temperature, reaching 38.5 °C. One of two sets of blood cultures obtained on admission revealed a gram-positive bacillus with terminal spores in the anaerobic bottle. This was identified as C. paraputrificum by matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) and 16 S rRNA gene sequencing. 16 S gene sequencing of this strain to nearly full length (1440 bp) was performed at TechnoSuruga Laboratory (Shizuoka, Japan). This sequence best matched, at 99.8 % (1437 of 1,440 bp), those of the C. paraputrificum type strain and strain JCM 1293 (NCBI Reference Sequence accession no. AB536771). Based on the blood culture result for C. paraputrificum, the patient was treated with intravenous ampicillin/sulbactam for a total of 10 days. The laboratory parameters and clinical conditions improved during the ICU stay, and he was discharged from the ICU 4 days after admission. However, his abdominal manifestations including frequent loose, small amounts of bloody stools (>4 per day) persisted, together with low-grade fever and mild anemia not requiring blood transfusions. Clostridium difficile toxins A and B and glutamate dehydrogenase (GDH) antigen were negative in 2 stool samples taken 1 day apart, and the stools were negative for ova, parasites, and culture. The blood culture result for C. paraputrificum guided the investigation toward an abdominal source of infection, as this isolate has been associated with gastrointestinal pathologies. On day 35 of hospitalization, sigmoidoscopy demonstrated diffuse mucosal inflammation with loss of vascular markings due to engorgement of the mucosa, exudates, edema, touch friability, and spontaneous bleeding in the rectum. (Fig. 1). Histopathology revealed crypt disarray with no signs of crypt abscesses, and epithelial cell abnormalities including mucin depletion and neutrophil invasion. Furthermore, increased lamina propria cellularity, basal plasmacytosis, and lamina propria eosinophils (hematoxylin and eosin staining; ×20). (Fig. 2), and non-contrast-enhanced abdominal CT confirmed this colonic dilatation with no sign of thromboses or mechanical obstruction (Fig. 3b). Therefore, after multidisciplinary consultation, a diagnosis of ACPO was made, and conservative treatments such as total parenteral nutrition were initiated, followed by pharmacologic and endoscopic decompression therapy. However, as these treatments were unsuccessful, the dilated colon was resected on day 94 of hospitalization. The final impression diagnosis based on the clinical and imaging data was ACPO having occurred in a setting of presumptive C. paraputrificum bacteremia caused by undiagnosed ulcerative colitis.

Discussion

The present case of undiagnosed ulcerative colitis followed by acute colonic pseudo-obstruction, in a patient presenting with presumptive complicated C. paraputrificum bacteremia raises several important clinical issues. Importantly, it illustrates the fact that although C. paraputrificum is an infrequently isolated Clostridium species, it can cause severe invasive infections. Furthermore, in this case, bacteremia due to this organism was associated with underlying gastrointestinal

![Fig. 1. Sigmoidoscopy: Diffuse mucosal inflammation with loss of vascular markings due to engorgement of the mucosa, exudates, edema, touch friability, and spontaneous bleeding in the rectum.](image1)

![Fig. 2. Histopathology: Shows crypt disarray, epithelial cell abnormalities, increased lamina propria cellularity, basal plasmacytosis, and lamina propria eosinophils (hematoxylin and eosin staining; ×20).](image2)
pathology leading to defective integrity of the bowel mucosa, as has been reported previously. These findings suggest that even if a single blood culture is positive, which often suggests a contaminant, there is a need to investigate any abdominal source of infection in patients with *C. paraputrificum* bacteremia.

Anaerobes are recovered in 5% of cases of clinically relevant bacteremia [9]. *Clostridium* species represent 23% of the obligate anaerobic bacteria isolated from blood cultures, being the second most frequent anaerobes after Bacteroides [10]. Among *Clostridium* species, whereas *C. perfringens* is the most frequently isolated species, *C. paraputrificum* is isolated in only 1.4–2.3% of clostridial bacteremia cases and its clinical significance has not been well investigated [4, 5]. Several case reports of *C. paraputrificum* bacteremia have described a range of underlying diseases with an abdominal source of infection. To evaluate the association of *C. paraputrificum* bacteremia and gastrointestinal pathologies with defective integrity of the bowel mucosa, we exclusively analyzed similar cases in the English language literature published in the Medline/PubMed database from 1961 to 2022. The database search was conducted using the terms “*C. paraputrificum*” and “bacteremia.” This revealed 12 cases of *C. paraputrificum* bacteremia reported to date. Seven of those 12 cases were accompanied by gastrointestinal pathologies associated with defective integrity of the bowel mucosa, which was thought to be a portal for entry of this organism (Table 1) [6, 11–16]. In 4 of the 7 cases there were underlying diseases associated with immunocompromised conditions [11–14]. Four of the 7 patients died. In the detection of bacteremia, the general principle is that *Staphylococcus aureus*, *Streptococcus* species, *Enterococcus* species, gram-negative rods, and *Candida* species are often considered responsible for true bacteremia when present in blood cultures, even if only a single culture proves positive. On the other hand, bacteria that comprise the commensal flora of the skin, including *C. paraputrificum*, are often considered contaminants when present in blood cultures, especially if only a single culture is positive. However, previous studies of bacteria that also often contaminate blood cultures, such as *Corynebacterium* species, coagulase-negative *Staphylococci*, and *Cutibacterium* species, have claimed that it may be reasonable to consider a single positive blood culture as sufficient if a foreign intravascular device is present [1–3]. It has been argued that the definition of true bacteremia due to these organisms is that multiple sets of blood culture must be positive. In the setting of inflammatory bowel diseases, bacteremia has multiple etiologies. Defective integrity of the bowel mucosa and frequent endoscopic interventions in immunocompromised individuals are considered the primary causes [17]. In addition, an age of >65 years and multiple comorbidities are associated with an increased risk of bacteremia in hospitalized patients with inflammatory bowel diseases [18]. Our present patient had evidence of defective bowel mucosa integrity due to undiagnosed ulcerative colitis. We established a diagnosis of ulcerative colitis based on the presence of chronic diarrhea for more than four weeks, evidence of active inflammation on endoscopy, and pathologic findings. Since these features are not specific to ulcerative colitis, we excluded other causes of colitis to establish the diagnosis. In this case, the patient’s advanced age and immunocompromised condition resulting from treatment of prostate cancer could have been risk factors for the induction of bacteremia.

Acute colonic pseudo-obstruction (ACPO) is a disorder characterized by acute dilatation of the colon in the absence of an anatomic lesion that obstructs the flow of intestinal contents. ACPO usually involves the cecum and right hemicolon, although occasionally colonic dilatation extends to the rectum. ACPO usually occurs in hospitalized or institutionalized patients in association with a severe illness or after surgery and in conjunction with a metabolic imbalance or administration of culprit medications. The exact pathophysiology of ACPO is poorly

### Table 1

Summary of case reports with data on underlying disease with mucosal barrier breakdown and outcome in patients with *C. paraputrificum* bacteremia.

| Year | Authors            | Age | Sex  | Underlying diseases                  | Source of infection                  | Outcome     |
|------|--------------------|-----|------|-------------------------------------|-------------------------------------|-------------|
| 1961 | Wiot et al. [13]   | 52  | Female | diabetes mellitus                  | Acute mesenteric ischemia and bowel infarction | Died        |
| 1976 | Babenco et al. [14]| 88  | Male  | Polycythemia vera                   | Colonic neoplasms                   | Died        |
| 1996 | Nerad et al. [15]  | 32  | Male  | Acquired immunodeficiency syndrome  | Likely gastrointestinal              | Died        |
| 2015 | Shinha et al. [2]  | 65  | Male  | Acquired immunodeficiency syndrome  | Acute colonic necrosis              | Survived    |
| 2020 | Intra et al. [16]  | 78  | Male  | None                               | Colon neoplasm                      | Survived    |
| 2021 | Haider et al. [17] | 74  | Male  | None                               | Fulminant pseudomembranous colitis   | Died        |
| 2022 | Mostel et al. [18] | 88  | Male  | None                               | Presumptive appendicitis            | Survived    |

Fig. 3. (A) Abdominal x-ray: A dilated colon > 12 cm in diameter. (B) Non-contrast-enhanced abdominal CT: Colonic dilatation with no sign of thromboses or mechanical obstruction.
understood, but the prevailing hypothesis is altered regulation of colonic function by the autonomic nervous system, resulting in colonic distension in the absence of mechanical blockage. Surgical management is recommended for patients who have a cecal diameter of > 12 cm and in whom endoscopic decompensation and pharmacologic therapy have failed [19].

In conclusion, we have reported a rare case of presumptive complicating *C. paraputrificum* bacteremia in an elderly immunocompromised patient with an abdominal source of infection. We postulate that *C. paraputrificum* bacteremia caused by undiagnosed ulcerative colitis created ideal conditions for acute colonic pseudo-obstruction. Because patients with presumptive complicating *C. paraputrificum* bacteremia, even if only a single blood culture proves positive, may have defective integrity of the bowel mucosa, investigation of any abdominal source of infection should be considered.

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**Consent**

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**Ethical approval**

Not applicable.

**CRediT authorship contribution statement**

**Masahiko Kaneko:** Writing – original draft. **Chie Moriyama:** Writing – review & editing. **Yuya Masuda:** Writing – review & editing. **Hirosi Sawachika:** Writing – review & editing. **Hisaharu Shikata:** Writing – review & editing. **Shoichi Matsukage:** Writing – review & editing & Supervision.

**Conflict of interest statement**

The authors declare that they have no competing interests in relation to this study.

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**References**

[1] Boman J, Nilson B, Sunnerhagen T, Rasmussen M. True infection or contamination in patients with positive *Clostridium* blood cultures - a retrospective cohort study. Eur J Clin Microbiol Infect Dis 2022;41(7):1029–37. https://doi.org/10.1007/s10096-022-04458-9.

[2] Rasmussen M, Mohlin AW, Nilson B. From contamination to infective endocarditis - a population-based retrospective study of *Corynebacterium* isolated from blood cultures. Eur J Clin Microbiol Infect Dis 2020;39(1):113–9. https://doi.org/10.1007/s10096-019-03696-6.

[3] Finkelstein R, Fusman R, Oren I, Kassis I, Hashman N. Clinical and epidemiologic significance of coagulase-negative staphylococci bacteremia in a tertiary care university Israeli hospital. Am J Infect Control 2002;30(1):21–5. https://doi.org/10.1016/mic.2002.118406.

[4] Leaf J, Gregson DB, Ross T, Church DL, Laupland KB. Epidemiology of *Clostridium* species bacteremia in Calgary, Canada, 2000–2006. J Infect 2008;57(3):198–203. https://doi.org/10.1016/j.jinf.2008.06.018.

[5] Haddy RI, Nadkarni DD, Mann BL, Little DR, Clever RD, et al. Clostridial bacteremia in the community hospital. Scand J Infect Dis 2000;32(1):27–30. https://doi.org/10.1080/0306544000164173.

[6] Mostel Z, Hernandez A, Tatem L. *Clostridium paraputrificum* bacteremia in a patient with presumptive complicated appendicitis: a case report. IDCases 2022;27:e01361. https://doi.org/10.1177/000313481608200211.

[7] Coulie B, Camilleri M. Intestinal pseudo-obstruction. Annu Rev Med 1999;50:37–55. https://doi.org/10.1146/annurev.med.50.1.37.

[8] Vanek VW, Al-Salihi M. Acute pseudo-obstruction of the colon (Ogilvie’s syndrome). An analysis of 400 cases. Dis Colon Rectum 1986;29(3):203–10. https://doi.org/10.1097/00000665-00000016.

[9] Goldstein EJ. Anaerobic bacteremia. Clin Infect Dis 1996;23(Suppl 1):S97–101. https://doi.org/10.1093/clinids/23.supplement_1.s97.

[10] Cookrell 3rd FR, Hughes JG, Vetter EA, Mueller RA, Weaver AI, Lintrup DM, et al. Analysis of 281,797 consecutive blood cultures performed over an eight-year period: trends in microorganisms isolated and the value of anaerobic culture of blood. Clin Infect Dis 1997;24(3):403–18. https://doi.org/10.1093/clinids/24.3.403.

[11] Wiest JF, Felson B. Gas in the portal venous system. Am J Roentgenol Radium Ther Nucl Med 1961;66:920–9 (Available from). https://www.ncbi.nlm.nih.gov/pubmed/14040292.

[12] Babenko GO, Joffe N, Tischler AS, Kados E. Gas-forming clostridial mycotic aneurysm of the abdominal aorta. A case report. Angiology 1976;27(10):602–9. https://doi.org/10.1177/000331977602701007.

[13] Nerd JL, Pulvirenti JJ. *Clostridium paraputrificum* bacteremia in a patient with AIDS and Duodenal Kapost’s sarcoma. Clin Infect Dis 1996;23(5):1183–4. https://doi.org/10.1086/3351183.

[14] Shinha T, Hadi C. *Clostridium paraputrificum* bacteremia associated with colonic necrosis in a patient with AIDS. Case Rep Infect Dis 2015;2015:312919. https://doi.org/10.1155/2015/312919.

[15] Intra J, Milano A, Sarto C, Brambilla P. A rare case of *Clostridium paraputrificum* bacteremia in a 78-year-old Caucasian man diagnosed with an intestinal neoplasm. Anaerobe 2020;66:102292. https://doi.org/10.1016/j.anaerobe.2020.102292.

[16] Haider A, Alvi FX, Siddiqui A, Abbas H, Patel F. Fulminant pseudomembranous colitis leading to *Clostridium paraputrificum* bacteremia. Cureus 2021;3(3):e13763. https://doi.org/10.7759/cureus.13763.

[17] Kreuzpaimner G, Horndette D, Heyll A, Lößle B, Strohmeyer G. Increased risk of bacterial endocarditis in inflammatory bowel disease. Am J Med 1992;92(4):391–5. https://doi.org/10.1016/0002-9343(92)90269-h.

[18] Goren I, Brom A, Yanai H, Dagan A, Segal G, Israel A. Risk of bacteremia in hospitalised patients with inflammatory bowel disease: a 9-year cohort study. United European. Gastroenterol J 2020;8(2):195–203. https://doi.org/10.1177/205646191774524.

[19] Ross SW, Ommen B, Wormer BA, Walters AL, Augenstein VA, Heniford BT, et al. Acute colonic pseudo-obstruction: defining the epidemiology, treatment, and adverse outcomes of Ogilvie’s syndrome. Am Surg 2016;82(2):102–11. https://doi.org/10.1177/0003318616820021.