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【 CASE REPORT 】

Clostridium paraputrificum Bacteremia in an Older Patient with No Predisposing Medical Condition

Miho Fukui[1], Shunsuke Iwai[1], Ryunosuke Sakamoto[1], Hiroko Takahashi[1], Tsuneo Hayashi[1] and Tsuneaki Kenzaka[2]

Abstract:
We herein report a rare case of *Clostridium paraputrificum* bacteremia in an elderly (88-year-old) man without a predisposing medical condition. Although he had a history of anaerobic bacteremia approximately eight months prior to admission, no gastrointestinal disease was discovered. He was treated with intravenous ampicillin/sulbactam. This case suggests that *C. paraputrificum* bacteremia can result from only minor abnormalities in macroscopically normal mucosal barriers. To our knowledge, this is the first report of *C. paraputrificum* bacteremia in Japan.

Key words: *Clostridium paraputrificum*, bacteremia, underlying medical conditions

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Introduction

Clostridium species are anaerobic Gram-positive rod bacteria that can cause a broad range of invasive infections in humans, including myonecrosis, intra-abdominal infections, and bacteremia. Infection of *Clostridium* species occurs at a rate of 1.8 per 100,000 persons per year (1). Clostridial bacteremia is frequently associated with underlying medical conditions, such as colonic malignancy, acquired immunodeficiency syndrome (AIDS), hemodialysis, and inflammatory bowel disease (1-3).

Among *Clostridium* species, *C. perfringens* (42%), *C. septicum* (14%), *C. ramosum* (9%), *C. clostridioforme* (6%), and *C. difficile* (5%) are the most common cause of bacteremia. In contrast, *C. paraputrificum* has been identified in only 1% of cases (1). *C. paraputrificum* is an unfamiliar, infrequent isolate (2), and therefore, its clinical significance has not been well described.

We herein report a case of bacteremia caused by *C. paraputrificum* in an older patient without any underlying predisposing medical conditions and discuss the clinical importance of *C. paraputrificum*-related bacteremia.

Case Report

An 88-year-old man was admitted to our hospital with a fever and rigors that had begun the day before presentation. He had a 10-year history of hypertension, and approximately 8 months prior to the current admission, he had experienced an episode of pyogenic spondylitis caused by *Bacteroides fragilis*, for which he had been treated with intravenous ampicillin/sulbactam (3 g every 6 h) for 7 weeks, followed by oral amoxicillin-clavulanate potassium (500 mg every 8 h) for 8 subsequent weeks.

Upon admission, the following observations were recorded: blood pressure, 125/69 mmHg; pulse rate, 88 beats/min; respiratory rate, 20 breaths/min; and body temperature, 39.4℃. His physical examination findings were unremarkable. No notable abnormal findings were observed on a physical examination of the chest. The patient's laboratory findings were as follows: white blood cell count, 11,200×10^9/L (neutrophils, 89%); hemoglobin, 11.1 g/dL; platelets, 121×10^9/; C-reactive protein, 5.61 mg/dL, aspartate aminotransferase, 26 U/L; alanine aminotransferase, 15 U/L; lactic dehydrogenase, 257 U/L; blood urea nitrogen, 19.3 mg/dL; creatinine, 0.68 mg/dL; Na, 140 mEq/L; K 3.8 mEq/L; Cl, 107 mEq/L; blood glucose, 100 mg/dL; and hemoglo-

[1]Yoka Hospital, Japan and [2]Division of Community Medicine and Career Development, Kobe University Graduate School of Medicine, Japan
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Correspondence to Dr. Tsuneaki Kenzaka, smile.kenzaka@jichi.ac.jp

Table 1. Laboratory Data on Admission.

Parameter	Recorded value	Standard value
White blood cell count	11,200/μL	4,500-7,500/μL
Neutrophil frequency	89%	
Hemoglobin	11.1 g/dL	11.3-15.2 g/dL
Hematocrit	33.2%	36-45%
Platelet count	12.1×10^4/μL	$13\text{-}35\times10^4$/μL
Activated partial thromboplastin time	28.3 s	26.9-38.1 s
Fibrin degradation products	10.0 μg/mL	2.0-8.0 μg/mL
C-reactive protein	5.61 mg/dL	≤0.14 mg/dL
Procalcitonin	2.41 ng/mL	≤0.05 ng/mL
Total protein	7.5 g/dL	6.9-8.4 g/dL
Albumin	3.5 g/dL	3.9-5.1 g/dL
Total bilirubin	0.7 mg/dL	0.2-1.2 mg/dL
Aspartate aminotransferase	26 U/L	11-30 U/L
Alanine aminotransferase	15 U/L	4-30 U/L
Lactate dehydrogenase	257 U/L	109-216 U/L
Creatine phosphokinase	103 U/L	40-150 U/L
Blood urea nitrogen	19.3 mg/dL	8-20 mg/dL
Creatinine	0.68 mg/dL	0.63-1.03 mg/dL
Sodium	140 mEq/L	136-148 mEq/L
Potassium	3.8 mEq/L	3.6-5.0 mEq/L
Glucose	100 mg/dL	70-109 mg/dL
Hemoglobin A1c	5.4%	<6.5%

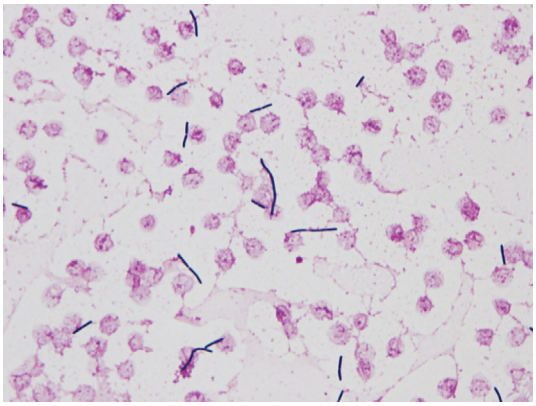

Figure. Gram stain of a blood culture showing Gram-positive rods with spores.

bin A1c (NGSP), 5.4%. Detailed laboratory findings are shown in Table 1.

Chest, abdominal, and pelvic computed tomography (CT), transthoracic echocardiography, abdominal ultrasound, and lumbar magnetic resonance imaging (MRI) yielded no abnormal findings and did not suggest a specific infection. Given the lack of signs of infection during the physical examination and lack of a specific diagnosis indicated by the available laboratory and imaging test results, the patient was placed under close inpatient observation without antimicrobial therapy.

Both sets of anaerobic cultures of blood samples obtained at admission yielded positive results on the second day of hospitalization. Gram staining revealed Gram-positive rods (Figure) that were identified on the third day of hospitalization as *C. paraputrificum* by Rapid ID 32A testing (bioMerieux SA, Marcy l'Etoile, France) in our laboratory. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS; Bruker Daltonics, Yokohama, Japan) was used to definitively identify the isolate as *C. paraputrificum*. Based on the results of antimicrobial susceptibility testing (Table 2), the patient was treated with intravenous ampicillin/sulbactam (3 g every 6 h). Antibiotic therapy alleviated the fever, and subsequent blood cultures conducted after two weeks of treatment yielded negative results.

Because the patient had a history of anaerobic bacteremia about eight months prior to admission, he was investigated for any predisposing medical conditions. Contrast-enhanced abdominal CT, gastroscopy, colonoscopy, small intestine capsule endoscopy, and transesophageal echocardiogram yielded no abnormal findings (e.g., colonic malignancy or inflammatory bowel disease). Laboratory findings excluded diabetes mellitus, HIV, and HTLV-1 infection. More than six months after discharge, the patient had not experienced a relapse.

Discussion

Only a few sporadic case reports of *C. paraputrificum* bacteremia have been reported in the literature. To our knowledge, this is the first report of *C. paraputrificum* bacteremia in Japan. Patients who develop *C. paraputrificum* bacteremia very often have underlying conditions that predispose them to infection, such as noncyclic neutropenia (4), alcohol abuse (5), diabetes mellitus (6), sickle cell ane-

Table 2. E-test MICs for *Clostridium Paraputrificum* Isolated from Blood Cultures of This Patient.

Antibiotic	MIC (μg/mL) for *Clostridium paraputrificum*
Penicillin G	0.25
Ampicillin	0.125
Ampicillin/Sulbactam	<4
Ceftazidime	8
Cefepime	2
Cefmetazole	<1
Flomoxef	<1
Meropenem	<0.25
Imipenem	0.5
Minocycline	<0.25
Clindamycin	0.5
Chloromycetin	1
Piperacillin/Tazobactam	<16
Metronidazole	2

MICs: minimum inhibitory concentrations

mia (7), malignancy (8, 9), and AIDS (2, 3). Clostridial bacteremia, more generally, is also frequently associated with underlying medical conditions such as colonic malignancy, AIDS, hemodialysis, and inflammatory bowel disease (1-3). The rarity of this case involves the lack of a predisposing medical condition for this patient, except for advanced age.

C. paraputrificum comprises part of the human microflora that resides on mucous membranes (10), and mucosal barrier breakdown can result in clostridial bacteremia (1). Although the patient had no gastrointestinal disease, he had suffered from anaerobic bacteremia twice within one year. In this context, the effects of aging on different organ systems, such as reduced homeostatic responses to injury, are pertinent (11). Increased colonic permeability consequent to the age-associated remodeling of intestinal epithelial tight junction proteins might be an important component of gastrointestinal dysfunction (12). The present case report showed that advanced age can be the only risk factor for *C. paraputrificum* infection.

Conventional *Clostridium* spp. classification methods rely on multiple microbiological and biochemical characteristics, including Gram stain morphology and carbohydrate fermentation profiles. Recently developed gene-sequencing techniques (e.g., 16S rRNA gene sequencing) have allowed for the identification of *Clostridium* genus members at the species level (1). Leal et al. reported the availability of susceptibility testing results for 135 of 138 cases of *Clostridium* spp. bacteremia; in addition, the overall clindamycin resistance rate was high, whereas most and all but one isolate remained susceptible to penicillin and metronidazole, respectively. Only two isolates of *C. paraputrificum* were identified in the 138 cases of *Clostridium* species bacteremia, and both were susceptible to penicillin and metronidazole but resistant to clindamycin (1). In another report, some *C. paraputrificum* isolates exhibited resistance to erythromycin, tetracycline, and penicillin (13). These data suggest that, in patients with suspected clostridial bacteremia, empiric treatment regimens should include metronidazole in order to minimize the risk of treatment failure; furthermore, clindamycin should not be used as an empiric monotherapy. Finally, the prognosis of *C. paraputrificum* bacteremia remains unclear due to the small number of cases.

In conclusion, we reported a rare case of *C. paraputrificum* bacteremia in an older patient with no predisposing medical conditions. Further studies are needed to elucidate the disease spectrum, pathogenesis, and risk factors of *C. paraputrificum*-related invasive infections, including bacteremia.

The authors state that they have no Conflict of Interest (COI).

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