

Clostridium paraputrificum Bacteremia in a Patient with Human Immunodeficiency Virus Infection: A Case Report and Literature Review

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Abstract: *Clostridium paraputrificum* (*C. paraputrificum*) is clinically important due to its association with underlying medical conditions. Infection with *C. paraputrificum* may worsen HIV prognosis, leading to acquired immunodeficiency syndrome. However, it is not frequently isolated and its susceptibility to antibiotics has not been well studied. Our report examines the case of a patient with human immunodeficiency virus (HIV) infection, who was diagnosed with *Clostridium paraputrificum* bacteremia. A 59-year-old male was admitted to hospital with a medical history of human immunodeficiency virus (HIV), hepatitis C virus (HCV), and neck pain. Following episodes of high fever, the patient received a full work up to test for sepsis. Blood culture revealed bacterial growth, and MALDI-TOF mass spectrometry confirmed the diagnosis of *Clostridium paraputrificum* bacteremia. The patient received treatment with meropenem and vancomycin antibiotics, which cleared the infection after 48 hours; however, inflammatory markers remained high. To date, a limited number of reported cases of *C. paraputrificum* exist; thus, this case report contributes valuable information to the literature to improve our understanding of its action and resistance profiles and aid future bacteremia management.

Keywords: clostridia, gram-positive bacteria, anaerobe, pathogen, hepatitis C, hepatitis B

Background

Clostridium species (*spp.*) are obligatory, anaerobic, gram-positive bacteria responsible for a wide range of invasive infections in humans, including bacteremia.¹ The genus is large and diverse, composed of >164 species, such as *Clostridium perfringens*, *Clostridium botulinum*, *Clostridium tetani*, and *Clostridium difficile*, which can cause clinical syndromes in humans. *Clostridium* can be difficult to treat due to its capacity to produce antibiotic-resistant endospores.² Blood infections with this bacteria have been frequently reported in patients with underlying medical diseases, such as colon cancer, acquired immunodeficiency syndrome (AIDS), hemodialysis, inflammatory enteropathy, septic arthritis, and sickle cell disease.^{3–6} The mortality rate of clinically relevant clostridial bacteremia ranges from 29% to 35%, and the risk factors for mortality are liver disease and older age.⁷

Despite the numerous complications associated with *Clostridium spp.* infections, *C. paraputrificum* is not well described. The aim of this article was to present a case report of a patient with HIV infected with *C. paraputrificum* bacteremia and provide a brief overview of relevant literature. Our findings will further our understanding of the impacts of anaerobic pathogens on human health and help inform the development of more effective treatment management of *Clostridium spp.*; particularly, patients with underlying medical conditions.

Case

Initial Presentation & Past History

The patient was a 59-year-old male from Dammam, Saudi Arabia with a history of HIV for 15 years, who was non-compliant to HIV treatment for five years. The patient last visited the HIV clinic in December 2020 and blood tests showed a viral load of 9340 copies per mL. Furthermore, this person had a history of HBV (immune to hepatitis B due to natural immunity), chronic non-treated HCV, diabetes mellitus type II for three years, hypertension (HTN), smoking and active drug abuse for heroin and alcohol, chronic kidney disease stage III, and a previously treated cervical spine abscess with internal fixation surgery. The patient was prescribed tenofovir and emtricitabine; no antiretroviral resistance screening test was performed, and we could not obtain lymphocyte subset results. Prior to emergency department (ER) admittance, the patient had three months history of progressive neck pain, and sudden weakness in the upper and lower limbs the day before presenting to the ER; however, they experienced no numbness, loss of sphincter control, fever, night sweats, or weight loss. The results of the patient's physical examination, blood pressure and other vital signs were normal, and neuromuscular examination results were unremarkable. However, laboratory blood test results revealed a high white blood cell (WBC) count, decreased hemoglobin level (Hgb), and high platelet count (Plt). The patient's serum creatinine level was 2.54 mg/dL and blood urea nitrogen was 45 mg/dL. Notably, there were elevated levels of inflammatory markers, such as procalcitonin and C-reactive protein, and erythrocyte sedimentation rate. A brain computed tomography (CT) revealed chronic small vessel disease, with a number of lytic lesions on the patient's first cervical vertebra.

Present History

Seven days post admission, the patient experienced fever (38.8°C), in addition to persistent and uncontrolled high blood pressure; however, a physical examination showed no evidence of limited movement or mobility. Prior to receiving blood culture results for sepsis testing, vancomycin and meropenem antibiotics were empirically prescribed. The patient received a complete work-up, and was tested for complete blood count (CBC), C-reactive protein (CRP), procalcitonin, and blood and urine cultures.

Laboratory Investigation

The septic workup results showed a high WBC count and high levels of inflammatory markers, including CRP and procalcitonin (Table 1).

Microbiology Investigation

We incubated one set of blood culture vials in a BacT/Alert Virtuo system (BioMérieux, France) for 5 days, according to the internal policies and procedures of the microbiology laboratory at King Fahd Hospital of the University. After 72 hours of incubation, one of the two blood culture vials flagged positive, and direct Gram staining showed Gram-positive

Table 1 Laboratory Results for the Patient After Developing Fever

Test	Result	Normal Range
CRP	7.92 mg/dL	0.1–0.5 mg/dL
Procalcitonin	3.16 ng/mL	≤0.1 ng/mL
WBC	18.3 k/ μ L	4–11 k/ μ L
Hgb	11.9 g/dL	13–18 g/dL
Plt	476 k/ μ L	140–450 k/ μ L

Abbreviations: CRP, C-reactive protein; WBC, white blood cell count; Hgb, hemoglobin level; Plt, platelet count.

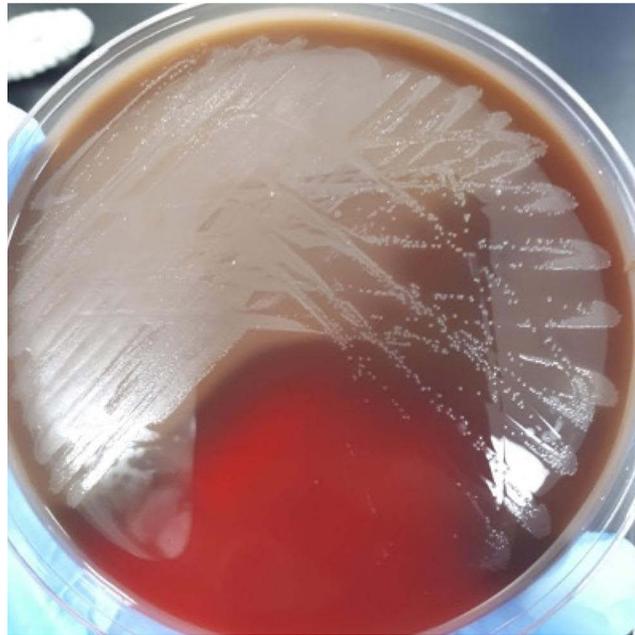


Figure 1 Nonhemolytic, translucent pinpoint colonies grew on anaerobic Brucella Agar.

Abbreviations: HIV, human immunodeficiency virus; *C. paraputrificum*, *Clostridium paraputrificum*, *Clostridium* spp., *Clostridium* species; HCV, Hepatitis C virus; MALDI-TOF, Matrix-assisted laser desorption/ionization-time of flight; HBV, hepatitis B virus; HTN, hypertension; ER, emergency department; WBC, white blood cell count; Hgb, hemoglobin level; Plt, platelet count; CT, computed tomography; CBC, complete blood count; CRP, C-reactive protein; CLSI, Clinical Laboratory Standards Institute.

bacilli. Subsequently, the blood culture vials were sub-cultured on sheep blood, MacConkey, chocolate, and anaerobic Brucella agars.

After 48 hours incubation at 37°C, there was no growth present on sheep blood, MacConkey's, and chocolate agars. However, there was bacterial growth on anaerobic Brucella agar (Figure 1). We used Matrix-assisted laser desorption/ionization-time of flight-mass spectrometry (MALDI-TOF-MS) (VITEK MS; bioMérieux) and the Knowledge Base database (version 3.0) with a confidence value of 99.9% to identify *Clostridium paraputrificum*. Antibiotics-susceptibility tests for anaerobic organisms were not available in our routine diagnostic laboratory; therefore, we depended on 2022 Clinical and Laboratory Standards Institute (CLSI) cumulative data, which showed that *Clostridium* was sensitive to imipenem, meropenem, and metronidazole antibiotics. Urine analysis results were normal, and the urine culture showed no growth.

Treatment Plan and Outcome

Forty-eight hours following treatment with vancomycin and meropenem antibiotics, the patient clinically improved, the fever subsided, and blood cultures showed no growth. All subsequent cultures were negative, but inflammatory markers remained high. On day 12 of admission, the patient experienced sudden cardiac arrest due to reflex arrhythmia caused by atlantoaxial subluxation and passed away.

Discussion

Clostridium spp. are widespread in nature owing to their ability to form resistant endospores.⁸ Infection with *Clostridium* species occurs at an annual rate of 1.8/100,000 persons,¹ and a mortality rate ranging from 29% to 35% from clinically relevant clostridial bacteremia. Risk factors for mortality include liver disease and older age,⁷ *Clostridium paraputrificum* is a rare isolate, comprising only ~1% of all *Clostridium* cases.¹

Clostridia are opportunistic bacteria, generally encountered in wounds, exudates, blood, and other normally sterile body fluids. Infection with *Clostridium* spp. may not develop into serious or progressive disease, unless conditions in the host are favorable. Owing to the inherent difficulty of performing susceptibility assays for anaerobes, new methods using phenotypic and molecular techniques are in development.²¹ Drugs lacking antimicrobial activity against various

Table 2 Summary of the Reported Cases of *Clostridium paraputrificum* Infections

Ref. #	Age (Years)	Sex	Chronic Disease(s)	Site	Treatment	Outcome
[3]	65	M	HIV, Hepatitis B, Hepatitis C, end stage renal disease, diabetes, atrial fibrillation	Blood	Vancomycin, tazocin, caspofungin, metronidazole	Cured
[4]	88	M	Hypertension	Blood	Ampicillin/sulbactam	Cured
[9]	47	F	Sickle cell disease, thalassemia	Synovial fluid	Vancomycin switched to flagyl	Cured
[5]	88	M	Hypertension, benign prostatic hyperplasia	Blood	Vancomycin, tazocin switched to Ampicillin/sulbactam then discharged on flagyl	Cured
[2]	52	F	Acute mesenteric ischemia, bowel infarction	Blood	No treatment	Died
[10]	88	M	Cancer colon	Blood and wound culture	Antibiotic and gas gangrene antitoxins	Died
[11]	10	F	Sickle cell disease	Blood	Penicillin	Cured
[12]	65	M	Aspiration pneumonia	Blood	Penicillin	Cured
[13]	38	F	Necrotizing enterocolitis	Colon and peritoneum	Cefotaxacin, ampicillin	Cured
[14]	32	M	HIV	Blood	Metronidazole	Died
[15]	70	F	Cancer breast, abdominal wall cellulitis	Abdominal wall swab	Meropenem, metronidazole	Cured
[16]	8	M	Protein energy malnutrition	Abdominal wall ulcer	Clindamycin, metronidazole	Cured
[17]	23	F	Liver abscess	Blood	Metronidazole	Cured
[18]	86	F	Septic arthritis	Synovial fluid	Ertapenem	Cured
[19]	78	M	Intestinal carcinoma	Blood	Metronidazole	Cured
[20]	74	M	HIV, diabetes, sickle cell anemia, malignancy	Blood	Vancomycin, meropenem, metronidazole	Died

Abbreviations: Ref. #, case reference number; Sex: M/F, Male/Female.

Clostridia include trimethoprim-sulfamethoxazole, ampicillin, and clindamycin. Notably, clostridia are not resistant to ampicillin-sulbactam, piperacillin-tazobactam, imipenem, metronidazole, and vancomycin. According to the reported cases in the literature, the most used therapy is a combination beta-lactam/metronidazole (Table 2).

Conclusion

Clostridium spp. are one of the most commonly isolated anaerobic pathogens. However, *C. paraputrificum* is rarely isolated. We presented a case study of a patient with multiple comorbidities and associated predisposing factors, such as hepatitis B, hepatitis C, and HIV with *C. paraputrificum* bacteremia. Further studies are needed to determine the associated risk factors and pathogenesis of *C. paraputrificum*.

Ethics Approval and Consent to Participate

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the consent document is available for review upon request from the Editor-in-Chief of this journal.

Consent for Publication

Consent for publication was not required for this case report in accordance with the legislation and the institutional requirement at Imam Abdulrahman Bin Faisal University.

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Disclosure

The authors declare that they have no competing interests in this work.

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