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Case Reports

# *Clostridium Cadaveris* Bacteremia in an Immunocompromised Host

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## Abstract

Clostridial bacteremia is an exceedingly rare clinical entity that can cause significant morbidity and mortality. Immunocompromised patients with insult to the gastrointestinal mucosa are especially prone to the development of clostridial sepsis based on limited existing literature. Here we report a case of a 65-year-old male nursing home resident with incompletely treated colorectal adenocarcinoma who was admitted for sepsis. He was found to have polymicrobial bacteremia with *Escherichia coli* and *Clostridium cadaveris*. He was successfully treated with intravenous piperacillin/tazobactam followed by an oral regimen of amoxicillin/clavulanic acid.

## BACKGROUND

*Clostridium cadaveris* is an uncommon bacterial pathogen that was first described when isolated from decomposing human bodies. It is an anaerobic gram-positive rod and normal constituent of the human gastrointestinal tract.[1] Patients with impaired gut mucosa or immunocompromising conditions are especially at risk for clostridial sepsis.[2] Although exceedingly rare, providers should understand who is at risk and therefore may benefit from anaerobic antimicrobial coverage.

## CASE PRESENTATION

A 65-year-old male nursing home resident with history of prior housing instability, major depressive disorder, type 2 diabetes mellitus, and incompletely treated, unresected colorectal adenocarcinoma presented to the Emergency Department (ED) for evaluation of acute onset nausea and vomiting. His emesis was non-bloody, non-bilious, and began one day prior to presentation in the absence of any sick contact or identifiable trigger. He reported associated malaise and tactile fever. He denied any abdominal pain, diarrhea, constipation, dysuria, or changes in urination.

On arrival in the Emergency Department, his vital signs were remarkable for a temperature of 99.3°F, heart rate of 108 beats/minute, and blood pressure of 82/53 mm Hg. His blood pressure improved with fluid resuscitation. On physical exam, he appeared frail and cachectic. Cardiovascular exam revealed sinus tachycardia with a regular rhythm. His abdomen was scaphoid, soft, and nontender to palpation. He had no suprapubic or costovertebral angle tenderness. A stage IV decubitus ulcer measuring 12 x 14 x 4 cm was noted along his sacrum with serosanguinous drainage present. There was no surrounding erythema, purulence, or malodor.

Laboratory workup was notable for a white blood cell (WBC) count of 32 x $10^3$/μL with 93.8% neutrophils (range: 4.5-11.0 x $10^3$/μL), a hemoglobin of 8.7 g/dL (range: 13.3-17.7 g/dL), and a serum creatinine of 1.24 mg/dL (range 0.52-1.28 mg/dL). His WBC was previously normal, and his serum creatinine was 1.04 mg/dL when measured at a clinic visit several weeks prior to presentation. Urinalysis was significant for moderate leukocyte esterase, nitrites, 43 WBC/high power field (HPF), and 7 red blood cells/HPF. Blood and urine cultures were collected. Computed tomography (CT) of the abdomen and pelvis showed a stable appearance to his known large, necrotic rectosigmoid mass. The mass was noted to abut the bladder, and gas was observed within the bladder raising suspicion for colovesicular fistula formation. A large decubitus ulcer and innumerable retroperitoneal lymph nodes were also noted and stable in size from his CT 2 months prior.

Given his fever and leukocytosis, he was started on intravenous vancomycin and piperacillin/tazobactam. It was initially presumed that the patient's sepsis stemmed from ascending pyelonephritis or an infected sacral decubitus ulcer. By hospital day #1, the patient's blood and urine cultures were growing a strain of extended-spectrum beta-lactamase (ESBL) *Escherichia coli (E. coli)*. His urine culture grew 15,000 colony forming units of this same strain of *E. coli*. Vancomycin was discontinued; his WBC count normalized and symptoms gradually improved. Discharge back to his skilled nursing facility was planned on a course of oral amoxicillin/clavulanic acid until the microbiology laboratory called to report an additional organism growing in his blood cultures from

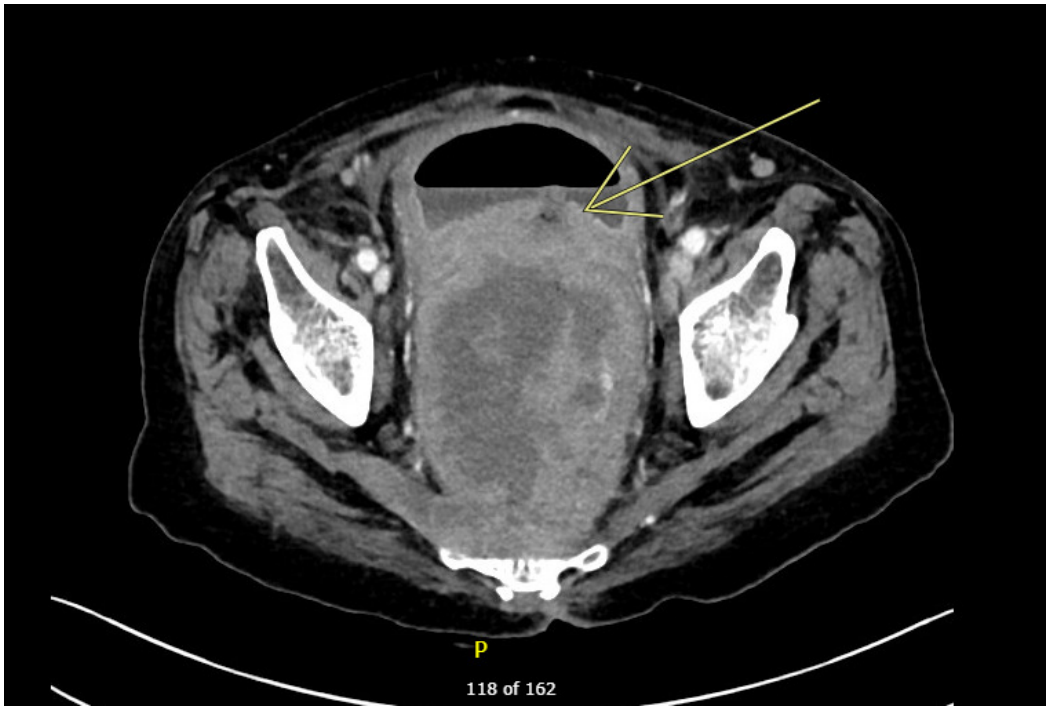


**Figure 1.** CT abdomen/pelvis with intravenous contrast demonstrating a large necrotic colonic mass arising from the rectosigmoid junction. The anterior margin of the mass abuts the posterior aspect of the bladder, prostate, and presacral region. Gas is seen within the mass consistent with necrosis. Additionally, there is gas within the bladder that raises concern for fistula formation (yellow arrow).

hospital admission – *Clostridium cadaveris (C. cadaveris)*.

Infectious Diseases consultation was requested to assist with source identification and tailoring of his antibiotic regimen. Infectious Diseases deemed the *C. cadaveris* to be pathogenic and hypothesized that his unresected, necrotic rectosigmoid mass was the source of his polymicrobial bacteremia via spontaneous bacterial translocation. Although the same strain of *E. coli* had been isolated in his urine, it was felt this more likely represented colonization due to the low number of colony-forming units, the patient's lack of genitourinary symptoms, and radiographic suggestion of a colovesicular fistula (**Figure 1**).

Repeat blood cultures were obtained on hospital day #2 and later demonstrated clearance of both the *E. coli* and *C. cadaveris*. The patient remained on amoxicillin/clavulanic due to its anaerobic coverage and his interval clinical improvement on this agent; the course was extended to a total of 14 days. The option of a palliative diverting colostomy was discussed with the patient due to its potential to mitigate his risk of future infection and rehospitalization. The patient declined surgical intervention in favor of a less invasive, more palliative-oriented approach. He was discharged back to his skilled nursing facility without recrudescence of his infectious symptoms or rehospitalization for several months. He was eventually re-hospitalized for hydronephrosis related to extrinsic ureteral compression by his rectosigmoid mass and later sepsis secondary to ascending pyelonephritis. Following these rehospitalizations, he elected to discharge back to his skilled nursing facility on hospice.

## DISCUSSION

*Clostridium cadaveris* is an uncommon bacterial pathogen that was first described in 1899 when it was isolated from decomposing human bodies.[1] Like other clostridial species, *C. cadaveris* is an anaerobic gram-positive rod and normal constituent of the human gastrointestinal tract. Limited case reports have been published describing *C. cadaveris* as the causative organism in spontaneous bacterial peritonitis, chronic osteomyelitis, and bacteremia stemming from a gastrointestinal source.[3-5] Only eight case reports have been published to date describing *C. cadaveris* bacteremia with several of these cases stemming from a gastrointestinal source.[6] Bacteremia with any clostridial species is exceedingly rare, accounting for 0.5-2% of all positive blood cultures.[7] Yet, the mortality rate for patients with medically managed clostridial bacteremia approaches 58%.[7] Given its potential to cause significant morbidity and mortality, greater awareness of this rare but virulent pathogen is needed.

Retrospective studies of patients with bacteremia involving any clostridial species identify the gastrointestinal tract as a common source. Less common sources of clostridial bacteremia include the hepatobiliary tree, lower urinary tract, and skin/soft tissues.[2,7] Necrotizing soft tissue infections such as gas gangrene are a noteworthy potential source for clostridial bacteremia, often with *C. perfringens* as the culprit pathogen.[7] In some cases, no convincing source can be identified even after obtaining cross-sectional imaging of the abdomen.[8] Translocation

of clostridial species into the bloodstream is thought to occur spontaneously and often transiently in immunocompromised hosts. Diabetes mellitus and underlying gastrointestinal or hematologic malignancy are frequently identified risk factors among patients with clostridial sepsis.[2] Based on a recent retrospective cohort study, bacteremia from clostridial species carried a very high relative risk (RR) for colorectal carcinoma, with *C. cadaveris* in particular having a RR of 13.7.[9]

Case reports by Gucalp et al. suggest gut barrier disruption and immunocompromised status are key risk factors for *C. cadaveris* infection.[10] One case described a 61-year-old with history of metastatic renal cell carcinoma involving the colon who underwent tumor embolization and was found to have a pericolonic abscess with accompanying *C. cadaveris* bacteremia post-procedurally. Another patient reported by Gucalp et al. described a 66-year-old with history of autoimmune hemolytic anemia on chronic prednisone (60 mg/day) and intravenous immune globulin who underwent polypectomy for colonic polyps and later developed *C. cadaveris* bacteremia. Both patients received antibiotics with anaerobic coverage upon identification of the *C. cadaveris* (imipenem and metronidazole, respectively), yet both experienced clinical deterioration and ultimately died.

These case reports by Gucalp et al. suggest that disruption of the gastrointestinal mucosa plays a role in the pathogenesis of *C. cadaveris* bacteremia. The exact mechanism may vary. In addition to tumor invasion and mechanical disruption via a procedure, another possible mechanism involves endotoxin lipopolysaccharides (LPS), which are produced by gram-negative organisms. These lipopolysaccharides are known to activate Toll-like receptors along the intestinal epithelium, triggering an inflammatory cascade that ultimately may impair the integrity of the intestinal barrier.[11] It is possible that in our patient's case, the LPS-producing *E. coli* created a portal of entry for the non-toxin producing *C. cadaveris* to then cross the disrupted gastrointestinal mucosa.

Due to its rarity, no guidelines exist to inform the optimal management of clostridial bacteremia, much less infections caused by *C. cadaveris*. Of the case reports that disclosed antimicrobial susceptibilities to *C. cadaveris*, all strains were susceptible to metronidazole.[5,10,12] Clindamycin resistance is well documented for clostridial species such as *C. perfringens* but not for *C. cadaveris*.[13] Similarly, the resistance profile of *C. cadaveris* against beta-lactams/beta-lactamase inhibitors is not well quantified. Few case reports document strains of *C. cadaveris* that were susceptible to such as ticarcillin/clavulanic acid and amoxicillin/clavulanate.[10,12] More recent cases of *C. cadaveris* infection have been treated with metronidazole or carbapenems such as meropenem or imipenem with cilastatin.[4-6] Our patient received intravenous piperacillin/tazobactam for less than 48 hours prior to being transitioned to a course of oral amoxicillin/clavulanic acid. Although sensitivities for his strain of *C. cadaveris* could not be obtained, his clinical improvement suggests his strain was susceptible to amoxicillin/clavulanic acid.

Although exceedingly rare, the significant mortality associated with clostridial bacteremia makes it a noteworthy clinical entity. It is challenging to discern whether this high mortality rate is attributable to the virulence of clostridial species themselves, the underlying immunosuppressing/malignant condition of the host, or some combination of the two. Anaerobic organisms are often more challenging to isolate on culture and Infectious Diseases Society of America (IDSA) guidelines do not routinely recommend obtaining anaerobic cultures when a community-acquired intra-abdominal infection is suspected.[14] The emergence of matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) technology may facilitate earlier detection of anaerobic organisms where it is available.[5,6] Our case highlights the importance of selecting empiric antimicrobials that provide anaerobic coverage when a gastrointestinal infection is suspected, especially in a patient with risk factors for nosocomial infection or immunosuppression. Our case also highlights the importance of rechecking for new culture growth prior to making decisions regarding antibiotic de-escalation. If antibiotic de-escalation had been guided solely by the initial growth of *E. coli* in our patient's blood and urine cultures, a fluoroquinolone could have been selected. This would not have provided adequate coverage for the *C. cadaveris* that was later isolated, and could have resulted in recrudescence of clinical symptoms, re-hospitalization, or even death.

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**Author Contributions**

All authors have reviewed the final manuscript prior to submission. All the authors have contributed significantly to the manuscript, per the International Committee of Medical Journal Editors criteria of authorship.

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accu-

racy or integrity of any part of the work are appropriately investigated and resolved.

**Disclosures/Conflicts of Interest**

The authors have no conflicts of interest to disclose.

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## REFERENCES

1. Klein E. Ein beitrag zur bakteriologie der leichenverwesung. Zentralblat fur Bakteriologie, Parasitenkunde. *Infektionskrankheiten und Hygiene*. 1899;1:278-284.

2. Yamamoto Y, Itoh N, Sugiyama T, Kurai H. Clinical features of Clostridium bacteremia in cancer patients: A case series review. *Journal of Infection and Chemotherapy*. 2020;26(1):92-94. doi:10.1016/j.jiac.2019.07.019

3. Herman R, Goldman IS, Bronzo R, McKinley MJ. Clostridium cadaveris: an unusual cause of spontaneous bacterial peritonitis. *Am J Gastroenterol*. 1992;87(1):140-142.

4. Corrigan RA, Lomas-Cabeza J, Stubbs D, McNally M. Clostridium cadaveris Osteomyelitis: an Unusual Pathogen which Highlights the Importance of Deep Tissue Sampling in Chronic Osteomyelitis. *J Bone Joint Infect*. 2020;5(2):96-100. doi:10.7150/jbji.43801

5. Li X, Wu X, Xu Y, Liu Y. First Report of Bacteremia Caused by Clostridium cadaveris in China. *Infect Drug Resist*. 2021;14:5411-5415. doi:10.2147/idr.s344062

6. Abarca J, Awada B, Itkin B, Milupi M. Poly-microbial *Clostridium cadaveris* bacteremia in an immune-compromised patient. *Oxf Med Case Reports*. 2023;2023(1):omac146. doi:10.1093/omcr/omac146

7. Rechner PM, Agger WA, Mruz K, Cogbill TH. Clinical Features of Clostridial Bacteremia: A Review from a Rural Area. *Clin Infect Dis*. 2001;33(3):349-353. doi:10.1086/321883

8. Hernandez Burgos PM, Nanjappa S, Snyder M, Bitetzakis C, Greene JN. Evaluation of Clostridium Bacteremia in the Cancer Population: A Case Series. *Infect Dis Clin Pract*. 2018;26(6):358-362. doi:10.1097/ipc.0000000000000655

9. Laupland KB, Edwards F, Furuya-Kanamori L, Paterson DL, Harris PNA. Bloodstream infection and colorectal cancer risk in Queensland Australia, 2000-2019. *The American Journal of Medicine*. 2023;136(9):896-901. doi:10.1016/j.amjmed.2023.05.003

10. Gucalp R, Motyl M, Carlisle P, Dutcher J, Fuks J, Wiernik PH. Clostridium cadaveris bacteremia in the immunocompromised host. *Med Pediatr Oncol*. 1993;21(1):70-72. doi:10.1002/mpo.2950210114

11. Stephens M, von der Weid PY. Lipopolysaccharides modulate intestinal epithelial permeability and inflammation in a species-specific manner. *Gut Microbes*. 2020;11(3):421-432. doi:10.1080/19490976.2019.1629235

12. Stolk-Engelaar V, Verwiel J, Bongaerts G, Linsen V, Lacquet L, Cox A. Pleural empyema due to *Clostridium difficile* and *Clostridium cadaveris*. *Clin Infect Dis*. 1997;25(1):160. doi:10.1086/516893

13. Leal 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. doi:10.1016/j.jinf.2008.06.018

14. Solomkin JS, Mazuski JE, Bradley JS, et al. Diagnosis and Management of Complicated Intra-abdominal Infection in Adults and Children: Guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2010;50(2):133-164. doi:10.1086/649554