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Clostridium innocuum Bacteremia in an AIDS Patient: Case Report and Review of the Literature

Nancy Crum-Cianflone, MD, MPH[1,2]

[1] TriService AIDS Clinical Consortium, Infectious Disease Clinical Research Program, Uniformed Services University of the Health Sciences, Bethesda, MD

[2] Infectious Disease Clinic, Naval Medical Center San Diego, San Diego, CA

Abstract

Clostridium innocuum is an unusual cause of infections in humans. This report describes the first published case of *C. innocuum* bacteremia in an AIDS patient and provides a review of the literature. The case suggests that recent *C. difficile* infection may be a risk factor for the subsequent development of C. *innocuum* bacteremia among immunosuppressed persons. Due to their intrinsic resistance to several common antibiotics, including vancomycin, *C. innocuum* infections are important to recognize.

Background

Clostridia species are gram-positive anaerobes that are normal flora of the oropharynx and gastrointestinal tract. Most clostridial infections are due to *C. perfringens* or *C. septicum*, whereas *C. innocuum* is a more unusual cause of infections in humans [1]. Prior case reports have described *C. innocuum* as a cause of abdominal sepsis and, rarely, bacteremia [2–4]. This report describes the first reported case of *C. innocuum* bacteremia in an AIDS patient.

Case Report

A 38-year-old African American male with AIDS was admitted for low grade fevers. He had previously been hospitalized for *Clostridium difficile* colitis and a necrotizing soft tissue infection of the right leg, which was culture-positive for methicillin-resistant *Staphylococcus aureus* (MRSA). Treatment consisted of daptomycin, imipenem, and oral vancomycin. The patient had a 12-year history of HIV infection; he had a CD4 count of 76 cells/mm^3 and a HIV viral load of >100,000 copies/ml. He had self-discontinued his HIV regimen. The patient had also been diagnosed with abdominal adenopathy and diarrhea due to *Mycobacterium avium* infection, but refused the multi-drug therapy.

On the day of admission, examination revealed a temperature of 100.8 °F, pulse of 93, and blood pressure of 104/48. His examination was noteworthy for a healing right leg wound. Abdominal examination was mildly distended, but there were no masses or hepatosplenomegaly. Laboratory investigation showed a white blood count of 6,000/ mm^3 with

Correspondence: Dr. Nancy Crum-Cianflone, c/o Clinical Investigation Department (KCA), Naval Medical Center San Diego, 34800 Bob Wilson Drive, Ste. 5, San Diego, CA 92134-1005. Phone: 619/532-8134/40; FAX: 619/532-8137; E-mail: nancy.crum@med.navy.mil.

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90% neutrophils, hemoglobin of 7.1 mg/dl, and platelet count of 64,000/mm^3. Chemistries were unremarkable except for a mildly elevated creatinine (1.5 mg/dl); liver function tests were normal. Stool studies and blood cultures were obtained on admission.

Due to concerns of continued infection of the leg and possible recurrent *C. difficile* colitis, daptomycin 4 mg/kg daily and oral metronidazole was begun. An anaerobic blood culture from admission became positive on hospital day three for a gram-positive rod. The organism was identified as a clostridium species, initially thought to be *C. difficile*. Three stool specimens were negative for *C. difficile* toxin, and an abdominal film showed mild obstruction without toxic megacolon. The blood isolate was sent to the Centers for Disease Control and Prevention (CDC) in Atlanta for further identification. The organism was an anaerobe, 1–2 mm in colony diameter, had yellow-green fluorescence, and was esculin positive. Further biochemical evaluation and fermentation tests identified the organism as *Clostridium innocuum*. The isolate was resistant to vancomycin. Therapy with metronidazole and daptomycin was continued and follow-up blood cultures were negative. The patient was switched to an oral regimen of metronidazole and linezolid for the *C. innocuum* bacteremia and wound infection with MRSA completing a total of 10 days of antibiotics. He restarted antiretroviral therapy and has had no further episodes of bacteremia.

Discussion

Clostridium innocuum was first described in human infections in the 1960s [5]. The name "innocuum" was chosen as a result of the organism's proposed lack of virulence. Although the organism was thought to be non-pathogenic due to the lack of toxin production, infections have been reported, especially among immunocompromised hosts. Clostridial species are inhabitants of the gastrointestinal tract; hence, compromise of the integrity gastrointestinal tract may lead to translocation with bacteremia. In the current case, previous *C. difficile* colitis may have predisposed to the *C. innocuum* bacteremia as suggested by another report [6]. This case may have an additional risk for *C. innocuum* bacteremia including a *M. avium* infection of the gastrointestinal tract.

A literature review was conducted using Ovid MEDLINE (1950–2008) and EMBASE (1980 to 2008) and the terms "*Clostridium innocuum*" and "bacteremia"; references of papers were also utilized to locate further cases. The review of the literature found 13 cases of *C. innocuum* bacteremia or endocarditis, including this case (Table 1) [1,4,7]. Three other cases of bacteremia were noted in the literature, but did not include details of the individual cases [2,8]. The median age of cases was 38 years (range 18–70 years), and 62% were male. All but one case had an immunocompromising condition, including malignancy (n=10), organ transplantation (n=1) and AIDS (n=1). This concurs with other reports suggesting that infections with "non-*perfringens*" clostridial species have a propensity to develop in immunocompromised hosts [8]. The most common presenting symptom of *C. innocuum* bacteremia was fevers of unknown etiology, with gastrointestinal symptoms being the second most common clinical manifestation.

Identification of *C. innocuum* is often more difficult than other clostridial species which are usually identified by simple laboratory tests. Members of the RIC group (*C. ramosum*, *C. innocuum*, and *C. clostridioforme*) are often mis-identified in laboratories due to their Gram stain variability, lack of spores, and unusual colony morphology. The isolate in this case report was initially identified as another species of clostridia at a local laboratory before being definitively identified at the CDC. A study examining three rapid identification kits found that none could accurately identify this organism, suggesting that more complex biochemical and fermentation methods as well as gas-liquid chromatography are required for *C. innocuum* identification [9].

Accurate diagnosis in cases of systemic infection is paramount, since this species displays greater resistance to antibiotics compared to other clostridia. For instance, many *C. innocuum* isolates have resistance to vancomycin with MICs of 4–16 mcg/ml [9,10]. Studies have shown that the resistance is intrinsic and related to the presence of two chromosomal genes allowing the synthesis of a peptidoglycan precursor with low vancomycin affinity [11, 12]. The presence of impaired susceptibility to vancomycin in a clostridial species should suggest that the isolate may be *C. innocuum* [6]. *C. innocuum* may become selected for as a consequence of prior treatment with oral vancomycin, for example, in the setting of a prior *C. difficile* infection. In addition to vancomycin, *C. innocuum* isolates often have decreased susceptibility to cephalosporins, clindamycin, and quinolones [4]. Antibiotics such as metronidazole and ampicillin-sulbactam are typically active against this organism [9]. The MICs for newer agents, such as linezolid and daptomycin, have been reported as 2–4 mcg/ml and 2–8 mcg/ml, respectively [10].

The outcome of clostridial infections are variable and depend on both the clostridial species and host. Some have suggested that *C. innocuum* isolates may be contaminants or represent transient bacteremia since usually only one blood culture is positive [1]. However, these cases often occur in the setting of immunosuppression and antibiotics are initiated immediately, given the potential for mortality, so the pathogenicity of *C. innocuum* in clinical specimens may be uncertain. As demonstrated by this review, severe *C. innocuum* infections have been well-described [1,4,7,8]. In addition to bacteremia, these organisms may cause empyema, pylephlebitis, and pelvic abscesses [2,3]. The survival of patients with an endovascular infection in this review was 46%; deaths were due to the infection and/or the underlying condition. Advanced age and malignancy may be associated with poor clinical outcome [13].

In summary, this is the first case reported of *Clostridium innocuum* bacteremia among an AIDS patient. Given the propensity of this infection to occur in immunocompromised hosts and the rising numbers of this patient population, clostridial infections may become more common. This case suggests a possible association between prior *C. difficile* infection treated with vancomycin and the subsequent development of *C. innocuum* infection. Clinicians should be aware of the difficulties identifying this organism and its intrinsic resistance to several common antibiotics including vancomycin.

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References

1. Bodey GP, Rodriguez S, Fainstein V, et al. Clostridial bacteremia in cancer patients. A 12-year experience. Cancer 1991;67:1928–42. [PubMed: 2004306]
2. Gorbach SL, Thadepalli H. Isolation of Clostridium in human infections: evaluation of 114 cases. J Infect Dis 1975;131:S81–5. [PubMed: 805193]
3. Saxena R, Adolph M, Ziegler JR, et al. Pylephlebitis: a case report and review of outcome in the antibiotic era. Am J Gastroenterol 1996;91:1251–3. [PubMed: 8651182]
4. Castiglioni B, Gautam A, Citron DM, et al. *Clostridium innocuum* bacteremia secondary to infected hematoma with gas formation in a kidney transplant recipient. Transpl Infect Dis 2003;5:199–202. [PubMed: 14987206]
5. Smith LD, King E. *Clostridium innocuum*, sp. n. a sporeforming anaerobe isolated from human infections. J Bacteriol 1962;83:938–9. [PubMed: 13914326]

6. Ackermann G, Tang YJ, Jang SS, et al. Isolation of *Clostridium innocuum* from cases of recurrent diarrhea in patients with prior Clostridium difficile associated diarrhea. Diagn Microbiol Infect Dis 2001;40:103–6. [PubMed: 11502376]

7. Cutrona AF, Watanakunakorn C, Schaub CR, et al. *Clostridium innocuum* endocarditis. Clin Infect Dis 1995;21:1306–7. [PubMed: 8589163]

8. Gottesdiener KM, Weinstein L. Clostridial bacteremia: patterns of infection. Infect Dis Clin Pract 1994;3:182–92.

9. Alexander CJ, Citron DM, Brazier JS, et al. Identification and antimicrobial resistance patterns of clinical isolates of *Clostridium clostridioforme, Clostridium innocuum,* and *Clostridium ramosum* compared with those of clinical isolates of *Clostridium perfringens*. J Clin Microbiol 1995;33:3209–15. [PubMed: 8586704]

10. Goldstein EJ, Citron DM, Merriam CV, et al. In vitro activities of the new semisynthetic glycopeptide telavancin (TD-6424), vancomycin, daptomycin, linezolid, and four comparator agents against anaerobic gram-positive species and *Corynebacterium spp*. Antimicrob Agents Chemother 2004;48:2149–52. [PubMed: 15155214]

11. Mory F, Lozniewski A, David V, et al. Low-level vancomycin resistance in *Clostridium innocuum*. J Clin Microbiol 1998;36:1767–8. [PubMed: 9620417]

12. David V, Bozdogan B, Mainardi JL, et al. Mechanism of instrinsic resistance to vancomycin in *Clostridium innocuum* NCIB 10674. J Bacteriol 2004;186:3415–22. [PubMed: 15150227]

13. Grasberger RC, Pietrafitta JJ, Deckers PJ. Non-spore-forming clostridial bacteremia. J Surg Oncol 1984;25:188–91. [PubMed: 6700232]

Table 1

Cases of *Clostridium innocuum* Bacteremia or Endovascular Infection

Case No.	Ref, Year	Age/Sex	Type of Infection	Predisposing Condition	Clinical Symptoms	Treatment	Outcome
1	[1] 1991	31/M	Bacteremia	Melanoma	Fevers, GI bleed	NR	Died*
2	[1] 1991	70/M	Bacteremia	Undifferentiated cancer	Abdominal pain, diarrhea	NR	Survived>30 days
3	[1] 1991	39/F	Bacteremia	Leukemia	Fevers	NR	Survived>30 days
4	[1] 1991	28/F	Bacteremia	Leukemia	Fevers	NR	Died*
5	[1] 1991	36/M	Bacteremia**	Lymphoma	Soft tissue infection near catheter site	NR	Survived>30 days
6	[1] 1991	65/M	Bacteremia**	Leukemia	Fevers	NR	Died
7	[1] 1991	54/M	Bacteremia**	Leukemia	Fevers	NR	Died
8	[1] 1991	49/M	Bacteremia**	Leukemia	Fevers	NR	Survived>30 days
9	[1] 1991	27/F	Bacteremia**	Leukemia	Ileus, GI bleed	NR	Died
10	[1] 1991	59/M	Bacteremia**	Leukemia	Fevers	NR	Died*
11	[7] 1995	18/F	Endocarditis	None	Dyspnea, cough, headache, stiff neck	Erythromycin, ceftriaxone	Died
12	[4] 2003	38/F	Bacteremia, abdominal hematoma	Kidney transplant, hepatitis C	Fevers and abdominal pain	I&D, penicillin G and clindamycin, followed by piperacillin/tazobactam and clindamycin (11 days)	Survived
13	[Current Case] 2008	38/M	Bacteremia	AIDS	Fevers	Metronidazole and daptomycin, then metronidazole and linezolid***	Survived

NR, not reported

* Responded to antibiotic therapy, but died of another condition

** Infection was polymicrobial

*** Antibiotic therapy also for MRSA soft tissue infection