



## Case report

## *Clostridium botulinum* – like organism bacteremia in a user of black tar heroin



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## ABSTRACT

Wound botulism due to introduction of the anaerobic bacteria, *Clostridium botulinum*, into otherwise sterile, relatively anaerobic tissue is a known complication of black tar heroin use. The treatment of wound botulism requires prompt initiation of antitoxin as well as antimicrobial therapy. We report the case of a patient with polymicrobial bacteremia that included a *Clostridium botulinum*-like organism who underwent successful treatment of their anaerobic infection with antibiotics and surgical debridement.

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## Case presentation

A person with a history of intravenous and subcutaneous methamphetamine and heroin use presented with a 4-day history of lower extremity swelling, abdominal pain, fatigue, and malaise. They described their abdominal pain as 8/10 severity, centered in the right lower quadrant with radiation to the bilateral shoulders. The patient reported associated nausea, vomiting, orthopnea, and increased abdominal girth. They also noted bilateral arm wounds, which were bandaged. They did not have a history of valvular or cardiac disease.

On physical exam, the patient was found to be afebrile (37.4 °C) with a heart rate of 98, a blood pressure of 109/69 mmHg, and a respiratory rate of 21. They were found to have a regular heart rhythm without heart murmurs or elevated jugular venous pressure. The patient's abdomen was tender and distended. They had 2+ pitting edema bilaterally to the knee, and diffuse scarring across both arms and legs. Multiple purulent, ulcerated lesions with necrotic appearing bases were present on the patient's forearms. There was an additional round, 1 cm fluctuant distal right forefinger lesion present without splinter hemorrhages or Janeway lesions. The patient was awake, alert and oriented, with a normal

cranial nerve exam, and intact strength and sensation to light touch in the bilateral upper and lower extremities.

The patient was started on empiric vancomycin for suspected soft tissue infection. Initial blood cultures grew methicillin-resistant *Staphylococcus aureus* (MRSA), and transthoracic echocardiogram was initially suspicious for echodensities on the aortic, mitral, and tricuspid valves. However, subsequent transesophageal echocardiogram did not show valvular lesions concerning for endocarditis. The patient was transitioned to daptomycin and ceftaroline for treatment of MRSA bacteremia. The patient was screened for Hepatitis C Virus (HCV), and was found to have a positive HCV antibody, but with an undetectable viral load on subsequent nucleic acid amplification testing. HIV testing was negative. Opioid use disorder and opioid withdrawal were managed with methadone and consultation of an addiction medicine team.

On hospital day 3, two of three original blood cultures turned positive for *Clostridium botulinum*, identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF; Bruker microflex; BIOTECON Diagnostics). On further questioning, the patient endorsed the use of black tar heroin. Close neurologic monitoring, including twice daily negative inspiratory force evaluation, was initiated to assess for the development of clinical botulism. However, the patient remained neurologically intact throughout admission. Polymerase chain reaction (PCR) was performed on an isolate of the bacteria at the Utah Department of Health to identify the presence of one or more of the genes for botulinum neurotoxin (BoNT), and the isolate was found to be

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negative for BoNT genes. The case was discussed with the Utah Department of Health (UDH) and Centers for Disease Control (CDC), and the administration of antitoxin was deferred given the fact that the patient's strain of *Clostridium* appeared to be nontoxicogenic, and there was no neurologic dysfunction clinically apparent.

Due to the concern for wound botulism secondary to parenteral injection of black tar heroin, the patient underwent extensive debridement of their bilateral forearm wounds and finger lesion. Wound cultures grew MRSA, *Prevotella*, and *Eikenella corrodens*. The patient was transitioned to metronidazole and daptomycin to cover *C. botulinum*, MRSA, and the other organisms detected in their wounds.

Repeat blood cultures were negative and the patient remained clinically stable. Despite plans to continue intravenous antimicrobial therapy for a total of 4 weeks, the patient elected to leave the hospital on hospital day 9 before arrangements could be made for gold standard therapy. The patient was provided prescriptions for linezolid and metronidazole, as well as contact information for an addiction clinic.

The patient has since returned to the clinic and hospital several times for management of MRSA complications, such as drainage of abscesses; however, repeat cultures have been negative for *Clostridium* species and they have remained neurologically intact without evidence of clinical botulism.

## Discussion

*C. botulinum* is a sporulating, gram positive, rod shaped, strictly anaerobic bacterial pathogen classically associated with the clinical syndrome of botulism, a flaccid paralysis which is mediated by botulinum neurotoxin (BoNT). There are nine distinct serotypes of BoNT, four of which are associated with human disease. The toxins are encoded by mobile genetic elements that enable the horizontal transfer of toxin-encoding genes between isolates. Each toxin begins as a single polypeptide chain of minimal potency before being cleaved via bacterial protease into two smaller chains becoming exponentially more potent. This cleaved serotype A chain becomes, based on molecular weight, the most potent toxin found in nature [1]. While most strains of *C. botulinum* only express one toxin serotype, isolates expressing two or even three subtypes have been reported [2,3]. Similarly, non-toxicogenic strains of *C. botulinum* have previously been described, though these are often classified as "*C. botulinum*-like" as they do not produce neurotoxin [4]. Nontoxicogenic *C. botulinum*-like organisms, such as *Clostridium sporogenes*, are rarely considered pathogenic, though a few cases of bacteremia, septicemia and soft-tissue infections have been described by these organisms in the past [5].

Wound infections due to *C. botulinum* have been rising in prevalence [6]. Historically associated with contaminated wounds from trauma or surgery, it has recently been associated with subcutaneous and intramuscular black tar heroin (BTH) use [7]. BTH has grown in popularity among patients with Opioid Use Disorder in the United States since the 1970s. Compared to pure heroin, BTH is cheaper to make because it is less refined and is often cut with a number of substances that increase the risk of wound botulism. BTH also causes greater degrees of venous sclerosis, decreasing limb circulation and a making limb tissue more anaerobic [8]. The increase of wound botulism associated with BTH use has been widely noted [7,9,10]. Wound botulism presents as a descending paralysis due to neurotoxin locally produced by *C. botulinum*. Early symptoms may include double or blurred vision, ptosis, dysphagia, and dry mouth. Death is often secondary to respiratory failure. Anaerobic substrate in wounds allows Clostridial spores to germinate often in the absence of classic signs of infections such as erythema, warmth, purulence,

and pain [7,11]. While nontoxicogenic *C. botulinum*-like organisms do not produce neurotoxin and will not cause paralysis, they also thrive in anaerobic environments like the wounds generated by black tar heroin use. They have been reported as a cause of necrotizing soft tissue [12], bacteremia [5,13], liver abscess [14], and empyema [13].

Clostridial bacteremia carries a high degree of morbidity and mortality. In a 2008 review of 138 patients with Clostridial bacteremia, a 30 % in-hospital mortality was observed [15]. In a 2018 study of *C. botulinum* isolated from infants with infant botulism, isolates of several strains of *C. botulinum* showed susceptibility to a wide range of antimicrobials, including penicillins, cephalosporins, fluoroquinolones, and trimethoprim-sulfamethoxazole [16]. There was one isolate resistant to penicillin, and clinical cases involving penicillin and metronidazole resistant *C. botulinum* have been reported [17]. The antibiotic susceptibility of *C. sporogenes*, the most commonly reported nontoxicogenic *C. botulinum*-like organism, was tested in a 1980 study and found to be similar to *C. botulinum*, with susceptibility to metronidazole, penicillins, and cephalosporins. Notable differences included greater susceptibility to vancomycin and resistance to clindamycin and aminoglycosides [18]. Given the high morbidity and possibility of resistant isolates, antimicrobial susceptibility testing of pathogens in cases of nontoxicogenic *C. botulinum*-like organisms is advisable. Unfortunately, susceptibility testing was not performed for the isolate of this patient and was unavailable for testing retrospectively.

Patients with opioid use disorder are at risk for many infectious conditions in addition to Clostridia, such as endocarditis, Hepatitis C, and HIV infection. In studies of endocarditis patients with opioid use disorder, use of medications for opioid use disorder (MOUD) was associated with a higher rate of receiving gold standard therapy for endocarditis [19], and lower mortality while actually receiving MOUD, though retention in MOUD programs post-discharge was low [20].

## Conclusion

Our case illustrates the challenge of managing polymicrobial infection in patients who use parenteral drugs. As rapid diagnostic testing becomes more widely available, the identification of uncommon pathogens like *C. botulinum* and its closely related nontoxicogenic strains requires clinical correlation to determine an appropriate treatment strategy. The use of black tar heroin increases the risk of developing soft-tissue infections caused by anaerobic organisms, and substance use disorder should be addressed as part of every patient's treatment plan.

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The authors report no declarations of interest.

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## Consent

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## CRediT authorship contribution statement

**Therese Battiola:** Writing - original draft. **Kristen Saad:** Writing - original draft. **Taylor Nelson:** Writing - original draft. **Nick Tinker:** Writing - review & editing. **Aaron Crosby:** Writing - original draft, Writing - review & editing.

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