A Case Report of Wound Botulism — Rare Disease on the Rise with the Opioid Crisis

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Abstract

Wound botulism is a rare, underrecognized life-threatening illness caused by a toxin produced by Clostridium botulinum, a spore-forming anaerobic bacterium. Approximately 20 cases are reported in the United States each year, mostly from California. Most wound botulism cases occur in drug injectors, particularly among those using black tar heroin. The initial presentation of botulism may overlap with other diagnoses, including opioid intoxication and pre-existing neurological disease, making accurate diagnosis difficult. A healthy 40-year-old patient with a history of injecting black tar heroin presented to an emergency department complaining of generalized weakness and throat discomfort. He was given antibiotics and was sent home. The next day, the patient presented to another emergency department with additional complaints of slurred speech and blurring of vision. He was admitted for a possible cerebrovascular injury. In the absence of positive findings from laboratory or imaging studies, botulism was considered. The patient decompensated and was intubated. Botulism antitoxin was given, and the patient eventually recovered. Prompt decision-making based on clinical suspicion and an informed presumptive diagnosis, administration of botulism antitoxin, and aggressive provision of supportive care can arrest the progression of paralysis and be life-saving. With the rise of opioid use in the United States, leading to a reversion to heroin as a cheaper form of opioids, cases of wound botulism may be on the rise. Clinician attentiveness to obtaining substance history and being aware of botulism presentation may lead to life-saving treatments for these patients.

Keywords

Botulism, black tar heroin, intravenous drug users, Botulism antitoxin

Abbreviations and Acronyms

BAT = botulinum antitoxin
BoNT = botulinum neurotoxin
CDC = US Centers for Disease Control and Prevention
ED = emergency department

Introduction

Botulism occurs when spores of *Clostridium botulinum* germinate to toxin-producing bacilli in an anaerobic environment. Wound botulism is a rare, reportable, life-threatening disease that occurs mostly in drug injectors, especially among those using black tar heroin in conjunction with skin popping (subcutaneous and inadvertent intradermal injection). We report here a case of wound botulism in a 40-year-old intravenous black tar heroin user whose initial presentation was non-specific.

Case Report

A 40-year-old heroin user with no pertinent past medical history initially presented to an emergency department (ED) with subjective complaints of generalized weakness, difficulty swallowing, dysphonia, and sensation of something “stuck” in his throat for 1 day. The patient’s significant other reported that the patient was walking, talking, and eating as usual despite the above complaints. The patient was subsequently sent home with antibiotics.

On the next day, his condition worsened despite taking the prescribed antibiotics. He presented to a different ED with additional complaints of slurred speech and double and blurry vision. In ED, the patient was not in acute distress with a blood pressure of 110/80, temperature of 98.6°F, and respiratory rate of 18 with oxygen saturation of 95%. He was noted to have rotary nystagmus, dysarthria, and motor strength of 4/5 in all extremities but no pronator drift. The extremity exam was notable for track marks bilaterally on the arms and hands, with an abscess on the left forearm. He had symmetrical facies, intact light touch, 2/4 deep tendon reflexes on all extremities, and physiologic plantar reflexes bilaterally. Computed tomography of the head, electrocardiography, chest X-ray, complete blood count, and comprehensive metabolic panel were all unremarkable. A urine drug screen was positive for opiates, and he reported using black tar heroin intravenously almost daily for the past 6 months, including recent skin popping. The patient was admitted for management of a possible cerebrovascular injury and was treated with an aspirin suppository. The left forearm abscess was drained later that day, and a culture was sent. The patient was continued on antibiotics.

On the second hospital day, the patient underwent brain magnetic resonance imaging, which showed no abnormality. The patient’s neurological symptoms persisted with no improvement. A neurologist was consulted, and Guillain-Barre syndrome, myasthenia gravis, and botulism were considered. Lumbar puncture showed no albuminocytologic dissociation for Guillain-Barre syndrome or any other abnormalities. A myasthenia gravis panel was sent to a laboratory in the continental United States, but results were not expected for at least a week—ultimately, these were negative. The Hawai‘i State Department of Health and the Centers for Disease Control and Prevention (CDC)
were notified and consulted for assistance in managing possible botulism. Following the discussion, the CDC authorized the release of botulism antitoxin (BAT). For further diagnostic purposes, a sample of the patient’s blood was sent to the CDC.

On the third hospital day, the patient started to experience dyspnea, which subsequently required intubation. The BAT arrived and was administered, and the patient was transferred to a facility supporting a higher level of care.

On the fourth hospital day, anti-GQ1b IgG antibody was sent for possible Miller-Fisher syndrome, a variant of Guillain-Barre syndrome, before empiric treatment of intravenous immunoglobulin for Guillain-Barre syndrome was initiated. The result came back a few weeks later and was negative. Nerve conduction studies and electromyography showed changes consistent with a presynaptic neuromuscular deficit as seen in botulism. Supportive care was continued.

The patient was extubated on his ninth day in the hospital. He recovered steadily; however, the patient continued to fail the swallow test and was discharged home with a gastrostomy feeding tube after 2 ½ weeks of hospitalization.

The patient’s cultures from the left arm abscess, spinal fluid, blood, urine, and sputum were all negative. A report from the CDC was received almost 50 days after the patient was tested, indicating the presence of BoNT type B.

**Discussion**

BoNT is produced by *Clostridium botulinum* and is recognized as one of the most lethal poisons by the World Health Organization and poses a major bioweapon threat. Assuming an average weight of 70 kg per person for the 5.6 billion people in the world, only 39.2 g of pure BoNT would be sufficient to eradicate humankind. There are 7 types of BoNT, toxins A-G, where toxins A, B, E, and rarely F can cause botulism in humans. All the serotypes of BoNT interfere with neural transmission by irreversibly blocking the release of acetylcholine, which is the principal neurotransmitter at the neuromuscular junction, thus causing muscle paralysis.

**Epidemiology**

The CDC warns that botulism is frequently misdiagnosed. Wound botulism is rare, and only approximately 20 cases are reported every year in the United States. According to National Survey on Drug Use and Health, the number of heroin users has been on the rise since 2007 with a slight decrease in 2017; however, no overall increase in the wound botulism cases between 2001 and 2017 has been noted. Any type of botulism is a reportable disease to the CDC, and in Hawai’i, to the state health department. During 2001–2016, 353 wound botulism cases were reported to the CDC, of which 291 cases (82%) were from California. Botulism is rarely reported outside California, but this may represent underdiagnosis elsewhere. In Hawaii, only 1 case of wound botulism was reported during 2001–2017.

**Risk Factors**

One of the major risk factors for wound botulism is intravenous drug use and skin popping. *Clostridium botulinum* spores, which are not killed by heat, germinate and produce BoNT in an anaerobic environment, such as puncture wounds from heroin injection and necrotic tissue created by skin popping. Another risk factor is intravenous administration of black tar heroin, which is usually made in Mexico and is cheaper than regular heroin due to its adulteration and lower purity (average purity, 27.1%). It is unclear how black tar heroin becomes contaminated.

From 2005 to 2017, 93% (222 out of 239) of the wound botulism cases in the United States were noted to be from injection drug users. In a wound botulism outbreak in San Diego County, California, which occurred between 2017 and 2018, there were 9 wound botulism cases reported; all 9 patients reported using intravenous heroin. Of these, 7 patients (78%) used black tar heroin, and 6 patients (67%) admitted to skin popping. The patient in this case report was a black tar heroin user who acknowledged skin popping.

**Signs and Symptoms**

According to Rao et al, there were 332 botulism cases reported in the United States between 2002 and 2015; most had descending paralysis (93%), subjective muscle weakness (85%), shortness of breath (65%), and cranial palsies such as dysphagia (86%), blurred vision (80%), and slurred speech (78%). Autonomic dysfunction such as dry mouth and fluctuating blood pressure and heart rate may also be present. Botulism usually progresses to symmetric descending flaccid paralysis and ultimately respiratory muscle paralysis and may result in death.

Initial presentation of botulism may be non-specific, such as generalized weakness and throat discomfort like in this patient. This type of non-specific presentation might lead to confusion with other diagnoses. Peak and colleagues noted that the symptoms of wound botulism often overlap with the symptoms of opioid intoxication or neurologic syndromes such as Guillain-Barré syndrome. In this patient, Miller Fisher syndrome and myasthenia gravis were also considered.

Myasthenia gravis is an autoimmune disease that presents a variable combination of weakness of the extraocular, bulbar, limb, and respiratory muscles, which is similar to our patient’s presentation. A hallmark of myasthenia gravis, however, is the presence of fluctuating muscle weakness that improves with rest, which our patient did not have. The patient’s myasthenia gravis panel also came back negative.
Patients with Guillain-Barre syndrome suffer from a flaccid, fairly symmetrical ascending paralysis, depressed deep tendon reflexes, and, at times, autonomic dysfunction, such as extreme hypertension or hypotension. Guillain-Barre syndrome is often seen after gastrointestinal infection with *Campylobacter jejuni* and respiratory infection, such as with Epstein-Barr virus. Lumbar puncture shows elevated protein, known as albuminocytologic dissociation, in 50% to 75% of patients. In this patient, deep tendon reflexes remained normal, and he denied having a recent infection before the onset of symptoms. Lumbar puncture results were also normal.

Miller Fisher syndrome is a variant of Guillain-Barre syndrome, which can present with the clinical triad of ophthalmoplegia, ataxia, and areflexia and, to a lesser degree, with mild motor weakness and bulbar palsies as in this patient. It accounts for between 1% and 5% of all Guillain-Barre cases in Western countries and twice as common in men than women with the median age of onset in the fifth decade. Anti-GQ1b IgG antibody can be used for diagnosis, which is present in 85% of the patients and was negative in this patient. Although Miller Fisher syndrome usually follows a self-limiting course, the usual treatment for Guillain-Barre syndrome, such as intravenous immune globulin and supportive care, may be used to hasten recovery.

**Diagnosis**

Diagnosing wound botulism can be challenging due to the lack of an immediately-confirmatory test and the presence of confounding symptoms that overlap with other neurologic syndromes or opioid intoxication. Confirmatory diagnosis requires growth of *Clostridium botulinum* from stool or wound cultures or the presence of toxin in the serum or other body fluid. The latter test is performed by the CDC or another designated lab depending on the state. As the confirmation test may take weeks to months, a high index of clinical suspicion, including a history of intravenous drug use and neurologic symptoms, should prompt early treatment and administration of BAT, rather than waiting for lab results. Patients suspected of having wound botulism who fit the clinical picture but without laboratory confirmation should still be considered as having probable wound botulism because the sensitivity of the mouse lethality bioassay, the gold standard to confirm botulism, is only 68%.

**Treatment**

BoNT causes paralysis by binding on the presynaptic neuron of the neuromuscular junction and irreversibly blocking acetylcholine release. Treatment for botulism is BAT to neutralize free BoNT in the bloodstream and stop the progression of the paralysis. Recovery of BoNT affected neurons occurs by the sprouting of nerve terminals and the formation of new synaptic contacts, which usually takes 2 to 3 months. Prompt diagnosis is essential in treatment for botulism and can be life-saving. When botulism is suspected, the state health department and the CDC should be contacted. If clinical consultation with both agencies supports botulism, BAT can be obtained. BAT is available only from the CDC due to its limited use and relatively short expiration date. The antitoxin is stored at the CDC Quarantine Stations located in major airports around the nation. In our case, BAT was available in 1 day.

**Prognosis**

During 1975–2009, mortality from wound botulism in the United States was approximately 5%, but recently, mortality from this disease decreased to about 1.5% (2010–2017). Mortality depends on various factors, including the type of toxin, where type F has the higher mortality while type B toxin (as in this patient) has lower mortality. The sequelae of wound botulism are similar to other types of botulism. Some who survive may have fatigue and shortness of breath for years. Fortunately, many people recover fully, but it may take months, and patients may require extended rehabilitation therapy.

**Conclusion**

Wound botulism is a rare disease that may be fatal if untreated, with approximately 20 cases per year reported in the United States. It is even rarer in the state of Hawai‘i, where only 1 wound botulism case has been reported between 2001 and 2017. Its association with the use of black tar heroin has been long known. Botulism’s initial presentation can be non-specific and may be misdiagnosed as opioid intoxication or another neurological disease. The treatment is supportive care and BAT, which needs to be given promptly to have any significant effect. Obtaining an accurate substance use history and an awareness of the characteristic botulism presentation may lead to prompt diagnosis, administration of BAT, and provision of supportive care and ultimately may be life-saving. In injection drug users, generalized weakness, blurry vision, slurred speech, paralysis, or dyspnea should prompt the clinician to strongly consider the possibility of wound botulism. Despite the syndrome’s rarity, the rise in the national use of heroin can be expected to produce an associated rise in such co-morbidities.
References