CASES

Botulism presenting as dyspnea and respiratory failure in the Canadian Arctic

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Competing interests: None declared.

This article has been peer reviewed.

The authors have obtained patient consent.

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***CMAJ* 2016. DOI:10.1503/cmaj.150941**

A 58-year-old Inuvialuit woman presented to her health centre in the western Canadian Arctic with acute-onset (over one day) dyspnea without chest pain or fever. She had tachypnea with increased work of breathing. A chest radiograph appeared normal. The patient soon had a decreased level of consciousness and required positive pressure ventilation to maintain adequate oxygenation and ventilation. She remained hemodynamically stable.

An airplane ambulance was flown to her community, and the patient was intubated by the paramedics. The neurologic examination was notable for bilaterally dilated (6 mm) pupils; findings were otherwise normal, including strength and deep tendon reflexes. Obtaining a detailed history from the patient in this context was challenging. Her husband reported that she had complained of dry mouth and mild nausea one day before her breathing difficulties. She had a smoking history of 40 pack-years, with no important medical history or medications. No one in her family or community reported being ill.

At the regional hospital, a computed tomography scan of the patient's chest (to rule out pulmonary embolism) showed only minimal bibasilar atelectasis. The patient was given methylprednisolone, bronchodilators and intravenous azithromycin treatment for possible exacerbation of chronic obstructive pulmonary disease. Gas exchange was noted to be excellent on minimal ventilator settings, and she was extubated. Immediately after extubation, severely increased work of breathing developed, with no audible breath sounds on auscultation. Hypercarbic respiratory failure quickly developed, and the patient was intubated again.

Further collateral history was obtained from the family. The patient's family lived near the Beaufort Sea and regularly ingested *maktak* (whale blubber, in this case beluga). The meat had been stored in a refrigerator that had not been functioning properly. No other family or community members were ill, but the patient's husband asked whether botulism was responsible for his wife's illness.

Botulism was strongly suspected at this point. However, antitoxin was not immediately available locally. On day 2 after presentation, the patient was transferred to the intensive care unit at a tertiary care centre, and arrangements were made to test the patient's serum and the source whale blubber for toxin bioassay. Other more common causes, including myasthenia gravis and Guillain–Barré syndrome (Miller Fisher variant), were ruled out by the treating team. Seven days after the initial presentation, the patient's serum was found to be positive for botulinum neurotoxin serotype E by means of mouse neutralization assay at a national reference testing centre.

On day 7 after presentation, heptavalent botulinum antitoxin was administered to the patient. Despite the delay in administration of the antitoxin, she made a complete recovery and was discharged from hospital less than four weeks after presentation.

KEY POINTS

- Foodborne botulism, rare elsewhere in the developed world, is relatively common in coastal Arctic communities.
- Marine mammal and fish products are the most common vehicles for type E foodborne botulism in Canada.
- Typically, patients present with rapid progression of cranial nerve abnormalities, followed by descending flaccid paralysis, which may lead to respiratory failure.
- Once foodborne botulism is suspected, antitoxin should be administered as soon as possible without awaiting confirmatory testing.

Discussion

Clostridium botulinum is an anaerobic spore-forming bacterium naturally occurring in soil and aquatic sediments worldwide. By weight, botulinum toxin is the most poisonous substance to humans.[1] There are seven known serotypes of

botulism (designated A through G), but almost all cases in humans are caused by serotypes A, B and E.[2] In foodborne botulism, preformed toxin is absorbed systemically and blocks neurotransmission at presynaptic motor nerve terminals by inhibiting acetylcholine release.[1]

Botulism cases in most of the developed world are usually associated with home-preserved dishes or fermented uncooked foods.[1] In Canada between 1985 and 2005, the mean incidence rate of foodborne botulism was 0.03 per 100 000 population.[3] However, certain communities are disproportionately affected, and much higher incidence rates have been reported in some coastal communities. The mean rate among Inuit of Nunavik (in the Arctic region of Quebec) is 50.5 per 100 000 population, more than 1600 times higher than the rate for the rest of Canada.[3]

In the circumpolar world (including the Canadian north, Alaska, parts of Russia, Greenland and Scandinavia), most cases of foodborne botulism are associated with fish or marine mammal products and involve the type E neurotoxin.[2,4] The *C. botulinum* spores in Arctic coastal soils are resistant to lower temperatures, which may allow spore germination under partial freeze–thaw temperatures common to the Arctic in the summer months.[2] Marine mammal products, including aged seal meat (*igunaq*) or flippers (*utjaq*), beluga skin and blubber (*maktak*, elsewhere referred to as *maktaaq*) or meat, and walrus, as well as fish products, such as aged salmon eggs ("stink eggs"), are the predominant vehicles for type E botulism in Canada.[3]

The risk of contamination of marine mammal meat during butchering under field conditions is high because the organism is ubiquitous in the coastal environment.[3] In Alaska, outbreaks have been associated with uncooked aquatic game, including fish, whales, seals, walruses and beavers. Two-thirds of botulism outbreaks affecting Alaskan Native people during 2000–2007 involved foods preserved in nontraditional ways, such as the use of sealed plastic or glass containers. These methods are likely to provide the anaerobic conditions and warmer, above-ground temperatures that favour toxin elaboration by *C. botulinum*.[5]

Clinical presentation and diagnosis

Adults with foodborne botulism usually experience neurologic symptoms 12–36 hours after ingestion of the preformed toxin; the incubation period ranges from hours to one week. A prodrome of gastrointestinal (nausea, vomiting, abdominal pain, diarrhea) and autonomic (severe dry mouth) symptoms may develop. Typically, patients with botulism present with distinctive symmetrical cranial nerve palsies. Blurred vision, mydriasis, diplopia, nystagmus, dysphagia, dysarthria and facial weakness are common. Subsequent descending flaccid paralysis proceeds rapidly, often over a period of hours, and affects the muscles of the neck, shoulders, upper and then lower extremities. Deep tendon reflexes become impaired. Respiratory failure from paralysis of the diaphragm and accessory breathing muscles, or occasionally also from pharyngeal collapse, may ensue and jeopardize the airway. Involvement of the autonomic nervous system may result in orthostatic hypotension.[6,7]

In certain clinical settings, including known local epidemics or in northern coastal Arctic communities where foodborne botulism is less rare, botulism toxicity may be easily recognized because of a common exposure. However, missed or delayed diagnosis may still occur. The differential diagnosis of botulism includes Guillain–Barré syndrome (Miller Fisher variant), myasthenia gravis, brainstem stroke, Lambert–Eaton syndrome, organophosphate poisoning and tick paralysis.[6]

Once suspected on a clinical and epidemiologic basis, the diagnosis may be confirmed in the laboratory by isolation of botulism toxin from the patient's serum, gastric secretions or stool, or from the food sample itself. Confirmatory testing with an enzyme-linked immunoassay or mouse bioassay is performed at reference laboratories,[8] and results can take several days to a week.

Treatment

Treatment of foodborne botulism is primarily supportive, including mechanical ventilation when necessary. Antimicrobial agents do not affect the toxin, which is preformed at the time of ingestion. Timely intravenous administration of an equine-derived botulinum antitoxin can arrest the progression of paralysis by neutralizing toxin molecules not yet bound to nerve endings.[9] For maximum effectiveness, the antitoxin should be given within 24 hours after symptom onset, many days before toxin bioassay results are available.[6] Clinical recovery correlates with the formation of new presynaptic end plates and neuromuscular junctions.[9] Antitoxin use is infrequently associated with hypersensitivity reactions, including anaphylaxis, urticaria and serum sickness.[1,2] Skin testing may be performed before intravenous administration of antitoxin,[3] although it is generally not feasible in remote Arctic health centres. Treatment of anaphylaxis should be readily available in settings where antitoxin is administered.[2,9]

Antitoxin as a treatment of clinical foodborne botulism is well established, and it is unlikely that randomized controlled trials will ever be conducted. It has a known mechanism of action

with biologic plausibility, and it is supported by evidence from a large number of observational human and experimental animal studies.[6] Uncontrolled observational studies in humans have shown an association between early antitoxin administration and decreased mortality, time on a ventilator and length of hospital stay.[6]

A retrospective study involving 70 patients with type E botulism in Canada reported a decrease in the median length of stay from 11 to 5 days with antitoxin administration.[3] More recently, a placebo-controlled trial of antitoxin treatment in infant botulism showed a decrease in the length of hospital stay, the time on a ventilator and the duration of tube feeding in the treatment group compared with the placebo group.[10]

Delays in treatment

Botulism is frequently underdiagnosed because of its rarity and the unfamiliarity of clinicians with the disease in most of the developed world. In a retrospective study that examined 203 cases of foodborne botulism in the state of Alaska, initial misdiagnosis occurred in 28% of single cases and 18% of multiple-case outbreaks. Initial misdiagnosis was associated with a median two-day delay in administration of antitoxin.[5] Because access to antitoxin and to mechanical ventilation and intensive care for patients in northern and remote communities frequently depends on air transport to regional centres, early recognition is all the more critical in such settings.[2]

Foodborne botulism, rare in much of North America, is relatively common in coastal Canadian Arctic communities. Although botulism can lead to fatal respiratory muscle failure, rapid recognition provides an opportunity for early administration of botulinum antitoxin and improved clinical outcomes. Clinicians should include botulism in the differential diagnosis of patients from coastal Arctic communities who present with respiratory distress, and they should not hesitate to administer antitoxin if clinical suspicion is high.

Health Canada resources for clinicians

Botulism: guide for health professionals (www.hc-sc.gc.ca/fn-an/legislation/guide-ld/botulism-botulisme-prof-eng.php)

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Contributors: Claudia Kraft and Terry Wuerz contributed equally to the drafting of the article. Leah Seaman provided details of the specific case and obtained consent from the patient. Substantial revisions were provided by Jennifer Cram, with additional revisions by Leah Seaman. All of the authors approved the final version of the article to be published and agreed to act as guarantors of the work.

The section Cases presents brief case reports that convey clear, practical lessons. Preference is given to common presentations of important rare conditions, and important unusual presentations of common problems. Articles start with a case presentation (500 words maximum), and a discussion of the underlying condition follows (1000 words maximum). Visual elements (e.g., tables of the differential diagnosis, clinical features or diagnostic approach) are encouraged. Consent from patients for publication of their story is a necessity. See information for authors at www.cmaj.ca.