Botulism in Patients Who Inhale Cocaine: The First Cases in France

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We describe 2 cases of mild botulism in patients who inhaled cocaine. Botulism, though rare, is increasing in incidence among illicit drug users. To our knowledge, these are the first cases of botulism in illicit drug users in France. Clinicians should be aware of this phenomenon; botulism should be considered in illicit drug users with neurological symptoms.

Botulism has long been considered to be a foodborne infection that is caused by ingestion of food contaminated with the botulinum toxin. A new mode of presentation is surfacing in illicit drug users, in which the organism enters the body at sites of subcutaneous or intramuscular injections. Worldwide, >90% of all reported cases of wound botulism in injection drug users have occurred in the United States [1]. Recently, cases have been reported in the United Kingdom and elsewhere in Europe [2–4]. Wound botulism associated with injection of black tar heroin seems to be linked to heroin or to the substances added to it and not to the skin or the environment of the user [5]. To our knowledge, only a few cases of wound botulism have been reported previously in individuals who inhale cocaine [6, 7]; we report the first cases in this patient population in France.

Case 1. A 28-year-old man who used cocaine intranasally presented to an emergency department with a 12-h history of confusion, acute diplopia, and diarrhea. Clinical symptoms had appeared 2 h after he began inhaling cocaine. He denied injecting the drug into his muscles (also called "skin popping") and consuming food canned at home. Clinical examination showed mydriasis, whereas the arterial pressure and respiratory rate were normal. He was observed over a 24-h period, but he refused hospital admission and returned home. Five days later—6 days after inhaling cocaine—his symptoms persisted, and he was admitted to the hospital. He reported not having inhaled cocaine since the previous examination. His confusion had resolved, but the patient reported loss of visual accommodation with blurred vision. Dry mucosa syndrome was observed, and the gag reflex was absent, but no dysphagia was noted. The patient complained of constipation. Electromyography performed on day 7 of the illness did not demonstrate presynaptic block. Blood samples were obtained on days 3 and 6 of the illness and sent to the French National Reference Centre for Botulism for detection of botulinum toxin. Toxin was detected using a bioassay in mice, which is the standard reference method [8]. Mouse lethality testing confirmed the presence of botulinum toxin type B.

For this mild form of botulism, in which there was an absence of severe signs of illness and a tendency for symptom regression within the 5-day period before hospital admission, the patient benefited from supportive care and received macrolide treatment for 10 days but did not receive an antitoxin. Ten days later, clinical examination confirmed that all symptoms had resolved. Findings of a radiograph did not demonstrate sinusitis.

Case 2. The patient in case 1 was questioned about similar cases of illness, which, that same day that he was admitted to the hospital, led us to examine a 27-year-old cocaine user who also had ingested the drug intranasally. He described loss of visual accommodation and blurred vision, dry mucosa syndrome, and constipation that had occurred 6 days before presentation to the hospital—6 h after he had inhaled cocaine from the same sample as the first patient. The symptoms regressed over a 3-day period. He reported inhaling a smaller amount of cocaine, compared with the first patient. All symptoms disappeared on the day he was examined. The test to detect botulinum toxin type B in a serum sample had a negative result.

These 2 patients had inhaled cocaine 2 or 3 times weekly for many years. Clinical symptoms appeared after they inhaled cocaine purchased from a new dealer for the first time. They did not share equipment. No meals or gatherings were attended by the patients, and no common food item had been eaten recently, including food canned at home or vacuum-packed foods.

Discussion. Botulism is usually considered to be a foodborne infection. However, although wound botulism is considered to be rare, its incidence is increasing among illicit drug

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users. To our knowledge, these are the first cases of botulism associated with inhaling cocaine in France.

There are 3 naturally occurring epidemiologic types of botulism: foodborne, intestinal colonization, and wound [9]. Cases of wound botulism have been reported in injection drug users [1–5, 7, 10]. The cases appearing in France are not surprising, because cases have been reported in illicit drug users in other countries in Europe, Great Britain, Ireland [2], Switzerland [3], and Norway [4]. Most cases have occurred in patients who inject cocaine by skin popping. Nevertheless, 2 cases of botulism that occurred after intranasal use of cocaine have been reported [6, 7]. Those 2 patients presented with sinusitis, and, in 1 case, a sinus aspirate sample grew *Clostridium botulinum*. Moreover, inhalational botulism and iatrogenic botulism resulting from injection of botulinum toxin for cosmetic or therapeutic purposes have been reported [9]. In our patients, foodborne botulism and intestinal colonization were unlikely. Our patients injecting drugs, and no abscesses or wounds were identified. No clinical or radiologic data were consistent with sinusitis. Nevertheless, sinus drainage was not performed in these 2 patients, and an infectious focus can be very small [6]. Thus, according to previous cases, *C. botulinum* sinusitis remains a likely mode of contamination. Moreover, inhalational botulism with direct absorption through the nasal mucosa can be considered.

Street cocaine may contain numerous adulterants; moreover, in the cases of these patients, the samples they purchased might have been hidden in soil. Although the cocaine these patients used was unavailable for culture or detection of botulinum toxin, *C. botulinum* is ubiquitous in the environment.

In these 2 cases, the incubation period would have been hard to determine, because these 2 patients inhaled cocaine a few times weekly. Nevertheless, clinical symptoms appeared a few hours after they inhaled cocaine that had been purchased for the first time from a new dealer, whereas previous samples of cocaine had been purchased from dealers who had supplied the drug to the patients previously. The very mild symptoms that were confined to a few cranial nerves and the gastrointestinal area may imply that a minute amount of toxin was inhaled with the cocaine.

The diagnosis was established using a bioassay to detect botulism toxin. Sinus aspiration can be performed for patients with evidence of sinusitis [7]. Any material obtained from aspiration should be cultured anaerobically to isolate *C. botulinum*. A real-time PCR assay has been proposed but needs to be evaluated with a greater number of patients [11].

Differential diagnoses should be carefully considered [2, 9]. Even if a diagnosis of botulism is usually established on the basis of clinical symptoms, other diseases can be confused with it. Guillain-Barré syndrome follows an acute infection, presents in 95% of cases as an ascending paralysis, and never occurs in outbreaks. Myasthenia gravis should be considered, and the Tensilon test should be administered when in doubt, even if borderline Tensilon test results have been reported for patients with botulism [9]. No history of shellfish consumption that would suggest paralytic shellfish poisoning was reported by these patients. Cutting agents, such as atropinic derivates, could have been introduced into the cocaine. In our 2 cases, the association of ophthalmoplegia and constipation led to the diagnosis of botulism for the first patient, and the second case was identified through specific questioning of the index case patient about other possible illnesses.

Botulism should be considered in drug users who present with cranial nerve palsy, dry mucosa syndrome, dysphagia, confusion, or all of these symptoms, even if the patients have not injected drugs. Epidemiologic research is needed, because the number of cases could increase with the increasing numbers of illicit drug users. Thus, all cases of botulism should be reported to the appropriate government agency.

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