Botulism is a rare neuroparalytic disease caused by a potent neurotoxin produced by *Clostridium botulinum*. There are different clinical types of botulism. Early diagnosis of the condition is essential for effective treatment. We report a case of food-borne botulism in identical twins characterized by severe initial oral involvement and a review of the literature about the condition. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:e15-e18)

Clinical features as well as medical history and physical examination are essential in the early diagnosis and management of this potentially lethal disease. However, because of the rarity of the disease, several differential diagnoses are usually provided by health practitioners. Interestingly, acute hyposalivation and dry mouth are often included in the early clinical features of botulism.1-4

We report a case of food-borne botulism in identical twins characterized by severe initial oral involvement, and we review the literature about the condition.

**CASE REPORT**

A 30-year-old man (A.L.) without any known underlying disease was referred to the Dentistry Unit, University of Parma, by the Emergency Services for a diffuse xerostomia associated with dysphagia. Signs and symptoms had been present for 2 days, and the patient had difficulty in eating and speaking. He also reported blurred vision.

At clinical examination the oral mucosa appeared extremely dry, sticky, and inflamed. The amount of saliva had decreased (0.1 mL/5 min) and there was a foamy white...
coating on the tongue as well as the mucosa. The lips were dry and cracked, and signs of angular cheilitis were also present. These features were also diffuse through the pharynx (Figs. 1 and 2).

The patient’s medical history revealed past acute viral hepatitis caused by hepatitis B virus (HBV), but blood tests excluded the presence of a chronic infection. He was a non-smoker and did not report any alcohol, drug, or other substance abuse. In the clinical interview, he reported that both he and his identical twin (who were university students from Southern Italy sharing a flat in Parma) were affected by abdominal pain and difficulty in eating. Their general practitioner had prescribed anti-acid tablets for 4 days (Gaviscon 500 mg + 267 mg 3 times per day) with complete symptom resolution. However, they both suddenly complained of oral dryness associated with dysphagia and the need for frequent ingestion of fluids. They also stated that they were experiencing stress in that period because they had not informed their family, who were waiting for the graduation ceremony, that neither of them had passed their university examinations.

The patient’s twin (A.C.) had a more severe ocular involvement (anysocoria, diplopia, photophobia, blurred vision) and nausea associated with the above-reported oral symptoms. In addition, he complained of generalized weakness. A cranial computerized tomographic scan was performed and revealed no anomalies. He was then hospitalized at the Neurologic Unit, University of Parma, for an in-depth neurologic evaluation. All the hematologic, toxicologic, and virologic examinations performed were negative apart from positive HbsAg, anti-HbcAg antibody, and anti-HbeAg antibody, revealing a chronic status of HBV infection of which the patient was already aware.

The neurologic examination showed a reduced bilateral photomotor reflex to direct and consensual stimulus. No extraocular muscle dysfunction was observed on examination, but the patient experienced diplopia. In addition, a low hyposthenia under resistance (4/5) was recorded on the superior right arm with difficulty in fine motility.

In addition, to exclude any structural and/or inflammatory diseases of the central nervous system, a series of neuroimaging (cerebral and cervical magnetic resonance imaging with and without contrast agent) and cerebrospinal fluid analyses were also performed, but no alterations were detected.

During hospitalization, autonomic signs became evident, with constipation, xerostomia, and xerophthalmia in both of the twins, suggesting the hypothesis of food-borne botulism. An electrophysiologic study was performed in both patients, showing an incremental response to high-rate stimulation, especially at rates >20 Hz, after repetitive nerve stimulation testing of the abductor digiti minimi. Single-fiber electromyography in the frontal, orbicular oculi, and extensor indicis proprius revealed an incremental jitter with block. To confirm the botulism, serum and feces from both patients as well as food samples (home-made preserved vegetables eaten by the twins in the days before hospitalization) were submitted to the Istituto Superiore di Sanità. Neurotoxigenic Clostridia was detected in fecal samples in one of the 2 patients (A.L.) and in spinach and mushrooms in olive oil that both had previously eaten. Results of toxin detection in serum, feces, and food samples were negative.

Due to the limited neurologic symptoms and the improved photomotor reflex as well as constipation, no systemic therapy was administered to the patients. Topical applications of salivary substitutes and antimycotic rinses (nystatin 100,000 U 4 times per day) were given to both the patients to reduce oral dryness. Two months from the diagnosis electrophysiologic studies performed in both patients were normal.

During hospitalization an anxious personality profile correlated with particular stressful events was evident for one of the twins; he was then referred to the Psychiatric Unit for further evaluations.

**DISCUSSION**

The classic and oldest recognized form of botulism occurs after the ingestion of food (usually inadequately processed food) contaminated with a preformed neurotoxin produced by C. botulinum. Interestingly, alimentary factors promoting bacteria growth and toxin elaboration are an anaerobic milieu, a pH of <4.6, low oxygen tension, high water content, and a temperature of 4-121°C. Initial signs and symptoms of the disease
develop within a few hours (12-36) of the ingestion of the contaminated food mainly with gastrointestinal symptoms (nausea, vomiting) that may precede neurologic features. Home-canned foods constitute the major source of intoxication, particularly where a tradition of consuming home-made and fermented food is still present (e.g., Alaska and Eastern Europe). Most cases are sporadic, but outbreaks may occur, usually involving 2-3 patients. In the USA, a total of 153 cases of botulism were reported by the Centers of Disease Control in 2008 and 18 (12%) were accounted for by food-borne forms. In Italy, the last outbreak was reported in 1996, when dozens of people were hospitalized all over the country due to botulinum intoxication; the vehicle was a batch of mascarpone cheese, commercially produced in northern Italy, traditionally used for the “tiramisù” dessert. However, owing to the Italian tradition of preparing home-made preserved vegetables, food-borne botulism remains a public health problem, with a mean of 20-30 new cases reported every year. A total of 300 cases between 1996 and 2006 have also been reported by the Italian Health Ministry.

Infant botulism results from the absorption of toxins produced in situ by *C. butulinum* that can temporarily colonize the intestinal tract of some infants <12 months of age. This variant of the disease is currently the most common form of botulism in the USA (111 new cases in 2008). Colonization may occur because the infant bowel tract lacks both protective bacterial flora and *Clostridium*-inhibiting bile acids found in the normal adult intestinal tract. Epidemiologic data has implicated honey consumption as a risk factor for the disease, with microbiologic surveys reporting that honey accounts for ~20%-25% of cases.

A form of adult intestinal toxemic botulism has also been identified, which is caused by the absorption of toxins produced in situ by rarely occurring intestinal colonization in adults. Wound botulism is caused by the contamination of wounds with *C. butulinum* spores that proliferate and produce toxins locally. Until the 1990s the condition was considered to be extremely rare; lately, most cases of this type of botulism have been reported in injected drug users in association with subcutaneous tissue injection or “skin-popping” (i.e., injection of drug into tissues instead of veins). Clinical features are similar to those reported for the foodborne type, apart from the absence of gastrointestinal symptoms. Usually, a small abscess at injection sites in a drug abuser combined with compatible clinical signs are essential elements to establish the correct diagnosis.

All forms of botulism may result in a pure motor paralysis, because only peripheral cholinergic synapses are affected and clinical manifestations of the disease are due to a progressive neuromuscular blockade. However, the early neurologic features include difficulty in swallowing followed by ocular anomalies (ptosis, diplopia, blurred vision) and proximal muscle weakness. Autonomic symptoms include anhydrosis with severe dry mouth and throat (often associated with mucosal erythema and pain) and postural hypotension. The disease may rapidly progress in severe cases, with involvement of respiratory muscles determining respiratory failure. Oral manifestations, particularly acute hyposalivation and xerostomia, are usually recorded as first neurologic signs and symptoms of the diseases. Interestingly, a study on the detection of disease outbreaks caused by biowarfare agents (such as botulism) by the use of oral diseases has been recently published.

Treatment of botulism consists mainly in advanced supportive care with particular attention to respiratory status and administration of a botulinum antitoxin that can arrest the progression of the paralysis and decrease its duration. However, the antitoxin should be given early in the course of the disease (ideally <24 hours after the onset of symptoms), because of its ability to neutralize only toxin molecules that are not bound to nerve endings. Furthermore, a series of adverse side effects (e.g., anaphylaxis, hypersensitivity reactions) are associated with antitoxin administration.

Botulism diagnosis may present difficulties, especially if it occurs as a sporadic case or if the relationship between foodstuff ingestion and symptom development is unclear.

In the present case report, we describe a diffuse oral involvement due to botulism infection. In particular, one of these 2 young patients complained during the first clinical examination of an extremely dry mouth characterized by an acute appearance without any apparent connection with known underlying disease or drug administration.

As reported, botulism is a rare condition and does not represent the first disease to eliminate when trying to establish the correct diagnosis, especially for a such sporadic (isolated) case. In addition, the importance of the stress experienced by the twins was underlined by both the patients and their family, which led the doctors to first consider the possibility that the patients had taken recreational drugs or a substance affecting the autonomic system, with possible side effects on salivary glands as well as the ocular system. This hypothesis was formed on the basis that the difficulty of informing the family about their failure to graduate may have pushed them to create a state of illness to facilitate the confession. For this reason, each patient was interviewed separately with only the doctor present and the hospitalized twin also underwent toxicologic examina-
tions. As reported, all of the evaluations gave a negative response.

Differential diagnosis of botulism included a series of neurologic disorders (such as Guillain-Barré syndrome, myasthenia gravis, tick paralysis, diphtheritic neuropathy). The combination of neurologic findings and specific laboratory tests usually provides highly sensitive clinical diagnosis pending laboratory confirmation. As reported in this case, an electrodiagnostic study may be particularly helpful in confirming the suspected clinical diagnosis while awaiting microbiologic and bioassay tests.\textsuperscript{1,2,21,22}

Dentists are not usually involved in the diagnostic process of botulism, because oral involvement is clearly associated with other more evident clinical signs that are often more characteristic of the pathology. However, as in this case, sometimes the presence of particularly severe oral manifestations, in combination with other data, may suggest that dentists, as well as oral medicine practitioners, could assist other health specialists in the detection of rare diseases such as botulism.

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REFERENCES

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