Botulism – A brief review based on a case

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ABSTRACT
Foodborne botulism is a serious, acute disease with digestive and neurological symptoms. It results from ingestion of food, containing toxins formed by Clostridium botulinum. There has been an increase in the incidence in Portugal and Spain. The authors report a case of botulism that culminated in the identification of a common origin for four other cases. It was a patient of 47 years with a clinical picture of diplopia, dysphagia, fever, dizziness, blurred vision, dry mouth and constipation and gastrointestinal complaints. He ingested smoked product 48-72h before resorting to the emergency room. He was interned for study. Changes in EMG compatible with presynaptic neuromuscular block were found. Serum toxin and suspicious food product were isolated and identified. He recovered completely from the clinical picture with support therapy and physiotherapy.

The authors intend to alert to a disease that although not rare, presents difficulties in the diagnosis, being this one essentially clinical with suggestive epidemiological context, confirmed by electromyographic changes and identification of the toxin.

INTRODUCTION
Botulism is a flaccid neuroparalytic disease induced by a potent toxin produced by the bacterium Clostridium botulinum. Justinus Kerner, in 1820, recognized for the first time the association between the occurrence of paralytic disease and the ingestion of sausages, in an outbreak that affected 230 people1.

Six epidemiological types are described: food botulism, wound botulism, infant botulism, botulism of indeterminate classification, inhaled botulism, and iatrogenic botulism.

Some strains (A and B) produce proteolytic enzymes that spoil contaminated food leaving an unpleasant appearance, odor and taste. Eight types of toxins are described: A – H. Toxins A, B, E and, rarely, F, G, H cause disease in humans. Unlike the spores (destroyed if T.ª> 120ºC), the toxin is sensitive to the heat, being destroyed at temperatures ≥ 80ºC2-3.

CLINICAL CASE
A 47-year-old caucasian man recurred to the emergency room (ER) due to nausea, food vomiting, diarrhea and fever (Tª: 38ºC). He was discharged with the diagnosis of acute gastroenteritis and medicated with ciprofloxacin (750mg, 12 / 12h) and Saccharomyces boulardii. The next day he started with blurred vision, diplopia, dysphagia for liquids and sensation of abdominal distension, resorting again to the ER. He presented without nausea, vomiting, diarrhea or fever. He had intaked smoked products (“alheiras” and chorizo) in the previous weekend (48-72 hours before admission).

In the ER, he was hemodynamically stable and afebrile. He presented conscious, cooperative and oriented; with mydriatic pupils, poorly reactive to light; he was closing the left eye to avoid the discomfort caused by diplopia; he had no changes in facial sensitivity, no facial paresis. He had symmetrical elevation of the palate, dysphonia, but without aggravation of dysphonia with fatigability maneuvers. He had no change in sternocleidomastoid muscles and trapezoids. No deviations of the tongue in the protrusion were seen or motor difficulties or changes in limb or trunk sensitivity. He presented flexion in the cutaneous-plantar reflex, bilaterally. No dysmetria was seen. The gait was normal and had no dysphagia for liquids and solids.

He was stained and hydrated; without signs of respiratory distress; Abdomen was soft and depressible, painless to palpation, with no defense; without peripheral edema.

The analytical study had no significant abnormalities. The LCR from lumbar puncture was rock water type and values were in the normal range. Chest X-ray, abdominal ultrasound, brain-CT and brain MRI were also performed and showed no significant changes.

He was evaluated by Ophthalmology that diagnosed bilateral paresis of the third cranial nerve. He was also evaluated by Neurology who placed the diagnostic hypothesis of Miller-Fisher Syndrome. Human immunoglobulin was administered for three days. He was then admitted to the Internal Medicine Service. An electromyography was performed and revealed alterations compatible with presynaptic neuromuscular block. He was transferred to UCIM for respiratory monitoring. Due to the suspected botulism the “Instituto Ricardo Jorge” was contacted and the serum was sent for toxin research. The case was signed to health delegate for attempted recovery of suspect food samples. Despite the strong suspicion of food botulism, it was decided not to administer botulinum antitoxin (evolution of symptoms greater than 24-48 hours). Four days after admission the diagnosis of Botulism was confirmed, with a positive type B botulinum toxin in serum.

The patient recovered from paresis of the third pair, with resolution of dysphagia for liquids or solids and progressive improvement of dyspnea with kinesitherapy. He was discharged after 21 days of hospitalization oriented to the external consultation of Internal Medicine.

Five cases of food botulism were reported by the “Direção Geral da Saúde de Portugal” in the same month, laboratory confirmed, without death records. A common origin associated with the ingestion of smoked food products (“alheiras”) was identified. Shortly thereafter, they were withdrawn from the market.

DISCUSSION
All forms of botulism result from the absorption of botulinum toxin into the circulation. It binds irreversibly to synaptotagmin II at the neuromuscular junction, preventing the release of acetylcholine, conditioning dysfunction both in the muscle
and in the autonomic nervous system. The recovery of synaptic function requires the regeneration of a new presynaptic terminal, a process that may take as long as 6 months. The adrenergic synapses are not affected by the toxin and the blood-brain barrier does not allow its passage4,5.

Epidemiology

Although considered to be rare and serious, there has been an increase in incidence in Portugal since 1970. In 2004, four cases associated with the consumption of ham and one case of canned tuna were identified. In 2009, one case related to canned sausages was reported and finally in 2015, five cases were confirmed, by consumption of “alheiras” (includes case described)5.

In Spain, in the period from 1997 to 2015, 154 cases of botulism were identified, most of them associated to foodborne botulism6.

Clinical manifestations

The incubation period is variable, from 12-36h up to one week. The clinical picture can range from mild complaints to death within the first 24 hours. It is associated with prodromes: nausea and vomiting, abdominal pain, diarrhea, dry mouth and dysphagia, which may remain throughout the evolution of the disease. The involvement of the cranial nerves is frequent: blurred vision (secondary to fixed dilation of the pupils and paralysis of the cranial nerves III, IV, VI); diplopia; nystagmus; ptosis eyelid; dysphagia; dysarthria and weakness of the facial mime muscles. There is a decreasing and symmetrical muscle weakness that usually progresses to the trunk and upper limbs and subsequently to the lower limbs. Respiratory difficulty due to diaphragmatic paralysis and / or upper airway compromise is often seen and also urinary retention, constipation and hypotension7-11.

Electromyography may suggest the diagnosis: low amplitude M waves; short low-voltage explosions in motor units; excessive potential for action; repetitive nerve stimulation is associated with a significant increase in the M. wave amplitude. Leukocyte count, cytobacterial study of CSF and VS are generally normal. The lumbar pucture for the exclusion of meningitis or encephalitis is not generally indicated2,5,9.

Differential diagnoses should include: Myasthenia Gravis, Lambert-Eaton myasthenic syndrome, Guillain-Barré, Neuroborreliosis, Poliomyelitis, heavy metal poisoning and stroke. The presence of toxin in the blood confirms the diagnosis and is detectable up to twelve days after ingestion. Samples of feces, vomit, and suspect foods may also reveal the toxin, which together with clinical manifestations, can establish the diagnosis. In Portugal, the samples are sent to “Instituto Ricardo Jorge” (anaerobic culture medium).

Treatment

All patients with signs, symptoms and suspected botulism should be hospitalized and monitored, monitoring signs and symptoms of respiratory failure, which is the main cause of death. Early intubation and mechanic ventilation drastically reduces the risk of death. Orotracheal intubation is recommended if there is respiratory insufficiency / loss of airway patency or vital capacity <30% of predicted value.

Heptavalent equine antitoxin is used in children > 1 year and adults (human immunoglobulin for infant botulism, children <1 year). It contains antibodies to seven of the eight toxins identified. If botulism is suspected and symptoms are progressing, it should be administered as soon as possible (24-48 hours), and should not be delayed by the lack of analytical results. It may cause sensitization and anaphylaxis and should only be given to patients at high risk of disease.
In Portugal, most of the cases described are associated with the ingestion of type B toxin and were associated to mild symptoms. The use of antitoxin was not necessary.\textsuperscript{2,5,7}

**Prevention**

Appropriate techniques for preparing homemade preserves allow the spores to be destroyed: cooking times, pressure (using “pressure cookers”) and temperature. Damaged conserved products should be avoided. The botulinum toxin is highly thermolabile, so it is recommended to cook the homemade preserves at 100 °C for 10 minutes before being consumed.

**Prognosis**

Botulism usually requires hospitalization for one to three months. The mortality ranges from ≤5-8% and <1% in infant botulism and <4% in food. Wrong/late diagnosis and toxin A are factors of worse prognosis. Patients precociously hospitalized and under respiratory monitoring usually recover completely. If the patient has moderate illness, the symptoms usually resolve within the first 3 months. Those who have severe disease and require prolonged mechanical ventilation, may sustain neurological deficits for years.\textsuperscript{10-11}

**REFERENCES**