Notes

# Remembering botulism

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**Abstract**

Based on her own case, the author makes some comments about food-borne botulism, highlighting five main issues: 1) botulism is not as rare as we used to think; 2) its mortality is far from being as high as we believed in; 3) not only typical industrial or home canned food is related to this disease; 4) its diagnosis is rare and difficult, mainly because it's not considered; 5) patients affected by botulism are frequently labeled with other diagnoses.

Keywords: clostridium, botulism, spore, toxin, acetylcholine, accommodative paresis, diplopia, dysphagia, respiratory failure.

Clostridium botulinum, the organism responsible for botulism, was discovered by Prof. Emile van Ermengem in 1896, while he was investigating a mysterious disease that had struck a group of musicians of an orchestra, after they had eaten ham, killing tree of them.[1]

This spore-forming, gram-positive anaerobic bacillus can cause three different types of infections: food poisoning in adults through the ingestion of food products contaminated with a pre-formed toxin; infection through contaminated wounds; and infant botulism caused by the ingestion of spores that produce toxin in the infant's intestine.[1,2]

Eight types of toxins are currently known (A, B, Ca, Cb, D, E, F, and G), but only serotypes A, B, E and very rarely F, contaminate human beings.[2]

The toxin irreversibly binds to the cholinergic receptors located in the presynaptic membrane of the nerve terminals, destroying them and preventing the release of acetylcholine. Recovery is only possible through the formation of new nerve terminals, which explains the persistence of symptoms for several weeks or months.[1]

The short introduction above refers to a case I experienced myself around three years ago, which made me rethink my ideas about this disease.

In fact, about twenty years ago, during my general intern practice, I attended some Departments of Internal Medicine and Infectious-Contagious Diseases. I recall having the impression, at that time, that botulism was a very serious intoxication, caused by an extremely potent toxin produced by Clostridium botulinum, which was generally found in spoiled home-made preserves, and which would almost always result in death due to paralysis of the respiratory muscles. It was considered a rare disease, and the probability of seeing a patient with botulism was extremely remote, therefore this diagnostic hypothesis was highly theoretical.

A few years later, more precisely, in 1987, in the final exam of my specialization in Ophthalmology, one of the members of the jury asked me to talk about the causes of paralysis of accommodation.

I remember mentioning, among other causes, botulinum intoxication. Nevertheless, I still had the idea that botulism was a disease that was only cited in books, but did not exist in the real world, as no one had never actually seen it for real.

Therefore, when I had an episode of intestinal cramps, diarrhea and vomiting about three years ago, I thought I had a simple gastroenteritis caused by one of the foods I had consumed on the previous day. And when, on the following day, I started having dysphagia and intense epigastric pains that were making my respiratory movements difficult, the most probable hypothesis was a perforated duodenal ulcer or pancreatitis. I underwent an abdominal echogram which revealed no abnormality, and an endoscopy, which revealed only mild gastritis, to which my complaints of dysphagia were attributed, albeit without some reticence. However, my mucosa were becoming increasingly drier and I was constantly thirsty, so that I had to keep a bottle of water with me at all times, which was soon empty. My colleagues and I were not able to identify my complaint, and I began to suspect there might be an abnormality with my neurotransmitters, particularly the acetylcholine neurotransmitter. Also, my bowel had stopped working

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properly, which caused me no great concern for the first two or three days, but after a week, I started to think that such a marked immobility was not normal. In fact, I had paralytic ileus, for which condition no reason could be found. It was only after around eight days after the initial symptoms that I realized I was not able to read a newspaper or some medical journal I was trying to read, as my vision was blurry and I could only read with the aid of a magnifying glass. At that moment, that question from my final specialization exam suddenly popped into my head: "Tell me the causes of paralysis of accommodation". Within seconds, although still incredulous, the word BOTULISM came to my mind. Little by little, the pieces of this puzzle started to come together and everything began to make sense. The diagnosis was never confirmed by laboratory tests, as only one of the three mice injected with my blood proved to be frail for several hours, which was hardly surprising, as we will see below. However, the symptoms persisted for around three months, and I only started to gradually improve after that time, which made my personal and professional life a little complicated.

It was this curious, unexpected and almost fatal episode that made me reflect on and start to pay special attention to botulism. After carrying out bibliographical research on the topic, I came to some curious conclusions, practically of which contradicted with the ideas I had held so far, and which I think most doctors still hold concerning this intoxication, namely:

1. Botulism is not as rare a disease as is generally believed. In fact, in recent years, several articles have been published on outbreaks or, more accurately, foci of botulinum intoxication, in the United States and several European countries, including England, France and Italy. These foci generally affect groups of people, whether family members or not, who have ingested the same contaminated food, either at home or at the same restaurant. Between 1965 and 1990, a hundred and eight cases were seen at the Department of Infectious-Contagious Diseases of Poitiers University Hospital.[3] In 1985, in Vancouver, Canada, thirty-six cases of botulism were diagnosed in people who had eaten food from the same restaurant, in the space of six weeks.[4] In 1989, the largest outbreak of botulism was recorded in the Great Britain, affecting thirty-six people.[1] In 1993, an outbreak of botulism affected eight people in a small town in Georgia, United States.[5] Between December 31, 1993 and January 12, 1994, twelve cases of botulinum intoxication were diagnosed in the town of Sion, Switzerland, after individuals had eaten ham.[6]

2. Although Clostridium botulinum produces the most potent toxin ever known[1] and although it takes only 1g to cause the deaths of seventeen million people,[7] botulism is far from being a mortal disease, since the different pathogenicity of the various toxins that most frequently affect human beings (serotypes A, B and E) can produce varied symptoms with different degrees of severity. While serotypes B and E generally cause moderately severe symptoms, serotype A seems to cause the most serious forms of the disease, almost always requiring respiratory support, and sometimes causing death.[5] In the last thirty years, the use of anti--toxin and, above all, assisted ventilation, has reduced the mortality rate from 60% to 25%.[2]

3. The vehicle of the toxin is far from being limited to the traditional home-made preserves or industrial canned goods. Outbreaks of botulism have been described after the ingestion of varied foods that include yogurts, smoked or salted meat and fish, garlic butter, cereal, honey, uncooked fish, shellfish, cheese, etc..[1,4,6,8] The common attribute of all these foods is the fact that they were not cooked at a temperature sufficient to kill off the toxin (boiling at 100ºC for ten minutes) or to destroy the spores that are extremely resistant and must be exposed at temperatures of around 120ºC for around thirty minutes.[9]

4. Botulism is still a rarely diagnosed disease, for two essential reasons. First, diagnoses are usually established for diseases that are thought of by doctors, and botulism is a disease that is almost never thought of, perhaps because it is still believed to exist only in Medical books. Second, it is a disease that is difficult to diagnose because: there is an incubation period that can range from a few hours to ten days or more;[4] the symptoms may not be very explicit and may be limited to simple gastroenteritis, moderate dysphagia, diplopia or difficulty reading, and may therefore be attributed to other, more recent pathologies. Also, in some cases, respiratory insufficiency can develop so quickly that timely diagnosis is impossible.

5. The initial diagnosis that is most frequently attributed to patients who are later diagnosed with botulism is related to the main mentioned symptoms: viral or bacterial gastroenteritis (gastrointestinal symptoms), diabetes mellitus (intense thirst and con-

sequent polyuria), Guillain-Barré syndrome (flaccid paralysis), transient vascular stroke (diplopia, dysarthria, dysphagia and other pareses), myasthenia gravis (ptosis and generalized muscle weakness), diphtheria (dysphagia and dysphonia), astigmatism or glaucoma (blurred vision), psychiatric disorders, etc. Some cases were reported of patients with paralytic ileus who underwent exploratory laparotomy to clarify a possible intestinal obstruction.[1,2,4,8]

Due to the five points above, it is essential to make us rethink our attitude towards botulinum intoxication, since although rarely diagnosed, is surely far more common than is believed. Doctors should bear this disease in mind and pay attention to a group of signs and symptoms that can point to the diagnosis. In a patient with gastrointestinal symptoms, dry mucosa, dilated pupils and complaints of dysphagia, diplopia or blurred vision, it is essential to keep this diagnostic hypothesis in mind. An exhaustive investigation of all food consumed by the patient in the ten days prior to the onset of symptoms is essential. It is also important to find out whether the patient knows any other people with the same symptoms, and whether they ate the same meal. The fact that foods contaminated with this toxin taste and look normal, and the intoxication can occur by ingestion of even a tiny amount (the lethal dose = 1 mg/kg), means patients often fail to consider that they could have eaten contaminated food.[2]

Confirmation of this condition through laboratory tests is very difficult, since the toxin is only detected in 13% to 28% of the blood samples collected more than two days after ingestion of the contaminated food, and only 36% of the coproculture are positive if they are performed more than three days after ingestion of the toxin.[8] Because the incubation period is very long, laboratory confirmation is only obtained in around half of suspected cases. The diagnosis is, therefore essentially clinical, and the earlier it is established, the better, since the anti-toxin is only of use if it is administered before the toxin is irreversibly bound to the neuro-receptors.[1] Treatment should include support and monitoring measures, since the symptoms appear gradually and respiratory paresis can develop at a later stage.

In my case, everything indicated that the food responsible for causing me to go through such difficulties was no less than our 'loyal friend' - cod fish. In fact, on the eve of the initial symptoms, I recall I had tasted (surely a lot less than 1 mg) a salad made with various ingredients, among which was shredded, raw cod fish. My colleague from Instituto Ricardo Jorge, whom I contacted, had no doubts in confirming this hypothesis. It is known that the intestines of some fish and shellfish can be contaminated by type E toxin, deriving from the ingestion of contaminated plankton.[10] When these food products are consumed raw, or are not cooked at a sufficiently high temperatures, or for long enough to destroy the spores, they become an unsuspected medium of poison for human beings. In Portugal, where the habit of eating cod - cooked in the most varied ways - is deeply-rooted, special attention should be paid when eating the "harmless" raw cod fish salads that are so common in certain households and restaurants. ■

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