

# Foodborne botulism, a forgotten yet life-threatening disease: a case report

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**Abstract. – OBJECTIVE:** Botulism is a very rare disease in Switzerland, with less than one case per year, an incidence of 0.01 cases for 100,000 inhabitants. Indeed, over the past ten years, 9 cases have been reported to Public Health registry. Foodborne botulism (FB) is caused by ingestion of preformed botulinum neurotoxin. Characteristic features should be rapidly recognized, and prompt treatment should be administered to avoid further progression towards respiratory failure and death.

**CASE REPORT:** We report the case of a patient who developed gastrointestinal symptoms just after a sandwich consumption followed by rapidly progressive cranial nerve impairment, truncal muscle weakness in a descending pattern and respiratory failure requiring mechanical ventilation. The diagnosis of foodborne botulism was delayed due to differential diagnosis considerations. Specific antitoxin therapy was administered immediately after firm clinical conviction of botulism, without waiting for serologic results that later confirmed the diagnosis. As expected, muscle weakness recovery was slow, with persistent chronic deficits nine years later.

**CONCLUSIONS:** This case highlights differential diagnosis issues of botulism. These include acute neuromuscular disorders such as myasthenia gravis, Guillain-Barré syndrome, or tick-borne encephalitis. The importance of careful medical history and repeated clinical evaluation to avoid misdiagnosis can be lifesaving. Our case highlights the typical warning signs.

*Key Words:*

Botulism, Intensive care, Neuromuscular disorder, Muscle weakness, Neurotoxin.

botulinum neurotoxin. Contaminated food with this toxin results from incorrect food handling, most often homemade canned food. Early characteristic symptoms of FB are acute onset of ocular neurological deficits (diplopia, palpebral ptosis), bilateral symmetrical descending flaccid paralysis, without sensory deficit, in an alert and afebrile patient. If not recognized and adequately treated early, respiratory failure requiring mechanical ventilation may develop, leading eventually to death. Early administration of specific antitoxins cannot reverse the weakness already installed but can stop disease progression. Our case points out the diagnostic traps to overcome.

## Case Report

A man in his 50s with previous medical history of asymptomatic chronic hepatitis B, presented to the emergency department of Lausanne Hospital in 2013 with eyelid drop, double vision, slurred speech, marked drooling with difficulty swallowing and tracking objects, and progressive dyspnea. The symptoms had started 24 hours prior to admission within minutes after ingestion of a sandwich purchased at a fast-food shop. Initial symptoms were nausea along with several episodes of vomiting, headache, vertigo and horizontal diplopia. Temperature was 36.8°C, heart rate 90 bpm, blood pressure 125/80 mmHg, respiratory rate 28/min and oxygen saturation 98%. Neurological examination showed dysarthria, dysphagia, horizontal diplopia, bilateral palpebral ptosis, and right tongue deviation. Furthermore, he was unable to keep his head in upright posture. He had no motor or sensory deficit in limbs.

The basic metabolic panel, complete blood count and C-reactive protein were within normal

## Introduction

Foodborne botulism (FB) is a rare, potentially fatal illness, caused by consumption of preformed

limits. In the cerebrospinal fluid (CSF) analysis, glucose and protein levels were normal with no cells or microorganisms. Serology tests for Borrelia and Syphilis were negative. Brain magnetic resonance imaging was normal. Nerve conduction studies (NCS) were considered normal including repetitive nerve stimulation of 3 nerve-muscle couples of the bulbar region.

The patient was admitted to the intermediate care unit with a presumptive diagnosis of generalized myasthenia gravis (MG). A pyridostigmine test (60 mg Mestinon®) was performed with partial improvement of muscle strength after 1 hour, a slight increase in vital capacity (VC), but no effect on the bilateral ptosis. During the next 24 hours, despite intravenous infusion of 0.5 g/kg of immunoglobulins (Privigen®) and 60 mg of Mestinon® treatment every 3 hours, the patient developed a respiratory failure (RF) with VC decrease to 0.8 L and hypercapnia, requiring transfer to the Intensive Care Unit (ICU). He then presented a sudden respiratory arrest needing emergency intubation and mechanical ventilation: 2 sessions of plasmapheresis were then performed. The patient was fully awake and totally ventilator dependent. He was able to shake hands vigorously, to write and move his forearms and legs with no difficulty: muscle strength (Medical Research Council) scored 48/60. Strength discrepancy between limb and trunk muscles and rapid muscle weakness progression despite the recommended treatment for presumed MG prompted to reconsider this diagnosis. During repeated NCS, an abnormal reduction of the amplitude of motor responses of the median and ulnar nerves following stimulation at the wrist was recorded. However, the amplitude of the responses increased by 15% after a train of 10 repeated nerve stimulations at 30 Hz. These features were highly suggestive of a pre-synaptic block of the neuromuscular junction (NMJ), characteristic of botulism. Specific antitoxin was then immediately given without waiting for mouse inoculation testing results. The results for pooled serum testing for botulinum neurotoxin A/B/E were positive: unfortunately, due to a limited volume of remaining pretreatment serum, no further testing could be done.

The patient recovered slowly and returned home after 4 months in the ICU and 2 months of rehabilitation. Nine years later, he is still complaining of fatigability and difficulty breathing either when walking long distances, or when carrying heavy loads. Due to these limitations, he had to change his professional activity.

Public health office investigations revealed that the botulinum neurotoxin originated from a home-canned food, consumed a week prior to admission. Analyses in the fast-food shop were negative.

## Discussion

Botulism is a rare and almost forgotten disease: it can evolve over days without rising suspicion, being often misdiagnosed as MG or Guillain Barré syndrome (GBS). And yet, it requires urgent treatment that can limit disease progression and prevent persistent deficits or death. Our case illustrates the diagnosis pitfalls.

*C. botulinum* is a Gram positive, anaerobic, spore forming, rod shaped bacterium, which produces botulinum neurotoxins. It is ubiquitous, worldwide, on vegetables, fruits, in water and soil. There are 8 serotypes of toxins designated A through G with the more recent discovery of H: serotypes C and D produces only animal disease<sup>1,2</sup>.

According to their pathogenic mechanism, 6 forms of botulism are described<sup>3</sup>: FB, wound, infantile, adult intestinal, iatrogenic and inhalational botulism (the last 3 are anecdotic).

FB essentially occurs after domestic intoxication rather than with industrial food. Incorrect preparation of cans is responsible for the food contamination by the heat resistant spores of *C. botulinum*, which later germinate in the preserved food and produce toxin<sup>3</sup>. Incubation period varies from several hours to 2 weeks. Usually, symptoms occur within 12-36 hours with a range between 4-8 days. This extremely variable range contributed to initial misdiagnosis in our patient.

Clinical manifestations are due to neurotoxin firmly binding to a presynaptic receptor in the peripheral cholinergic ganglia and in NMJ, inhibiting neurotransmitter release. Peripheral cholinergic system involvement is predominant. The adrenergic system is later affected with limited clinical manifestations. Gastrointestinal symptoms, cranial nerve involvement with ophthalmoplegia, palpebral ptosis, dysphagia, dysarthria follows. Unreactive dilated pupils are present in 25% of cases and are helpful in distinguishing MG from botulism. The symptom triad most often found is acute onset of symmetrical descending flaccid paralysis<sup>4</sup>, involving the pharyngo-laryngeal muscles (the so-called "bulbar palsy"), with no sensory impairment and no fever. Table

I shows a diagnostic tool based on frequency of signs and symptoms present in confirmed botulism patients<sup>5</sup>.

A hallmark of botulism is the striking complete paralysis of upper trunk muscles with RF requiring invasive mechanical ventilation, with preservation of limb muscle strength, as observed in our patient<sup>5</sup>. Moreover, patients are alert, without any central nervous system or sensory impairment. Definite diagnosis is based upon identification of the toxin in different samples (serum, stool, vomits, contaminated food, and wounds). The results may take up to 4 days; therefore, the treatment should be administered promptly based only on clinical suspicion without waiting for laboratory confirmation<sup>3</sup>.

The recommended diagnostic workup aims at excluding other acute neuromuscular disorders:

- In GBS and its variants, paralysis is usually ascending and predominates in extremities. Tendon reflexes are abolished, and pain and sensory involvement increase by the stretching of the Lasègue maneuver. CSF shows isolated increased protein levels. In addition, NCS shows abnormalities of motor responses or prolonged latencies of motor and sensory evoked responses<sup>3</sup>.

- In tick-borne encephalitis, the disease manifests itself as meningitis, encephalitis or meningoencephalitis. Myelitis and spinal paralysis with bi-brachial paralysis are also possible. Pleocytosis is found in CSF. The main method of diagnosis is the detection of specific antibodies in patients' sera combined with typical clinical signs. NCS is normal, but signs of denervation may be recorded in the involved muscles<sup>3</sup>.

- A motor improvement following a Mestinon<sup>®</sup> or an edrophonium test is not specific to MG but can be observed in all peripheral motor disorders.

- The most sensitive NCS test for the diagnosis of botulism is the demonstration of a block of the NMJ at the presynaptic level: firstly, a train of low-frequency stimulation with decremental responses in amplitude is suggestive of a neuromuscular disease of pre- (botulism or Lambert-Eaton, congenital myasthenic syndrome: CMS) or post-synaptic (MG or CMS) origin. Secondly, the demonstration of an increase in amplitude of evoked motor responses ("potentiation"), by a train of high frequency stimulation is characteristic of a disease of the pre-synaptic junction<sup>3</sup>. The sensitivity of these features is high. However, if the responses are of very low amplitude or if the trains of stimulation are performed immediately after clinical examination, motor "potentiation" cannot be demonstrated. This was the case in our

**Table I.** Six symptoms out of the 12 "Dozen Ds" suggested by Horowitz et al<sup>5</sup> were present in our patient.

12 Symptoms	Present
Dry mouth	No
Diplopia (double vision)	Yes
Dilated pupils	No
Droopy eyes (ptosis)	Yes
Droopy face	No
Diminished gag reflex	No
Dysphagia (difficulty swallowing)	Yes
Dysarthria (difficult phonation/ whispered speech)	Yes
Dysphonia	No
Difficulty lifting head	Yes
Descending paralysis	Yes
Diaphragmatic paralysis	No

patient leading to initial misdiagnosis.

Antitoxin administration is the only specific available treatment<sup>3,6</sup>. Currently used antitoxin is a heptavalent botulinum antitoxin. This equine-derived immunoglobulin contains Fab and F(ab')<sub>2</sub>, neutralizing the 7 botulinum serotypes A through G, and possibly against H. Potential *C. Botulinum* and toxins in the intestine can be addressed by prescribing purgatives and enema.

The prognosis depends on the clinical presentation and prompt antitoxin administration. This toxin is the most potent known poison today: it affects synapses in an irreversible way so that synapses must regenerate, explaining the length of the recovery. The mortality rate varies between 4-8%, but series are too small to enable its exact evaluation. In a large cohort, poor outcome was observed in patients presenting with shortness of breath, impaired gag reflex and no diarrhea<sup>7</sup>. In the same cohort a decline in general health persisted after a median time of 4.3 years, with functional limitations, including fatigue, generalized weakness, dry mouth, difficult lifting objects, and exertional dyspnea<sup>5</sup>.

## Conclusions

Botulism should be evoked in an afebrile patient presenting with acute progressive descending symmetrical paralysis associated with unreactive pupils (1/4 of patients), blurred vision, ophthalmoplegia, palpebral diplopia, dysphagia, and preservation of sensory senses. Although FB may develop in clusters, isolated episodes are quite the rule nowadays. A high clinical suspicion and precise knowledge of neuromuscular diseases are mandatory for early diagnosis of this rare but potentially fatal disease.

The striking discrepancy between severe head and trunk paralysis and preserved peripheral limb muscle strength is a hallmark of progressing botulism. The challenge is to recognize and treat it early.

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#### Authors' Contribution

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