Clinically and electrophysiologically diagnosed botulinum intoxication

Dilcan Kotan,¹ Recep Aygul,² Mustafa Ceylan,² Yalcin Yilikoglu²

¹Sakarya University Medical Faculty, Sakarya, Turkey
²Department of Neurology, Ataturk University Faculty of Medicine, Erzurum, Turkey

Correspondence to

Dr Dilcan Kotan,
 Sakarya University Faculty of Medicine, Sakarya, Turkey;
 dilcankotan@yahoo.com

SUMMARY

In this case report, clinical and electrophysiological findings of 43-year-old female patient who developed *Clostridium botulinum* intoxication after consumption of home-made canned food are presented. Following the sudden onset of severe nausea and vomiting, diplopia, blurred vision, bilateral ptosis, weakness, speech and swallowing difficulties have developed and the patient declared that she has just tasted the canned beans after she had rinsed them several times. The case, where serological tests cannot be performed, was diagnosed clinically and treated with antitoxin immediately. During follow-up, consecutive nerve stimulation was performed and significant incremental response was observed. There was an improvement in symptoms within 2 weeks, and in 5 or 6 weeks the symptoms had disappeared completely. Electrodiagnostic studies revealed that the findings turned to normal. The case showed that immediate antitoxin treatment is life-saving even the diagnosis of botulinum intoxication is based on clinical findings.

BACKGROUND

Botulism is a rare, but fatal illness that can develop after oral ingestion of toxin made by the bacterium *Clostridium botulinum*.¹ After absorption into the bloodstream, botulinum toxin reaches to peripheral cholinergic synapses and binds to presynaptic nerve ending irreversibly at the neuromuscular junction and other peripheral autonomic synaptic receptors, where it inhibits the release of acetylcholine.^{2–3} While neuromuscular junction, peripheral ganglia, postganglionic parasympathetic nerve endings are affected primarily, CNS is not affected. Here, the elements of the mechanism responsible for neurotransmitter release are exposed to proteolytic activity of the toxin.^{4–5} Incubation period averages 18–36 h. Clinical findings include nausea/vomiting, abdominal pain, cranial nerve palsy (diplopia, dysarthria, dysphagia, ptosis and mydriasis), symmetric descending paralysis, respiratory failure, blurred vision, dry mouth, constipation, urinary retention and decreased deep tendon reflexes.^{6–7} Botulinum antitoxin has been shown to accelerate neuromuscular conduction by increasing the secretion of acetylcholine from the nerve endings.^{4–8} Function can be recovered by the sprouting of nerve terminals.⁹ Electrodiagnosis tests are helpful for diagnosis. Nerve conduction studies show normal amplitude and latency of sensory action potentials. Repetitive stimulation at 20–50 Hz shows incremental response for most cases.^{10–11} Electromyography is a suitable diagnostic method for the confirmation of the diagnosis in early diagnosis and in cases when a serological examination cannot be conducted. This study presents a 43-year-old female patient who

developed botulism after ingesting a grain of home-made canned beans steeped in water, showed significant incremental response in EMG and recovered completely after the application of antitoxin.

CASE PRESENTATION

A 43-year-old, right-handed woman presented with a 2-day history of nausea and severe vomiting. The next day she had a pain in her throat and arm, weakness in arm, difficulty with swallowing and speech disturbance, and the other day she developed double vision. She stated that 3 days ago she had washed the homemade canned beans several times because of bad smell and steeped in water, then tasted and gave up eating. Neurological examination at her presentation revealed that she was fully conscious, the speech was hypophonic, the uvula was in the midline but gag and swallowing reflexes were impaired, dysphagia was present, pupils were 5–6 mm in diameter and light reflexes were weak, horizontal eye movements were 2–3 mm whereas vertical movements were completely limited, the ptosis was present at the level of the right pupil and in the middle of the left pupil (figure 1), both orbicularis oculi muscles were weak, the tongue moved just up to the mouth commissure, muscle strength was 4/5 in the neck flexor, 4/5 in the proximal muscles of the upper and lower extremities and 4 +/5 in the distal of the upper extremities, plantar responses were flexor and ve DTRs were hypoactive. The patient's personal and family medical history was unremarkable. The patient was diagnosed as food-borne botulinum intoxication based on history and clinical findings, and poison control centre was called to provide antitoxin. Despite the patient being fully conscious, she was monitored in intensive care unit due to the lack of gag and swallowing reflexes, oral intake was stopped in order to prevent aspiration, and parenteral nutrition was started. Botulinum antitoxin was obtained after 12 h, and after the application of the test dose without any reaction, two doses of antitoxin were administered as 500 ml with slow intravenous infusions 8 h apart. Six days after the onset of neurological symptoms, electrodiagnostic studies showed that sensory nerve conduction was normal, motor nerve CMAP amplitudes were slightly lower and there was more than 50% increase in the amplitudes after 10 s of maximal muscle. Consecutive ulnar nerve stimulation with bipolar surface electrodes applied on abductor digiti minimi muscles showed aggravated incremental response on the high frequencies (20–30 Hz; figure 2). Our diagnosis was supported electrophysiologically as well as by clinical findings in this case where serological tests cannot be done. At 15 days after treatment the patient had

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Figure 1 In the first examination of the patient bilateral ptosis and near total ophthalmoplegia were observed.

improvement and she totally recovered in 5–6 weeks (figure 3). In our case, the fast recovery starting from the second week was thought to be related to less amount of toxin and an early treatment with antitoxin.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of botulism includes Guillain-Barré syndrome, myasthenia Gravis and Lambert Eaton myasthenic syndrome (LEMS) that cause acute flask paralysis.

TREATMENT

The only specific treatment for botulism is administration of botulinum antitoxin.

DISCUSSION

The botulinum toxin is the most potent toxin known in the world.^{12 13} The *C botulinum* bacteria were found in 1895 by Emile Van Ermengem, and it was found in 1949 that the toxin blocks the neuromuscular junction.¹⁴ The botulinum intoxication develops as a result of intake of previously developed toxin through the foods prepared under improper conditions. In our case, the intoxication findings developed after tasting a spoiled home-made canned food.

In the USA, during 1990–2000, the median number of food-borne botulism cases per year was 23 (range, 17–43 cases). Most cases are sporadic (ie, they are not part of outbreaks); outbreaks are typically small, involving two or three persons. Nevertheless, outbreaks caused by commercial or restaurant-prepared foods do occur.¹⁵ As our case is the only individual who ate the canned among the family, it is a sporadic one.

Guillain-Barré syndrome is a relatively common, inflammatory demyelinating polyneuropathy of unknown aetiology.¹⁶ Typical Guillain-Barré syndrome is associated with motor weakness. It begins as proximal lower-extremity weakness and ascends to involve the upper extremities, truncal muscles and head. In our case, Guillain-Barré syndrome was not considered, because the initial symptoms of nausea and vomiting had started after the ingestion of canned food, cranial nerve involvement

was evident and the motor weakness was not progressive and significant.¹⁷

Myasthenia Gravis is an immunological disorder of neuromuscular transmission in which muscle weakness results from an autoantibody-mediated depletion of acetylcholine receptors at the neuromuscular junction.¹⁸ The edrophonium test shows an unequivocal positive response. The symptoms usually become apparent within 2 years. The disease is treated with cholinesterase inhibitors (pyridostigmine).¹⁹ In our case cholinesterase inhibitor (neostigmine) was administered, but since no signs of recovery have been observed, and the onset of symptoms was sudden and did not show any fluctuation, the diagnosis of myasthenia gravis was not considered.²⁰ LEMS is an important diagnostic challenge at this point. LEMS is a myasthenia-like syndrome which does not involve ocular and bulbar muscles, but is associated with weakness in extremities.^{19 21} LEMS is common in men with intrathoracic tumours, and the lack of an underlying cancer and sudden onset of the disease has made us move away from this syndrome.²²

Botulism included characteristic EMG findings. Decremental response to repetitive nerve stimulation at low frequency (3 Hz) facilitated response to repetitive nerve stimulation at high frequencies (10–50 Hz) and low compound muscle action potential (CMAP). Motor nerve CMAP amplitudes of our patient were slightly lower, and there was more than 50% increase in the amplitudes after 10 s of maximal muscle and consecutive ulnar nerve stimulation showed aggravated incremental response on the high frequencies (20–30 Hz).

Botulism, although very rare, causes high morbidity and mortality.²³ When gastroenterological and neurological findings are observed after the ingestion of food, especially botulinum intoxication should be considered and treatment should be started without any delay.²⁴ Antitoxin can arrest the progression of paralysis and decrease the duration of paralysis and dependence on mechanical ventilation. Antitoxin should be given early in the course of illness, ideally <24 h after the onset of symptoms,²⁵ because antitoxin neutralises only toxin molecules that are yet unbound to nerve endings. Animal experiments confirm this relationship.²⁶ Administration of one vial of botulinum antitoxin produces serum levels of toxin type-specific antibodies capable of neutralising serum toxin concentrations manyfold in excess of those reported for patients with botulism.

Varma *et al*²⁷ have reported that the mortality rate of 706 patients who received in-patient antitoxin administration with food-borne botulism diagnosis between 1980 and 2002 was 8%. The mortality rate reported due to botulinum intoxication ranges between 5% and 15% in the literature.⁷ It has been reported that there was not observed any mortality in 209 patients that were received botulism diagnosis and administered with antitoxin in an epidemic in 2006 in Thailand.²⁸ Persons who may have been exposed by consumption of implicated foods should be observed closely, and if they develop symptoms compatible with botulism, they should be treated with antitoxin immediately. Experimental evidence concerning the amount of circulating antitoxin needed to counteract botulinum toxin poisoning by antitoxin therapy is not fully documented. The outcome of treatment depends, as it does in other comparable

Figure 2 Evident incremental response on the high frequencies (20–30 Hz) with consecutive nerve stimulation.

Figure 3 The examination performed in the second week showed an improvement in ptosis and eye movements.

conditions, largely on the time interval elapsing after the onset of symptoms before the peak of absorbed antitoxin is reached. This principle is illustrated in reported animal experiments.²⁹

In order to ensure the quickest possible neutralisation of all toxin in the tissue and fluids, it is advisable to give immediately 7500 IU of type A and 5500 IU of type B intravenously diluted in 0.9% saline for intravenous infusion at a 1 : 10 dilution. We applied two doses of botulinum antitoxin A. In our case, antitoxin was administered before respiratory arrest developed, and a significant improvement was observed in the patient's symptoms as a result of early treatment. In conclusion, further evaluation and treatment of cases of suspected botulism should not be delayed, and botulinum antitoxin application must be remembered as the basic treatment method.

Competing interests None.

Patient consent Obtained.

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