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Case Report

Serum False-Positive Botulism in Guillain-Barré Syndrome

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A 30-year-old man of Guillain-Barré syndrome (GBS) had atypical descending weakness and history of exposure to expired canned meat, which caused confusion with botulism. His serum showed false-positive botulism type B by the standard mouse bioassay. The diagnosis of axonal GBS was based on clinical and electrophysiological evidence. This report highlights the fact that GBS can present descending weakness and serum false-positive botulism.

1. Introduction

Botulism is a potential lethal neuromuscular junction disease caused by botulinum neurotoxin. It is characterized by the acute onset of symmetric, descending paralysis with prominent bulbar palsies, which usually starts from ocular musculature. The autonomic dysfunctions are prominent. Guillain-Barré syndrome (GBS), an immune-mediated neuropathy, exhibits a similar clinical picture as botulism. Rapidly progressive weakness and areflexia often lead to bulbar and respiratory compromise. GBS usually presents ascending weakness, but atypical distribution of weakness can be observed occasionally. Herein, we report a case of axonal GBS with atypical descending pattern of weakness and serum false-positive botulism type B, which makes a diagnostic challenge. We discuss the differential diagnosis for these two potential lethal diseases based on the clinical, electrophysiological, laboratory evidences.

2. Case Report

A 30-year-old man ate expired canned meat on 23 December 2007 (day 1), and then he had dizziness and constipation on the next day. Sore throat and mild dyspnea developed on day 3. Bulbar weakness occurred on day 4. Descending weakness progressed in the following days from his upper limbs to lower limbs, and he was unable to walk on day 7.

He came to our hospital on day 14 because of the progressive weakness. Upon arrival, physical examination showed dyspnea and abdominal distension. Neurological examination revealed clear consciousness with prominent bulbar palsies, including facial diplegia, dysarthria, dysphagia, and dysphonia. Pupil reflexes and extraocular movements were intact. Generalized weakness and hyporeflexia were noted. Complete blood count, serum chemistry, urinalysis, and brain CT showed normal results. Serum, vomit, and stool samples were sent for botulism exam. Both slow (3 Hz) and rapid (30 Hz) repetitive nerve stimulation tests (RSTs) did not show significant abnormal results. Nerve conduction study (NCS) showed reduction of overall compound motor action potentials (CMAP) but relatively preserved sensory nerve action potentials (SNAP) (Table 1). Autonomic dysfunction was indicated by decreased heart rate variation and absent sympathetic skin response at soles bilaterally. The cerebrospinal fluid (CSF) studies showed no significant abnormality.

The symptoms worsened gradually. The patient complained of distal paresthesia with sensory disturbances in position and light touch modalities over his toes. All limbs failed to achieve antigravity strength on day 16. Because respiratory distress ensued, endotracheal intubation with mechanical ventilation was applied. Serum positive botulism was reported but with undetermined subtype on day 20. The subacute disease course, sensory dysfunction, and normal RST favored GBS over botulism. The patient underwent 6 sessions of plasmapheresis and recovered gradually.

Botulism type B was detected in serum by standard mouse bioassay, but the cultures of both vomit and stool were negative for *Clostridium botulinum* [1]. The follow up of NCS on day 25 showed profound reduction of CMAP and

Table 1: The electrophysiological study results on day 14 and day 25 after onset.

(a) Day 14

Motor NCS	DL (ms)	CV (ms)	Amp (mV)	F (ms)
Median n	3.9 (3.6 ± 0.4)[1]	62.5 (57.8 ± 4.2)	1.8 (11.9 ± 3.7)	31.6 (25.4 ± 2.2)
Ulnar n	3.3 (2.8 ± 0.4)	58.3 (61.4 ± 3.7)	6.6 (11.7 ± 3.1)	28.3 (25.0 ± 2.1)
Peroneal n	NR (4.2 ± 0.5)	NR (48.6 ± 4.4)	NR (6.0 ± 2.5)	NR (44.7 ± 3.7)
Tibial n	4.3 (2.9 ± 1.0)	46.9 (50.5 ± 5.3)	2.6 (13.1 ± 5.0)	50.6 (45.0 ± 4.8)
Sensory NCS	DL (ms)	Amp (μV)		
Median n	2.4 (2.5 ± 0.2)	59.8 (33.0 ± 13.4)		
Ulnar n	2.5 (2.5 ± 0.2)	31.2 (26.1 ± 12.0)		
Sural n	3.2 (3.0 ± 0.3)	6.1 (12.5 ± 5.2)		

(b) Day 25

Motor NCS	DL (ms)	CV (ms)	Amp (mV)	F (ms)	
Median n	5.2	53.4	1.2	30.3	
Ulnar n	4.1	52.9	5.7	27.6	
Peroneal n	NR	NR	NR	NR	
Tibial n	5.8	45.8	1.0	52.1	
Sensory NCS	DL (ms)	Amp (μV)			
Median n	2.7	51.4			
Ulnar n	3.0	30.4			
Sural n	NR	NR			
Needle EMG	Ins Act	Rest PSW	Fib	Recruitment	Polyphasic MUAP
Brachioradialis	Increased	2+	2+	Reduced	Increased
Vastus medialis	Increased	2+	2+	Reduced	Increased
Gastrocnemius	Increased	3+	3+	Reduced	Increased
T paraspinal muscle	Increased	2+	2+	Reduced	Increased

Amp = amplitude, CV = conduction velocity, DL = distal latency, EMG = electromyography, Fib = fibrillation, F = F latency, Ins Act = insertion activity, MUAP = motor unit action potential, n = nerve, NCS = nerve conduction study, NR = no response, PSW = positive sharp wave, T = thoracic.
[1]Normal value (mean ± standard deviation) [2].

SNAP. EMG revealed spontaneous denervation activities in all the muscles sampled at limbs and trunk, compatible with polyradiculoneuropathy with axonal degeneration (Table 1).

3. Discussion

It seems that our patient had axonal GBS with serum false-positive botulism. History of exposure to high-risk food, the clinical course of descending weakness, and presentation of autonomic dysfunction led to the possibility of botulism. However, the follow up of electrophysiological studies confirmed its diagnosis as GBS.

Both GBS and botulism are critical issues for patients with rapid onset of flaccid paralysis, which can result in respiratory failure. Early diagnosis of botulism is very important, because adequate treatment decreases morbidity and mortality. The diagnosis is based on positive laboratory studies of *Clostridium botulinum* and its exotoxin [1]. The mouse bioassay remains the gold standard test for biologically active neurotoxins. However, this method has some disadvantages and may result in errors in clinical practices. First, mice can die nonspecifically during the procedure.

Serum false-positive botulism via mouse bioassay has been reported in GBS and Miller-Fisher syndrome (MFS) [3, 4]. Second, the standard mouse bioassay requires 4 days, but antitoxin should be given as soon as possible. Several rapid in vitro assays, such as immunological methods, molecular detection, and genetic characterization, have been developed to confirm the mouse bioassay but are not widely available [1].

Clinical symptoms and signs cannot offer enough information for distinguishing botulism from GBS, especially the motor-predominant variants. Autonomic dysfunctions develop in both diseases, which confuse clinical physicians further. Some GBS have descending weakness instead of the typical ascending pattern [5]. In this situation, ocular manifestations play a key role at initial stage. The acute descending paralysis of botulism usually begins in ocular musculature with presentation of impaired accommodation (100%), reduced pupil light reflex (83%), and diplopia (44%) [6]. In contrast, GBS relatively spares the eyes, except variants with prominent ophthalmoplegia such as MFS. However, one case who had GBS mimicking botulism with ophthalmoplegia as the initial symptom of the descending paralysis has been

reported [7]. Patients of MFS combined with autonomic dysfunctions are indistinguishable from botulism clinically, especially those with rare pupil involvement [8].

Electrophysiological, CSF, and immunological studies are also necessary for differential diagnosis. Electrophysiological studies give early clues for botulism. Rapid (20 to 50 Hz) RST shows incremental responses in more than 60% of patients [9]. Instead, classic electrophysiological findings of GBS may not be evident within 2 to 4 weeks. CSF studies may not be diagnostic within 2 weeks. Positive anti-ganglioside antibodies favor GBS, and anti-GQ1b presents in more than 85% of patients with MFS, but these two methods are not popular in all hospitals [5].

We believe this case is the first report of axonal GBS with history of exposure to high-risk food, descending weakness, and serum false-positive botulism via mouse bioassay. Clinicians should pay attention to all the possible potential confusion.

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