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【 CASE REPORT 】

Takotsubo-like Myocardial Dysfunction in a Patient with Botulism

Shuichi Tonomura[1], Yoshiaki Kakehi[1], Masatoshi Sato[2], Yuki Naito[1], Hisao Shimizu[1], Yasunobu Goto[3] and Nobuyuki Takahashi[1]

Abstract:
Botulinum toxin A (BTXA) can disrupt the neuromuscular and autonomic functions. We herein report a case of autonomic system dysfunction that manifested as Takotsubo-like myocardial dysfunction in a patient with botulism. Takotsubo syndrome results in acute cardiac insufficiency, another fatal complication of botulism in addition to respiratory muscle paralysis, particularly in patients with cardiovascular disease.

Key words: botulism, botulinum toxin A, Takotsubo syndrome, autonomic failure

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Introduction

Botulism is usually caused by the ingestion of toxins produced by the spore-forming obligate anaerobic bacillus *Clostridium botulinum*. Improved food sanitation control over the past several decades has reduced the incidence of food-borne botulism in Japan. There are five botulinum toxins, designated A to G. Botulinum toxin type A (BTXA) prevents acetylcholine release from the presynaptic membrane by cleaving a 25-kDa synaptosomal-associated protein at neuromuscular junctions, postganglionic parasympathetic nerve endings, and peripheral ganglia, resulting in motor and autonomic paralysis (1). Clinically, the most critical symptom of botulism is dyspnea due to respiratory muscle paralysis. Autonomic symptoms, blurred vision, dry mouth, orthostatic hypotension, and constipation are other typical symptoms but are regarded as non-fatal. Takotsubo syndrome, an acute reversible apical ventricular dysfunction caused by sympathetic neuronal and catecholamine surge (2), can result in acute cardiac insufficiency, particularly in patients with a history of cardiovascular disease.

We herein report the first case of BTXA toxicity resulting in Takotsubo-like myocardial dysfunction due to autonomic failure. The patient's written consent for the publication of this article was obtained, and any information, including illustrations, have been anonymized as far as possible.

Case Report

A 63-year-old man with a history of aortic valve replacement with an artificial heart valve for aortic stenosis presented to the emergency department with nausea, vomiting, blurred vision, and xerostomia a few days after he had eaten an insufficiently cooked instant meal (cooked in a sealed plastic pouch).

An initial neurological examination revealed only bilateral ptosis and hoarseness; however, hypoxic respiratory failure, increased blood pressure, and tachycardia occurred within a few hours. After incubation and respiratory assistance, chest X-ray revealed aspiration pneumonia and cardiogenic collapse. Two-dimensional echocardiograms revealed apical ballooning without myocardial infarction, findings consistent with Takotsubo syndrome (Figure A, B).

Intensive care for circulatory support was initiated; left ventricular dysfunction was transiently improved, but he had rapidly progressive internal and external ophthalmoplegia, flaccid quadriplegia, and ventilation failure due to respiratory muscle paralysis worsened on the Day 2. Electromyography (EMG) with nerve conduction studies of the radial, median, ulnar, and sural nerves showed decreased compound muscle action potential amplitudes and normal con-

[1]Department of Neurology, Nara City Hospital, Japan, [2]Department of Infectious Disease, Nara City Hospital, Japan and [3]Department of Intensive Care Unit, Nara City Hospital, Japan
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Correspondence to Dr. Shuichi Tonomura, tono0822shuichi@gmail.com

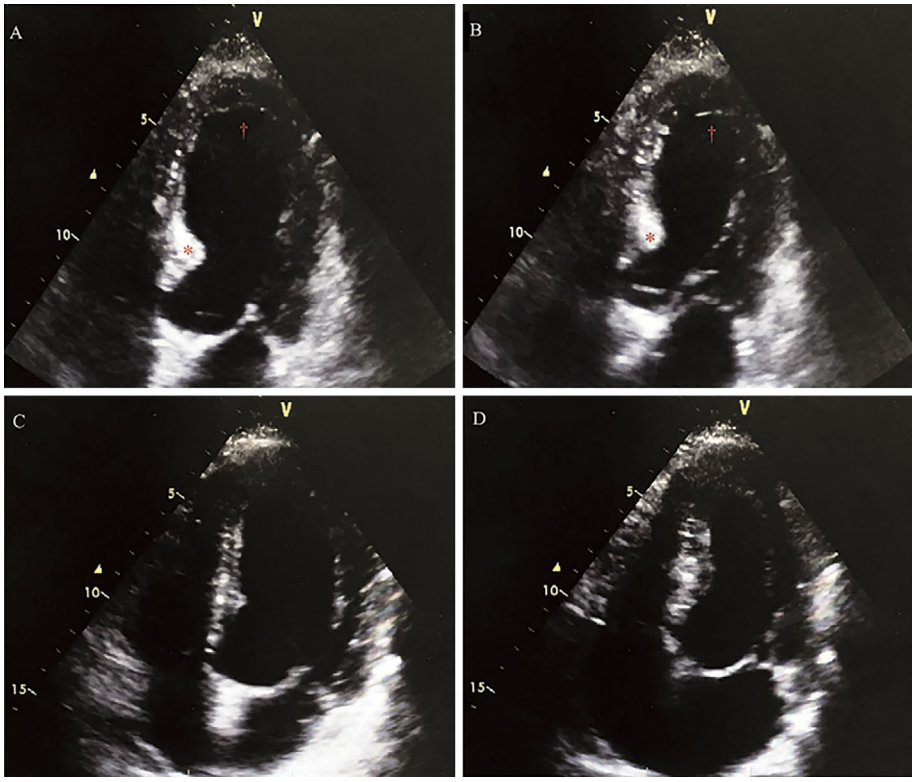

Figure. **Two-dimensional echocardiogram. Two chamber view of the left ventricle during diastole (A) and systole (B) showing akinetic and balloon apex in systolic (*) and alternatively normal contractile base (†), consistent with the findings in Takotsubo syndrome. After 14 days, wall motion normalized in diastolic (C) and systolic (D) phases. Two-dimensional echocardiogram.**

duction velocities. The sensory responses had normal amplitudes and latencies. Repetitive nerve stimulation at 3 Hz shows a decrement of 10%. Rapid repetitive stimulation at 50 Hz shows no increment. Acute inflammatory demyelinating polyneuropathy and myasthenia gravis were excluded by the clinical course, EMG, brain magnetic resonance imaging, and serum autoantibody assays. The tests for toxins in mice using inoculation of the patient's serum and stool revealed BTXA. Trivalent ABE antitoxin on Day 7 was not successful in preventing further worsening. Under intensive monitoring and treatment of the circulatory and respiratory symptoms, the autonomic dysfunction and muscle paralysis gradually ameliorated.

Discussion

To our knowledge, this is the first case of Takotsubo-like myocardial dysfunction in a patient with botulism; however, we believe that this condition has likely also been observed previously in studies on autonomic dysfunction due to botulism (3). Autonomic failure due to botulism had been considered to account for some cases of sudden infant death syndrome (4) as well as arrhythmias and electrocardiographic changes in adults (5). In our case, we hypothesized that the suppression of acetylcholine release in the peripheral ganglia and postganglionic parasympathetic nerves by the botulinum toxins strengthened the postganglionic sympathetic nerve effects, which has norepinephrine as the primary transmitter. When a sympathetic surge occurs, contraction of the resistance vessel rapidly increases the cardiac afterload through α-receptor activation, and hypercontraction of the left ventricle increases mechanical wall stress in the apex through β-receptor activation, resulting in Takotsubo syndrome (2).

Furthermore, both the severity of botulism and the cardiovascular disease history of the patient may have contributed to the patient's condition. First, BTXA is longer-acting than other botulinum toxins, particularly botulinum toxin type E (BTXE), which is a more common cause of food-borne botulism (6). Although both BTXA and BTXE degrade the same synaptosomal-associated protein, the protease activity of BTXA is stronger than that of BTXE and acts more rapidly and for longer in presynaptic neurons. Second, the EMG findings showed almost complete denervation of the neuromuscular junctions, suggesting that the patient may have been exposed to a large amount of BTXA (7). Lastly, the patient's medical history likely increased the vulnerability of his circulatory system to autonomic dysfunction. A recent study reported that severe autonomic failure is a significant predictor of mortality in patients undergoing aortic valve replacement and hypothesized that this stems from the abnormal activation of the autonomic cardiac reflex (8).

A preclinical study recently showed the retrograde transport of BTXA to upstream neurons (9). Furthermore, pa-

tients with cervical dystonia treated with BTXA reported autonomic symptoms, and a quantitative investigation revealed mild subclinical abnormalities in autonomic cardiovascular regulation and cardiopulmonary baroreflex sensitivity in healthy adults (10). We herein report autonomic dysfunction as a major complication of BTXA, particularly in patients with a medical history of cardiovascular disease.

The authors state that they have no Conflict of Interest (COI).

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