

## Takotsubo cardiomyopathy following severe tetanus

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### Abstract

Takotsubo cardiomyopathy is considered a neurogenic heart disease resulting from impaired autonomic function and is known to be associated with various neurological and medical conditions. To our knowledge, although tetanus is frequently accompanied by autonomic instability, there has been no report of Takotsubo cardiomyopathy in patients with tetanus. Here we describe a patient with Takotsubo cardiomyopathy as a manifestation of autonomic instability in severe tetanus.

### INTRODUCTION

Takotsubo cardiomyopathy, also called apical ballooning syndrome, is characterized by transient left ventricular cardiac dysfunction mimicking myocardial ischemia, but without evidence of coronary artery occlusion.<sup>1-2</sup> Although Takotsubo cardiomyopathy has been increasingly investigated recently, the understanding of its pathogenesis is limited. Some reports describe that autonomic dysfunction associated with acute medical illness might attribute to the development of Takotsubo cardiomyopathy.<sup>3-4</sup> Autonomic instability with abnormal heart rate, labile blood pressure, myocardial dysfunction and sympathetic over activity are relatively common in tetanus.<sup>5</sup> Overdrive of sympathetic activity associated with change of catecholamine levels was suggested as the plausible mechanism of sympathetic dysfunction in tetanus.<sup>6-7</sup> Cardiac dysfunction in tetanus might be attributed to catecholamine-associated sympathetic over activity as well as catecholamine-induced myocardial damage.<sup>3</sup> We report a patient with tetanus suffering cardiac dysfunction manifesting as Takotsubo cardiomyopathy.

### CASE REPORT

A forty-year-old woman was admitted to the otolaryngology department with difficulty in swallowing. Initially she underwent conservative management under the impression of pharyngeal spasm. She worked as a fisher and remembered several minor trauma from fish-hooks. She had no history of tetanus immunization. There was no remarkable history of medical illness, medication and exposure to cardiotoxic or vasoconstrictive

agents. On admission, the blood pressure was 110/80 mmHg and the pulse regular at 80 beats per minute. Initial laboratory tests were within normal range except for a mildly raised erythrocyte sedimentation rate (ESR) 27 mm/hr (normal range 0-20mm/hr), C-reactive protein (CRP) 3.582 mg/dL (normal range 0.02-0.3mg/dL) and white blood cell count (WBC) 12900/ $\mu\ell$  (normal range 3500-9700/ $\mu\ell$ ), were suggestive of ongoing inflammation or infection.

Her symptoms became worse two days after admission, with her jaws becoming tightly clenched. Severe trismus developed with sustained spasm of facial muscles (risus sardonius) a sign often observed with tetanus. Nuchal rigidity also developed with repeated muscle spasm in the neck. On the second day, acute respiratory failure resulted due to reduction of chest wall compliance and laryngeal spasm developed. Emergency tracheostomy and subsequent mechanical ventilation were applied. She was transferred to the neurology department for critical care. Based on the clinical presentation suspicious of tetanus, human tetanus globulin (intravenous, 250 IU) was immediately given to the patient, though the titer of anti-tetanus antibody IgG before the injection of tetanus immunoglobulin was within normal range (<0.01 IU/mL). Computed tomography of the brain and neck, electroencephalography and cerebrospinal fluid analysis were performed to exclude secondary causes of progressive caudal spread of spasm and rigidity, but revealed no abnormalities. Intermittent injection of diazepam did not control her symptoms.

On the third day of hospitalization, she suddenly complained of chest tightness with hyperhydrosis over the trunk. Her blood pressure lowered to

80/50 mmHg with heart rate 85 or lower beat per minute. Electrocardiography showed a T-wave inversion in leads II, III, aVF and V3-6, suggesting inferolateral cardiac ischemia (Figure 1). Serum CK-MB and troponin-T were elevated to 11.56 and 0.182 ng/ml respectively, (normal range <6.3, <0.1 ng/ml, each). Her blood pressure could not be elevated despite continuous and maximum infusion of inotropic agents. Emergency trans-thoracic echocardiography revealed wall abnormalities in the apical and midportion of the left ventricle, sparing basal segments (Figure 2). Ejection fraction (EF) was 42%. Subsequent coronary angiography showed normal coronary arteries with normal flow without vasospasm. As the patient's condition was suggestive of Takotsubo cardiomyopathy, it was decided to continue with conservative treatment. Her neurological condition including trismus and nuchal rigidity gradually stabilized. She did not complain of further chest discomfort. Blood pressure and cardiac enzyme levels normalized by the eighth day of hospitalization. A follow-up echocardiography performed 13 days after admission showed improved left ventricular wall motion and normalized ejection fraction of 65%. She was discharged 15 days after admission and after 12 months of serial follow-up, she remained normal without any complications.

## DISCUSSION

We present a case of reversible acute myocardial

dysfunction, so called Takotsubo cardiomyopathy following severe tetanus. Takotsubo cardiomyopathy is similar to acute coronary syndrome except that there is no angiographic evidence of obstructive coronary artery disease. It is characterized by distinctive abnormality of left ventricle contraction with akinesia or dyskinesia of the apical and/or midventricular segments of the left ventricle together with hypercontractility of the base.<sup>8</sup> Its pathogenesis is still debated. Some investigators suggest that it could be explained by ischemia. However, evidence implies participation of the sympathetic nervous system and excessive catecholamine levels in its pathogenesis.<sup>9,10</sup> There are some cases of Takotsubo cardiomyopathy related to sympathetic stimulation resulting from stress, exercise or sympathomimetic drugs.<sup>11,12</sup> Additionally, the distinctive left ventricular dysfunction is compatible with a neural causation, and is not explained alone via coronary vascular territory.<sup>11</sup> Although most adrenergic nerve endings are thought to be located around the base of the left ventricle, there is some evidence that the apex has a greater density of adrenergic receptors, making it more susceptible to catecholamine-induced microvascular dysfunction and to direct myocardial damage.<sup>13-14</sup>

The tetanus toxin may lead to catecholamine release and affect the autonomic nervous dysfunction (sympathetic hyperactivity) through its prolonged stimulation of the sympathetic nervous system or relative imbalance of sympathetic and

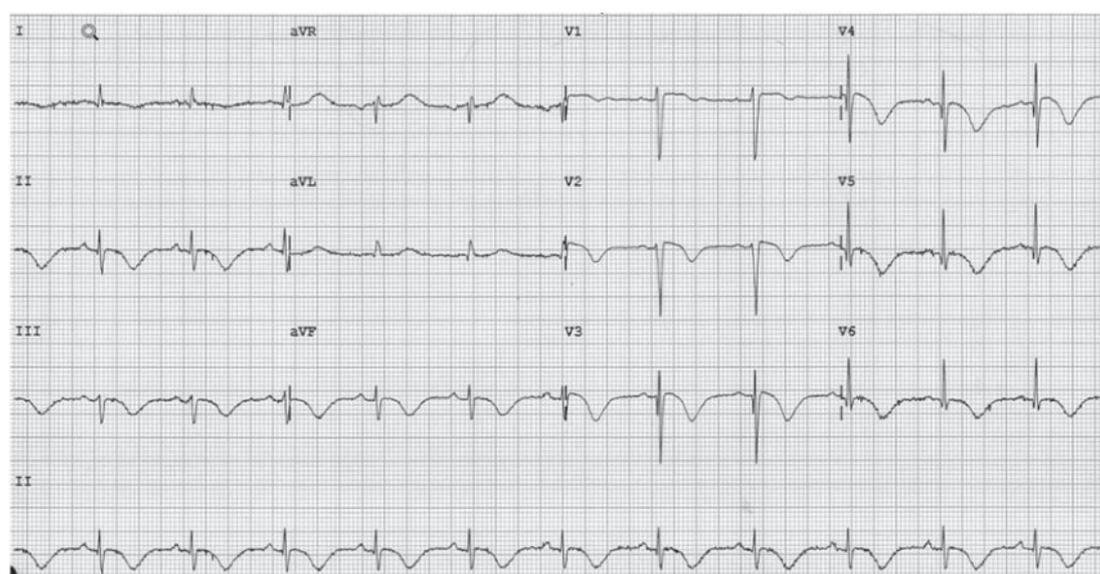


Figure 1. Electrocardiography performed after chest tightness, fluctuated blood pressure showed a T-wave inversion in leads II, III, aVF and V3-6, suggesting inferolateral cardiac ischemia.

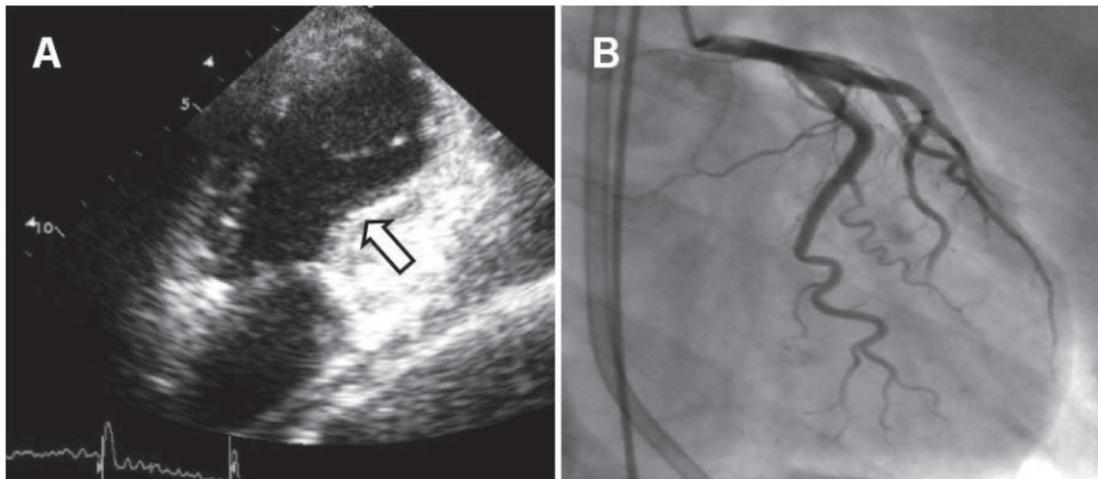


Figure 2. Echocardiography showed distinctive left ventricle contraction pattern (apical ballooning) in systole (A). Coronary angiography of left main coronary artery showed no abnormal finding (B).

parasympathetic nervous system, regardless of its level.<sup>15</sup> Also, myocardial damage caused by catecholamine or direct action of tetanus toxin (cytokine-mediated) could be involved in cardiac dysfunction.<sup>16</sup> In this patient, the sudden elevation of cardiac enzymes and the lack of changes in arterial blood pressure and heart rate despite the continuous infusion of inotropic agents implies that the cardiomyocytes were also impaired. Therefore, this case suggests that catecholamine release or sympathetic hyperactivity could be a common (or shared) pathogenesis involved in autonomic instability of tetanus and Takotsubo cardiomyopathy. The autonomic manifestations in tetanus are variable and the treatment of those differs in individuals. Takotsubo cardiomyopathy can be expectantly treated with conservative management. Thus, the recognition of Takotsubo cardiomyopathy triggered by tetanus and several conditions resulting in sympathetic stimulation and the urgent management of underlying tetanus are important for clinicians to recognise.

The diagnosis of tetanus was based on the history and clinical manifestations, which were compatible with those observed in this patient. Strychnine poisoning, orofacial infection or trauma, rabies and drug-induced dystonic reaction were all excluded as differential diagnosis from thorough history taking, medication history and physical examination. To our knowledge, this is the first report of Takotsubo cardiomyopathy developing in severe tetanus with autonomic instability and acute respiratory failure.

## DISCLOSURE

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Conflict of interest to declare: None

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