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Takotsubo cardiomyopathy in a patient with theophylline toxicity

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Abstract

Takotsubo cardiomyopathy typically involves transient left ventricular apical ballooning triggered by emotional or physical stressors. We present a case of the ophylline toxicity with takotsubo cardiomyopathy. A 73-year-old woman was transferred to the emergency department of our hospital because convulsions developed during intravenous administration of theophylline at another hospital. The intermittent convulsions were abated with diazepam followed by phenytoin, however, chest pain occurred with ST-segment elevation on electrocardiography and an apical ballooning of the left ventricle on echocardiography. Conservative treatment was continued since the patient had not accepted invasive procedures including cardiac catheterization. On the next day after admission, the creatine kinase MB isoenzyme level slightly elevated, 35 U/l, without newly developed abnormal Q waves. It was later confirmed, based on additional information from his primary care doctor and family members, that the patient had been addicted to the ophylline for several years. The serum the ophylline levels were 34.8 mg/lon admission and 20.2 mg/lone day after admission, respectively.

Keywords

addiction; takotsubo cardiomyopathy; theophylline; toxicity

Introduction

Takotsubo cardiomyopathy is typically characterized by chest symptoms, ST-segment elevation, and transient left ventricular wall motion abnormalities, mimicking acute myocardial infarction [1,2]. This condition has been frequently associated with emotional triggers or physical triggers, and accompanied by coexisting medical conditions including an acute episode of a neurologic or psychiatric disorder [3,4]. Here, we present a case of the ophylline toxicity with takotsubo cardiomyopathy.

Case Report

A 73-year-old woman was admitted to our hospital with impaired consciousness and intermittent convulsions. A few hours before admission, the patient visited another hospital and asked a physician to administer theophylline. The patient was reportedly alert and not distressed, but convulsions developed five minutes after the intravenous drip of 125 mg theophylline was started. The total amount of theophylline given was unknown. The convulsions resolved spontaneously, but the level of consciousness

was drowsy (Japan Coma Scale 30). The blood pressure was 170/80 mmHg and the oxygen saturation was 97% with the patient breathing ambient air. She was transferred to the emergency room of our hospital. The patient had no remarkable medical history except for a self-reported asthma. The patient reported that medication was inhalation for asthma, which was not exactly determined. She had allergies to aspirin, ceftriax one, and steroids. She did not smoke, drink alcohol, or use illicit drugs.

On examination, she was not organized. The systolic blood pressure was 200 mmHg, the pulse was 108 beats per minute, the temperature was 37.4°C, and the oxygen saturation was 98% in ambient air. No rales or gallop rhythm were heard in the chest. A chest radiograph showed cardiomegaly with a cardiothoracic ratio of 63% and no pleural effusion. The lactate dehydrogenase was 383 U/l, the levels of urea nitrogen and creatinine were 33 mg/dl and 1.75 mg/dl, respectively, the creatine kinase was 194 U/l, and the C-reactive protein was 2.08 mg/dl. The complete blood counts were normal, as were the liver function test and the levels of sodium and potassium. Convulsions infrequently developed, along with rolling of the eyes, but spontaneously stopped within a minute; no life-threatening arrhythmia, such as ventricular tachycardia or ventricular fibrillation, was detected on the monitor during her attacks.

The patient requested for theophylline obsessively and violently, but theophylline was not resumed without her being informed of it. The convulsions were treated with diazepam of 5 mg, followed by phenytoin of 250 mg, accompanied with intravenous saline fluid. Her condition had gradually stabilized, but chest pain developed with an increase in ST-segment elevation (**Figure**). Echocardiography showed apical ballooning of the left ventricle, without pericardial effusion or valvular heart disease. The patient was treated conservatively because she did not agree for invasive procedures including cardiac catheterization.

On the next day, electrocardiography showed a slight improvement in ST-segment elevation without newly developed abnormal Q waves. The creatine kinase was high (2191 U/l) but the MB isoenzyme remained low (35 U/l or 1.6%); the troponin T level was 2.710 ng/ml (reference value, <0.100). His primary care doctor and family members reported that she had been addicted to theophylline and visited frequently other clinics or hospitals for the request of theophylline. She was arbitrarily discharged 24 hours after admission, and lost to follow-up. It was later confirmed that the levels of theophylline were increased to 34.8 mg/l (therapeutic range, 10 to 20 mg/l) on admission and 20.2 mg/l one day after admission, respectively.

Discussion

This is a rare case of theophylline toxicity with chest pain and ST-segment elevation. Given the apical ballooning of the left ventricle and minimal elevation of cardiac enzymes, a diagnosis of takotsubo cardiomyopathy was considered reasonable, although neither coronary angiography nor ventriculography was performed.

Since the first report by Sato et al. in 1990 [5], takotsubo cardiomyopathy has gained worldwide recognition [3,4,6,7]. In an international registry of 1750 patients with takotsubo cardiomyopathy [3], approximately three fourths of the patients had emotional triggers, physical triggers, or both preceding the onset of this condition. More recently, takotsubo cardiomyopathy is reported to be provoked not only by negative triggers such as grief, anger, or fear but also by positive triggers including a birthday party or

wedding, winning jackpots at the casino, and becoming a great grandmother [4]. In our case, an emotional stress before theophylline could be a negative trigger to develop takotsubo cardiomyopathy, but, given her clinical course, a relief after the administration of some theophylline should be considered as a positive trigger. The presence of a psychiatric condition (i.e., a binge pattern of theophylline) is consistent with the diagnosis of takotsubo cardiomyopathy because more than 40% of patients in this situation had psychiatric illness [3].

Theophylline has been widely used in the management of airway diseases for almost a century since its first clinical use in 1922 [8]. Nevertheless, attention should be paid in the use of theophylline, because of the close relationship between an effective concentration of 10 to 20 mg/l and harmful concentration of >25 mg/l [8]. Japanese guidelines for adult asthma have not recommended theophylline as a first-line treatment in the management of acute exacerbations because of safety concerns [9]. The side effects of theophylline include headache, nausea, and vomiting, mainly by phosphodiesterase inhibition [10,11]. It is reported that convulsions and arrhythmias can be provoked by adenosine receptor antagonism under higher plasma levels of theophylline [8,12]. Our patient showed the plasma level of 34.8 mg/l on admission, along with convulsions and premature atrial contractions, findings consistent with theophylline toxicity. Theophylline is predominantly metabolized by cytochrome P450 enzymes in the liver [8], with an average half-life of 7.2 hours in nonsmokers [13], which could be influenced by many factors [8,13]. Oral activated charcoal and charcoal hemoperfusion are recommended in the management of theophylline toxicity; hemofiltration should be considered in severe cases, such as sustained convulsions or hemodynamic instability [14,15]. No specific treatment other than hydration was initiated in our case because of her preference. The incidence of theophylline toxicity as a cause of takotsubo cardiomyopathy remains unclear, but it seems extremely rare. So far, to our knowledge, there is no case report of theophylline-associated takotsubo cardiomyopathy except for two abstracts [16,17], both of which are likely to report the same case.

This case highlights the importance of understanding the diversity of takotsubo cardiomyopathy. Further study is warranted to examine the possible side effects of theophylline as a trigger of takotsubo cardiomyopathy

Figures

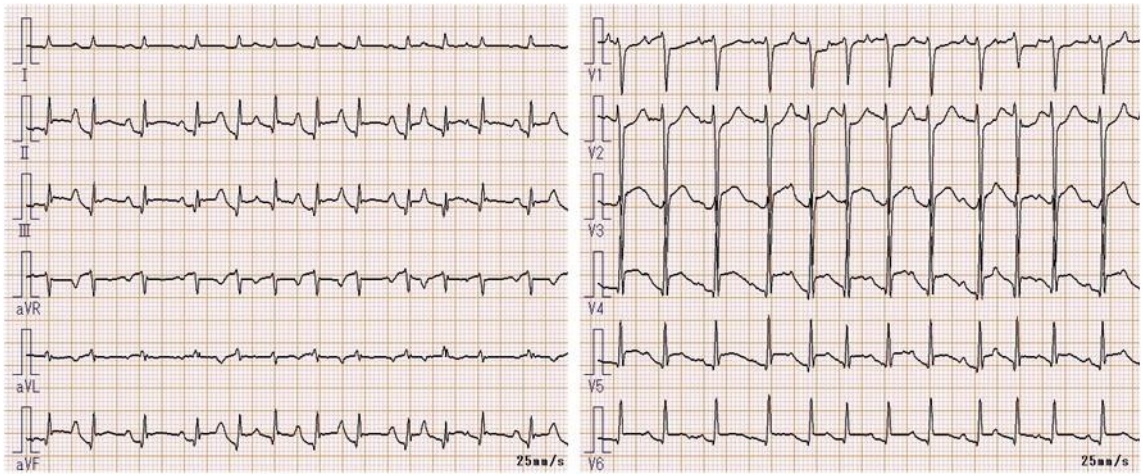

Figure 1: Electrocardiography ST-segment elevation is shown in leads I, II, III, aVF, and V_3 to $V_6$with frequent premature atrial contractions.

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