A MAN WITH TRANSIENT LEFT VENTRICULAR APICAL BALLOONING SYNDROME (TAKOTSUBO CARDIOMYOPATHY) MIMICKING ACUTE MYOCARDIAL INFARCTION

Chen-Tung Hsu, Rei-Yeuh Chang, Cheng-Kang Chen

Abstract

Transient left ventricular (LV) apical ballooning syndrome is a recently described entity characterized by chest symptoms associated with electrocardiographic changes and mild elevation of cardiac enzymes. The clinical presentation mimics acute myocardial infarction, but these patients have no significant stenosis of the coronary artery. We describe a 63-year-old man with dyspnea and chest tightness which occurred after progressive lower back pain. He was diagnosed and managed as a case of acute myocardial infarction initially. Apical akinesis with ballooning was noted during left ventriculography. However, coronary angiography did not show obstructive coronary stenosis. One month later, follow-up echocardiogram demonstrated complete resolution of the LV wall abnormalities. Transient LV apical ballooning syndrome should be included in the differential diagnosis of patients with an acute myocardial infarction, especially following a stressful trigger.

Key words: Takotsubo cardiomyopathy, Transient left ventricular apical ballooning, Acute myocardial infarction

Introduction

Transient left ventricular (LV) apical ballooning syndrome, also known as Takotsubo cardiomyopathy, is a recently described entity characterized by chest symptoms associated with electrocardiographic changes (ST elevation or T-wave inversions) and mild elevation of cardiac enzymes. The clinical presentation mimics acute myocardial infarction, but these patients have no significant stenosis of the coronary artery. Typically, the transient LV dysfunction may present with akinesis or hypokinesis of the mid-to-distal portion of the LV chamber with hyperkinesis of the basal segments. In 1991 Dote et al first described this transient LV systolic dysfunction as Takotsubo cardiomyopathy, named after the instrument with a round bottom and narrow neck used for trapping octopus in Japan. The syndrome is often triggered by an emotional or physical stress or acute medical illness, so the terms broken heart syndrome or stress cardiomyopathy have also been used. Those presenting with the syndrome are most commonly postmenopausal women. We describe a 63-year-old man with the typical characteristics of transient LV apical ballooning...
Case Report

A 63-year-old man presented to our emergency room because of dyspnea and chest tightness for four hours. The chest tightness was not associated with cold sweating or radiation. He had a long-standing history of hypertension and chronic kidney disease. He had been on hemodialysis for one year. His antihypertensive medications consisted of nifedipine OROS 60 mg and telmisartan 40 mg/day. The maintenance hemodialysis was relatively stable, and the appropriate dry weight had been maintained. Also, the patient had a six-week history of lower back pain with radiation to the right thigh and calf. His lower back pain had gotten worse in the past few days. On physical examination, his blood pressure was 190/82 mmHg, heart rate 90 beats per minute, and temperature 37°C. His palpebral conjunctiva were slightly pale. Bilateral crackles were noted in his lung fields. There was a soft II/IV systolic murmur over the left sternal border and apex. There were no other noteworthy findings.

Blood tests yielded the following: a white blood cell count of 17,710/uL (normal range: 3500-9900); hemoglobin level of 11.5 g/dL (normal range: 14-18); platelet count of 362,000/uL (normal range: 130,000-340,000); C-reactive protein level of 10.15 mg/dl (normal < 0.47); creatine kinase (CK) level of 75 IU/L (normal range 26-174); CK myocardial band (CK-MB) level of 2.4 IU/L (normal range 0.1-6.3); and troponin I level of 0.091 ng/ml (normal < 0.5). Chest X-ray demonstrated acute pulmonary edema. Electrocardiogram (ECG) revealed sinus rhythm with mild ST-segment elevation over leads V3 and V4 (Fig. 1A). Intravenous nitrate and supplementary oxygen were administered. Then the patient was admitted to our intensive care unit, where emergency hemodialysis was carried out for acute lung edema. His dyspnea and chest tightness improved after the above management. Twelve hours later, follow-up CK and CK-MB levels were 159 and 15.8 IU/L, respectively, and troponin I 2.744 ng/ml.

Fig. 1. (A) Admission electrocardiography showing mild ST-segment elevation in leads V3 and V4. (B) Electrocardiography 12 hours later showing deep, symmetric, T-wave inversion over leads V2-V6, I, II and aVL, and prolonged QT interval with QTc of 552 ms. (C) Electrocardiography 70 days later showing resolution of T-wave inversion.
Repeat ECG revealed deep, symmetric, T-wave inversion over leads V2-V6, I, II and aVL, and prolonged QT interval with QTc of 552 ms (Fig. 1B). The patient was treated with aspirin, clopidogrel, nitrate and heparin for suspicion of acute myocardial infarction. The cardiac enzymes peaked 24 hours later, with CK and CK-MB levels of 246 and 18.0 IU/L, respectively, and troponin I 5.288 ng/ml. Two days after admission, coronary angiography was performed and revealed no evidence of coronary artery stenosis (Figs. 2A, B). Left ventriculography showed apical akinesis and ballooning, and an ejection fraction of 40% (Figs. 2C, D). Transient LV apical ballooning syndrome was diagnosed. The patient received maintenance hemodialysis three times per week. The patient was discharged six day later and maintained on a regimen of aspirin, nitrates, bisoprolol, nifedipine OROS, telmisartan, acetaminophen and meloxicam.

He was admitted to our ward again because of low-grade fever and persistent lower back pain a few weeks later. The follow-up white blood cell count was 19520/μL, and C-reactive protein level was 22.480 mg/dl. Oxacillin-resistant *Staphylococcus aureus* was detected in all three sets of blood cultures. A technetium-99m methylene diphosphonate three-phase bone scan as well as a gallium-67 citrate scan confirmed osteomyelitis in the lower lumbar spine L4-L5. His lower back pain and low-grade fever subsided after medical treatment with vancomycin infusion. A transthoracic echocardiogram obtained one month after presentation demonstrated complete resolution of the LV wall abnormalities (Fig. 3). Seventy days later, follow-up ECG was normal (Fig. 1C).

![Fig. 2. Coronary angiography (left anterior oblique view) showing no significant stenosis (A: left coronary artery and B: right coronary artery). Left ventriculography showing apical akinesis and ballooning (C: end-diastole and D: end systole).](image-url)
Discussion

Transient LV apical ballooning syndrome is a still rarely diagnosed syndrome. After the initial recognition and description of the transient LV apical ballooning in Japanese population, the syndrome has now been reported worldwide.3-5 Because of its clinical and imaging characteristics, this syndrome is frequently misdiagnosed as an acute coronary syndrome. The diagnosis is usually confirmed when coronary angiography is normal or reveals mild abnormalities (<50% luminal stenosis). Although the true prevalence remains unknown, LV apical ballooning syndrome accounts for about 2% of ST-segment elevation infarcts.6 Our patient presented with the characteristics clinical features of the syndrome, acute onset of dyspnea and chest tightness. The characteristic ECG features of this syndrome are non-specific and include dynamic ST elevation (<2 mm) and/or T-wave inversion, with prolongation of QT interval in the anterior leads, as in our patient. In comparison to patients with anterior infarct, these ST elevations are less prominent. However, ECG does not have a predictive value allowing emergency differentiation of these entities.7 Our patient also had mildly elevated cardiac biomarkers. However, the levels of cardiac enzymes were lower than expected relative to the degree of LV dysfunction. Coronary angiography should be performed to exclude relevant coronary artery obstruction in patients presenting with transient LV apical ballooning syndrome. In acute stage, the left ventriculogram typically shows apical and/or midventricular wall motion abnormalities extending beyond a major epicardial coronary distribution. The condition does not always affect the apex, and midventricular ballooning with sparing the basal and apical segments can be present.8 We did not carry out cardiac magnetic resonance (CMR) imaging. However, CMR can provide morphologic and functional information on left ventricular function. CMR appears to be a useful tool to differentiate LV apical ballooning syndrome from myocardial infarction and myocarditis.9 Typically, late gadolinium hyperenhancement presents in patients with acute myocardial infarction or myocarditis. In contrast, almost all patients with LV apical ballooning syndrome have an absence of late gadolinium hyperenhancement, consistent with viable myocardium.

Fig. 3. Modified four-chamber view on transthoracic echocardiogram after one month demonstrating complete resolution of the LV wall abnormalities (left panel: end-diastole and right panel: end-systole).
One of the hallmarks of LV apical ballooning syndrome is that most affected patients are between 62 and 75 years, with a female predominance. Another feature of the syndrome is the occurrence of a preceding emotional or physical stress event in about two thirds of patients. However, our patient had all the characteristic clinical features of the syndrome except for his gender. There may be a higher prevalence of males among patients admitted to the medical intensive care unit. Fang et al reported 10 cases of transient LV apical ballooning syndrome in the Taiwanese population. Their series showed male preponderance (60% of cases), which was different from other studies. Of the 10 patients, 6 patients had physical illness and 2 patients died of sepsis from a pulmonary infection during admission. In our patient, progressive lower back pain might be the trigger event. Lower lumbar osteomyelitis with oxacillin-resistant *Staphylococcus aureus* sepsis was diagnosed a few weeks later. Acute medical illness, especially sepsis, appears to be the trigger of transient LV dysfunction. Park et al reported that 28% of consecutive patients admitted to the medical intensive care unit for acute medical illness developed transient LV wall-motion abnormalities involving the apical and midventricular segments consistent with transient LV apical ballooning syndrome. Sepsis was the only independent predictor for the developed of the stress cardiomyopathy. However, coronary angiography was not routinely performed to rule out obstructive coronary artery disease in this series. Although the mechanisms are not fully understood, the release of tumor necrosis factors-α and other cardiotoxic cytokines, as well as production of anaphylatoxins such as complement 5a might be involved in the molecular and cellular mechanisms responsible for transient LV dysfunction in sepsis syndromes.

The pathophysiological mechanism of transient LV apical ballooning is unknown. It has been suggested that transient multivessel epicardial spasm was relatively uncommon (1.4% and 28.6%, respectively). Coronary microvascular dysfunction may play a role in the pathogenesis of this syndrome. Bybee et al evaluated the coronary angiogram and thrombolysis in myocardial infarction (TIMI) frame counts in patients with transient LV apical ballooning syndrome. They reported abnormal TIMI frame counts in all three major epicardial coronary arteries during the acute phase of the syndrome. Nuclear studies documented abnormal myocardial perfusion in the absence of epicardial obstruction. However, it remains to be established whether impaired myocardial perfusion is a direct cause of the syndrome or a secondary phenomenon. Catecholamine-induced myocardial stunning is the most widely proposed mechanism because many patients have emotional or physical triggers. Moreover, wall motion abnormalities have been observed in diseases associated with high catecholamines, such as pheochromocytoma.

Wittstein et al reported that plasma catecholamine levels were markedly higher among those with stress-induced cardiomyopathy than among those with Killip Class III myocardial infarction. Since exaggerated sympathetic stimulation appears to play a major part in transient LV apical ballooning syndrome, this syndrome might be easily induced in hemodialysis patients, especially those under emotional or physical stress because of the increased sympathetic nerve activity that occurs with chronic kidney disease. In a Japanese multicenter study, four of 88 patients with transient LV apical ballooning syndrome were undergoing hemodialysis, suggesting that the prevalence of this syndrome in hemodialysis patients might be higher than that in the general population.

The optimal management of LV apical ballooning syndrome is uncertain, but supportive therapy according to the patient’s haemodynamic status invariably leads to spontaneous recovery. Every patient should be evaluated and treated as a case of acute myocardial infarction initially. Fibrinolytics should be avoided, and emergency coronary angiography would be a suitable strat-
egy in a patient suspected of LV apical ballooning syndrome. In the absence of contraindications, a short duration of anticoagulation and antiplatelet agents should be considered until LV dysfunction has normalized, with the aim of preventing formation of mural thrombi in patients with significant LV dysfunction. Complications, such as pulmonary edema, cardiogenic shock or ventricular tachyarrhythmia should be treated with standard therapies. Nevertheless, the prognosis of this syndrome is favorable; reported inhospital mortality rates range from 0% to 8%. Data from an animal model of takotsubo cardiomyopathy imply that its occurrence appears to be reduced after α- and β-blockade. After normalization of LV function, it is reasonable to consider chronic β-blocker therapy with the aim of preventing recurrence, which have been described as occurring in 3.5% of patients. Our patient did not experience recurrence of this syndrome over 20 months’ follow-up with chronic labetalol therapy.

Despite the absence of obstructive coronary stenosis, transient LV apical ballooning syndrome has a clinical presentation that is indistinguishable from that of an acute myocardial infarction. However, the managements and prognoses are very different. Urgent coronary angiography is indicated for the differential diagnosis and avoidance of exposure to inappropriate fibrinolytics. Transient LV apical ballooning syndrome should be included in the differential diagnosis of patients with an acute myocardial infarction, especially following a stressful trigger.

References

暫時性左心室心尖球狀突出症候群（Takotsubo心肌病變）—急性心肌梗塞的模仿者

許振東，張瑞月，陳政康

摘要

暫時性左心室心尖球狀突出症候群是一個最近被熱烈討論的心臟疾病。它的臨床表徵類似急性心肌梗塞，包括胸痛或呼吸困難、心電圖變化及輕微心臓酵素升高，但是，冠狀動脈無阻塞的情形。我們報告一位63歲男士，他的臨床症狀是漸漸加劇的下背痛，伴隨呼吸困難及胸悶。他最先被當成急性心肌梗塞來治療，然而，冠狀動脈無阻塞的情形，且左心室攝影發現有心尖球狀突出的現象。一個月後，追蹤心臟超音波發現左心室收縮功能完全正常。暫時性左心室心尖球狀突出症候群應該包含於急性心肌梗塞的鑑別診斷，尤其是有壓力誘發因子的病人。

關鍵詞：Takotsubo心肌病變，暫時性左心室心尖球狀突出症候群，急性心肌梗塞