CASE REPORTS/CLINICAL VIGNETTES

It's a Trap! Clinical Similarities and Subtle ECG Differences between Takotsubo Cardiomyopathy and Myocardial Infarction

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We describe a 65-year-old woman with a history of hypertension and smoking who presented with an acute episode of chest pain precipitated by severe emotional stress. Her initial electrocardiogram done in the emergency room showed non-specific T wave changes in the lateral leads and her cardiac troponin levels were mildly elevated. Because of her clinical presentation, she was admitted with a presumptive diagnosis of acute myocardial infarction and managed with antiplatelet and anticoagulant therapy. Coronary angiogram did not reveal coronary artery disease and left ventriculography showed findings consistent with apical ballooning syndrome or takotsubo cardiomyopathy. Subsequent electrocardiograms displayed dramatic changes including T wave inversions, QT interval prolongation and U waves. The patient remained asymptomatic and recovered uneventfully. Three weeks post-discharge, an echocardiogram documented resolved left ventricular dysfunction. We describe the clinical features and highlight the electrocardiographic findings that may help differentiate takotsubo cardiomyopathy from myocardial infarction.

KEY WORDS: takotsubo cardiomyopathy; apical ballooning; myocardial infarction; electrocardiogram.

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INTRODUCTION

In recent years, takotsubo cardiomyopathy or apical ballooning syndrome has been reported as a transient cause of left ventricular dysfunction. Its name is derived from the Japanese octopus trap called “takotsubo,” which resembles the appearance of the classic ventriculogram findings of apical ballooning during systole. It generally affects post-menopausal women who present with anginal symptoms induced by psychological or physical stressors. While it is increasingly acknowledged that takotsubo and myocardial infarction (MI) have analogous clinical presentations, knowledge of how to differentiate their electrocardiogram (ECG) features continues to evolve. Following a description of a patient with takotsubo cardiomy-

opathy who manifested with interesting ECG findings, we review current studies that contrast the ECG patterns of takotsubo with those of MI and discuss whether ECG can reliably distinguish either condition. Additionally, we describe the clinical course, complications, prognosis, treatment options and contemporary diagnostic approach of takotsubo cardiomyopathy.

CASE REPORT

A 65-year-old woman with history of hypertension, smoking, gastroesophageal reflux disease and family history of coronary artery disease presented to the emergency department complaining of severe chest pain. Her symptoms began 5 days prior to admission when she experienced episodic, “burning,” chest discomfort that she attributed to acid reflux. An hour before coming to the hospital and while watching her young grandkids, her pain intensified to 8/10, radiated to either side of her chest and was accompanied by nausea and diaphoresis. She had been taking enalapril 10 mg daily, nifedipine 30 mg daily, omeprazole 20 mg daily and aspirin 81 mg daily. She admitted being under a lot of stress lately, acting as surrogate caregiver for her grandchildren.

Physical examination revealed blood pressure of 108/73 mm Hg, heart rate of 110 beats per minute, respiratory rate of 20 per minute, and oxygen saturation of 96% on room air. She had no jugular venous distention. Her heart rhythm was regular. S1 and S2 were distinct and there were no murmurs, gallops, or rubs. Her lungs were clear to auscultation. There was no pedal edema. The remainder of the physical exam was unremarkable. Laboratory results, including a complete blood count and metabolic profile, were within normal range. Serum potassium level was 4.2 mEq/L (reference range: 3.5–5.1 mEq/L) and her serum calcium level was 8.8 mg/dL (reference range: 8.8–10.2 mg/dL). Initial ECG (Fig. 1) showed sinus tachycardia with Q waves in the inferior leads and flat T waves in leads I and aVL. Her initial troponin-I was elevated at 0.63 ng/dL (normal range <0.10 ng/dL). To evaluate for left ventricular wall motion abnormalities, a bedside transthoracic echocardiography was performed 1 hour post-admission that showed apical akinesis and basal hyperkinesis; left ventricular ejection fraction was estimated at 25%. She was promptly treated with aspirin, clopidogrel, metoprolol, nitroglycerin, atorvastatin, low-molecular weight heparin and eptifibatide. Cardiac catheterization performed the same day did not find any significant coronary artery disease. Left ventriculography confirmed ballooning of the apex during systole characteristic of takotsubo cardiomyopathy. Anticoagulation therapy was stopped thereafter.

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Figure 1. Initial ECG obtained 1 hour after onset of severe pain, demonstrating sinus tachycardia, Q waves in inferior leads (solid arrows) and non-specific T wave changes in lateral leads (broken arrows).

An ECG (Fig. 2) obtained 15 hours post-admission displayed persistently flattened T waves in lead I. New findings included T wave inversion in aVL, T wave changes in V4–5, QT interval prolongation (corrected QT=591 millisecond) and prominent U waves (best seen in V4 and V1 rhythm strip). Another ECG taken 42 hours from admission (Fig. 3) revealed more dramatic changes. There were diffuse T wave inversions in both limb and chest leads, most markedly deep in the leads V4–V6.

During her hospital stay, the patient remained clinically asymptomatic and was shortly discharged home. An echocardiogram done 3 weeks post-discharge showed normal wall motion and recovery of ejection fraction to 50%. ECG at

5 months displayed upright T waves in all leads and no ST-segment abnormalities.

DISCUSSION

The patient's clinical presentation, confounded by the presence of multiple risk factors for coronary artery disease, favored a misleading impression of MI. Takotsubo cardiomyopathy, otherwise known as transient left ventricular apical ballooning syndrome, broken heart syndrome, stress-induced or ampulla cardiomyopathy, is increasingly recognized as a

Figure 2. ECG obtained 15 hours after admission, showing T wave inversions in lead aVL and flattening in V4, V5 and lead I (solid arrows), as well as QTc prolongation and U waves (broken arrows).

Figure 3. ECG taken 42 hours from admission, revealing dramatic, deep T wave inversions (solid arrows).

differential diagnosis among postmenopausal women with suspected acute coronary syndromes. It is characterized by severe but transient left ventricular dysfunction and angiographically normal coronary arteries. First described in Japanese women by Dote et al.,¹ the condition derives its name from the striking resemblance of the left ventriculogram to the Japanese takotsubo octopus trap.

Takotsubo cardiomyopathy is a rare entity. A recent systematic review² estimated its prevalence to range between 0.7 to 2.5% with 90.7% female predominance and mean age of 62 to 76 years. Its exact prevalence, however, is unclear for a number of reasons: its novelty, diverse presentation, and population bias with potentially higher prevalence in “high-stress” urban settings than rural areas.^{3,4}

Its initial chief symptom is angina-like chest pain, followed by dyspnea,^{2-3,5} making it difficult to differentiate from MI based on symptom presentation. Less commonly, patients present with syncope and palpitations. An interesting characteristic of takotsubo cardiomyopathy is that it is typically preceded by a wide variety of emotional or physical stressors ranging from quarrels, accidents,^{6,7} natural calamities,⁸ to seizures,⁹ anaphylaxis,¹⁰ exercise stress test,¹¹ electrical cardioversion,¹² radiofrequency ablation,¹³ and sexual intercourse.¹⁴ Approximately one-third of patients do not have identifiable stress triggers.³

The most common acute ECG findings are ST segment elevation in the precordial leads and T wave inversions in most leads.^{2-3,5,15-20} Evolving T waves deepen further to their first negative peak within 3 days, transiently turn shallow, then become significantly deeper on their second negative peak in 2–3 weeks.^{21,22} T wave changes may revert to normal after about 2–4 months.^{3,22} Prolongation of corrected QT (QTc) interval may occur 48 hours from symptom onset²³ or may accompany the second phase of T wave inversions.²² Q waves in leads V1–V2 or V2–V3 are present in 56% of cases.¹⁹

Dynamic and diffuse T wave inversions, as observed in this case, are the most consistent ECG findings in takotsubo.²⁰ These changes should be differentiated from other condi-

tions,²⁴ including subarachnoid hemorrhage where markedly deep T waves also appear widely splayed and are associated with QT prolongation.²⁵ Neurogenic stunned myocardium induced by aneurysmal subarachnoid hemorrhage and takotsubo cardiomyopathy are believed to share the same mechanism of catecholamine excess.²⁶ Another notable differential diagnosis is Wellens' syndrome,²⁷ a condition characterized by deep T wave inversions typically in leads V2 to V4 and seen in asymptomatic patients with normal cardiac enzyme levels and evidence of critical left anterior descending stenosis.

Perhaps the most unique ECG finding of this case was the presence of prominent U waves. U waves were reported in one case series of ten patients with takotsubo²⁸ but their significance was not elucidated. Another case report²⁹ described the unusual presentation of takotsubo in a young woman who had a syncopal attack after torsade de pointes. Her ECG showed severe QTc prolongation and U waves; she was later diagnosed to have a sporadic long QT syndrome.

Because takotsubo cardiomyopathy mimics MI, several studies have examined their distinguishing ECG features. A retrospective case series by Ogura et al.³⁰ demonstrated that higher ST elevation voltage in leads V4–V6 than V1–V3, and absence of pathologic Q waves and reciprocal changes in the inferior leads showed high sensitivity and specificity to help differentiate takotsubo from anterior MI. More recently, however, two larger prospective studies^{19,20} demonstrated that ECG alone has insufficient value in emergency diagnosis of takotsubo to obviate the need for invasive and more definitive testing. Bybee et al.¹⁹ reported that while the takotsubo cohort had less prominent ST elevation and less frequent concurrent ST depression than subjects with anterior ST elevation MI (STEMI), these differences were relatively subtle. Sharkey et al.²⁰ found concurring results of lower mean magnitude of ST elevation in takotsubo than STEMI with significant overlap.

Clearly, patients with takotsubo cardiomyopathy and acute coronary syndromes present quite similarly. Moreover, cardiac biomarkers, including creatine kinase-MB fraction and troponin I and T, are elevated in majority of patients although to a

relatively lower degree than seen in MI.^{2,3} Using the modified Mayo Clinic criteria,³ a diagnosis of takotsubo cardiomyopathy can be made if all four conditions are met: (1) transient hypokinesia, akinesia, or dyskinesia of the left ventricular mid segments with or without apical involvement; the regional wall motion abnormalities extend beyond a single epicardial vascular distribution; a stressful trigger is often, but not always present; (2) absence of obstructive coronary disease or angiographic evidence of acute plaque rupture; (3) new electrocardiographic abnormalities (either ST-segment elevation and/or T wave inversion) or modest elevation in cardiac troponin, and; (4) absence of pheochromocytoma or myocarditis.

The prognosis of takotsubo cardiomyopathy is generally considered favorable^{5,16} where four-year survival is comparable to an age-matched and gender-matched population.³¹ Although majority of patients recover uneventfully, a study of 185 cases of Tako-tsubo reported complications in approximately one of five patients.³² The most common complications are heart failure, pulmonary edema, dynamic outflow tract obstruction and cardiogenic shock.^{2,3} A repeat echocardiogram is recommended 4 to 8 weeks after discharge to document complete recovery of left ventricular dysfunction. Third-degree atrioventricular blocks, ventricular arrhythmias, left ventricular thrombus formation and free wall rupture have been reported.^{2,5} Significant predictors of morbidity or mortality have not been ascertained.³²

In the absence of consensus treatment guidelines, management strategies of takotsubo cardiomyopathy are derived from case outcomes. Since the clinical and ECG presentation do not reliably distinguish takotsubo from MI, an invasive approach with coronary angiography and ventriculography is appropriate for patients with chest pain and ST elevation to establish the diagnosis.³³ Supportive measures comprise the cornerstone of therapy. Most experts recommend beta blockers in the acute phase for the postulated sympathetic overactivity and for long-term use to avoid recurrence.^{2,3} In contradiction, emerging data show that beta blockers, calcium channel antagonists and nitrates have limited efficacy in recurrence prevention.³⁴ Angiotensin converting enzyme inhibitors or angiotensin receptor blockers are indicated for the left ventricular dysfunction and may be discontinued with recovery of systolic function.³ Short-term anticoagulation with heparin or warfarin may be considered to prevent mural thrombus formation in the setting of severe systolic dysfunction.^{5,33}

In summary, clinicians should have a high index of suspicion for takotsubo cardiomyopathy among postmenopausal women who present with angina following acute stress and demonstrate ECG changes suggestive of ischemia. Generally, patients with takotsubo have lower ST elevation voltage and less frequent reciprocal changes compared to patients with STEMI. Furthermore, dynamic T wave inversions are characteristic of takotsubo. Although these ECG features add incremental diagnostic value, definitive diagnosis still requires invasive cardiac testing. Knowledge of these ECG differences may help medical professionals not to "fall into the trap" of misdiagnosing an MI.

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