

Atypical Presentation of the Broken Heart Syndrome Associated with Chronic Anxiety

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ABSTRACT

The “broken heart syndrome”, or Takotsubo cardiomyopathy, is an acute cause of transient left ventricular systolic dysfunction characterized by abrupt onset of chest symptoms, ECG changes and a mild rise in myocardial enzymes mimicking acute myocardial infarction. This condition is more common in postmenopausal women and is typically preceded by an intense emotional or physical stress or an acute illness. A higher prevalence of anxiety disorders in patients with this syndrome have also been reported recently. Apical ballooning with left ventricular akinesis or dyskinesia of distal one-third to two-thirds of the left ventricle in cardiac catheterization and absence of significant coronary obstruction is this hallmark of this condition. However, various morphologic variants with different ventricular region involvement have been reported including “an atypical variant” where the left ventricular hypokinesia is restricted to the midventricular segment without involvement of the apex. Here we present a case of 56-year-old female with a history of chronic anxiety who presented with retrosternal chest pain after her partner threatened to leave her. Her EKG showed diffuse T-wave changes with prolonged QT intervals. She also had modest elevation of cardiac enzymes.

Keywords: takotsubo cardiomyopathy, broken heart syndrome, anxiety.

INTRODUCTION

Broken heart syndrome, also called transient apical ballooning syndrome or Takotsubo cardiomyopathy, is an acute cause of cardiac dysfunction characterized by transient systolic dysfunction of the apical and /or mid-segments of the left ventricle. It mimics acute coronary syndrome without significant obstructive coronary vessel disease. First described in Japan, this condition has been increasingly reported in the western world.^{1,2} It is more common in postmenopausal women in their sixties and is frequently associated with intense emotional or physical stress.^{2,3,4,5} Characteristically, these patients present with any combination of substernal chest pain, dyspnea, modest elevation of cardiac enzymes and EKG changes.⁶ The exact mechanism of this condition is poorly understood but there is evidence supporting catecholamine excess, multivessel coronary artery spasm and microvascular dysfunction.^{7,8} There may be a higher prevalence of chronic anxiety disorder preceding the illness in these patients.⁹

We present a typical case of Takotsubo cardiomyopathy with atypical ventriculographic characteristics in a patient with long standing anxiety disorder.

CASE REPORT

A 56-year-old white female with a history of hypertension, type 2 diabetes mellitus and hyperlipidemia presented to the emergency room with retrosternal chest pain radiating to the throat and left arm. The pressure-like chest pain had an intensity of 7 on a pain scale of 0 to 10 and was associated with palpitations and shortness of breath. The chest pain started soon after an intense argument with her partner when he threatened to leave her. The emergency squad was immediately called and she was brought to the ER.

The patient was obese. Her past medical history was significant for hypothyroidism, depression and anxiety disorder as well. Her medication list included Aspirin,

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Levothyroxine, Metoprolol, Insulin, Celexa and Ativan. Her family history was significant for coronary artery disease and diabetes mellitus. She is an ex-smoker who stopped smoking at the age of 26. She denied ever drinking alcohol or taking recreational drugs.

During the initial evaluation, the patient did not report pain or distress but appeared slightly anxious. Her pulse was 68 beats per minute; BP was 142/55 mmHg; and respirations 18 breaths per minute. She was afebrile and was breathing room air with an oxygen saturation

of 100%. Her neck was supple and there was no jugular venous distension. Auscultation of the lungs revealed bilaterally decreased, but comparable, vesicular breath sounds. Her heart sounds were normal and without third heart sound or rubs. The point of maximum impulse was not displaced. Other than marked obesity, the examination of her abdomen was unremarkable. There was no neurological deficit. Her extremities were warm and all peripheral pulses were palpable and comparable bilaterally with no pedal edema. The rest of the physical examination was unremarkable.

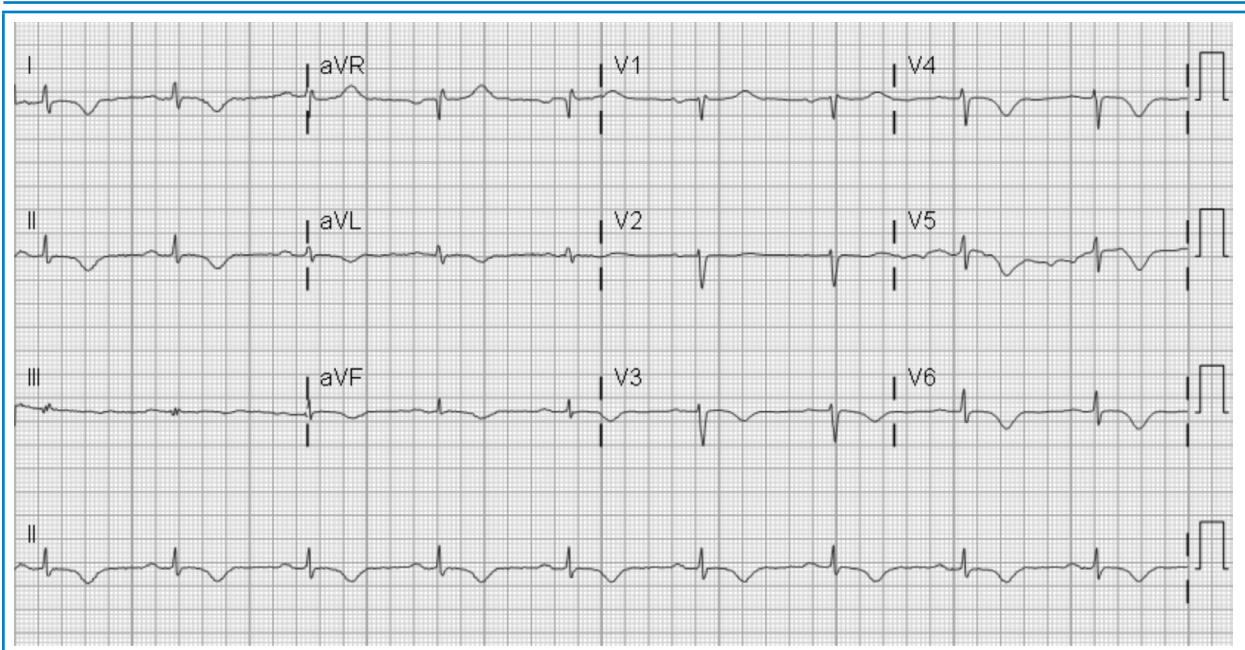


Figure 1. 12 Lead EKG..

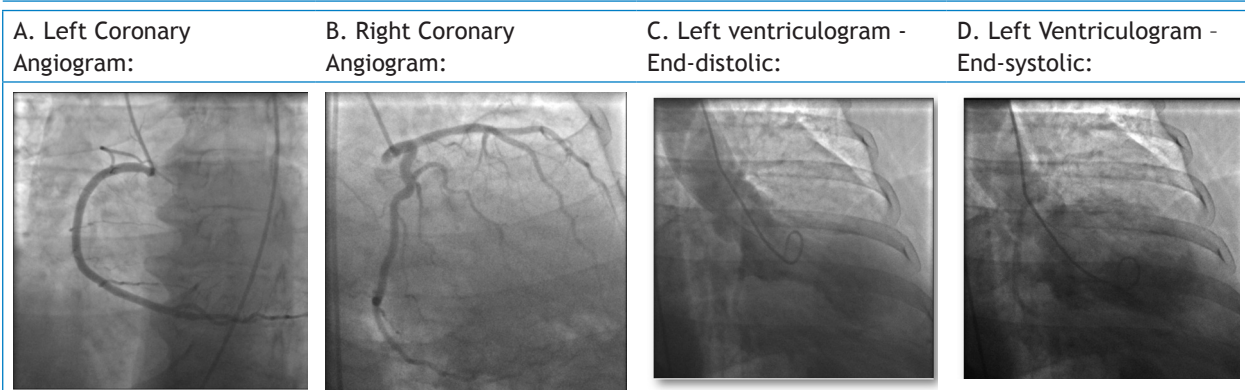


Figure 2. Left (A) and Right (B) Coronary Angiogram; End-diastolic (C) and end-systolic (D) left ventriculogram.

A 12-lead EKG showed sinus bradycardia with first degree atrio-ventricular block, prolonged QT interval and diffuse T-wave changes (Figure 1). Cardiac iso-enzymes were elevated with the Troponin I of 3.34 ng/mL and CKMB of 18.4 ng/mL. The second set of cardiac iso-enzymes increased to a Troponin I of 5.11 ng/mL and

CK-MB of 30.9 ng/mL. Since the patient was allergic to contrast dye, she was first managed conservatively with anticoagulation and eventually was scheduled for cardiac catheterization. A 2D-echocardiogram showed hypokinesia of the apex and a possible psuedoaneurysm.

The coronary artery angiography showed less than 20% stenosis in the left main coronary artery (LMCA), and the left ventriculogram showed severe hypokinesia in the anterolateral, anteroapical, inferoapical and apical regions with an ejection fraction of 30% (Figure 2). In the absence of coronary artery disease, this presentation was most consistent with a nonischemic cardiomyopathy.

In the light of her clinical presentation, the history of a serious argument with her partner, and the absence of a significant coronary artery disease, these findings conform to the clinical features of Takotsubo Cardiomyopathy.

The patient received aspirin, a beta-blocker, an ACE inhibitor and statin therapy. Her condition improved significantly within 4-5 days of admission and she was discharged home to continue the same pharmacotherapy. A follow-up echocardiogram was done in 4 months, and showed a well preserved left ventricular function with estimated ejection fraction of 60%.

DISCUSSION

Takotsubo or Stress-induced cardiomyopathy, is increasingly reported as a cause of nonischemic, transient left ventricular dysfunction. It is characterized by an abrupt onset of chest symptoms, ECG changes and a modest rise in myocardial enzymes mimicking acute myocardial infarction. These patients, who commonly have left ventricular wall motion abnormality, may initially receive treatment for acute coronary syndrome. However, there is no occlusive coronary artery disease.¹⁰

Stress-induced cardiomyopathy is much more common in women than men, accounting for 80% of cases in one prospective study.³ The mean age of presentation is 61 to 76 years.³ Intense emotional or physical stresses as well as acute medical illness are the frequent trigger factors.^{2,4,5} Studies have identified risk factors such as postmenopausal status. Two recent reports of familial cases, involving two sisters in one family and a mother and daughter in another family, raised the possibility of a genetic predisposition.^{11, 12}

There is a higher prevalence of chronic anxiety disorder preceding the illness in patients with stress-induced cardiomyopathy.⁹ Summers et al., in their retrospective case-control study, identified a higher prevalence of anxiety disorders in patients with condition and proposed chronic anxiety along with other psychological stresses as predisposing risk factors and acute anxiety as a triggering factor in the pathogenesis of stress induced cardiomyopathy. This association is plausible because acute emotional stress is a well-recognized trigger for takotsubo cardiomyopathy.⁹

The exact mechanism is unknown and there are no large cohort studies to examine this association. But several studies have identified a positive relationship between psychological stress factors and cardiovascular morbidity and mortality. Negative emotions such as anxiety and depression, stress and social factors have pathophysiological effects on cardiovascular diseases. These psychological factors cause activation of the hypothalamic-pituitary-adrenal and sympathetic nervous systems, serotonergic dysfunction, secretion of proinflammatory cytokines, and platelet activation and may lead to atherosclerosis.²⁰ The same mechanism could precipitate myocardial dysfunction that occurs in stress-induced cardiomyopathy.⁹

The diagnosis of stress-induced cardiomyopathy is suspected in a postmenopausal woman who presents with acute chest pain after an intense psychological stress and the presence of EKG abnormalities that are out of proportion to the degree of cardiac enzyme elevation.⁶ Classically, apical ballooning with akinesis or dyskinesia of the apical one-half to two thirds of the left ventricle is seen on the left ventriculography or echocardiography leading to a reduced ejection fraction.^{4,13} However, other morphologic variants have also been described recently. In one study, about 40 percent of patients had transient left ventricular hypokinesia restricted to the midventricular segment ("atypical variant") without involvement of the apex.¹⁴

The exact mechanism of left ventricular dysfunction has yet to be established. However, available evidence supports the role of excess catecholamine in response to stress, which has been suggested to cause diffuse microvascular spasm and endothelial dysfunction resulting in myocardial stunning¹⁵ or direct catecholamine-associated myocardial toxicity.¹⁶ Typically, microvascular vasospasm is seen in multiple coronary artery territories; however, single arterial spasm has also been reported. A few studies have suggested that wall motion abnormality in transient cardiomyopathy may not always be limited to the apical segment of the left ventricle. In some instances it may involve mid-ventricular segments as well.^{7, 8} Regional differences in the density of cardiac adrenoreceptors might explain the typical form of Takotsubo cardiomyopathy, while inter-individual differences in location and density of these receptors may explain the development of atypical variants.¹⁷

In our subject, the diagnosis of Takotsubo cardiomyopathy was established based on a typical presentation of acute coronary syndrome preceded by strong emotional stress. The patient was found to have significantly elevated levels of troponin and CK-MB. The EKG showed diffuse T-wave inversion and prolonged QT interval which is

a less common finding in this condition. ST-segment elevation is reported as the most common EKG finding in Takotsubo Cardiomyopathy.¹⁸

Additionally, our patient had an atypical presentation on the left ventriculogram. Only the inferio-basal segment of the left ventricle was contracting well. The anterolateral, anteroapical, apical, inferoapical segments were severely hypokinetic.

Different morphologic presentations may be explained by the effect of aging on adrenoceptor location and density as well as the dynamic variation in the sensitivity of the cardiac adrenoceptors. The varying levels of stress and resulting catecholamine excess may also play a role.^{17,19} There are reports of cases initially presenting as an atypical variant of Takotsubo Cardiomyopathy with subsequent occurrence revealing typical ventriculographic features.^{17,19}

In conclusion, variation in the regional myocardial hypokinesias should be considered, and recognized, as a part of Takotsubo Cardiomyopathy. It should no longer be regarded as just an apical ballooning syndrome.¹⁹ The presence of chronic anxiety disorder should be recognized in the pathogenesis of Takotsubo Cardiomyopathy. If the association is proven by larger studies, it would be possible to prevent recurrences by actively treating the psychiatric condition.⁹

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