GLOBAL CARDIOLOGY SCIENCE & PRACTICE
A Qatar Foundation Academic Journal

OPEN ACCESS

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Apical ballooning with mid-ventricular obstruction: the many faces of Takotsubo cardiomyopathy

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ABSTRACT

Takotsubo cardiomyopathy (TTC) is a transient left ventricular dysfunction due to akinesia of the left-ventricular (LV) mid-apical segments (apical ballooning), which can cause severe reduction in LV systolic function. The typical clinical picture of TTC include chest pain, electrocardiographic changes consisting of mild ST-segment elevation followed by diffuse deep T-wave inversion, QTc interval prolongation and mild troponin release in the absence of significant coronary stenoses. The syndrome often affects post-menopausal women and is triggered by sympathetic overstimulation, like intense physical or emotional stress, so that it is called the "broken heart syndrome". Although left-ventricular systolic dysfunction usually fully recovers within few days, heart failure can still complicate the early phase. We report a case of stress-induced cardiomyopathy that had full recovery after 4 weeks of follow up. The main electrocardiographic, angiographic and imaging features are discussed.

Keywords: Takotsubo, stress-induced, cardiomyopathy, electrocardiogram, T-waves, myocardial edema

http://dx.doi.org/10.5339/gcsp.2013.22

Submitted: 21 February 2013
Accepted: 14 March 2013

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Cite this article as: Spadotto V, Elmaghawry M, Zorzi A, Migliore F, Marra MP. Apical ballooning with mid-ventricular obstruction: the many faces of Takotsubo cardiomyopathy, *Global Cardiology Science and Practice* 2013:22 http://dx.doi.org/10.5339/gcsp.2013.22

CLINICAL SUMMARY

A 66-year-old female presented to the emergency department for chest pain of recent onset (30 min) that occurred after a stressful disagreement with her spouse. The patient was a smoker with history of systemic hypertension and borderline hypercholesterolemia. At the time of admission, blood pressure was 95/60 mmHg, heart rate was 72 bpm, O_2 saturation in room air was 100%, and physical examination revealed a 3/6 pansystolic mid-apical heart murmur with no signs of heart failure. The presenting electrocardiogram (ECG) showed Q waves and ST-segment elevation in the inferior leads with an apparent J wave in leads I, V5, 6 (Fig. 1). Troponin I level was 0,048 μg/L (normal value < 0, 045 μg/L). The patient underwent urgent coronary angiography that demonstrated no atherosclerotic coronary artery lesions and mild systolic milking of the mid to distal segments of the left anterior descending artery (LAD) (Fig. 2). Catheterization of the left ventricle (LV) revealed mild reduction of LV ejection fraction (47%) due to apical akinesia, severe dynamic mid-ventricular gradient, and severe mitral regurgitation (Fig. 3). The echocardiogram showed mild reduction of LV ejection fraction (52%) due to apical akinesia, and moderate mitral regurgitation with systolic anterior motion (SAM) of the anterior mitral leaflet caused by the hyperkinetic basal segments, which also generated a peak intra-ventricular gradient of 48 mmHg. According to the Mayo Clinic criteria, the patient was diagnosed with Takotsubo cardiomyopathy (TTC).[1] She was admitted to the cardiac intensive care unit for monitoring and was treated with beta-blocker in order to reduce the intraventricular gradient.[2] Subsequently, the ST-segment elevation was substituted by diffuse T-wave inversion and QT interval prolongation, which reached the maximal amplitude by day four (Fig. 4). The same day cardiac magnetic resonance showed intense myocardial edema of the mid-apical LV segments and a small apical thrombus (Fig. 5). The regional distribution of myocardial edema coincided with the repolarization abnormalities in leads I, II, III, avF, V3-6; while the positive T waves in V1-2 are concordant with lack of edema in the basal septum by CMR. The patient was discharged after 8 days on beta-blocker, ACE-inhibitor and warfarin therapy. Full recovery of the LV function with complete dissolving of the thrombus and normalization of the ECG was observed after 4 weeks follow-up.

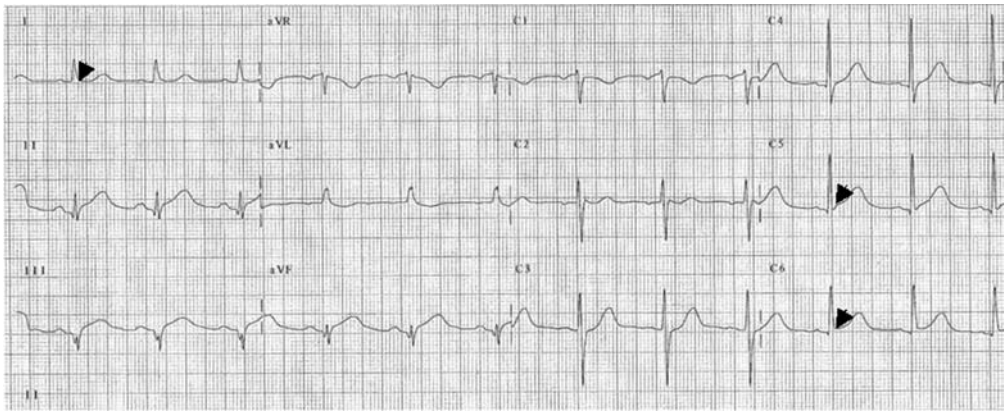

Figure 1. Admission electrocardiogram, characterized by Q waves and ST-segment elevation in the inferior limb leads, mimicking an inferior acute myocardial infarction. Note J wave elevation in I, V5,6 (arrows).

DISCUSSION

TTC is an acute cardiovascular disease characterized by transient LV systolic dysfunction in the absence of critical coronary stenosis, often precipitated by an intense acute emotional or physical stress.[1] The syndrome usually affects post-menopausal women and presents with chest pain, ST-T segment changes at the ECG, and slightly elevated cardiac enzymes so that it is often misinterpreted as an acute myocardial infarction. However, the regional distribution of both echocardiographic and ECG abnormalities goes beyond the distribution of a single coronary artery.[3] Typical TTC is characterized by mid-apical akinesia ("apical ballooning") but atypical ("apical sparing") variants have also been described.[4,5] Patients with atypical TTC are younger and exhibit more often a hyperadrenergic state than those with typical TTC; however, both typical and atypical variants can occur in the same patient.[6]

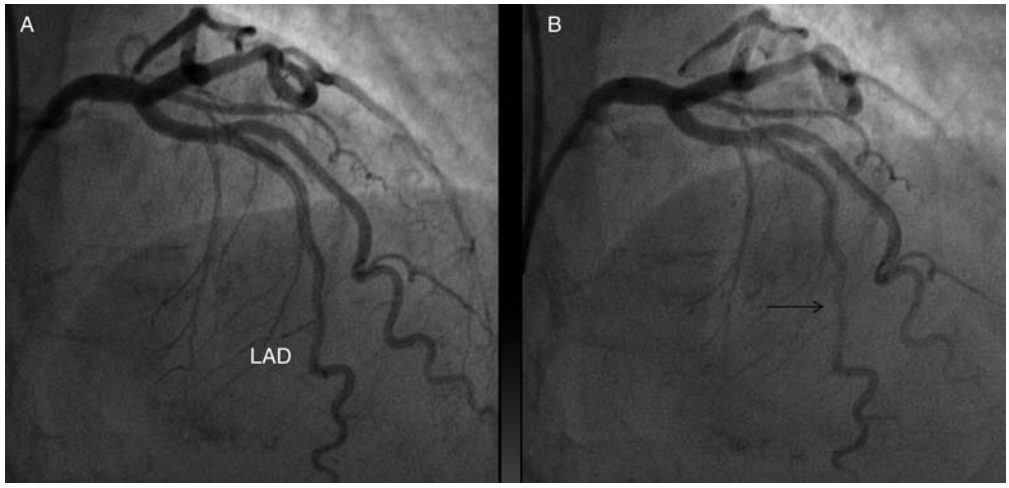

Figure 2. A: Coronary angiogram frame in diastole, showing normal left coronary system with no obvious atherosclerotic lesions. B: Coronary angiogram frame in systole, showing mild milking effect in mid to distal segment of left anterior descending artery (arrow). LAD: left anterior descending coronary artery.

The ECG changes of typical TTC tend to follow a certain pattern. In the acute phase, there is mild and diffuse ST-segment elevation in precordial leads, usually in V3-6, with concomitant ST-segment depression in aVR.[7] Prominent J-waves may precede the appearance of ST-segment elevation.[8] The ST-segment elevation is later replaced by diffuse T-wave inversion and QTc interval prolongation.

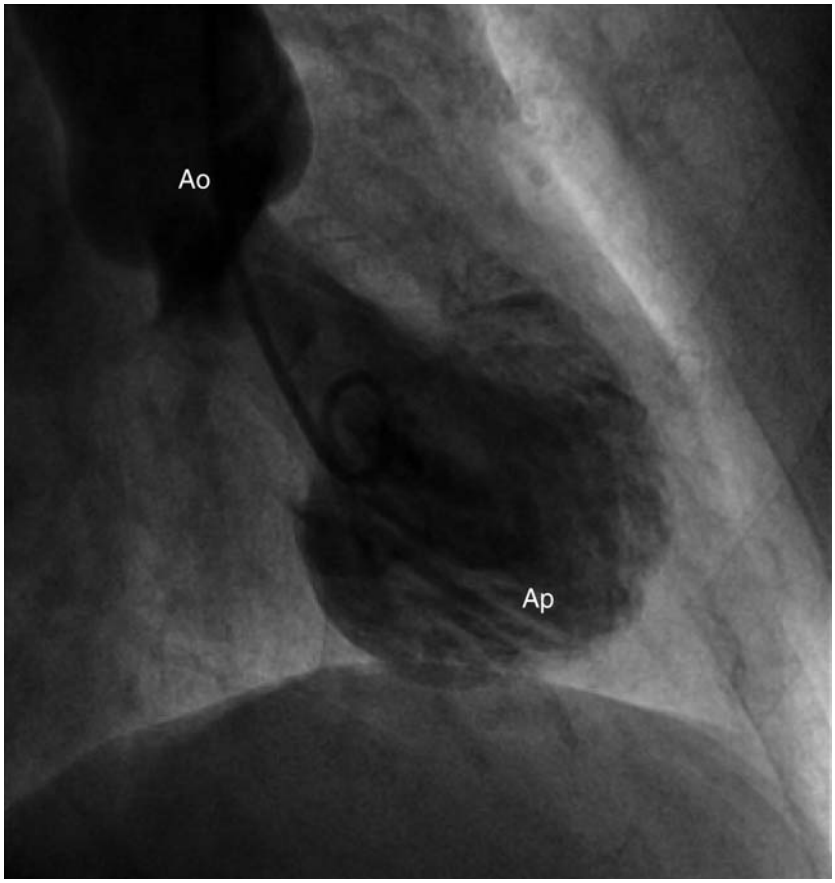

Figure 3. Ventriculography frame in systole, showing apical akinesia ("apical ballooning") and mitral regurgitation secondary to the systolic anterior movement of the anterior mitral leaflet generated by the hyperkinetic basal segments. Ap: left ventricular apex; Ao: aortic root.

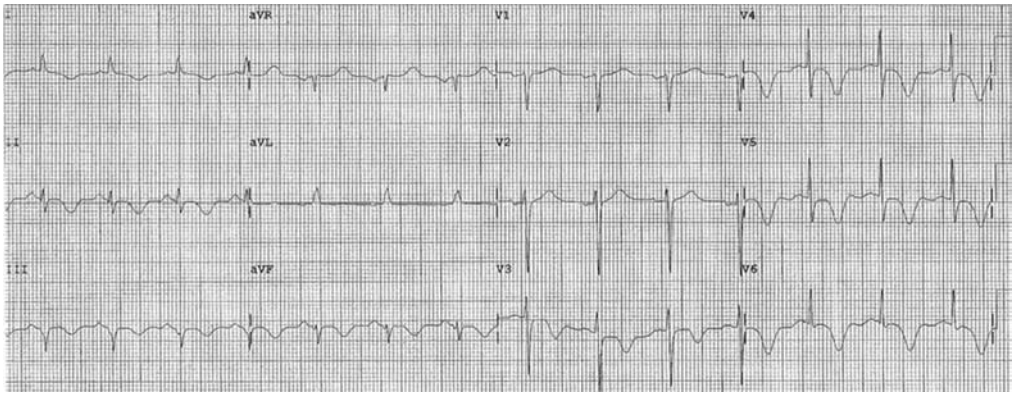

Figure 4. Electrocardiogram acquired at the time of cardiac magnetic resonance (day 4). Note deep T wave inversion in I, II, III, avF, V3-V6, with marked QTc interval prolongation.

The T-wave inversion reaches its trough by day 3–4 (by this time LV function is starting to recover); it tends to revert to normal by day 7–10; then it becomes negative again. The ECG completely normalizes after several weeks from the acute episode.[7] Cardiac magnetic resonance rules out an acute myocardial infarction by showing the absence of gadolinium late-enhancement. Moreover, T2 sequences reveal myocardial inflammation (edema) in the affected LV segments which resolves at follow-up in concomitance with normalization of the LV systolic function and ECG changes.[9,10] In a study on 20 patients with typical TTC forms, T wave inversion in surface ECG coincided and qualitatively correlated with the apicobasal gradient of myocardial edema as evidenced by T2-weighted signal intensity of CMR.[10] The parallel time course of repolarization abnormalities as well as the correlation between the edema signal intensity and the degree of T-wave inversion and QTc interval prolongation

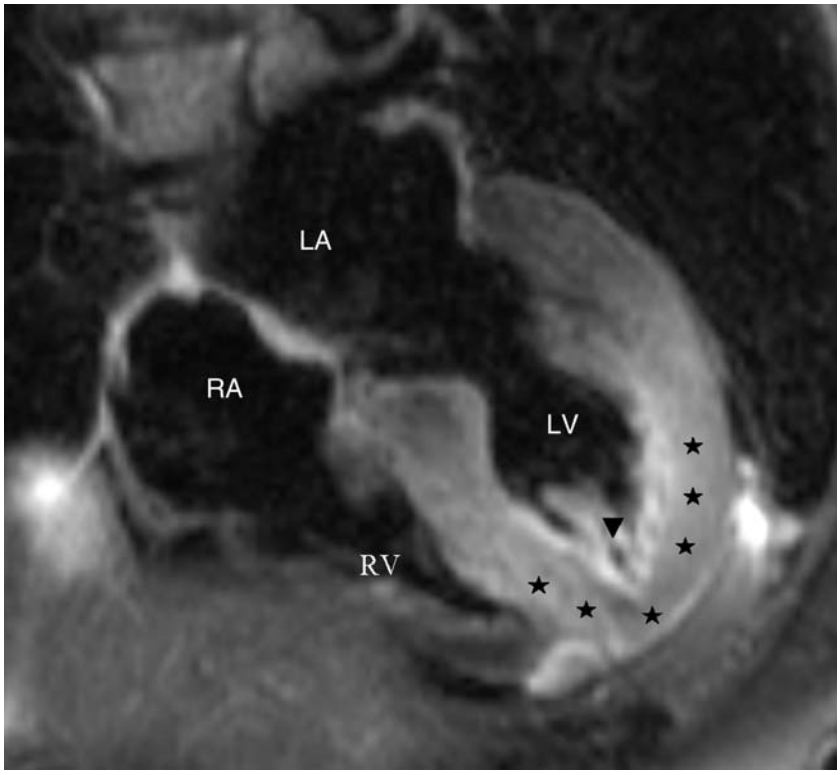

Figure 5. Cardiac magnetic resonance, T2 sequences, 4 chamber long-axis view showing high signal intensity (myocardial edema) in the mid-apical left-ventricular segments (stars) and a small apical thrombus (arrow head). LA: left atrium; LV: left ventricle; RA: Right atrium; RV: right ventricle.

suggests a possible role of myocardial inflammation in giving rise to the repolarization abnormalities typical of the subacute phase of TTC. The interstitial edema could create intramyocardial repolarization inhomogeneity, which can be either transmural (between endocardial and epicardial layers) or regional (from apical to basal segments).[10]

Although full recovery of the LV dysfunction is typically observed within few days, TTC is not an entirely benign condition as complications such as acute heart failure, dynamic intraventricular obstruction with mitral regurgitation and SAM of the mitral valve, life-threatening ventricular arrhythmias, or apical LV thrombosis may be observed.[3,11–13] In fact, in a series of 68 patients with TTC, two elderly patients (85 years old) with acute mitral regurgitation died during hospitalization due to refractory cardiogenic shock and refractory heart failure associated with pneumonia, respectively.[13] The mechanism of mitral regurgitation during TTS is likely due to the altered spatial relationship between mitral leaflets and the subvalvular apparatus, caused by the apical ballooning.[13] In addition, in the same series, SAM occurred in 36% of patients with mitral regurgitation. SAM of the mitral valve possibly results from the LV apical dyskinesia, abnormal papillary muscle tethering forces, mitral valve displacement, and the hypercontractile basal LV segments.[13] The therapy for TTC is usually supportive but it is important to identify and correct any potential triggering factors to avoid recurrences.[14]

The main hypothesis for the pathophysiology of TTC is that an increase in the level of serum catecholamines secondary to a stressful event may cause either microvascular coronary spasm or direct myocardial toxicity leading to a reversible myocardial inflammation and dysfunction.[3] The sympathetic overstimulation can also be caused by pheochromocytoma, exogenous sympathomimetics or withdrawal of sympathetic antagonists, such as opioids.[3,14–16] In a recent *in vivo* rat model, high intravenous epinephrine, but not norepinephrine, bolus produced a reversible LV apical depression associated with basal hyper-contractility, mimicking typical TTC. The myocardial contractility depression was prevented via Gi inactivation by pertussis toxin pretreatment. This epinephrine-induced effect can be explained by the agonist effect of epinephrine on β2AR-Gs at low doses and for β2AR-Gi at high doses, with a differential apico-basal gradient in β2ARs distribution. In the same work, further *in vitro* studies demonstrated that the high dose epinephrine can induce cardiomyocyte cardiodepression and cardioprotection in a β2AR-Gi dependent manner. The authors suggest this epinephrine β2AR-Gi signaling may have evolved as a cardioprotective strategy to limit catecholamine-induced myocardial toxicity during acute stress.[17] A recent clinically based study showed that myocardial bridging of the LAD artery was detected in 76% of TTC patients either by angiography or MSCT.[18] This observation proposes that TTC results from a complex physiological interplay between surging circulating catecholamines and transient coronary flow insufficiency. However, further experimental and clinical studies are needed to prove this hypothesis.

CONCLUSION

We reported a case of typical TTC, precipitated by an emotional stress and complicated by SAM of the anterior mitral leaflet, severe intraventricular gradient and apical thrombus. Supportive therapy and time lead to full recovery. TTC is a stress-reversible acute myocardial dysfunction that should be recognized as a cause of chest pain and ST-segment elevation, typical of post-menopausal women. Emotional, physical, or iatrogenic sympathetic stimuli may contribute to the development of TTC. Although long-term follow-up is favorable, severe complications can occur in the acute phase.

Authors disclosures

None.

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