

Delayed onset Takotsubo syndrome following exercise ECG: a case report

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Background

Takotsubo syndrome usually occurs immediately following a physical or emotional trigger. In some cases, a triggering stress may not be evident. A delayed manifestation of the syndrome may account for such cases.

Case summary

An asymptomatic 69-year-old woman presented for a routine cardiac check-up, which revealed normal electrocardiogram (ECG), echocardiography, and exercise ECG. She did not complain of any chest pain during or immediately after the tests. After about 24 h, she developed chest pain for which she was admitted with the provisional diagnosis of acute coronary syndrome. ECG showed dynamic T-wave changes with QTc prolongation. Cardiac biomarkers were mildly elevated. Characteristic reversible left ventricular dysfunction in absence of coronary stenosis ultimately led to the diagnosis of Takotsubo syndrome.

Discussion

Our case represents a delayed occurrence of Takotsubo syndrome triggered by a treadmill exercise stress test, which manifested about 24 h following the stressor. Such delayed manifestation may account for those cases of Takotsubo syndrome where no immediate triggering stressor is evident.

Keywords

Takotsubo syndrome • Delayed onset • Treadmill exercise ECG • Case report

Learning points

- Although a triggering stress is often present in Takotsubo syndrome, the temporal relation between the trigger and the cardiac event is variable and may not always be easily apparent.
- Delayed manifestation of Takotsubo syndrome following a stressful event may account for some of the cases of Takotsubo syndrome where no immediate physical or emotional stressors are found.

Introduction

Takotsubo is characterized by acute, reversible left ventricular (LV) dysfunction in the absence of significant angiographic coronary stenoses.^{1,2} The syndrome is often triggered by emotional or physical stress, leading to a hypersympathetic state and catecholamine excess³ and is normally expected to occur soon after the stressful event. In some cases, however, no trigger is evident. We report a case of Takotsubo syndrome provoked by treadmill exercise electrocardiogram (ECG), which manifested about 24 h following the treadmill test.

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Timeline

Day	Event
Day 0	Routine cardiac check-up. Normal resting electrocardiogram (ECG), echocardiography, and treadmill exercise test.
Day 1	Presented with chest pain to emergency department and was admitted in coronary care unit. ECG revealed QT prolongation along with T inversion in aVL. Cardiac biomarkers mildly elevated. Started on treatment on the presumed diagnosis of non-ST-elevation myocardial infarction.
Day 2	Chest pain resolved within a few hours. ECG revealed further QT prolongation along with tall T in V3–V6, new T inversion in III and aVF, and normalization of T wave in aVL. No further chest pain. Echocardiography revealed mild concentric hypertrophy of left ventricle, akinetic apex, preserved overall left ventricular systolic function (left ventricular ejection fraction: 50%), and reduced diastolic compliance along with mild mitral regurgitation. Coronary angiography revealed normal coronary arteries. Left ventricular angiography revealed apical systolic ballooning.
Day 3	ECG revealed reduction in QT prolongation.
Day 4	Normalization of ECG changes. Shifted to general ward.
Day 5	Recovers uneventfully, discharged.
One week post-discharge	Echocardiography revealed resolution of wall motion abnormalities.

Case presentation

An asymptomatic 69-year-old hypertensive Indian woman arrived at our hospital for a routine cardiac check-up. She had no other significant cardiovascular and non-cardiovascular comorbidities. The tests revealed normal resting ECG and only mild concentric LV hypertrophy (maximum wall thickness 1.3 cm) on echocardiography. In the exercise ECG, she managed 4 min 8 s on the Bruce protocol achieving 86% of the maximum predicted heart rate. The test was stopped for shortness of breath. No ST segment changes were seen. She did not complain of any chest pain during or immediately after the tests.

On the following day after about 24 h of exercise ECG, she developed a constricting type of chest pain and was brought in to the A&E department within 4 h of symptom onset.

General examination was unremarkable. Pulse was 90/min and blood pressure was 130/80 mmHg. Jugular venous pressure was not raised. No abnormal heart sounds or murmurs were audible.

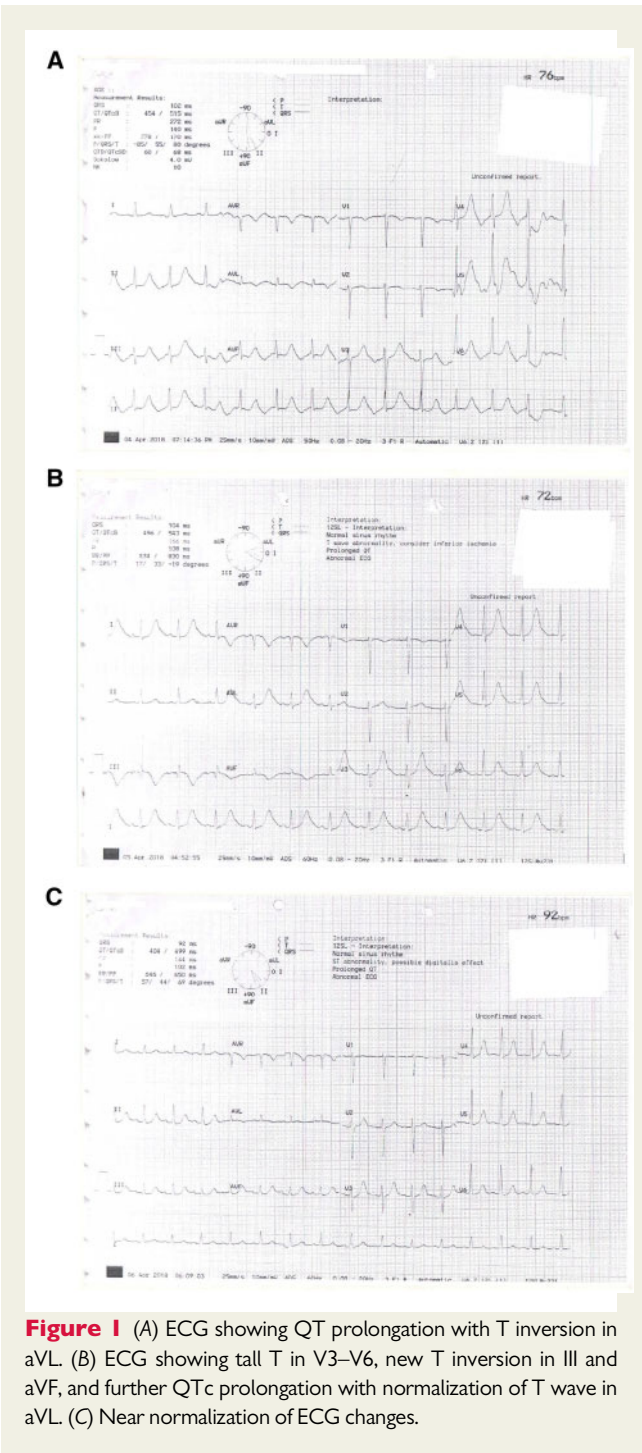


Figure 1 (A) ECG showing QT prolongation with T inversion in aVL. (B) ECG showing tall T in V3–V6, new T inversion in III and aVF, and further QTc prolongation with normalization of T wave in aVL. (C) Near normalization of ECG changes.

ECG done on admission showed QT prolongation along with T inversion evident only in aVL (Figure 1A). Cardiac biomarkers done on admission were mildly elevated; CPK-MB was 42 U/L (normal range <24 U/L) and Troponin I was 0.18 ng/mL (normal range <0.01 ng/mL).

N-terminal prohormone of brain natriuretic peptide was also raised at 2018 pg/mL (normal range for age <900 pg/mL). Echocardiography revealed mild concentric hypertrophy of left ventricle (maximum wall thickness 1.3 cm), dyskinetic apex with hyperkinetic basal LV wall, preserved overall LV systolic function (ejection fraction about 50% measured by Simpsons biplane method), and

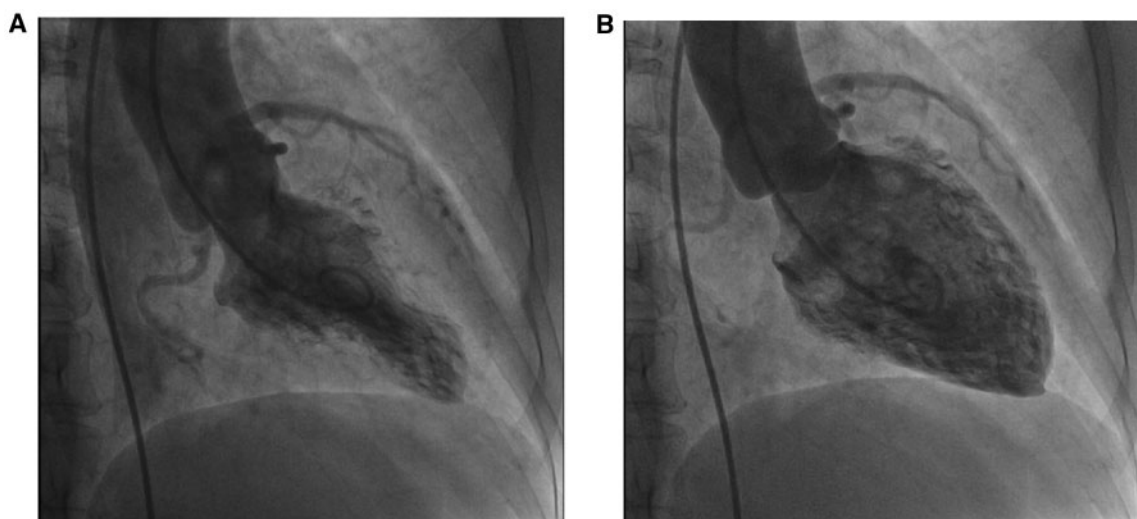


Figure 2 Left ventricular angiography in (A) systole showing apical ballooning and (B) diastole.

reduced diastolic compliance along with mild mitral regurgitation. Right ventricular size and systolic contraction were normal.

She was started on anti-platelets, statin, beta-blocker, subcutaneous low molecular heparin, and intravenous nitrates on the presumed diagnosis of non-ST-elevation myocardial infarction. Her symptoms settled with treatment, but on the following day ECG showed tall T in V3–V6, new T inversion in III and aVF, and normalization of T wave in aVL (Figure 1B). Further increase in QTc interval was also noted. Electrolytes were normal. She underwent coronary angiography which revealed normal coronary arteries. Apical systolic ballooning was seen on LV angiography (Figure 2A and B). The ECG changes and QTc prolongation normalized within 72 h of admission (Figure 1C). She had an uneventful recovery and was discharged on the fourth day only on ramipril 2.5 mg once daily and aspirin 75 mg once daily, with the plan to discontinue aspirin on normalization of LV wall motion abnormalities.

A follow-up outpatient echocardiography in a week's time showed resolution of wall motion abnormalities. Aspirin was discontinued and ramipril dosage was optimized. She was planned for long-term follow-up. She was recommended to avoid intense physical exercise and not to repeat exercise ECG in future.

Urinary metanephrines were checked post-discharge and was found in the normal range.

Discussion

In our case, an acute coronary syndrome—like presentation with elevated cardiac biomarkers, transient T wave changes with QTc prolongation on the ECG, and characteristic reversible apical systolic ballooning in the presence of normal coronary arteries, established the diagnosis of Takotsubo syndrome.⁴

The patient denied any stressful event in the days prior to the occurrence of chest pain. Therefore, no identifiable stressor other than exercise ECG testing was evident. As catecholamine surge induced by the stressor is widely accepted as the probable aetiology, the manifestation

of the syndrome is expected to occur soon after the triggering stress. In our case, it occurred about 24 h after the presumed trigger. A delayed catecholamine surge, however, is not unknown. Delayed onset up to 48 h has been reported after an acute cerebral event.⁵

The distinction between Takotsubo cardiomyopathy and other forms of MINOCA (myocardial infarction with non-obstructive coronary arteries) may be sometimes challenging. Coronary artery spasm or vasospastic angina is usually associated with ST-segment shift that was not seen in this case. Although provocative test with acetylcholine has been shown to be safe when used by experienced researchers, we did not perform the test as it is generally avoided during the acute phase.⁶ Moreover, Takotsubo cardiomyopathy may be associated with abnormal vasomotor function and coronary vasospasm with acetylcholine could be demonstrated even in about one-fifth of the cases with the syndrome.⁷ Unavailability of cardiac magnetic resonance imaging is a study limitation that we acknowledge.

Although various physical or emotional stressful situations have previously been reported as triggers for Takotsubo syndrome,^{8,9} no trigger was identifiable in about 30% of cases.^{10,11} A delayed manifestation of the syndrome may account for some of the cases of Takotsubo syndrome where no immediate stressors are apparent.

Lead author biography



Dr. Aruni Ghose has just graduated (MBBS) from NRS Medical College & Hospital, Kolkata in 2019 where he was awarded with Honours in Anatomy, Physiology and Pharmacology. He is keen on learning and journal writing. He looks forward to start a career in Surgical Training in the UK.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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