CASE REPORT

Takotsubo cardiomyopathy case series: typical, atypical and recurrence

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SUMMARY

Takotsubo cardiomyopathy (TCM) is characterised by a transient left ventricular (LV) dysfunction, ECG changes that can imitate acute myocardial infarction and positive cardiac biomarkers in the absence of obstructive coronary artery disease. The exact pathogenesis of TCM is unclear but emotional or physical stress is a common denominator. We present three cases encompassing a spectrum of the disease: A typical TCM with apical LV dyskinesia, an atypical TCM with mid-ventricular regions affected and a TCM recurrence. Our cases show that TCM symptoms vary between individuals and may vary in the same patient. All our patients reported acute emotional stress prior to the onset of symptoms, had LV systolic dysfunction, positive cardiac biomarkers and non-obstructed coronary arteries. In all cases, LV systolic dysfunction eventually improved. TCM may account for 0.7–2.5% of acute coronary syndromes. It is more prevalent in the female population and can reoccur. Treatment is mainly supportive.

BACKGROUND

Takotsubo cardiomyopathy (TCM) is also known as stress cardiomyopathy,¹ broken heart syndrome² and transient left ventricular (LV) apical ballooning syndrome.³ It is characterised by a transient LV dysfunction, ECG changes that can imitate an acute myocardial infarction and a release of myocardial enzymes in the absence of obstructive coronary artery disease.⁴ The syndrome was first described in Japan, in 1991, when authors observed that the shape of an affected left ventricle is similar to a tako-tsubo, a Japanese pot for fishing octopus.⁵

Although most common symptoms include chest pain and dyspnoea, more serious presentations, such as cardiogenic shock or ventricular fibrillation were also described.^{4 6} The prevalence of stress cardiomyopathy is estimated at 0.7–2.5% of acute coronary syndromes (ACSs)^{3 6 7} and it most commonly affects postmenopausal women.^{4 6} The exact pathogenesis of TCM remains unclear,² however, preceding acute emotional or physical stress is a common denominator.^{4 6} A recent meta-analysis of acute mortality in TCM showed that this condition may not be as benign as previously believed with 1.7% of patients dying due to cardiac complications and 2.8% due to underlying non-cardiac conditions.⁸ Male gender and stress cardiomyopathy secondary to other life-threatening disorders were identified as risk factors.⁸

Echocardiogram in TCM shows LV systolic dysfunction (LVSD) with regional wall motion abnormalities extending beyond a single epicardial vessel distribution.⁷ Akinesis/dyskinesia affects either

apical (typical TCM) or mid-ventricular LV segments (atypical TCM).^{3 7} Most frequent ECG changes include ST segment elevations, T wave inversions and pathological Q waves.^{3 4 6} Coronary angiography is commonly normal or confirms only mild, non-occlusive atheromatous changes.^{4 6 7}

Strikingly, in the majority of patients, the LVSD improves rapidly within days to weeks.^{4 6} TCM can reoccur with a reported recurrence rate in the region of 5–7%.^{7 9}

CASE PRESENTATION

Case 1: Patient 1 was a 74-year-old Caucasian woman who presented to accident and emergency (A&E) department after two episodes of shortness of breath. The second episode was associated with severe, pressure-like chest pain which initially responded to short-acting nitrates but later required intravenous opiates. Her medical history included hypertension, hyperlipidaemia, polymyalgia rheumatica, temporal arteritis and a diagnosis of possible angina made by her general practitioner. A stress trigger was identified as her husband's relapse of bipolar affective disorder and a perceived lack of social and family support.

Case 2: Patient 2 was a 60-year-old Caucasian woman who presented to A&E with a 3-day history of worsening, central, pleuritic chest pain associated with breathlessness, presyncopal symptoms, palpitations, increased sweating and fever. Her medical history included hyperlipidaemia and spondylosis. A stress trigger was identified as the 1 year anniversary of her husband's sudden death.

Case 3, first presentation: Patient 3 was an 80-year-old Caucasian man who presented to A&E with a 2 h history of central, heavy chest pain. His background included hyperlipidaemia, hypertension and a history of smoking. The stress trigger was identified as the recent bereavement of his wife.

Case 3, second presentation: Patient 3 represented 2 years later with a sudden onset of breathlessness and sweating in the middle of the night. Patient reported attempting to reconstruct his wife's memorial stone in preceding days which lead to high levels of emotional anguish.

INVESTIGATIONS

Case 1: On admission, patient 1 was hypoxic and her chest X-ray (CXR) was consistent with pulmonary oedema. ECG showed sinus rhythm, LV hypertrophy with strain pattern laterally and ST segment elevations in anterior leads (figure 1). Peak serum troponin T (TnT) was 0.17 µg/L (normal range 0–0.03 µg/L). Invasive coronary angiogram revealed

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Reminder of important clinical lesson

non-obstructive coronary artery disease with 45% stenosis in the mid-left anterior descending artery and 30% stenosis in the right coronary artery. Left ventrioculography (LV-gram) showed moderate LVSD with apical ballooning (figure 2). A subsequent echo revealed mildly dilated LV with an estimated ejection fraction (EF) of 41%, markedly impaired apical regions with good basal contraction. There was moderate aortic regurgitation (AR) and mild mitral regurgitation (MR).

Case 2: On admission, ECG showed sinus rhythm with T wave inversions inferiorly and Q waves in anterior leads (figure 3). CXR was unremarkable. Laboratory tests showed a peak serum TnT of 0.20 µg/L (normal range 0–0.03 µg/L), elevated white cell count of $15.3 \times 10^9/L$ (normal range $3.5\text{--}11.0 \times 10^9/L$) and C reactive protein of 158 mg/L. Initial physical examination suggested a possibility of a new systolic murmur; however, this was not confirmed on subsequent examinations.

Figure 1 Patient 1, admission ECG.

Figure 2 Patient 1, left ventrioculography.

Figure 3 Patient 2, admission ECG.

Figure 4 Patient 2, left ventriculography.

Coronary angiogram revealed normal and smooth coronary arteries. LV-gram showed a moderately impaired LV systolic function (LVSD) with ballooning and hypokinesia in mid-ventricular—basal segments (figure 4). Echo showed LVSD with an estimated EF of 35%. Anterior wall, septum and inferior wall were hypokinetic.

Case 3, first presentation: On admission, ECG showed sinus rhythm with Q waves and ST segment elevations in anterior leads and T wave inversions in inferior and lateral leads (figure 5). CXR was unremarkable. Peak serum TnT was 0.42 µg/L (normal range 0–0.03 µg/L). Coronary angiogram revealed left anterior descending and right coronary artery plaque disease, without any obstructive lesions. LV-gram confirmed mild LVSD and apical ballooning (figure 6).

Case 3, second presentation: Patient 3 was clinically and radiologically in pulmonary oedema. ECG showed Q waves with ST elevations in septal leads, T wave inversions in inferior leads and biphasic T waves in lateral leads (figure 7). Serum TnT peaked at 0.11 µg/L (normal range 0–0.03 µg/L). Coronary angiogram revealed a moderate, non-obstructive lesion in the left anterior descending artery and diagonal artery bifurcation. LV-gram again confirmed apical ballooning (figure 8).

DIFFERENTIAL DIAGNOSIS

Case 1: Non-ST elevation myocardial infarction (NSTEMI) leading to LVSD and pulmonary oedema was the main differential diagnosis. This was excluded once a stress trigger was identified and a coronary angiography was performed, with evidence of non-obstructive coronary artery disease and typical apical ballooning.

Figure 5 Patient 3, first presentation, admission ECG.

Case 2: NSTEMI was the main differential diagnosis. Infective endocarditis was considered due to a possibility of a new systolic murmur and raised inflammatory markers. A diagnosis of atypical TCM was established post coronary angiogram and once a stress trigger was identified.

Case 3, first presentation: NSTEMI was the main differential diagnosis until a coronary angiogram was performed and a diagnosis of typical TCM was made.

Case 3, second presentation: Although a recurrence of TCM was suspected, patient was also treated as NSTEMI initially. A coronary angiogram and LV-gram images were reviewed with an invasive cardiologist and a consensus was reached that this presentation was likely due to a recurrence of TCM and that coronary artery lesions were non-obstructive. Owing to high blood pressure, pheochromocytoma was queried, however, blood pressure easily responded to antihypertensive treatment, 24 h metadrenaline levels came back as normal and MRI revealed normal adrenal glands.

TREATMENT

Case 1: Patient 1 initially received conventional ACS treatment which consisted of dual antiplatelet therapy, low molecular weight heparin (LMWH) and statin. She also received intravenous diuretics and glyceryl trinitrate as treatment for pulmonary oedema. Once this resolved, ACE inhibitor and β blocker were added.

Once TCM was diagnosed, full ACS treatment was stopped and patient was discharged home on aspirin, statin, diuretics, ivabradine, ACE inhibitor, long-acting nitrate and B-blocker.

Figure 6 Patient 3, first presentation, left ventriculography.

Case 2: Patient 2 initially received conventional ACS treatment which included: dual antiplatelet therapy, LMWH, ACE inhibitor, β -blocker and statin. After a diagnosis of TCM, patient was discharged on aspirin, β -blocker, ACE inhibitor and statin. Spironolactone was added on initial follow-up visit.

Case 3, first presentation: Conventional ACS treatment with dual antiplatelet, LMWH, β -blocker, statin and sartan was started after admission. Prior to discharge, LMWH was stopped and the remaining medications continued with a plan to stop clopidogrel 1 year after the admission.

Case 3, second presentation: Similar to his previous admission, patient 3 was initially treated with conventional ACS therapy. He also required intravenous diuretics to treat pulmonary oedema. On discharge he was on aspirin, statin, sartan, B-blocker and dihydropyridine calcium channel blocker.

OUTCOME AND FOLLOW-UP

Case 1: After discharge, patient 1 was readmitted 3 days later with sudden onset resting chest pain associated with breathlessness and nausea. There were no significant changes on her repeated echo or ECGs, and TnT results continued to fall from the previously elevated value. Her symptoms improved with an increased dose of diuretics and ivabradine, and patient was subsequently discharged. Five months after initial presentation, patient continued to experience breathlessness and intermittent chest pains, and she underwent a transoesophageal echocardiography (TOE) to reassess her valvular pathologies. TOE showed normal LV dimensions and good LV systolic function, severe AR

and severe MR. Patient subsequently underwent a mitral valve repair and aortic valve replacement.

Case 2: Postcoronary angiogram patient developed hospital-acquired pneumonia and was treated with intravenous antibiotics. A repeated echocardiogram, 6 weeks after discharge, revealed normal LV systolic function with estimated EF of 68% and no residual wall motion abnormalities.

Case 3, first presentation: Patient 3 quickly improved after the admission and a repeated echocardiogram 6 months later revealed no more than mildly impaired LV function (EF 52%) and no evidence of apical ballooning.

Case 3, second presentation: After second discharge, patient 3 was readmitted 3.5 months later for the third time with another episode of pulmonary oedema. Serum TnT peaked again at 0.11 $\mu\text{g/L}$ (normal range 0–0.03 $\mu\text{g/L}$). Echocardiogram at the time revealed mild-moderate LVSD (EF 44%), and patient was treated conservatively for a third recurrence of TCM. A stress trigger was not identified on this presentation. On discharge he was put on regular spironolactone and loop diuretic.

Seven months after third presentation, his echo showed normal LV function, his blood pressure was well controlled and he was discharged from the clinic.

DISCUSSION

TCM is a complex condition and its pathogenesis is not fully understood.² Theories trying to explain the mechanism behind it include: multivessel coronary vasospasm; myocardial microvascular dysfunction; aborted myocardial infarction caused by

Figure 7 Patient 3, second presentation, admission ECG.

Figure 8 Patient 3, second presentation, left ventriculography.

transient thrombotic occlusion; LV outflow tract obstruction; blood-borne catecholamine cardiac toxicity; cardiac sympathetic disruption and norepinephrine seethe and spillover.² Initially TCM was thought to be a geographical and racial phenomenon.⁵ However, since initial reports, cases were also described in Europe and America^{1–4 6 7} and it is felt that stress cardiomyopathy may account for 0.7–2.5% of ACSs.^{3 6 7}

As shown by our cases, LV ballooning syndrome can present with a variety of physical signs and symptoms which vary between patients and may vary in the same individual with TCM recurrence. Although reported female prevalence among patients with TCM is estimated at 87–94%, males may not only be affected by this condition but we are reporting on TCM recurrence in a male patient.

Within LV ballooning syndrome, there are two recognised forms as illustrated by our patients: typical with apical LV regions affected and atypical with mid-ventricular ballooning.

What our patients had in common, and what is shown in literature,^{4 6 7} is an identifiable stress trigger, symptoms and signs mimicking ACS, coronary angiogram showing normal coronary arteries or non-obstructive coronary lesions, and eventual full resolution of LV dysfunction and wall motion abnormalities.

In the absence of studies comparing and evaluating TCM treatment, therapy remains empirical and supportive,⁴ mostly focusing on heart failure management. There is also currently no evidence that treatment prevents stress cardiomyopathy recurrence.¹⁰ However, the number of patients described in studies is too small to draw any firm conclusions.^{9 10}

Contributors JL was involved in the literature search, review of medical notes/results, preparation of figures, drafting of the manuscript. VC was involved in the literature search, review of medical notes/results, drafting of the manuscript. PS was involved in the supervision and revision of the manuscript.

Competing interests None.

Patient consent Obtained.

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Learning points

- ▶ Takotsubo cardiomyopathy (TCM) commonly mimics acute myocardial infarction and its prevalence is estimated at 0.7–2.5% of acute coronary syndromes.
- ▶ Although exact pathogenesis of TCM is unknown, it usually affects postmenopausal women and a physical or emotional stress trigger is a common denominator.
- ▶ Two types of TCM are recognised: typical with apical left ventricular regions dyskinesia and atypical with mid-ventricular ballooning.
- ▶ TCM therapy remains empirical and supportive, mostly focusing on heart failure management.
- ▶ Although, in the majority of patients, the left ventricular systolic dysfunction improves rapidly within days to weeks, recent meta-analysis estimates in-hospital mortality at 4.5% due to cardiac and non-cardiac complications and as such, this condition may not be as benign as previously believed.

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