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CASE REPORT
Coronary intervention

Takotsubo cardiomyopathy in patients with borderline stenosis of the left anterior descending artery and vasospastic angina: to stent or not to stent? A case report

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Background Takotsubo cardiomyopathy (TCM) is a complex disease that resembles the clinical presentation of acute myocardial infarction with non-obstructive coronary arteries. The aetiology remains elusive despite the comprehensive nature of current guidelines meticulously detailing the diagnostic process.

Case summary We present the case of a 64-year-old female who presented with a clinical profile consistent with non-ST elevation myocardial infarction, confirmed by elevated cardiac enzyme levels. Echocardiography raised suspicions of TCM. Angiography presented a challenge, revealing a 65% stenosis of the left anterior descending artery (LAD). Based on the collected evidence, we decided to delay and ultimately forgo LAD revascularization while identifying epicardial vasospasm through a provocation test as a possible cause underlying TCM.

Discussion Conducting an acetylcholine provocation test, as recommended by the European Society of Cardiology guidelines for patients with ischaemia and no obstructive coronary artery disease unveiled severe diffuse vasospasm affecting both the LAD and circumflex arteries. The intricate interplay of pathophysiological mechanisms and clinical presentations necessitates ongoing exploration to uncover the mysteries and refine our diagnostic and therapeutic strategies.

Keywords Cardiomyopathy • Heart failure • Myocardial infarction • Takotsubo • OCT • Case report

ESC curriculum 2.1 Imaging modalities • 2.3 Cardiac magnetic resonance • 3.2 Acute coronary syndrome • 3.4 Coronary angiography • 6.5 Cardiomyopathy

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Learning points

Importance of comprehensive diagnostic evaluation:

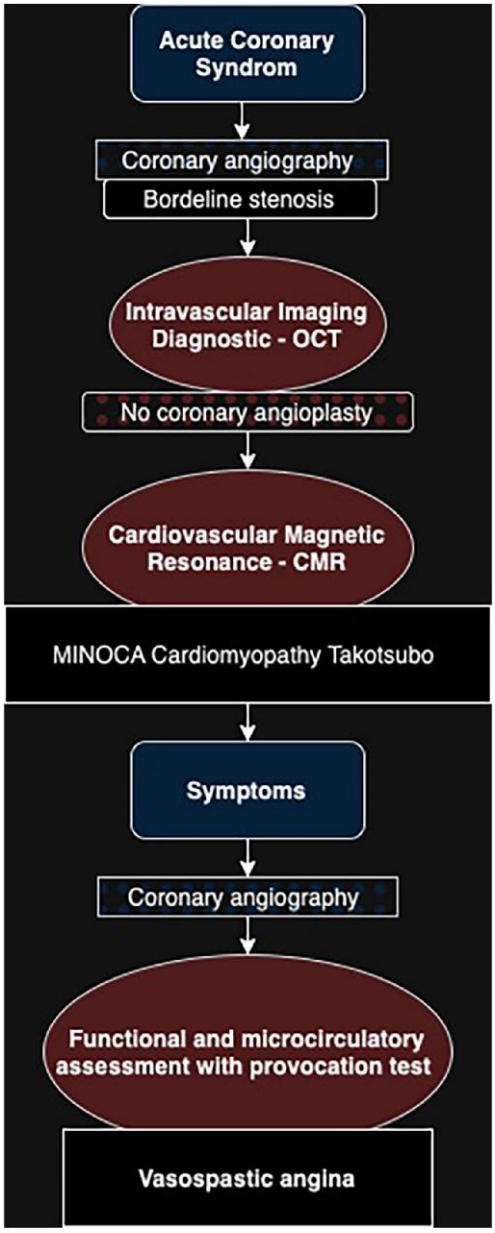
- Despite initial findings suggestive of non-ST elevation myocardial infarction, the patient underwent extensive diagnostic procedures, including coronary angiography, optical coherence tomography (OCT), left ventriculography, and magnetic resonance imaging, to ensure that there was no ischaemic reason for takotsubo cardiomyopathy (TCM). Consider using OCT to exclude plaque rupture or thrombus-containing lesions in myocardial infarction with non-obstructive coronary arteries patients, especially in borderline lesions in left anterior descending artery.
- Combining ischaemia exclusion with a provocative acetylcholine test is crucial in confirming the diagnosis. Vasospasm is considered a potential mechanism in TCM.

Introduction

Takotsubo cardiomyopathy (TCM), colloquially known as stress cardiomyopathy, emerges in response to a surge of catecholamines prompted by acute stress, leading to cardiac dysfunction.[1] The aetiological triggers include physical or emotional stressors.[2,3] These symptoms, mirroring acute myocardial infarction in the absence of obstructive coronary disease, manifest as a transient impairment of left ventricular function. A hallmark of TCM is the emergence of regional wall motion abnormalities, notably characterized by a distinctive ballooning of the left ventricle. These motion aberrations expand beyond the confines of a single vascular territory, typically concentrating at the apex of the left ventricle.[4,5] The clinical manifestation of TCM mirrors the presentation of acute coronary syndrome (ACS). Thus, a meticulous process of differential diagnosis is imperative, involving the exclusion of all causes related to myocardial infarction with non-obstructive coronary arteries and myocarditis.[6] Despite extensive research, the pathophysiology of TCM still needs to be partially understood. A prominent and widely accepted hypothesis suggests that the origin of ventricular dysfunction in this condition lies in the catecholamine theory. The surge of acute stressors triggers an increase in neuropeptide and catecholamine concentrations (dopamine, epinephrine, and norepinephrine) during the acute phase of TCM, ultimately contributing to left ventricular dysfunction.[7] A recent investigation has highlighted a distinct impairment in myocardial blood flow within the apex region relative to the base. This was observed alongside a downregulation of various genes. Notably, these changes were found to reverse when global cardiac function was restored.[8] This evidence strongly supports the theory that microvascular disease or potential vasospasm plays a crucial role in the pathogenesis of TCM.

The pathophysiology of vasospastic angina shares a similar foundation, characterized by an exaggerated vasospastic reaction resulting from heightened neuropeptide and catecholamine concentrations within coronary vessels. Though this underlying commonality in pathophysiology results in diverse clinical presentations, it has been sporadically reported in the literature.[9] The aetiology of TCM remains elusive. The multifaceted interplay of factors driving the onset and progression of TCM continues to elude complete comprehension, emphasizing the need for ongoing research and exploration.

Summary figure



Case presentation

A 64-year-old female was admitted to the emergency department with suspected ACS. She had experienced a sudden onset of chest pain 3 h before admission. The patient's clinical presentation was consistent with non-ST elevation myocardial infarction, supported by elevated cardiac enzymes, including troponin T levels of 0.583 μg/L (<0.014) and Creatine kinase-MB levels of 34 U/L (<24). The electrocardiogram did not show specific ischaemic changes. Echocardiography revealed a characteristic presentation suggestive of TCM. The imaging displayed akinesis of the apical region of the left ventricle, accompanied by left ventricular ballooning and adequate contraction of the basal regions. The patient's left ventricular ejection fraction (LVEF) was severely reduced, measuring 25%. Notably, a significant emotional stressor, the death of her spouse, was identified in her medical history. The patient had several risk factors for atherosclerosis, including diabetes mellitus, hypertension, and hypercholesterolaemia. Invasive coronary angiography revealed non-obstructive coronary artery disease, characterized by a 65% stenosis in the proximal segment of the left anterior descending artery (LAD). Optical coherence tomography (OCT) confirmed the presence of an atherosclerotic plaque in the LAD proximal region, devoid of signs of instability, plaque rupture, or thrombus formation (*Figure 1*).

Left ventriculography supported the diagnosis of TCM, revealing reduced left ventricular systolic function accompanied by characteristic apical ballooning. An extensive diagnostic approach, including magnetic resonance imaging (MRI), was undertaken to ascertain the nature of the injury and exclude alternative explanations. The assessment confirmed the non-ischaemic nature of the injury while effectively ruling out myocarditis and other potential aetiologies. Therapeutic measures included a comprehensive regimen, such as dual antiplatelet therapy (acetylsalicylic acid 75 mg and clopidogrel 75 mg), angiotensin-converting enzyme inhibitor (perindopril 5 mg), beta-blocker (nebivolol 1.25 mg), mineralocorticoid receptor antagonist (eplerenone 50 mg), statin (rosuvastatin 10 mg), long-acting nitrate (isosorbide 50 mg), and insulin therapy (detemir and aspart). Subsequently, the patient showed significant improvement following rehabilitation. A follow-up echocardiogram 5 days later demonstrated a substantial enhancement in systolic function (LVEF 50%), with slight impairment of apical regions but robust basal contraction. An MRI provided additional insights into the patient's condition 2 weeks later. The MRI revealed an ejection fraction of 56% and correctly proportioned heart chambers. The assessment indicated an increased fluid volume within the pericardial sac, extending to 6 mm behind the lateral wall. A late enhancement sequence revealed intramural signal augmentation in the basal regions of the lateral and posterior walls. These changes were consistent with myocardial damage of a non-ischaemic aetiology. At this point, the patient's medical management shifted towards conservative treatment, given the mild stenosis observed in the LAD. Six months later, the patient underwent a repeat coronary angiography, which was included in the MOSAIC-Cor study.[10] This comprehensive evaluation entailed accurate assessments of both epicardial fractional flow reserve (FFR) and functional microcirculation assessment, coupled with an acetylcholine provocation test to examine epicardial vasospasm. The LAD's FFR was measured at 0.84, indicating minimal ischaemic pressure drop.

No microcirculation dysfunction was observed in the left anterior descending or circumflex branches (LAD: IMR 17, CFR 2.4; LCx: IMR 18, CFR 2.1). However, during the acetylcholine provocation test, the patient experienced severe chest pain, ST elevation in V1–V2, and non-sustained ventricular tachycardia. Severe vasospasm was identified in the distal segments of all branches, with nitroglycerine initially failing to alleviate the spasm (*Figure 2*). Subsequent escalation of nitroglycerine dosages eventually mitigated the spasm. This constellation of symptoms and responses led to the diagnosis of vasospastic angina. A repeat echocardiography exhibited preserved LVEF (60%) and symmetrical myocardial contractility. Consequently, the patient was discharged with a calcium channel blocker (diltiazem 60 mg × 2)

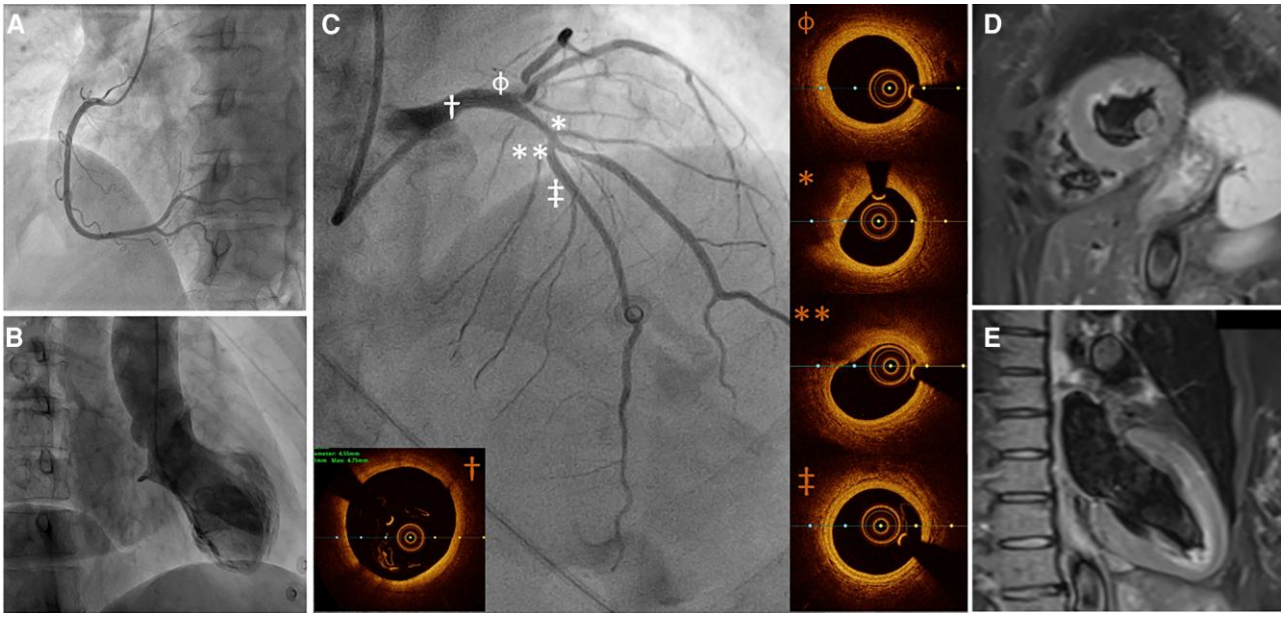


Figure 1 Initial assessment of the patient during takotsubo cardiomyopathy development. (*A*) Right coronary artery. (*B*) Left ventriculography—showing akinesis of the anterior wall. (*C*) Left coronary artery showing a borderline narrowing in the proximal part of the vessel, with optical coherence tomography (* and **) showing atherosclerotic plaque without rupture or dissection (†, left main artery; Φ, proximal left anterior descending artery; ‡, distal left anterior descending artery). (*D*, *E*) Magnetic resonance imaging of the heart. T1-mapping—showing no ischaemic injury in the left ventricle.

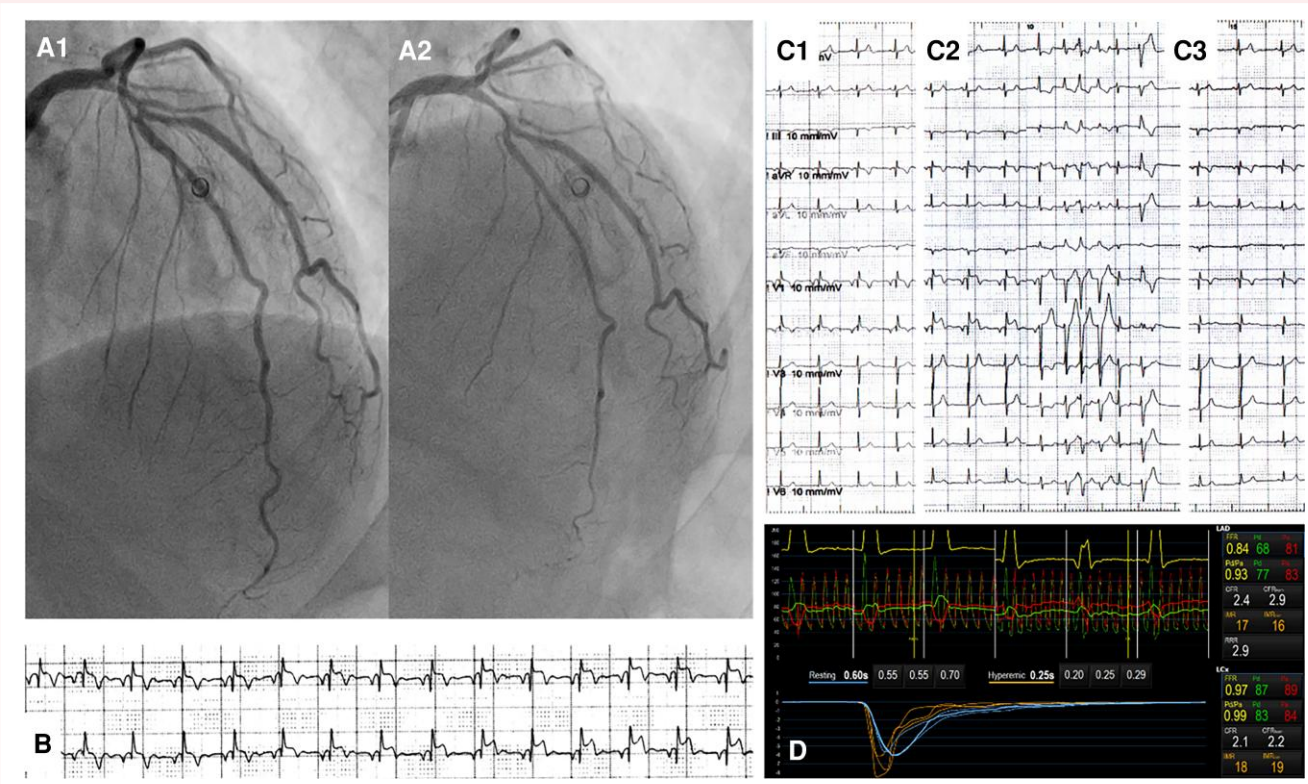


Figure 2 Delayed, complex assessment of coronary vessels. (*A1*) Left coronary artery baseline. (*A2*) Left coronary artery after acetylcholine administration. (*B*) Dynamic changes over time in electrocardiogram in V1 and V2 showing ST elevation. (*C*) Electrocardiogram. (*C1*) Baseline. (C2) After acetylcholine administration, prolonged pain not responding to typical nitroglycerine administration. (*C3*) Final electrocardiogram after regression of changes in angiography and pain. (*D*) Microcirculation assessment, showing normal pressures and resistance in the coronary microcirculation.

regimen instead of a beta-blocker, with dosage adjustments planned for the follow-up period. Six months after the change in pharmacotherapy, the patient was contacted by telephone and asked mainly about the symptoms. The patient denied any symptoms (CCS 0; NYHA 0) and is taking medications as stated in the discharge card from the hospital stay.

Discussion

Takotsubo cardiomyopathy is an intriguing medical condition that has gained the attention of researchers and clinicians. While it was once considered rare, ongoing studies and registries have revealed its true prevalence. Current estimates suggest that TCM accounts for approximately 0.7–2.5% of ACS cases, making it a significant cardiac entity within this diagnostic realm.[9] The pathophysiological mechanisms linking stress-related catecholamine surges to left ventricular apical ballooning presentation involve several hypotheses.[2,11] Firstly, the concept of coronary flow decrease without vasospasm suggests that acute stress releases substantial amounts of catecholamines, constricting microcirculatory vessels. This constriction reduces blood flow to specific myocardial regions, leading to transient ischaemia and the characteristic regional wall motion abnormalities seen in TCM. Secondly, the idea of vasospastic angina proposes that acute stress-induced catecholamine surges can trigger sudden contractions of smooth muscles within coronary arteries, causing vasospasm.[2,12] This acute constriction restricts blood supply to heart parts, resulting in ischaemia. The resulting oxygen and nutrient deficits can lead to the abnormal ventricular contraction pattern characteristic of TCM. Unlike traditional angina resulting from physical exertion or atherosclerosis, vasospastic angina in TCM arises directly from the impact of catecholamines on coronary arteries. Lastly, the notion of direct myocardial toxicity emphasizes the harmful effects of elevated catecholamine levels on cardiomyocytes. Prolonged stimulation of cardiac beta-adrenergic receptors by catecholamines can disrupt normal cellular processes and damage cardiomyocytes.[5,11] This cellular damage leads to compromised contraction and relaxation of the heart muscle, resulting in the hallmark ventricular ballooning and dysfunction characteristic of TCM.

The literature contains limited data on the simultaneous occurrence of coronary vasospasm and TCM.[13] A notable case report documented patients diagnosed with TCM who exhibited multivessel vasospasm during angiography.[14] This report represents a rare instance in the literature, as no previous publications demonstrated the replication of clinical symptoms such as ST elevation and chest pain following recovery from TCM.

In the case of our patient, a typical presentation of TCM was evident, and a thorough diagnostic evaluation helped exclude alternative diagnoses, confirming the primary diagnosis. Given its borderline stenosis, a crucial clinical decision emerged concerning the revascularization of the LAD.[12] The approach was cautious, opting for further data acquisition before the intervention. This contrasts with the usual tendency for immediate percutaneous coronary intervention in cases of ACS associated with LAD narrowing. Initial diagnostic investigations, including MRI and OCT, confirmed a non-ischaemic aetiology for the injury, reducing the urgency for immediate revascularization.[15] Subsequent assessments, including FFR and coronary flow reserve, as well as an acetylcholine provocation test, revealed severe diffuse vasospasm

affecting both the LAD and circumflex arteries, which was included in the MOSAIC-Cor study.[10] This finding highlights the limited literature on the vasospastic mechanisms underlying TCM in such cases. Given the intricate and multifaceted nature of TCM, it is crucial, particularly in an ACS setting, to adopt a comprehensive perspective that considers the various possibilities for the observed injury. The complex interplay of pathophysiological mechanisms and clinical presentations necessitates ongoing research to uncover the mysteries of TCM and to refine diagnostic and therapeutic strategies.

Lead author biography

Dr Bartłomiej M. Guzik is a Jagiellonian University professor specializing in interventional cardiology. He holds several key positions, including senior consultant at John Paul II Hospital in Krakow and a proxy to vice-rector for humanitarian aid at the Jagiellonian University. Dr Guzik has a significant academic and clinical footprint, evidenced by his publications and involvement in advanced medical procedures. His international experience includes fellowships and medical missions in places like Glasgow and East Africa, contributing to his global perspective in cardiology. Additionally, he engages in community service through the Order of Malta.

Consent: The authors confirm that they have obtained permission from the patient to publish this case report, following the Committee on Publication Ethics (COPE) guidelines.

Conflict of interest: None declared for all the authors.

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Data availability

The data underlying this article are available in its online supplementary material (https://osf.io/yghv4/?view_only=74c43293a42e4e31976056f7dfa9b085).

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