

MINOCA-induced apical ballooning case report: a diagnostic conundrum

Moez Dugarwalla ^{1*}, Polyvios Demetriades ¹, Martin Been¹, and Jamal Nasir Khan^{1,2}

¹University Hospitals Coventry and Warwickshire NHS Trust, Clifford Bridge Road, Coventry CV2 2DX, UK and ²University of Warwick, Coventry, CV4 7AL, UK

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Background

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is a recently described phenomenon where no flow-limiting lesions are noted on coronary angiography in a patient with electrocardiogram changes, elevated cardiac biomarkers, and symptoms suggesting acute myocardial infarction. Patients with MINOCA can also potentially develop structural cardiac defects through ischaemic injury. Therefore, the absence of a flow-limiting lesion on angiography coupled with structural defects (e.g. apical ballooning) can very easily result in a diagnosis of Takotsubo cardiomyopathy (TTC). This can lead to potentially serious consequences since treatment options between TTC and MINOCA are different.

Case summary

We report a case of a patient presenting with features suggestive of TTC but where the final diagnosis was of a MINOCA that induced an apical ventricular septal defect (VSD). Reaching the correct diagnosis proved challenging given that there is no gold standard diagnostic modality for diagnosing MINOCA.

Conclusion

Imaging adjuncts played a vital role in both diagnosing the underlying MINOCA as well as revealing and planning closure of the resultant VSD. Cardiovascular magnetic resonance imaging played an instrumental role in establishing the patient's primary pathology and in planning a remediation of the structural defect. Structural myocardial defects in a patient with a diagnosis of TTC should prompt clinicians to further investigate whether there is an underlying infarct aetiology (MINOCA).

Keywords

Myocardial infarction with non-obstructive coronary arteries • MINOCA • Takotsubo cardiomyopathy • Ventricular septal defect • Cardiovascular magnetic resonance • Case reports

* Corresponding author. Tel: +447852229855; e-mail: moez.dugarwalla@gmail.com

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Learning points

- A new ventricular septal defect (VSD) in association with an initial diagnosis of Takotsubo cardiomyopathy must prompt further assessment of the precise aetiology and raise the suspicion of myocardial infarction with non-obstructive coronary arteries (MINOCA).
- There is no gold standard diagnostic modality for MINOCA at the time of coronary angiography: intravascular ultrasound, optical coherence tomography, and computed tomography coronary angiography can potentially reveal plaque rupture/fissure/ulceration suggesting recanalized culprit vessel and hence infarct.
- Severity (transmurality, presence of microvascular obstruction/intramyocardial haemorrhage) rather than size (number of segments of left ventricle) of a myocardial infarction has implications in the development of a post-infarct VSD.
- Clinicians should remain vigilant to the development of potentially fatal structural complications such as VSDs especially in late presenting myocardial infarcts.
- Intracoronary imaging and provocation testing may currently be a relatively underutilized tool in the diagnostic armoury in MINOCA.

Introduction

Takotsubo cardiomyopathy (TTC) is characterized by chest pain typically resulting in transient left ventricular (LV) apical ballooning and systolic dysfunction. Patients are often initially assumed to be having an acute myocardial infarction (MI) as the chest pain is usually accompanied by ST-segment elevation on electrocardiogram (ECG) and elevated cardiac biomarkers. Apical ballooning observed on angiography in the absence of flow-limiting coronary lesions supports a diagnosis of TTC. Association of TTC with myocardial structural defects is not well established, however, there are case reports in the literature base supporting this notion.

A newer entity of acute cardiac event that is increasingly recognized is that of an acute MI clinical presentation with no flow-limiting coronary artery lesion seen on angiography, termed 'myocardial infarction with non-obstructive coronary arteries' (MINOCA). MINOCA, like other ischaemic myocardial pathologies, is associated with risk of developing structural abnormalities. As a result, distinguishing between TTC and structural abnormalities secondary to MINOCA are crucial as treatment and prognosis for the two differ significantly.

Timeline

Case presentation

An 80-year-old female with no significant medical history presented with sudden onset, left-sided chest pain. Twelve-lead ECG (*Figure 1*) performed a few minutes after the onset of chest pain by the ambulance crew resulted in a diagnosis of acute anterior ST-elevation myocardial infarction. Upon arrival to our institution, she was administered oral loading doses of antiplatelet medications (aspirin 300 mg and ticagrelor 180 mg) and transferred to the cardiac catheter laboratory for emergency invasive coronary angiography with a view to percutaneous coronary intervention (PCI). Prior to angiography, a full cardiovascular examination excluded a murmur and there were no signs of a cardiac shunt.

Coronary angiography demonstrated mild, non-flow-limiting stenosis in the proximal left anterior descending (LAD) artery which was not felt to be unstable by the interventional cardiologist and hence intracoronary imaging and provocation testing were not performed (*Video 1*). The remaining arteries had minor, non-flow-limiting atheroma (*Figure 2*). Left ventriculography showed apical ballooning consistent with TTC (*Video 2*) and in the absence of flow-limiting coronary artery disease and presence of laminar (Thrombolysis in Myocardial Infarction-3) flow, a decision was

Admission to Emergency Department	An 80-year-old female presented with left-sided chest pain, anterior ST-segment elevation myocardial infarction, and elevated serum high-sensitivity troponin-T
30-Min post-admission	Underwent invasive coronary angiography with view to proceeding to primary percutaneous coronary intervention. Mild non-flow-limiting atheroma only in coronary arteries. Left ventriculography reveals apical ballooning
Day 2	New pansystolic murmur on physical examination. Contrast echocardiography reveals apical ventricular septal defect (VSD) and left ventricular ejection fraction of 40%
Day 3	Develops signs and symptoms consistent with a urinary tract infection. Additionally, developed new onset atrial fibrillation with fast ventricular rate
Day 10	Cardiovascular magnetic resonance imaging confirmed acute transmural myocardial infarction in the mid-left anterior descending artery territory with akinesis of the left and right ventricular apices and associated apical VSD
Day 14	Discussed at Cardiology/Cardiothoracic Multidisciplinary Team meeting. Concluded that VSD was secondary to ischaemic pathology. A consensus was reached in favour of percutaneous device closure
Day 17	VSD corrected percutaneously which significantly reduced shunting
Day 21	Hospital discharge
1-Month post-discharge	Reviewed in clinic, tolerating activities of daily living with no angina or cardiovascular limitations

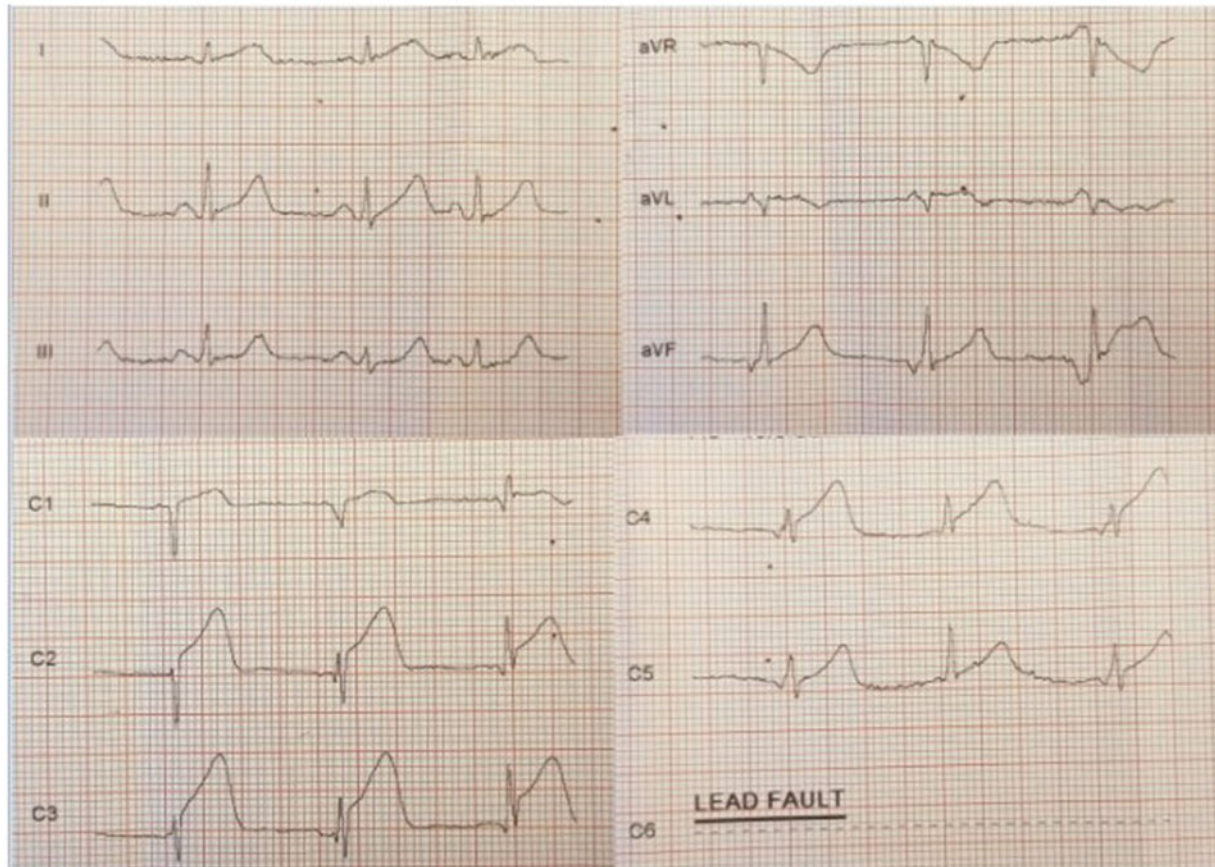


Figure 1 Twelve-lead electrocardiogram performed by ambulance crew.

made not to proceed to PCI. The initial diagnosis of TTC was established by angiographic assessment.

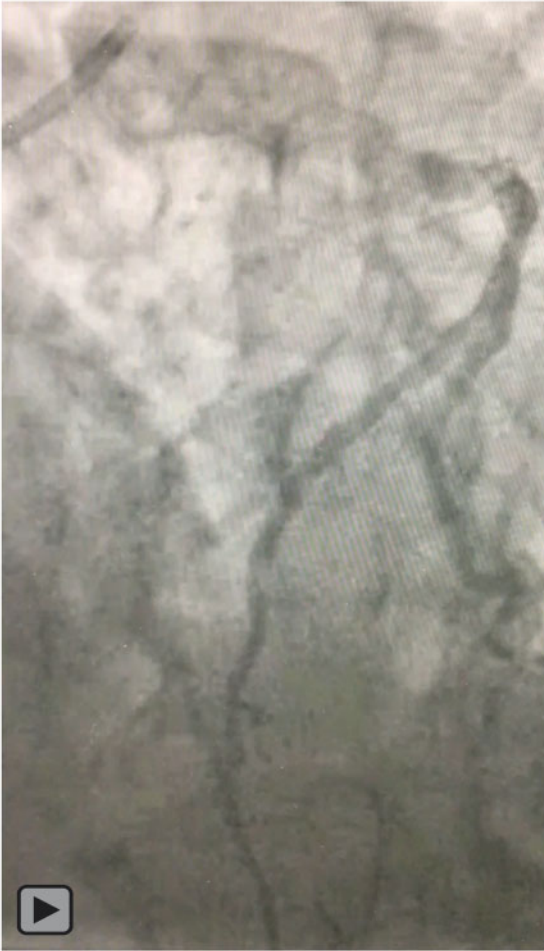
Relevant admission blood tests are shown in *Table 1*. Serum Troponin-T was significantly elevated at 1940 ng/L. An angiotensin-converting enzyme-inhibitor and a beta-blocker were commenced. The following day, a physical examination revealed a new pansystolic murmur. After discussion with the patient's primary care provider, there was no previously documented cardiac murmur. Urgent contrast-enhanced echocardiography performed the day after admission (*Video 3*) showed a significant apical septal defect suggestive of a ventricular septal defect (VSD). LV systolic function was moderately impaired with an ejection fraction of 40% in the presence of dyskinesis of all four apical LV segments resulting in apical ballooning. There was no LV outflow tract obstruction, systolic anterior motion of the mitral valve or mitral regurgitation. These echocardiographic findings could be consistent with TTC, however, the presence of a VSD raised the suspicion of an alternative diagnosis.

Repeat ECG on Day 2 (*Figure 3*) showed progressive deep T wave inversion in anterolateral leads. By Day 3, the patient developed urosepsis with atrial fibrillation, hyperactive delirium, and hyponatraemia. The patient became clinically unstable requiring intravenous antibiotics and careful fluid balance monitoring. Due to the development of a VSD, the diagnosis of TTC was re-evaluated. Cardiovascular

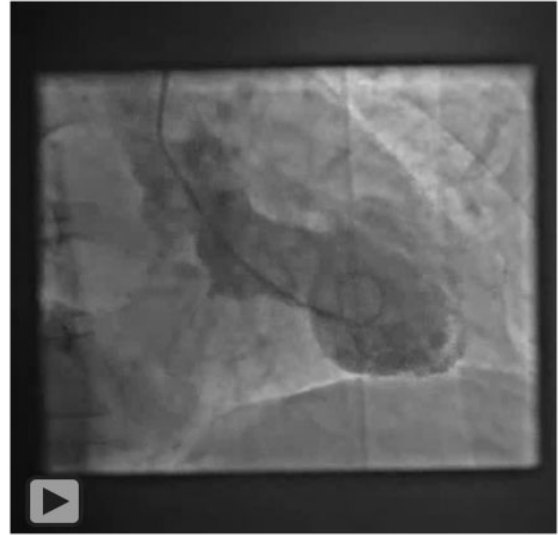
magnetic resonance (CMR) imaging was performed on Day 10 once the patient was clinically stable and her delirium resolved, permitting safe and feasible CMR imaging.

CMR demonstrated transmural late gadolinium hyperenhancement (LGE) at the apical septal, apical anterior, and apical inferior LV segments with extension into the apical right ventricular (RV) which became subendocardial on extension into the mid-septal and mid-anterior segments, in keeping with acute transmural MI in the mid-LAD territory. There was resultant akinesis of the LV and RV apices and associated apical VSD measuring 9 mm × 12 mm with Qp:Qs 2.7 (RV stroke volume = 2.7 × LV stroke volume) in keeping with significant left-to-right shunting (*Supplementary material online, Video S1*). No significant valve dysfunction was present thus allowing this method of Qp:Qs calculation to be employed. Oedema imaging was not performed in order not to jeopardize the ability to perform LGE imaging as the patient struggled with breath-holding and tolerating the study.

Following joint cardiology and cardiothoracic surgery multidisciplinary team discussion, the diagnosis was revised to an anterior MI with spontaneous LAD recanalization. The prospect of surgical intervention was assessed. The P-Poosum score was calculated; the predicted mortality was 26.7% and predicted morbidity 79.9%. The



Video 1 Invasive angiography demonstrated mild, non-flow-limiting disease in left anterior descending artery which was not felt to be unstable.



Video 2 Contrast-enhanced left ventriculogram demonstrating apical ballooning.

consensus was that percutaneous device closure would be the best option due to prohibitively high surgical risk.

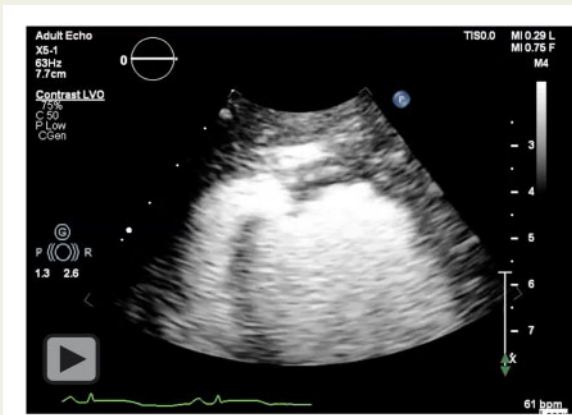
Under general anaesthesia and transoesophageal echocardiographic (Supplementary material online, Video S2) and fluoroscopic guidance, the VSD was found to be serpiginous. Successful percutaneous closure was achieved with the deployment of three Amplatzer Vascular Plugs-II: 9 mm × 22 mm, 12 mm × 9 mm, and 9 mm × 20 mm (Supplementary material online, Video S3) with resultant significantly reduced shunting (Supplementary material online, Video S4). Following an uncomplicated recovery, the patient was discharged after 4 days, with recovery to her baseline functional status and mobilization with no cardiovascular symptoms. At clinic review 1-month later she remains well with no intrusive cardiovascular symptoms. ECG findings (Figure 4) showed the same T wave



Figure 2 Invasive coronary angiography showing only mild, non-flow-limiting lesion in the proximal left anterior descending artery—the lesion is indicated with a white arrow.

Table 1 Relevant blood tests on admission

Blood analysis	Result	Normal reference range
Serum haemoglobin	145 g/L	Men: 135–180 g/L Women: 115–160 g/L
Serum white cell count	$16.96 \times 10^9/L$	$4.0\text{--}11.0 \times 10^9/L$
Serum neutrophil count	$13.48 \times 10^9/L$	$2.0\text{--}7.0 \times 10^9/L$
Serum platelet count	$252 \times 10^9/L$	$150\text{--}400 \times 10^9/L$
Serum high-sensitivity Troponin-T	1940 ng/L	<14 ng/L

**Video 3** Contrast-enhanced transthoracic echocardiogram demonstrating defect apical ventricular septal defect.

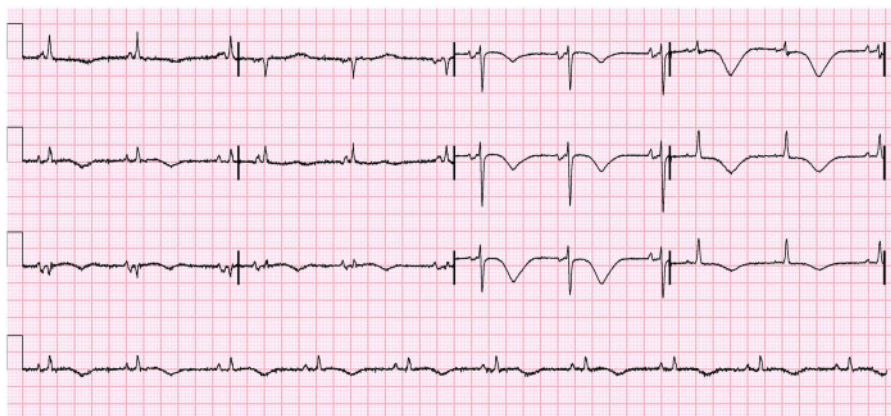
CMR was arranged 4 months post-device closure. This showed a mildly dilated LV with thinned and akinetic apical segments. All other segments were normokinetic with uniformly normal wall thickness (max 8 mm basally). Mild LV systolic dysfunction with an ejection fraction of 60% (previously 50%) was present. All three VSD devices were well seated with only minimal residual shunting ([Supplementary material online, Videos S5 and S6](#)). No valvular abnormalities noted apart from mild tricuspid regurgitation. The symptoms are stable and annual cardiology follow-up is being arranged.

Discussion

TTC refers to characteristic apical ballooning of the LV during end-systole akin to a Japanese octopus trap. It has also been described as ‘broken heart syndrome’, stress cardiomyopathy, and ‘apical ballooning syndrome’.¹ It is a transient cardiomyopathy due to myocardial stunning, with typically complete myocardial recovery. Rarely it can take atypical forms with stunned basal or mid-ventricular segments.

Principally, published diagnostic criteria require clear morphological evidence of TTC in combination with reliance on excluded

inversion anteriorly and no significant ST-segment changes. The patient was re-reviewed again in clinic after referral from her Primary Care Physician as she complained of mild breathlessness. A repeat

**Figure 3** Repeat 12 lead ECG on Day 2 showing progressive deep T wave inversion in anterolateral leads.

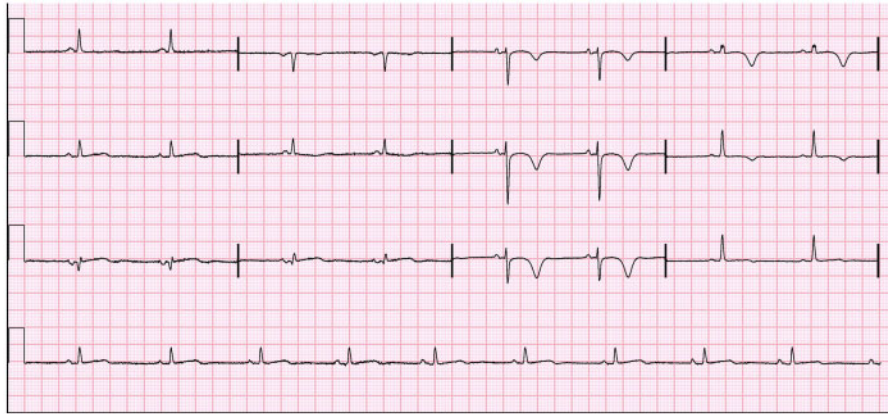


Figure 4 12 lead ECG 1 month post VSD closure.

pathology. Most of the published criteria (e.g. Mayo Clinic Diagnostic Criteria² and Gothenburg³) stipulate that a flow-limiting coronary artery culprit lesion must be excluded. In our case, the preliminary diagnosis of TTC was due to the observed apical ballooning in the context of mild, non-flow-limiting coronary lesions.

Structural myocardial defects post-MI are uncommon complications, but associated with high mortality. Acute VSD is a serious mechanical complication with a mortality rate of >90% if managed conservatively. Septal interventricular rupture typically occurs 48–96 h post-infarct and has been observed in patients with LAD and right coronary artery lesions due to their septal blood supply.⁴ The site of a septal rupture is largely attributed to the diseased artery. Septal defects post-infarct can vary in morphology.⁴ The site and serpiginous characteristic of the VSD in our patient was more in keeping with a post-infarct rather than congenital VSD.

The mechanism of rupture in acute MI is thought to be related to transmural necrosis and possibly intramyocardial haemorrhage (IMH). However, in TTC the mechanism of wall rupture is thought to be due to contraction band necrosis caused by catecholamine cardiotoxicity. Lu *et al.*⁵ described a case of VSD in association with TTC but could find no causative mechanism. A systematic review by Kumar *et al.*⁶ identified only 12 patients between 1950 and 2009 with TTC and associated cardiac rupture (cardiac rupture shares the same pathophysiology as a VSD but occurs at the free wall). This implies that this complication is extremely rare in the context of TTC. In our case, the development of a VSD questioned the diagnosis of TTC.

The unique ability of CMR to directly visualize MI characteristics refuted the initial working diagnosis of TTC and confirmed the correct diagnosis of acute transmural MI with VSD.

A more recent subclassification of MI is MINOCA. According to the European Society of Cardiology, non-obstructive (<50%) coronary artery disease in patients with symptoms related to myocardial ischaemia and ST-segment elevation does not discount an aetiology related to atherothrombosis.⁷ Whilst in the case described, there

was only mild LAD plaque disease, this was deemed to be the spontaneously recanalized culprit responsible for an acute transmural infarct presenting as a MINOCA.

CMR plays a crucial role in establishing a diagnosis of MINOCA. CMR allows direct visualization of myocardial oedema, MI, microvascular obstruction, and IMH. Dastidar *et al.*⁸ compared the impact of the timing of CMR in troponin-positive acute coronary syndrome patients, showing that CMR established a definitive diagnosis in 70% of patients and made a significant impact in diagnosis and/or management in 66% patients.⁸ CMR helps establishing the underlying pathophysiology and distinction between the three main differentials of acute MI, myocarditis, and TTC. The former may be explained by plaque rupture, plaque erosion, or ulceration with spontaneous autolysis leaving a seemingly benign lesion on angiography. CMR is the only imaging modality able to demonstrate myocardial oedema. On CMR, the subsequent pattern of late gadolinium enhancement [LGE (scarring)] allows distinction between the three differentials. MI is typically associated with subendocardial or transmural LGE, myocarditis typically results in subepicardial or mid-wall LGE whereas there is typically no LGE present in TTC. Oedema is seen in all three phenomena in keeping with the presence of an acute insult.⁹

The European Society of Cardiology Working Group MINOCA position paper highlights the potential importance of intracoronary imaging [intravascular ultrasound, optical coherence tomography (OCT)] and intracoronary provocation testing in identifying acute plaque events and coronary vasospasm as a cause of MINOCA.¹⁰ Recently, a prospective study of 40 MINOCA subjects demonstrated that by coupling OCT and CMR, the substrate and diagnosis of MINOCA was established in 100% of cases.¹¹ Intracoronary imaging and provocation testing may currently be a relatively underutilized tool in the diagnostic armoury in MINOCA.

Our case highlights the importance of multimodality imaging and particularly the crucial role of CMR in establishing prompt and correct diagnosis in MINOCA. Mechanical complications such as VSD should alert clinicians to question an original diagnosis of TTC.

Lead author biography



Moez Dungarwalla is currently a GP trainee in London. He developed a keen interest in Heart Failure and looking to improve management of heart failure patients in the community as well as develop community heart failure services.

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 authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: There are no conflicts of interests for any of the authors.

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