


A valuable cardiac magnetic resonance investigation after MINOCA/takotsubo Syndrome: a case report

Snehasis Pradhan* , Nedall Zalloum, Gresa Kciku and Hans-Joachim Trappe

Department of Cardiology and Angiology, Marien Hospital Herne, Ruhr-University of Bochum, Herne, Germany

Abstract

Myocardial infarction with non-obstructive coronary arteries is a working diagnosis that includes takotsubo cardiomyopathy/syndrome (TTS). Cardiac magnetic resonance (CMR) is useful for establishing the underlying aetiology of myocardial infarction with non-obstructive coronary arteries during the acute phase, but its role in follow-up is less well established. A 35-year-old man with several cardiac risk factors presented 3 days after his sister's death with biochemical and clinical features of acute myocardial infarction without coronary artery obstruction on angiography but with diagnostic features of TTS on CMR, including oedema but no late gadolinium enhancement. Subsequent CMR 3 months later revealed left ventricular late gadolinium enhancement suggesting previous acute myocardial infarction. Although the initial diagnosis of TTS was robust according to established criteria, it remained uncertain whether the later ischaemic injury was related to an ischaemic event at presentation or occurred in the intervening period. Nevertheless, CMR may have an extended role in the follow-up of these patients and may reveal additional, actionable pathology.

Keywords MINOCA; Takotsubo; Cardiac magnetic resonance; Late gadolinium enhancement

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*Correspondence to: Snehasis Pradhan, Department of Cardiology and Angiology, Marien Hospital Herne, Ruhr-University of Bochum, Hoelkeskampung 40, Herne 44625, Germany. Tel: 02323-499-1604; Fax: 02323-4993301.

Email: snehasis.pradhan@ruhr-uni-bochum.de

Introduction

Myocardial infarction with non-obstructive coronary arteries (MINOCA) is characterized by (i) clinical evidence of an acute myocardial infarction (MI); (ii) normal or near-normal coronary arteries on coronary angiography; and (iii) no clinically overt specific cause for the acute presentation.^{1–3} MINOCA can be a diagnostic challenge, because it can be caused by several clinical entities or uncertain aetiology. MINOCA represents a working diagnosis that requires exclusion of other causes of elevated troponin [takotsubo cardiomyopathy/syndrome (TTS), myocarditis, and other cardiomyopathies] and non-cardiac pathologies (pulmonary embolism and renal impairment).⁴ The European Society of Cardiology proposed a diagnostic classification scheme for MINOCA,³ but there are still no formal management guidelines.

Cardiac magnetic resonance (CMR) imaging performed early after admission will, in many MINOCA cases, help to establish the diagnosis. Late gadolinium enhancement (LGE) on CMR is particularly useful, because ischaemic and infarct-related changes tend to delay gadolinium enhancement in the subendocardium or transmurally in a vascular distribution.⁵ In contrast, non-ischaemic myocardial changes tend to delay enhancement in more than one vascular territory and are often mid-wall rather than subendocardial or transmural.⁵ Whether CMR may be useful after the initial management of MINOCA and related conditions is uncertain.

Here, we report a case of a man presenting with features of acute MI, without obvious coronary artery obstruction, and with diagnostic features of TTS. This case allows us to review the clinical dilemmas posed by the working diagnosis of MINOCA and the utility of CMR in its immediate and follow-up management.

Case report

A 35-year-old obese man (body mass index 42 kg/m²), previously diagnosed with a history of chronic depression, diabetes, hypertension, and tobacco use, was admitted to the emergency department 3 days after his sister's death. He presented with severe intermittent retrosternal chest pain radiating to the left arm and jaw. His heart rate was 120 b.p.m. and blood pressure 190/112 mmHg. A pericardial rub and vesicular breath sounds were present, but heart sounds were normal, and there were no murmurs. There was no oedema and no pleural effusions on chest X-ray. His depression had interfered with his adherence to his prescribed hydrochlorothiazide, ramipril, amlodipine, moxonidine, metoprolol tartrate, metformin, amitriptyline, and fluoxetine.

His complete blood count, biochemistry, coagulation profile, D-dimers, and C-reactive protein were within normal limits. Initial B-type natriuretic peptide was elevated at 3900 pg/mL (normal <125 pg/mL). Cardiac enzymes were elevated, with a high-sensitivity cardiac troponin of 837 pg/dL (normal <14 pg/dL), total creatine phosphokinase of 1353 IU/L (normal <174 IU/L), and maximum creatine kinase myocardial band of 185 IU/L (normal <25 IU/L). Electrocardiogram (ECG) demonstrated normal sinus rhythm with extreme left axis deviation, ST elevations in V2 to V4, and T-wave inversion in I, aVL, and V5–V6 (Figure 1A). Because an evolving ST-elevation myocardial infarction was suspected, aspirin, heparin, and atorvastatin were administered.

Emergency angiography confirmed mild atheromatosis without obstruction, coronary dissection, myocardial bridging, or embolism (Figure 2A–C). Ventricular angiography

Figure 1 Twelve lead electrocardiograms. (A) Initial electrocardiogram during angina at presentation showing ST-segment elevation in the anterolateral leads. (B) Electrocardiogram 2 days later showing prominent symmetric negative T-waves in I and aVL and regression of the ST-segment elevation.

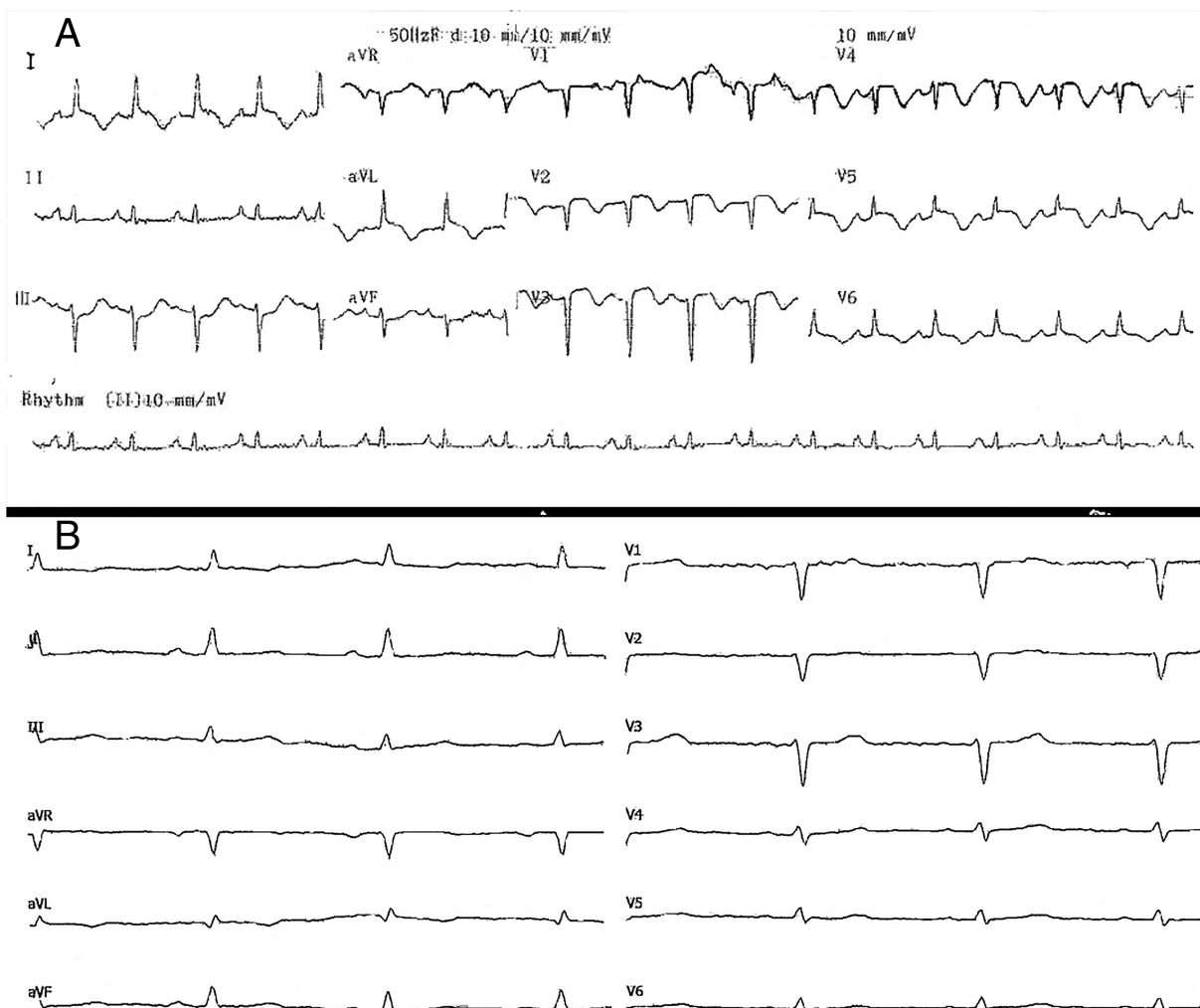
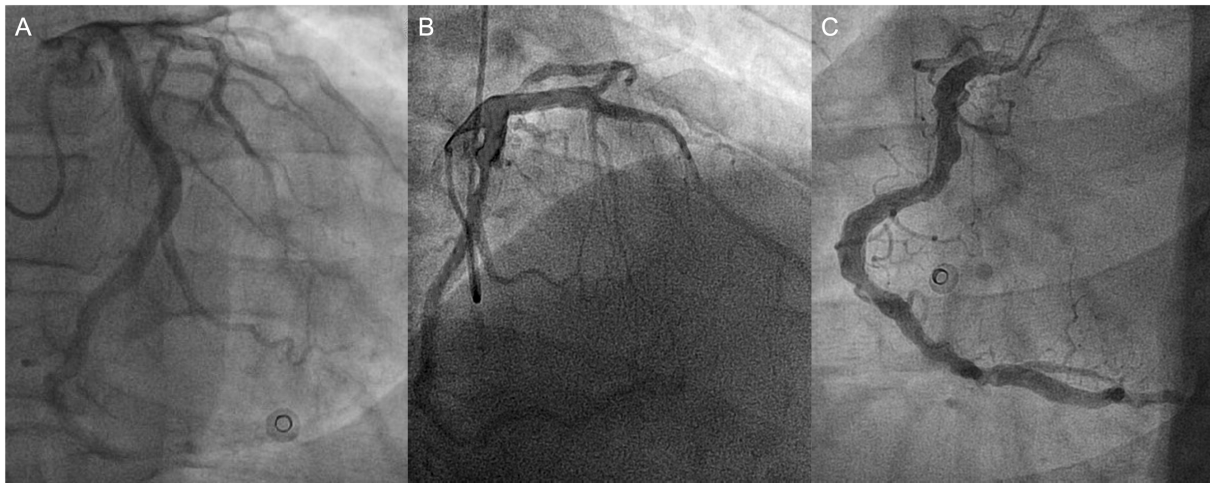


Figure 2 Angiograms showing (A) left circumflex artery in caudal right oblique view; (B) left anterior descending artery in the cranial right oblique view; and (C) right coronary artery in the left caudal view with mild atherosclerosis without coronary artery lesions.



revealed a severely reduced left ventricular ejection fraction (15%), elevated left ventricular end-diastolic pressure (32 mmHg), and basal hyperkinesia and apical ballooning indicative of TTS (*Figure 3*), confirmed by on-table echocardiography.

Over the next 24 h, his pain resolved, together with the ST-segment elevation. (*Figure 1B*). CMR without T1 mapping performed the next day detected mild left ventricular hypertrophy and dilatation in standard scout sequences. Systolic function was severely restricted with a typical wall motion pattern extending beyond a single coronary territory, and

the overall ejection fraction (EF) was estimated to be slightly improved but still <30%. Black blood T2-weighted mapping revealed high signal intensity in the apical and anteroseptal–apical segments suggesting the presence of myocardial oedema (*Figure 4A,B*) but no LGE (*Figure 5A,B*).

Transthoracic echocardiography 48 h later showed mid and apical left ventricular hypokinesia with apical ballooning of the left ventricle and an EF of 30–35%. His high-sensitivity cardiac troponin had reduced from a peak of 918 pg/dL on Day 2 to 212 pg/dL by Day 4. A presumptive diagnosis of TTS was made based on an European Society of Cardiology

Figure 3 Left ventriculography during the acute stage showing typical mid-apical ballooning during systole in keeping with takotsubo cardiomyopathy: (A) end-diastole and (B) end-systole.

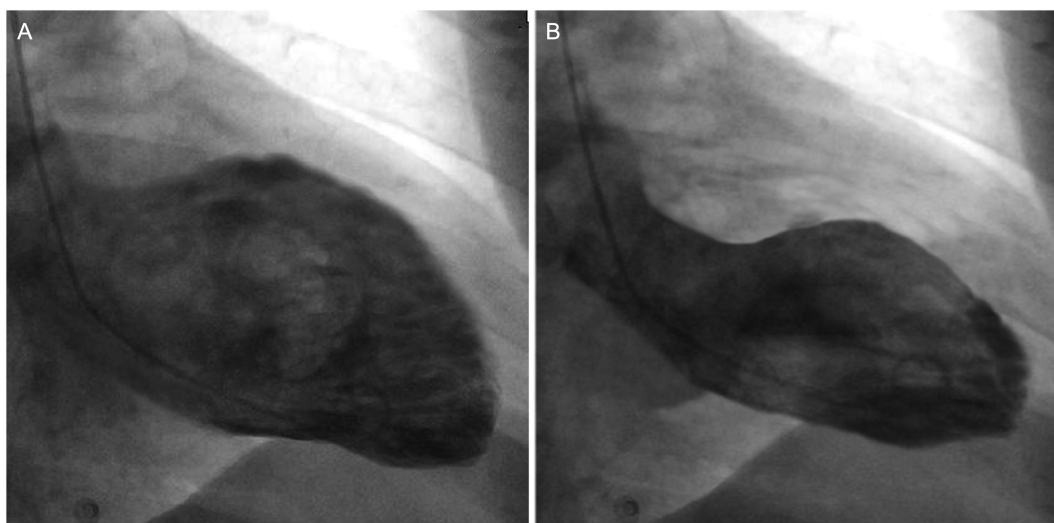
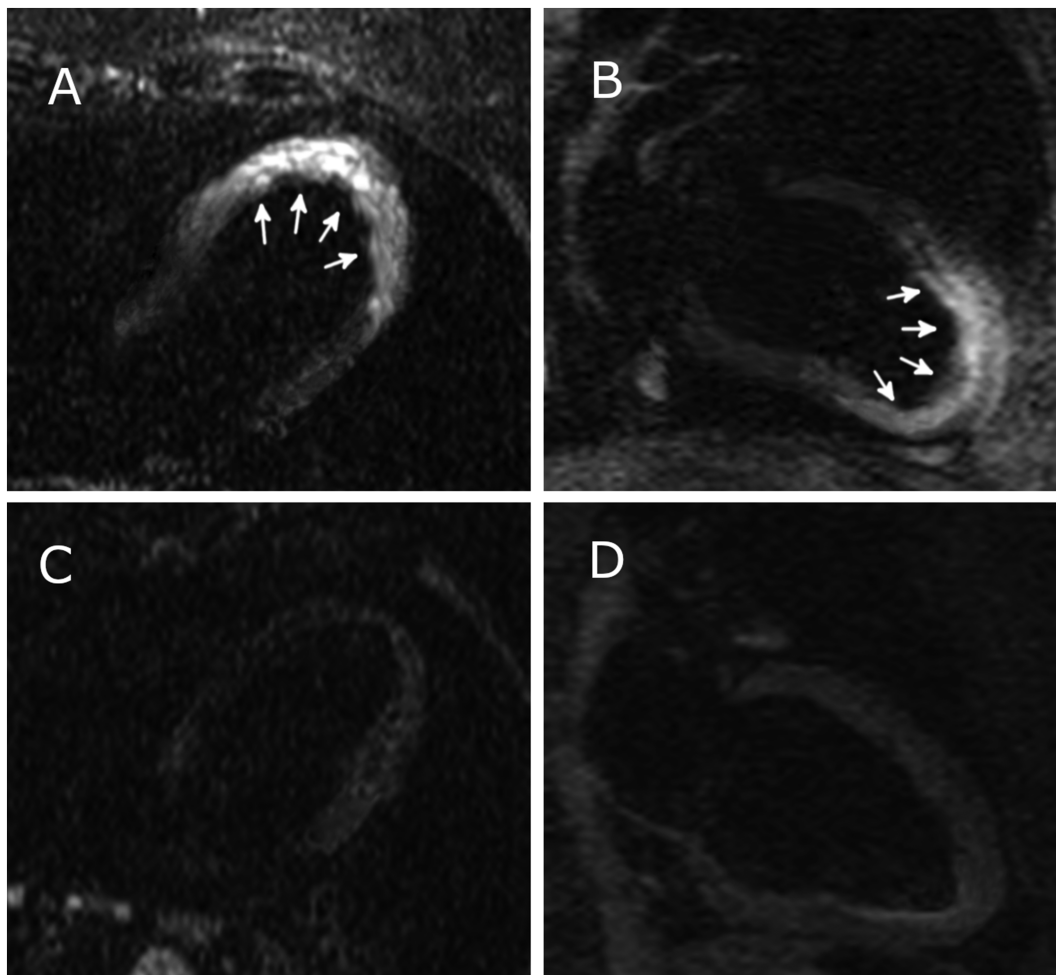


Figure 4 Cine cardiac magnetic resonance T2-weighted short-time inversion recovery images: (A) four-chamber view and (B) two-chamber view at presentation showing transmural signal hyperintensity (myocardial oedema) in the mid-apical segments of the left ventricle at presentation. (C and D) At 3 month follow-up showing regression of the myocardial oedema: (C) four-chamber view and (D) two-chamber view.



InterTAK diagnostic score for TTS⁶ totalling 69 (84.7% probability).

Aspirin and statins were commenced, complete heart failure therapy was started, and a wearable cardioverter defibrillator was sited. The patient was discharged from hospital on Day 6 with psychiatric follow-up.

At 3 month follow-up, the patient was clinically stable, and cardiac markers and ECG were normal. Follow-up CMR showed significantly improved left ventricular function with an EF of 59% and no oedema (*Figure 4C,D*). However, subendocardial LGE was noted in the apicolateral and mid-anterior wall of the left ventricle (*Figure 5C,D*). On the basis of this CMR finding of myocardial necrosis, we again diagnosed MINOCA. A paradoxical embolus was excluded by transoesophageal echocardiography. Additional clopidogrel was started as a part of a dual antiplatelet regimen for

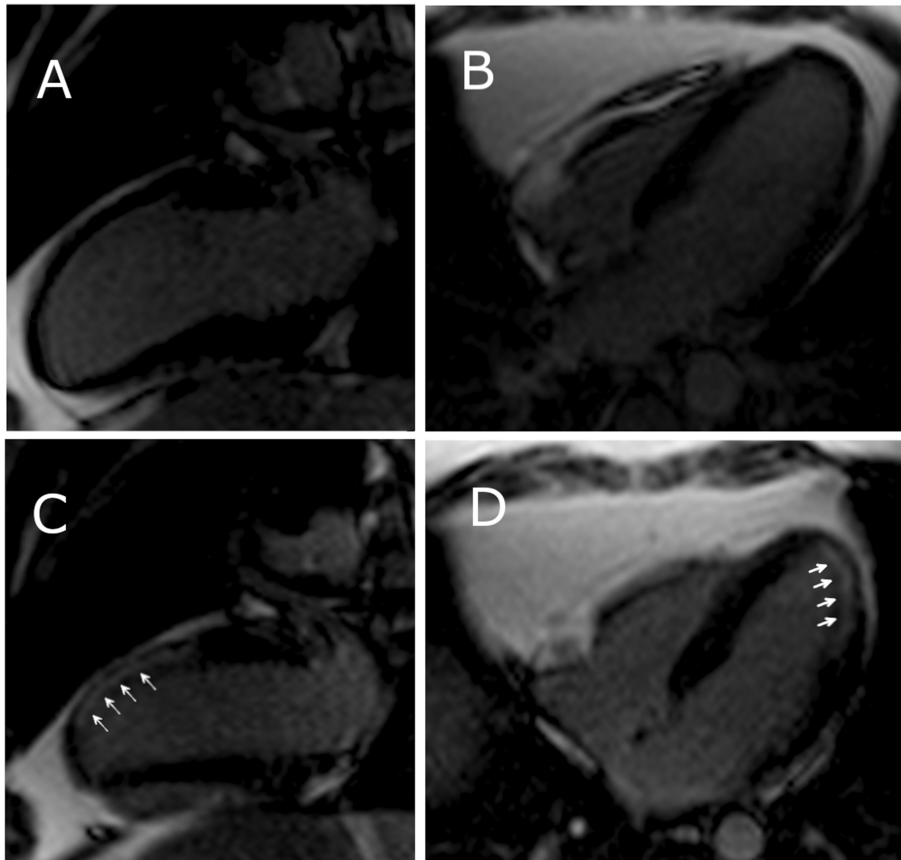
12 months. There were no new developments at 6 and 12 month follow-up.

Discussion

Here, we present a case of a man with several cardiac risk factors who was initially diagnosed with TTS but who subsequently showed LGE suggestive of an ischaemic event. This case provides the opportunity to discuss MINOCA, TTS, and the role of CMR in managing these patients.

The history of chronic depression, an emotional trigger, cardinal symptoms of acute coronary syndrome, elevated cardiac biomarkers, and angiographically demonstrated non-obstructive coronary arteries with typical ventricular

Figure 5 Cardiac magnetic resonance late gadolinium enhancement images: (A) two-chamber view at presentation and (B) four-chamber view at presentation. (C and D) At 3 month follow-up; arrows denote subendocardial late gadolinium enhancement within a single coronary territory: (C) two-chamber view and (D) four-chamber view.



apical ballooning suggested TTS with high probability by InterTAK diagnostic criteria.⁶ Furthermore, the resolving ECG abnormalities, decreasing trend in cardiac biomarkers, absence of LGE, and typical oedema on CMR along with left ventricular ejection fraction improvement within 48 h further suggested TTS.

Cardiac magnetic resonance is indicated in all patients presenting with MINOCA; CMR performed 48 h after cardiac catheterization secured a diagnosis in 97% of MINOCA cases, also revealing a higher prevalence of TTS through the presence of myocardial oedema and lack of LGE.⁵ The absence of LGE on CMR, as seen in our case, is a hallmark of TTS and suggests that the damage associated with apical ballooning is not irreversible. In most TTS patients including our own, oedema is present in regions with abnormal systolic function and is possibly due to inflammation, increased wall stress, and/or transient ischaemia⁷; oedema can also be seen in other, non-ballooning segments.⁸ The CMR features in TTS are different to the diffuse oedema with patchy epicardial and mid-wall LGE seen in myocarditis or the typical extensive

subendocardial to transmural LGE and focal transmural oedema in a coronary artery territory in acute MI.⁹

Our case was complicated by the discovery of subendocardial myocardial necrosis with associated LGE on follow-up CMR. This new finding suggested a “true” MI and raised a number of possibilities: (i) LGE may be a feature of late or resolved TTS; (ii) he had TTS but subsequently developed MI; and (iii) he had coexistent TTS and MI.

With respect to whether LGE may be a feature of late or resolved TTS, LGE has been uncommonly reported in TTS, with a distinctive transmural band appearing at the hinge points between the dyskinetic ballooning segments and the hypercontractile segments, so the pattern is unique to TTS.¹⁰ We did not observe this pattern here, making this possibility unlikely.

Our patient might have had another silent MI after discharge. In the SWEDEHEART registry, 6.3% of MINOCA patients suffered a new MI during follow-up.¹¹ At follow-up, our patient did not have any cardiac indicators to necessitate another coronary angiography; moreover, this was unlikely to

have changed the management, but angiography could be considered in patients with CMR features of new MI after MINOCA.

With respect to coexistent TTS and MI at presentation, plaque rupture, thromboembolism, superimposed vasospasm, or a combination of these processes with subsequent transient thrombotic coronary occlusion by a fast-dissolving clot is some of the proposed pathogenic mechanisms in TTS.¹² Our patient also had numerous cardiac risk factors and presented with typical features of MI. Spontaneous thrombolysis, which might have occurred here, is an endogenous protective mechanism against thrombus formation, even in the presence of a ruptured coronary plaque.¹³ In our patient, the severe chest pain and the antecedent emotional stress may have triggered TTS, similar to one other reported case of coexistent TTS and MI similarly suggested to be either MI-induced TTS or TTS with secondary plaque rupture.¹⁴ Another possible variant of this scenario is that our patient had prolonged coronary vasospasm of a major coronary artery during the acute phase (which might have contributed to CMR oedema), with or without superimposed TTS, that subsequently developed into a subendocardial infarct after discharge. Indeed, there have been isolated reports of concurrent coronary vasospasm and TTS.^{15,16} Given that the patient's EF returned to normal, it is perhaps more likely that the concurrent or subsequent ischaemic event had a transient aetiology rather than representing a "typical" occlusive MI.

The absence of LGE in the first CMR may have been due to the myonecrosis being below the sensitivity of detection. CMR may show large areas of myocardial oedema with or without small areas of necrosis in patients with MINOCA and plaque disruption, suggesting a transient compromise of flow in a larger vessel.¹⁷ Patients with normal CMR imaging tend to have lower peak troponin values, although peak troponin levels 100 times the upper limit of normal have been observed in the absence of LGE. Technological advances might help improve the specificity and sensitivity of CMR in MINOCA; for instance, with free-breathing high-resolution LGE CMR imaging¹⁸ or feature-tracking CMR.¹⁹

In the international expert consensus document on TTS,⁹ follow-up investigations mainly focus on using transthoracic echocardiography to monitor left ventricular function. Follow-up CMR is only advised in cases with persistent regional wall motion abnormalities to exclude MI or myocarditis. Our case suggests that CMR may be useful not only to confirm TTS (and its resolution) but also to detect any possible adverse sequelae or alternative aetiologies. The follow-up CMR changed the management in our case, because dual

antiplatelet therapy was indicated due to suspected or confirmed plaque disruption.

In conclusion, CMR is useful at the time of presentation in patients with MINOCA. A typical pattern of oedema and LGE, when present, permits localization of the myocardial damage and provides insights into the underlying ischaemic or non-ischaemic causes and the extent and impact of acute myocardial injury. In our case, the diagnosis of TTS seems robust, but it remains uncertain whether the ischaemic injury detected at follow-up was related to events at time of presentation or occurred in the intervening period. Nevertheless, our case shows that CMR may be useful in the follow-up of these patients and may reveal additional, actionable pathology.

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Conflict of interest

The authors declare that they have no competing interests.

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Not applicable.

Ethics approval and consent to participate

This study was performed in accordance with the principles of the Declaration of Helsinki, and the patient provided informed consent. As the current study was a case report, there was no ethics committee to approve the study.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor of this journal.

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