



Acute biopsy-proven lymphocytic myocarditis mimicking Takotsubo cardiomyopathy

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Endomyocardial biopsy (EMB), the diagnostic gold standard for myocarditis, has not been systematically performed in the reported case series of Takotsubo cardiomyopathy, although proposed Mayo Criteria specify exclusion of myocarditis. Moreover, there is no specific recommendation for infarct-like acute myocarditis in the recently published guidelines on the role of EMB. Here we present a thoroughly documented case fulfilling both the proposed Mayo criteria for Takotsubo cardiomyopathy and the World Health Organization criteria for active, virus-negative, immune-mediated myocarditis. Since myocarditis can mimic acute myocardial infarction with normal coronary arteries, EMB should be performed to rule out myocarditis in patients presenting with LV apical ballooning syndrome (or Takotsubo cardiomyopathy).

Keywords

Myocarditis • Takotsubo cardiomyopathy • Autoimmunity • Acute myocardial infarction with normal coronary arteries

Introduction

Although proposed Mayo Criteria specify exclusion of myocarditis in all cases presenting as Takotsubo cardiomyopathy,¹ endomyocardial biopsy (EMB), the diagnostic gold standard for myocarditis,^{2–4} is not systematically performed in these patients. Moreover, no specific recommendation for the clinical setting of infarct-like acute myocarditis is included in the recently published guidelines on the role of EMB.³

Case report

A 68-year-old woman with a family history of coronary artery disease, but with no other risk factors for atherosclerosis, no stressful events except for her brother's death 3 months before, no history of heart failure or coronary artery disease symptoms (such as dyspnoea or chest pain on exertion), no preceding febrile or suspected viral illness or elevated markers of inflammation, presented to the emergency department (ED) of our hospital. Forty-eight hours previously she had complained of

prolonged (4 h) oppressive retrosternal chest pain at rest, which had resolved spontaneously. The day before ED admission she had experienced intermittent chest discomfort, exacerbated by physical effort, with associated dyspnoea. On the day of ED admission, after mild physical activity (house keeping) she presented with intense chest pain (10/10) of about 3 h duration. On arrival, she was in sinus tachycardia with a heart rate of 120 b.p.m., her blood pressure was 120/70 mmHg; there were no heart murmurs, and no signs of acute heart failure. Her ECG showed diffuse ST elevation and inverted T waves on inferior and anterolateral leads (Figure 1A). Her troponin I level was elevated (4.24 µg/L). She received aspirin (160 mg) and unfractionated heparin administered as an intravenous bolus (60 IU/kg). Selective coronary angiography showed no obstructive coronary disease (there was a 40% stenosis in the proximal LAD) or angiographic evidence of acute plaque rupture (Supplementary material online, Video files A–D). Left ventriculography showed a normal left ventricular (LV) end-diastolic volume (69 mL/m²) with severely reduced LV ejection fraction (LVEF = 23%) and wall motion abnormalities in

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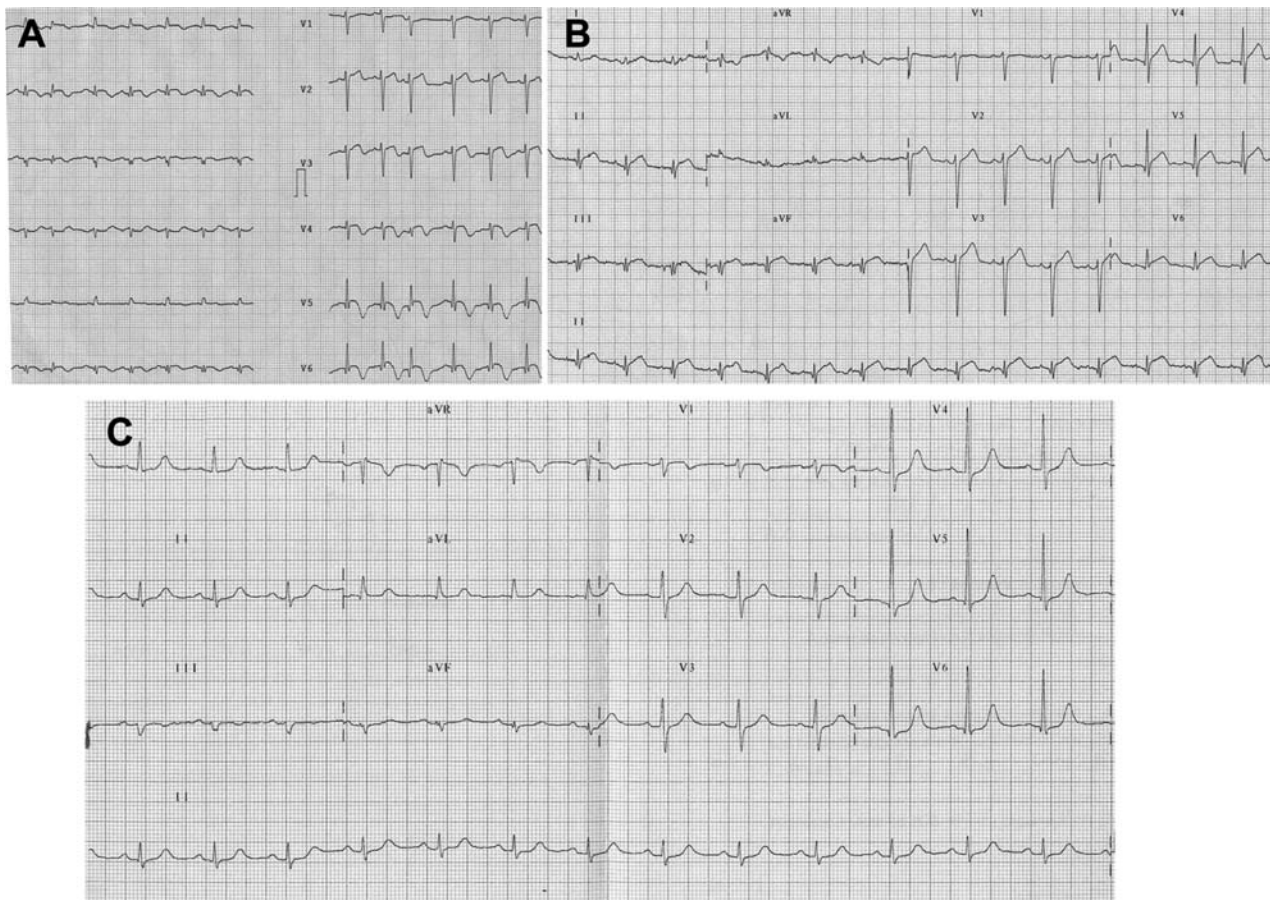


Figure 1 Echocardiography at diagnosis (A), at 1 week (B), and at last follow-up (C).

keeping with classical LV apical ballooning or Takotsubo cardiomyopathy (Supplementary material online, Video file E).¹

A right-ventricular EMB was performed. Cardiac magnetic resonance imaging (MRI) showed diffuse oedema and diffuse late-enhancement of the medial and apical portions of the left ventricle (Figure 2A and B, left panels). No signs of pericardial inflammation/effusion were present on cardiac MRI or transthoracic 2-dimensional echocardiography. Histological analysis on EMB showed diffuse lymphomonocytic infiltration and myocyte necrosis, not typical of myocardial infarction, but consistent with the Dallas diagnosis of active lymphocytic myocarditis (Figure 3A and B). Immunohistochemical analysis showed positive T lymphocytes (CD45 positive, Figure 3C, CD43 positive, not shown), sometimes activated (CD45RO positive, Figure 3D and E), cytotoxic T lymphocytes (CD8 positive, Figure 3F), and macrophages (CD 68 positive not shown). Polymerase chain reaction for common DNA and RNA cardiotropic viruses' genome (Adenovirus, Herpes simplex, Epstein-Barr, Cytomegalovirus, Enterovirus, Influenza A and B, Parvovirus B19, Hepatitis C) detection on EMB was negative. Serum cardiac-specific anti-heart auto-antibodies of IgG class were detected by indirect immunofluorescence test.

Follow-up echocardiography showed progressive regression of regional wall motion abnormalities and recovery of LVEF, with normal examination after 2 months. Normalization of ECG findings was partial at 1 week and complete at last follow-up (Figure 1B and C). Cardiac MRI findings were also normal at last follow-up (Figure 2A and B, right panels). The patient is asymptomatic at 4-year follow-up, and attends regular cardiological evaluations.

Discussion

The proposed Mayo Criteria specify exclusion of myocarditis in all cases presenting as Takotsubo cardiomyopathy.¹ However, in the reported case series of Takotsubo cardiomyopathy, EMB, the diagnostic gold standard for myocarditis, has not been systematically performed.²⁻⁴ In a recent large review, which included 286 patients from 14 studies, only 15 patients from 4 studies underwent EMB and these were all reported as negative for myocarditis.⁵⁻⁶

Here we present a case fulfilling both the proposed criteria of Takotsubo cardiomyopathy¹ and the WHO criteria of active, virus-negative, immune-mediated myocarditis.² In our recent large prospective study of biopsy-proven myocarditis, a pseudo-ischaemic

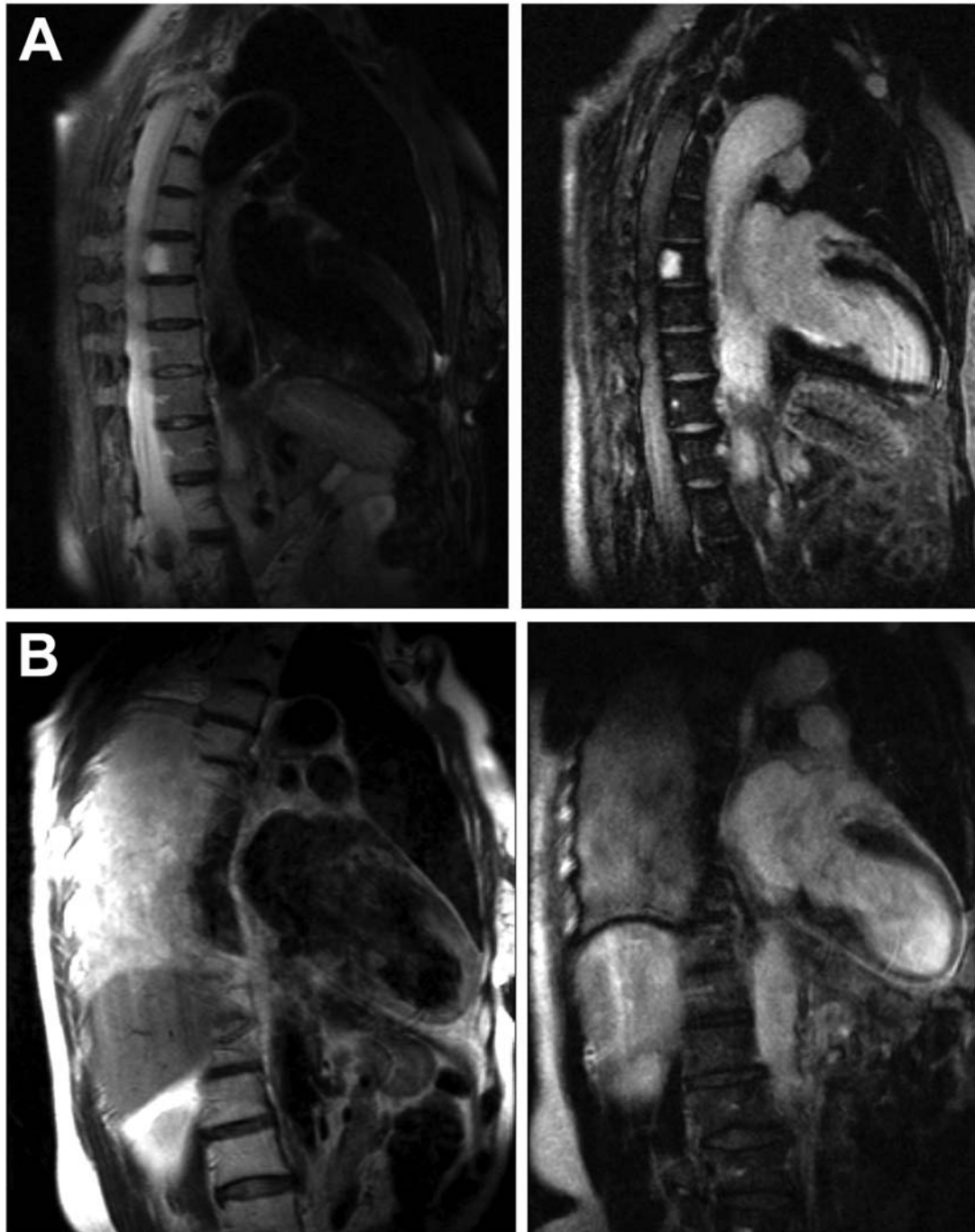


Figure 2 (A) T2-CMR findings: Left panel shows at diagnosis diffuse oedema of the medial and apical portions of the left ventricle. Right panel shows resolution of wall oedema at last follow-up. (B) Gadolinium-enhanced CMR findings: Left panel shows at diagnosis diffuse late enhancement in medial and apical portions of the left ventricle, a magnetic resonance imaging pattern not commonly observed in acute myocarditis. Right panel shows lack of late enhancement at last follow-up.

presentation with normal coronary arteries and troponin release was very common.⁷ In light of these findings, studies in which all patients presenting with LV apical ballooning syndrome (or Takotsubo cardiomyopathy) undergo EMB with histological (Dallas criteria) as well as current immunological, immunohistochemical

and molecular biology tools are warranted, in order to clarify the role of myocarditis (immune-mediated or viral) and its frequency in this condition.⁷ Such studies would also be important to clarify whether Takotsubo cardiomyopathy is a distinct nosographic entity or a syndrome.⁸⁻⁹

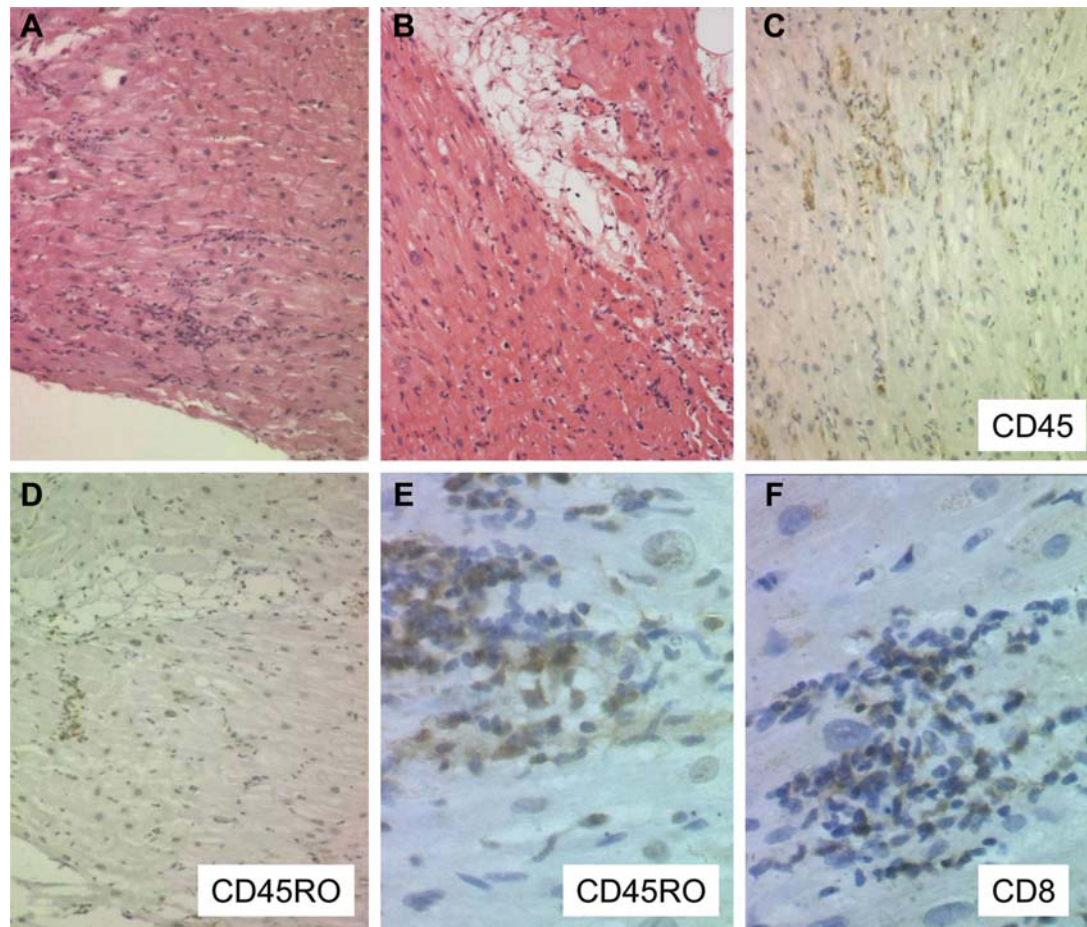


Figure 3 Endomyocardial biopsy showing diffuse inflammatory cell infiltrate and myocyte necrosis [(A and B) Haematoxylin–eosin stain, original magnification $\times 10$]. Immunohistochemistry revealed positive T lymphocytes [(C) CD45 positive stain, original magnification $\times 10$] sometimes activated (D and E) CD45RO positive stain; (D) Original magnification $\times 10$, (E) original magnification $\times 40$] and cytotoxic T lymphocytes [(F) CD8 positive, original magnification $\times 40$].

Supplementary material

Supplementary material is available at *European Journal of Heart Failure* online.

Conflict of interest: none declared.

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