CASE REPORT

'Clinically suspected myocarditis with pseudoinfarct presentation' complicated with left ventricular aneurysm

Annick Haouzi,¹ Ahmed Ahmed²

¹Heart and Vascular Institute, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, USA

²Department of Cardiology, St Bernards Heart and Vascular, Jonesboro, Arkansas, USA

Correspondence to

Dr Annick Haouzi,
ahaouzi@pennstatehealth.
psu.edu

Accepted 27 December 2017

SUMMARY

A 51-year-old man presented with chest pain, high troponin level, inflammatory syndrome and ST-segment elevation in the anterior leads. While the transthoracic echocardiogram (TTE) showed anteroseptal hypokinesis and apical akinesis, the coronary angiogram was normal. Cardiac MR demonstrated a typical aspect of myocarditis (multiple areas of mid-myocardial late gadolinium enhancement, sparing the subendocardial layer, along with oedema). The initial diagnosis was clinically suspected myocarditis with pseudoinfarct presentation. However, the short-term evolution was not typical of this syndrome, since an apical transmural scar with aneurysm developed within 2 weeks. Seven years later, the patient remained asymptomatic, while Q waves persisted in anterior leads along with an apical aneurysm on TTE. A transmural myocardial necrosis with aneurysm is an unusual complication of acute myocarditis. The potential mechanisms accounting for the development of these lesions are reviewed, and the clinical implications for the diagnosis and monitoring of acute myocarditis are discussed.

BACKGROUND

Acute myocarditis can often mimic an acute coronary syndrome.^{1–8} In the absence of coronary artery stenosis, cardiac MR (CMR) is helpful for initial assessment and follow-up.^{2, 9–14} Since the diagnosis of myocarditis requires an endomyocardial biopsy (EMB) to be confirmed, the term 'clinically suspected myocarditis with pseudoinfarct' has been proposed when EMB is not performed.¹⁰

We are presenting an observation where a clinically suspected myocarditis was complicated by the development of an apical left ventricular aneurysm. This complication, although uncommon, may be underestimated while its prognosis remains potentially threatening.

CASE PRESENTATION

A 51-year-old man with medical history of hypertension presented to the emergency department with a 3-day history of crescendo, mid-sternal, crushing chest pain without radiation, associated with nausea and vomiting. The pain was worsened with deep inspiration. The patient was subfebrile (37.8°C), normotensive (122/78 mm Hg) with tachycardia (100/min) and normoxic (arterial oxygen saturation 94% on room air). Auscultation of the heart and lungs was unremarkable.

INVESTIGATIONS

White cell count was elevated ($16.8 \times 10^9/L$ with 78% neutrophils) along with C reactive protein (12.0 mg/dL). The ECG showed diffuse ST-segment elevation, more pronounced in the anterior leads, and Q waves in the anterior and inferior leads (figure 1). The troponin-I level was elevated (28 ng/mL). Medical treatment with aspirin, clopidogrel, heparin and intravenous nitroglycerin was initiated.¹⁵ The emergent coronary angiogram revealed strictly normal coronary arteries without any atherosclerotic lesion (figure 2), whereas the left ventriculogram demonstrated anterior wall akinesis and apical dyskinesis. Transthoracic echocardiogram (TTE) showed a mildly dilated left ventricle (LV) with a slightly reduced ejection fraction (EF 45%) due to anteroseptal hypokinesis and apical akinesis along with a small LV apical thrombus. There was no pericardial effusion. Of note, apical LV wall thickness was normal at that time with no evidence of aneurysm.

OUTCOME AND FOLLOW-UP

The diagnosis of clinically suspected myocarditis with pseudoinfarct was proposed.¹⁰ The CMR study performed 13 days later demonstrated a mildly dilated LV with EF 47%, patchy mid-myocardial areas detected with late gadolinium enhancement (LGE), involving the septum, the distal anteroseptal and the proximal posterior walls, sparing the subendocardial layer in a typical myocarditis pattern (figure 3). T2-weighted high-intensity signal indicated myocardial oedema. The pericardium also exhibited LGE, suggesting associated pericarditis. There was also evidence of a newly developed apical aneurysm, with a thin, scarred myocardium (figure 4). Repeated TTE confirmed the aneurysm (2.2 cm width, 3.7 cm length).

Six months later, ECG still exhibited Q waves in anterior and inferior leads, and TTE revealed normal LV size with improvement of contractility, EF 55%, but persistence of an apical aneurysm without thrombus. After 7 years, the patient remained asymptomatic without any sign of heart failure, thromboembolic event or arrhythmia.

DISCUSSION

Myocarditis remains defined histologically as an inflammatory disease of the myocardium according to 1996 WHO,¹⁶ 2007 European Society of

CrossMark

To cite: Haouzi A, Ahmed A. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-222114

Figure 1 ECG on admission. Sinus tachycardia with diffuse ST elevation predominant in anterior leads (+4 mm) with Q waves in anterior and inferior leads, suggesting acute anteroseptal myocardial infarction.

Cardiology (ESC)¹⁷ and 2013 ESC working group on myocardial and pericardial diseases.¹⁰

The clinical diagnosis of acute myocarditis remains challenging due to the large spectrum of clinical presentations, ranging from asymptomatic non-specific ECG changes to heart failure, arrhythmias, cardiogenic shock or sudden death.^{2 13 18} Myocarditis mimicking acute myocardial infarct^{1 3-5 8 19-23} is a frequent mode of presentation.^{1 3 5 7 24} In a patient with sudden onset of chest pain, ECG changes and elevated cardiac enzymes, but with normal coronary angiogram, the diagnosis of myocarditis is suspected based on history of viral illness, fever, presence of inflammatory markers, global or regional ventricular wall motion abnormalities on the angiogram and/or TTE.⁹ CMR has become a major tool for *non-invasive* diagnosis of myocarditis, according to the 'Lake Louise criteria'.¹¹ However, EMB remains the gold standard to establish the diagnosis of acute myocarditis

and its aetiology, an approach that has been greatly enhanced by the addition of immunohistochemical analysis and viral genome search.¹⁰

The clinical course of an acute myocarditis is often benign with spontaneous resolution within 2–4 weeks in 50%–57% of cases, whereas 12% to 25% progress to severe dilated cardiomyopathy and heart failure.^{10 25 26} Indeed, acute myocarditis may sometimes evolve towards ongoing inflammation (autoreactive myocarditis), causing further myocardial injury and eventually leading to dilated cardiomyopathy and heart failure.^{10 18} A similar evolution has also been reported in myocarditis with pseudoinfarct, which despite a usual good prognosis has been found to develop a persistent reduced pump function in several retrospective studies.^{13 5}

The mechanism leading to the development of myocardial necrosis during myocarditis has been primarily accounted for

Figure 2 Coronary angiogram, right anterior oblique view of the left coronary circulation showing no evidence of atherosclerosis or thrombosis.

Figure 3 Three-chamber cardiovascular MRI view shows multiple areas of mid-myocardial late gadolinium enhancement involving the distal anteroseptal, the proximal and the mid-posterior walls of the left ventricle (arrows), sparing the endocardium, typical of myocarditis. There is also diffuse pericardial hyperenhancement suggesting associated pericarditis.

Figure 4 Left panel shows long-axis cardiovascular MRI view of the LV, 13 days after patient's presentation. The previously akinetic apex is now aneurysmal (white arrow). Right panel shows three-chamber CMR view of the LV with late gadolinium hyperenhancement. There is evidence of transmural distal septal and apical necrosis (white arrow) with white aspect while normal myocardium is black. CMR, cardiac MR; LV, left ventricle.

by direct viral infection and microvascular ischaemic injury. The latter results from endothelial dysfunction produced by intense focal inflammation.^{27–29} It has also been proposed that viral myocarditis could be associated with an exaggerated coronary vasoconstrictive response to acetylcholine, suggesting that coronary vasospasm may occur in these patients.³⁰ In addition, coronary thrombosis has been reported in fulminant,¹⁹ giant cell²⁰ or hypereosinophilic myocarditis.²² Regardless of the mechanisms, local myocardial necrosis can result in wall thinning and aneurysmal remodelling as demonstrated in animal models.^{31 32}

Ventricular aneurysms have been described in a variety of inflammatory myocardial diseases, but remain a relatively rare complication. Most cases are related to immune-mediated diseases such as sarcoidosis (10% of the patients with sarcoidosis have a ventricular aneurysm),³³ giant cell myocarditis,^{34–37} Behcet's disease^{34–37} or Takayasu's arteritis.^{34–37} The remaining observations are associated with bacterial (listeriosis, syphilis),^{38 39} fungal (aspergillosis),⁴⁰ parasitic (Chagas disease)^{41 42} or viral (particularly Coxsackievirus B)^{31 32 43–45} myocarditis. Frustaci *et al*⁴⁶ have found the presence of microaneurysms, sometimes multiple, located in the right or left ventricles, in about 3% of patients with EMB-proven myocarditis from viral or immunological origin. The prevalence of macroaneurysms remains unknown. While large aneurysms associated with myocarditis can lead to life-threatening LV free wall rupture,^{47 48} microaneurysms can be complicated by ventricular arrhythmias or Brugada syndrome.^{46 49} Nevertheless, microaneurysms with preserved pump function seem to have a favourable outcome, without any fatal arrhythmia in the study by Frustaci *et al*,⁴⁶ and may even sometimes get spontaneously occluded.

Data are not available to know if a specific antiviral, anti-inflammatory or immunomodulatory treatment would prevent the formation of aneurysms or more generally prevent myocardial necrosis and scar. Yet, there is evidence that the course of the disease may be stalled by these treatments. A study of 102 patients

with idiopathic cardiomyopathy showed an improvement in systolic function with immunosuppressive therapy only in the subgroup with evidence of inflammatory disease.⁵⁰ Recent clinical trials have since confirmed that the course of such 'reactive' myocarditis, that is, with active ongoing inflammation, could be improved with immunomodulation or antiviral therapy.^{51–54} The recent ESC recommendations support immunosuppressive therapy, including steroids, in selected cases with EMB-proven virus-negative myocarditis, but not in the presence of virus to avoid exacerbation in patients with ongoing infection. Identifying patients who could benefit from such aetiology-directed treatment justifies the current recommendations for EMB.^{7 10 18} Furthermore, since many of the myocarditis causes leading to aneurysm formation are immune-mediated and treatable (ie, sarcoidosis or giant cell myocarditis), EMB is also recommended in those patients.^{9 10 15}

In conclusion, clinically suspected myocarditis with pseudo-infarct presentation may be complicated by myocardial necrosis and development of an aneurysm. The prevalence of such aneurysms and their prognosis remain unknown. Since many aneurysms could be related to a treatable form of myocarditis, EMB should be proposed to establish the diagnosis, the aetiology and guide therapy. It would also provide a rational framework to understand better the natural history and time course of this heterogeneous disease.

Contributors AH contributed to the conception, design, acquisition, analysis and interpretation of data presented in the manuscript, drafted and revised the manuscript, approved the version to be submitted and will be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. AA contributed to the design of the work and the acquisition of data, drafted the original case report, provided some of the references, selected some of the figures, approved the version to be submitted and will be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Angelini A, *et al*. Myocarditis mimicking acute myocardial infarction: role of endomyocardial biopsy in the differential diagnosis. *Heart* 2000;84:245–50.
- 2 Caforio ALP, Marcolongo R, Basso C, *et al*. Clinical presentation and diagnosis of myocarditis. *Heart* 2015;101:1332–44.

Learning points

- Myocarditis with pseudoinfarct presentation may be complicated with ventricular aneurysm.
- Myocardial necrosis with left ventricular aneurysm can develop in myocarditis in the absence of coronary lesions.
- Since some aneurysms could be related to a treatable form of myocarditis, endomyocardial biopsy should be proposed to establish the diagnosis, the aetiology and guide therapy.

- 3 Pellaton C, Monney P, Ludman AJ, *et al.* Clinical features of myocardial infarction and myocarditis in young adults: a retrospective study. *BMJ Open* 2012;2:e001571.
- 4 Costanzo-Nordin MR, O'Connell JB, Subramanian R, *et al.* Myocarditis confirmed by biopsy presenting as acute myocardial infarction. *Heart* 1985;53:25–9.
- 5 Dec GW, Waldman H, Southern J, *et al.* Viral myocarditis mimicking acute myocardial infarction. *J Am Coll Cardiol* 1992;20:85–9.
- 6 Sarda L, Colin P, Boccaro F, *et al.* Myocarditis in patients with clinical presentation of myocardial infarction and normal coronary angiograms. *J Am Coll Cardiol* 2001;37:786–92.
- 7 Caforio ALP, Malipiero G, Marcolongo R, *et al.* Clinically suspected myocarditis with pseudo-infarct presentation: the role of endomyocardial biopsy. *J Thorac Dis* 2017;9:423–7.
- 8 Fan Y, Chen M, Liu M, *et al.* Myocarditis with chest pain, normal heart function and extreme increased troponin. *Int J Cardiol* 2016;209:307–9.
- 9 Agewall S, Beltrame JF, Reynolds HR, *et al.* ESC working group position paper on myocardial infarction with non-obstructive coronary arteries. *Eur Heart J* 2017;38:143–53.
- 10 Caforio ALP, Pankuweit S, Arbustini E, *et al.* Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur Heart J* 2013;34:2636–2648.
- 11 Friedrich MG, Sechtem U, Schulz-Menger J, *et al.* Cardiovascular magnetic resonance in myocarditis: a JACC white paper. *J Am Coll Cardiol* 2009;53:1475–87.
- 12 Laissy JP, Hyafil F, Feldman LJ, *et al.* Differentiating acute myocardial infarction from myocarditis: diagnostic value of early- and delayed-perfusion cardiac MR imaging. *Radiology* 2005;237:75–82.
- 13 Magnani JW, Dec GW. Myocarditis: current trends in diagnosis and treatment. *Circulation* 2006;113:876–90.
- 14 Lurz P, Eitel I, Adam J, *et al.* Diagnostic performance of CMR imaging compared with EMB in patients with suspected myocarditis. *JACC Cardiovasc Imaging* 2012;5:513–24.
- 15 Ibanez B, James S, Agewall S, *et al.* 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2017.
- 16 Richardson P, McKenna W, Bristow M, *et al.* Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the Definition and Classification of cardiomyopathies. *Circulation* 1996;93:841–2.
- 17 Elliott P, Andersson B, Arbustini E, *et al.* Classification of the cardiomyopathies: a position statement from the European society of cardiology working group on myocardial and pericardial diseases. *Eur Heart J* 2008;29:270–6.
- 18 Dennert R, Crijns HJ, Heymans S. Acute viral myocarditis. *Eur Heart J* 2008;29:2073–82.
- 19 Feng WH, Lin TH, Su HM, *et al.* Fulminant myocarditis complicated with obstructive ST-elevation myocardial infarction—a rare case report. *Am J Emerg Med* 2013;31:635.e1–635.e3.
- 20 Kwok OH, Chau EM, Wang EP, *et al.* Coronary artery disease obscuring giant cell myocarditis—a case report. *Angiology* 2002;53:599–603.
- 21 Morgan JM, Gray HH, Pillai RG. Coronary arterial occlusion and myocardial infarction in acute myocarditis. *Int J Cardiol* 1990;26:226–9.
- 22 Yamashita K, Nakamura T, Iio K, *et al.* Eosinophilic myocarditis complicated by acute myocardial infarction—a case report. *Angiology* 1997;48:1013–8.
- 23 Testani JM, Kolansky DM, Litt H, *et al.* Focal myocarditis mimicking acute ST-elevation myocardial infarction: diagnosis using cardiac magnetic resonance imaging. *Tex Heart Inst J* 2006;33:256–9.
- 24 Schultz JC, Hilliard AA, Cooper LT, *et al.* Diagnosis and treatment of viral myocarditis. *Mayo Clin Proc* 2009;84:1001–9.
- 25 Mason JW, O'Connell JB, Herskowitz A, *et al.* A clinical trial of immunosuppressive therapy for myocarditis. The Myocarditis Treatment Trial Investigators. *N Engl J Med* 1995;333:269–75.
- 26 D'Ambrosio A, *et al.* The fate of acute myocarditis between spontaneous improvement and evolution to dilated cardiomyopathy: a review. *Heart* 2001;85:499–504.
- 27 Choy JC, Lui AH, Moien-Afshari F, *et al.* Cocksackievirus B3 infection compromises endothelial-dependent vasodilation of coronary resistance arteries. *J Cardiovasc Pharmacol* 2004;43:39–47.
- 28 Mahrholdt H, Wagner A, Deluigi CC, *et al.* Presentation, patterns of myocardial damage, and clinical course of viral myocarditis. *Circulation* 2006;114:1581–90.
- 29 Schmidt-Lucke C, Zobel T, Schrepfer S, *et al.* Impaired endothelial regeneration through human parvovirus b19-infected circulating angiogenic cells in patients with cardiomyopathy. *J Infect Dis* 2015;212:1070–81.
- 30 Yilmaz A, Mahrholdt H, Athanasiadis A, *et al.* Coronary vasospasm as the underlying cause for chest pain in patients with PVB19 myocarditis. *Heart* 2008;94:1456–63.
- 31 Khatib R, Khatib G, Reyes MP, *et al.* The effect of subsequent myocardial damage on the expression of coxsackievirus B4 myocarditis and the development of ventricular aneurysms. *Eur Heart J* 1994;15:1140–3.
- 32 Hoshino T, Matsumori A, Kawai C, *et al.* Ventricular aneurysms and ventricular arrhythmias complicating Cocksackie virus B1 myocarditis of Syrian golden hamsters. *Cardiovasc Res* 1984;18:24–9.
- 33 Sekhri V, Sanal S, Delorenzo LJ, *et al.* Cardiac sarcoidosis: a comprehensive review. *Arch Med Sci* 2011;7:546–54.
- 34 Atzeni F, Sarzi-Puttini P, Doria A, *et al.* Behçet's disease and cardiovascular involvement. *Lupus* 2005;14:723–6.
- 35 Rose AG, Folb J, Sinclair-Smith CC, *et al.* Idiopathic annular submitral aneurysm associated with Takayasu's aortitis. A report of two cases. *Arch Pathol Lab Med* 1995;119:831–5.
- 36 Rose AG. Ruptured idiopathic left ventricular false aneurysm of the free wall associated with Takayasu's arteritis in a young child. *S Afr Med J* 1997;87 Suppl 3:C161–4.
- 37 Oommen A, Ramachandran P, Rao PV, *et al.* Dor's endoaneurysmorrhaphy in severe heart failure due to giant cell myocarditis. *Ann Thorac Surg* 2001;71:2036–8.
- 38 McCue MJ, Moore EE. Myocarditis with microabscess formation caused by *Listeria monocytogenes* associated with myocardial infarct. *Hum Pathol* 1979;10:469–72.
- 39 Chino M, Minami T, Nishikawa K. Ruptured ventricular aneurysm in secondary syphilis. *The Lancet* 1993;342:935–6.
- 40 Baumann S, Renker M, Schoepf UJ, *et al.* Invasive Cardiac Aspergillosis With Postinfectious Left Ventricular Aneurysm in a Patient With Acute Myeloid Leukemia. *Can J Cardiol* 2014;30:1463.e1–1463.e2.
- 41 Kransdorf EP, Fishbein MC, Czer LS, *et al.* Pathology of chronic chagas cardiomyopathy in the United States: a detailed review of 13 cardiectomy cases. *Am J Clin Pathol* 2016;146:191–8.
- 42 Aldama-Luebbert A, Nasrallah AT, Garcia E, *et al.* Ventricular aneurysm in Chagas' cardiomyopathy: clinical, epidemiologic, angiographic features. *Tex Med* 1976;72:55–60.
- 43 Morishita M, Oda A, Okayama A, *et al.* Acute myocarditis with localized left ventricular aneurysm: a report of three cases. *J Cardiol* 1988;18:553–64.
- 44 Matsumori A. Role of hepatitis C virus in cardiomyopathies. *Ernst Schering Res Found Workshop* 2006;55:99–120.
- 45 Way RC. Left ventricular aneurysm in rubella heart disease. *Am J Dis Child* 1971;121:451.
- 46 Frustaci A, Chimenti C, Pieroni M. Prognostic significance of left ventricular aneurysms with normal global function caused by myocarditis. *Chest* 2000;118:1696–702.
- 47 Kondo T, Nagasaki Y, Takahashi M, *et al.* An autopsy case of cardiac tamponade caused by a ruptured ventricular aneurysm associated with acute myocarditis. *Leg Med* 2016;18:44–8.
- 48 Lindblom RPF, Alström U, Zemgulis V. Dissecting ventricular pseudoaneurysm after perimyocarditis—a case report. *J Cardiothorac Surg* 2015;10:157.
- 49 Frustaci A, Priori SG, Pieroni M, *et al.* Cardiac histological substrate in patients with clinical phenotype of Brugada syndrome. *Circulation* 2005;112:3680–7.
- 50 Parrillo JE, Cunnion RE, Epstein SE, *et al.* A prospective, randomized, controlled trial of prednisone for dilated cardiomyopathy. *N Engl J Med* 1989;321:1061–8.
- 51 Wojnicz R, Nowalany-Kozielecka E, Wojciechowska C, *et al.* Randomized, placebo-controlled study for immunosuppressive treatment of inflammatory dilated cardiomyopathy: two-year follow-up results. *Circulation* 2001;104:39–45.
- 52 Frustaci A, Chimenti C, Calabrese F, *et al.* Immunosuppressive therapy for active lymphocytic myocarditis: virological and immunologic profile of responders versus nonresponders. *Circulation* 2003;107:857–63.
- 53 Kühl U, Pauschinger M, Schwimmbeck PL, *et al.* Interferon-beta treatment eliminates cardiotropic viruses and improves left ventricular function in patients with myocardial persistence of viral genomes and left ventricular dysfunction. *Circulation* 2003;107:2793–8.
- 54 Cavalli G, Pappalardo F, Mangieri A, *et al.* Treating life-threatening myocarditis by blocking interleukin-1. *Crit Care Med* 2016;44:e751–4.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow