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CASE REPORT

Acute fulminant necrotizing eosinophilic myocarditis: early diagnosis and treatment

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Abstract

Necrotizing eosinophilic myocarditis is a rare but potentially fatal condition that requires prompt recognition and treatment. We describe a case of a young athlete presenting with chest pain and breathlessness, with evidence of rapidly deteriorating cardiac function. The condition was successfully treated with corticosteroids, with no evidence of residual myocardial damage. This is the first reported case to demonstrate the utility of cardiac magnetic resonance imaging for diagnosis and monitoring response to treatment. It also highlights the value of endomyocardial biopsy in establishing a tissue diagnosis in cases of fulminant myocarditis, in order to direct treatment appropriately.

Keywords Myocarditis; Acute heart failure; Echocardiography; Magnetic resonance imaging; Endomyocardial biopsy

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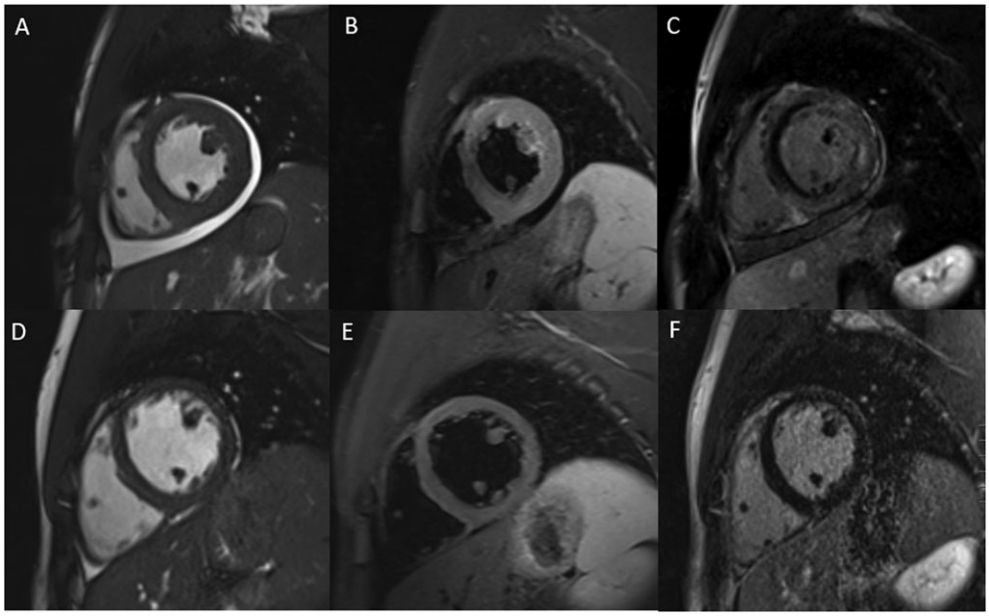
Case report

A 19-year-old professional sportsman was admitted because of acute central chest pain and breathlessness, which began during exercise. He has a history of asthma, treated with steroid and salbutamol inhalers, and hay fever. He was known to have a bicuspid aortic valve with moderate regurgitation. There was no history of foreign travel or medication changes. The chest pain resolved prior to admission. An electrocardiogram (ECG) revealed 2 mm ST elevation in leads I, II, V5, and V6, without reciprocal changes. An echocardiogram revealed a mildly dilated left ventricle, left ventricular ejection fraction (LVEF) 45–50% by visual estimation without regional wall motion abnormalities, and a small pericardial effusion. A computed tomography (CT) aortogram demonstrated normal origin of the coronary arteries, no evidence of proximal coronary disease or aortic dissection.

Troponin I was 13 530 ng/mL (normal range $<$40 ng/mL). He had a neutrophilia of 9.7 × 10^9/L and mild eosinophilia 0.6 × 10^9/L. Renal and liver function were normal, and C-reactive protein was 12 ng/mL. He underwent cardiac magnetic resonance imaging (MRI) on the day after admission. This revealed extensive myocardial oedema on T2 weighted short Tau inversion recovery (STIR) images, widespread late gadolinium enhancement, with moderate biventricular systolic dysfunction (*Figure 1*). His clinical condition worsened over the following 4 h, with profuse vomiting, tachycardia, and pallor. A repeat echocardiogram now showed severe biventricular systolic dysfunction, with a bright, thickened myocardium (*Figure 2*). He underwent right heart catheterization at the time of endomyocardial biopsy to assist in decisions regarding the need for inotropic and mechanical circulatory support: the right atrial pressure was 11 mmHg, wedge pressure 14 mmHg, and cardiac index 1.8 L/min/m^2. A left ventricular endomyocardial biopsy demonstrated an extensive infiltrate with abundant eosinophils, mixed with histiocytes, occasional plasma cells, and neutrophils (*Figure 3*). The histological diagnosis was a fulminant necrotizing eosinophilic myocarditis. He was treated with intravenous methylprednisolone (1 g daily for

Figure 1 Magnetic resonance imaging before (top row) and after (bottom row) treatment with corticosteroids. Pre-treatment images demonstrate thickening of left ventricular (LV) walls (A), extensive myocardial oedema on short Tau inversion recovery (STIR) images (B), and extensive late gadolinium enhancement (LGE) (C). Following treatment LV wall thickness returned to normal (D), with no evidence of myocardial oedema or LGE (E,F).



3 days), commenced on intravenous milrinone, and monitored in the intensive care unit. His symptoms improved within 12 h. He was weaned off milrinone and commenced on oral prednisolone 1 mg/kg/day and heart failure therapy (bisoprolol, ramipril, eplerenone, and furosemide). There was a progressive fall in serum Troponin I levels and a repeat echocardiogram on day 5 demonstrated a reduction in myocardial thickness and echo-reflectivity, with LVEF 72% (*Figure 2*). He was discharged on prednisolone 60 mg/day, alendronic acid, omeprazole, and heart failure therapy. Two weeks post-discharge, he was asymptomatic. Troponin levels were undetectable, and an ECG was normal. Repeat MRI confirmed normal biventricular function with no evidence of myocardial oedema or fibrosis (*Figure 1*). In a cardiopulmonary exercise test, he achieved 19 min of a modified Bruce protocol, with a peak VO2 of 40 mL/kg/min. His prednisolone has been weaned to 20 mg/day; he remains well with normal cardiac function by echocardiogram.

Discussion

Eosinophilic myocarditis is an uncommon condition; however, the true incidence is unknown. The prevalence in unselected autopsy series is 0.5–1% and higher in younger cohorts.[1] The most common causes are drug-induced hypersensitivity, parasitic infection, vasculitis, and granulomatous disorders. The Japanese Circulation Society produced guidelines on the diagnosis and management of myocarditis, which include diagnostic criteria for eosinophilic myocarditis.[2] Our patient fulfilled all of the minimally required conditions and also had an associated allergic condition, seen in approximately one-third of patients. The guidelines state that the disease can occur with a normal blood eosinophil count, and this appears to be particularly true of the necrotizing form, where around 40% of patients have a normal eosinophil count at presentation.[3] There does not appear to be a relationship between peripheral eosinophil count and disease severity.[4]

Fulminant necrotizing eosinophilic myocarditis (FNEM) is extremely rare. This is the first case report describing the MRI appearances both before and after treatment. Our patient presented with features of a fulminant myocarditis with ECG changes and raised troponin. Having excluded an acute coronary syndrome, we confirmed the diagnosis of myocarditis by MRI. A biopsy was required to establish the histological form of myocarditis because treatment depends on the nature of the inflammation.[5,6]

Fulminant necrotizing eosinophilic myocarditis presents as fulminant heart failure; the absence of extra-cardiac involvement distinguishes it from other forms of eosinophilic myocarditis such as hypersensitivity myocarditis (HSM).[7] A recent comprehensive literature review identified 21 published cases of FNEM, in which 15 patients survived and six died.[3] All patients had severe LV dysfunction, with many following a similar course of rapidly deteriorating cardiac function within days of admission. All of the

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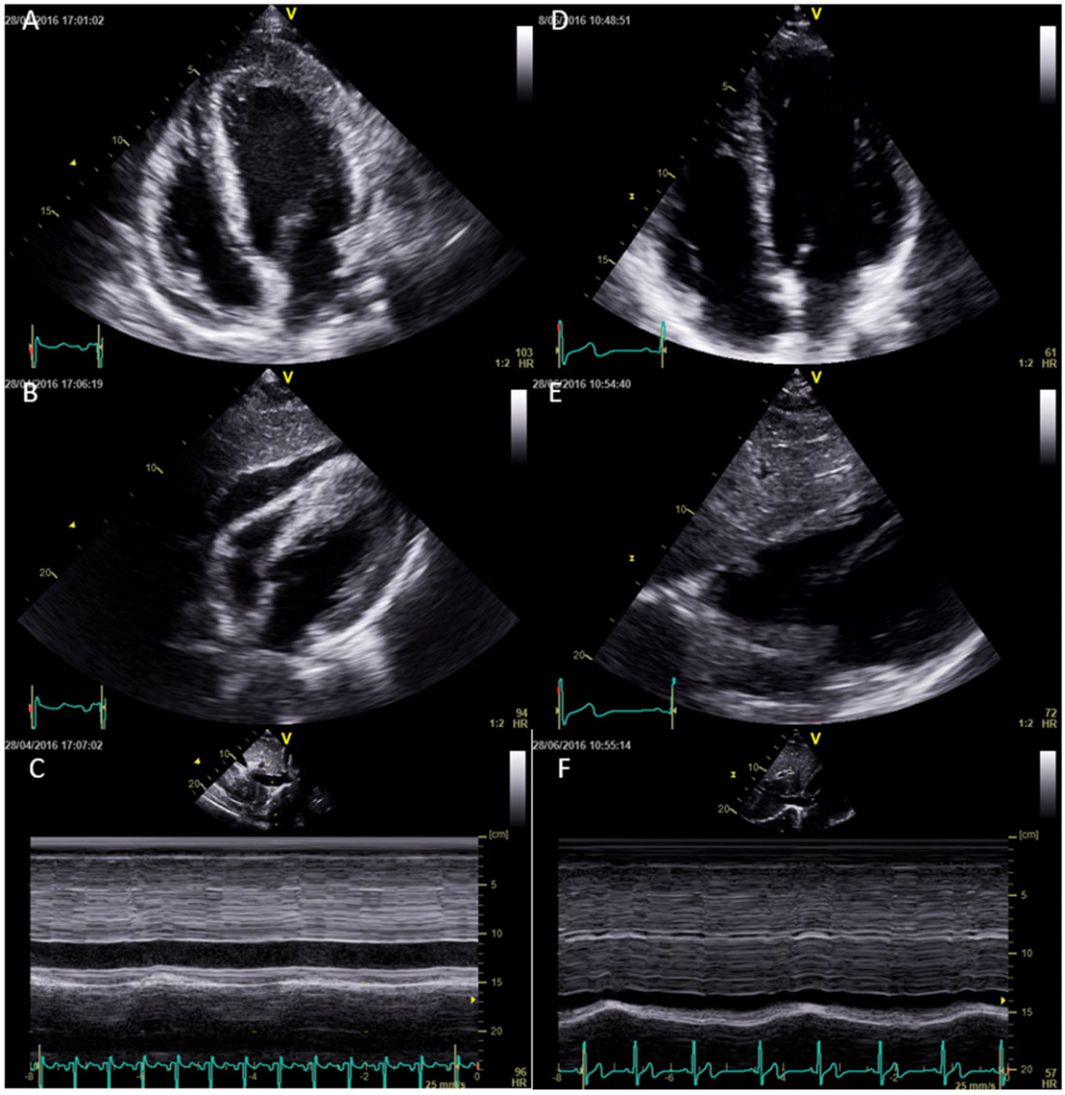
Figure 2 Echocardiogram images before (left column), and after (right column) treatment. Initial images revealed bright, thickened myocardium and a pericardial effusion (A,B), with a fixed, dilated inferior vena cava (C). Following treatment, there was complete resolution of these changes (D–F).



surviving patients were treated with high dose steroids; 14 out of 15 had complete recovery of ventricular function, with one partial recovery.

The key to successful treatment of this rapidly progressive and potentially fatal form of myocarditis is early recognition. This requires a systematic approach to rapidly exclude an ACS and use advanced imaging to establish the diagnosis of myocarditis and then endomyocardial biopsy to direct therapy. The use of steroid monotherapy in this condition was based on previous case reports and the known sensitivity of allergic eosinophilic disease to steroids.[8–11] Troponin measurements were useful for initial diagnosis and an early marker of treatment response. Serial echocardiograms were used to monitor the functional response to treatment and a follow-up MRI to characterize the myocardium and confirm the resolution of oedema without areas of scar. Cardiac MRI is increasingly utilized for diagnosing myocarditis, with a sensitivity of 76 to 100% and specificity of 91 to 100% in small series.[12] There are no specific MRI features that differentiate eosinophilic from other causes of myocarditis. It can be useful to help determine the most appropriate site for endomyocardial biopsy when there is patchy eosinophilic infiltration.

An interesting feature was that the cardiac symptoms were relatively short-lived, and gastrointestinal (GI) symptoms were the predominant feature. The GI symptoms were likely to be related to a combination of low cardiac output and hepatic congestion. The symptoms preceded left ventricular systolic dysfunction, when the echo showed

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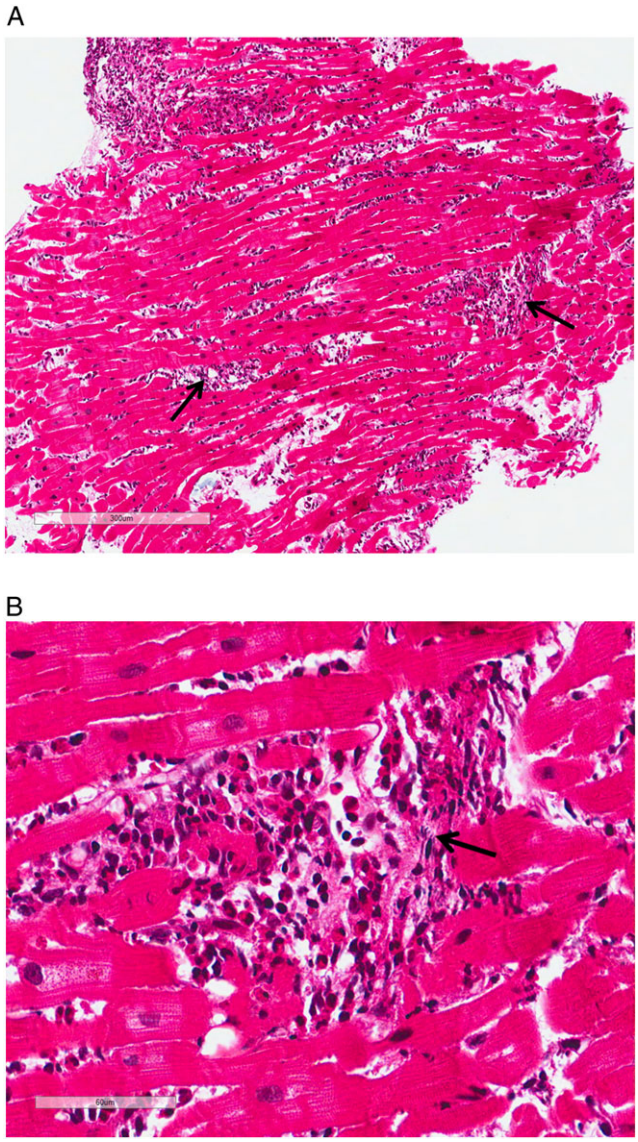
Figure 3 Endomyocardial biopsy of the left ventricle. (A) Haematoxylin and eosin stained slide of the endomyocardial biopsy showing the presence of an extensive patchy interstitial infiltrate with a marked presence of eosinophils (arrows). (Original magnification ×100). (B) Haematoxylin and eosin stained slide showing an infiltrate composing mostly of eosinophils mixed with a minority other inflammatory cells including monocytes (arrow). There is focal cardiomyocyte damage. (Original magnification ×400).



a constrictive–effusive physiology, with exaggerated respiratory variation in Doppler tricuspid inflow velocities, and a fixed dilated inferior vena cava. This would be consistent with infiltration of the pericardium and effusion leading to pericardial constraint, coupled with impaired left ventricular relaxation as a result of myocardial infiltration. It is recognized that adolescents with cardiomyopathy are more likely to present with GI symptoms than with classical heart failure symptoms.[13] It is important, therefore, to have a high index of suspicion for cardiac dysfunction in young patients presenting with a progressive unexplained GI disturbance.

In conclusion, FNEM is a rare, life-threatening disease that is eminently treatable if identified at an early stage. The key to success is a rapid systematic assessment using modern cardiac imaging and endomyocardial biopsy to establish a firm diagnosis. This can be best achieved by rapid access to a specialist advanced heart failure service.

Conflict of interest

None declared.

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