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CASE REPORT
Heart failure

A unique case report of relapsing eosinophilic myocarditis causing atrial myopathy and persistent sinus arrest

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Background Eosinophilic myocarditis (EM) is a rare and devastating condition. The underlying cause of EM is unknown, and the natural history is not well understood.

Case summary A 20-year-old male presented in cardiogenic shock with preceding 24-h history of pleuritic chest pain associated with nausea and vomiting. Electrocardiogram showed sinus tachycardia with widespread ST elevation, significantly raised high-sensitivity troponin T, and raised white cell count with eosinophilia. Transthoracic echocardiogram demonstrated severe left ventricular (LV) impairment and a moderate-sized pericardial effusion. Right ventricular (RV) endomyocardial biopsy and bone marrow biopsy were performed, with both demonstrating prominent eosinophilia. He was initiated on pulse methylprednisolone leading to rapid clinical improvement with normalization of LV function. Day 9 after discharge, he was readmitted to hospital with presyncope and right heart failure. Electrocardiogram revealed junctional escape rhythm, and cardiac magnetic resonance imaging showed scarring confined to the atria. The patient was treated with mepolizumab and underwent an electrophysiology study with electroanatomical mapping, demonstrating sinus arrest and the absence of electrical activity throughout the right atrium. After much deliberation, an implantable cardioverter-defibrillator was implanted with a deep septal RV pacing lead and an apical RV defibrillator lead.

Discussion We present a unique case of EM with two distinct phases: the first marked by severe LV impairment resolving with immunosuppression; the second characterized by atrial cardiomyopathy leading to persistent symptomatic sinus arrest necessitating permanent pacing. Close follow-up of EM after initial remission is essential to monitor for further complications including heart failure and arrhythmias.

Keywords Cardiomyopathy • Electroanatomical mapping • Electrophysiology • Bradycardia • Case report

ESC Curriculum 2.3 Cardiac magnetic resonance • 5.9 Pacemakers • 5.10 Implantable cardioverter defibrillators • 6.4 Acute heart failure • 6.5 Cardiomyopathy

Learning points

- Eosinophilic myocarditis (EM) can present as isolated atrial myopathy with symptomatic bradycardia, and long-term cardiac pacing may be necessary in the absence of electrical recovery.
- Targeted interleukin-5 inhibition with mepolizumab can be useful in treating relapsing EM.

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Introduction

Eosinophilic myocarditis (EM) is a rare disease marked by eosinophilic infiltration of the myocardium.[1,2] The underlying cause of EM is unknown, but it is often associated with other systemic disorders such as hyper-eosinophilic syndrome (HES).[2] Here, we present a case of relapsing EM causing atrial myopathy and persistent sinus arrest.

Timeline

Day 0	24-h history of pleuritic chest pain.
Day 1	Patient presents to hospital. Transthoracic echocardiogram revealed severe left ventricular (LV) systolic impairment and pericardial effusion.
Day 4	Transfer to cardiac transplant centre with endomyocardial and bone marrow biopsy demonstrating prominent eosinophilia. Diagnosed with eosinophilic myocarditis secondary to hyper-eosinophilic syndrome and treated successfully with pulse intravenous methylprednisolone.
Day 10	Discharged home with a tapering regime of oral prednisolone.
Day 19	Readmitted to hospital with symptomatic bradycardia, right heart failure, and elevated troponin. Electrocardiogram: junctional escape rhythm. Transthoracic echocardiogram: normal LV function. Treated with intravenous methylprednisolone, mepolizumab, and cyclophosphamide.
Day 40	Cardiac magnetic resonance showed late gadolinium enhancement confined to the atria.
Day 45	Persistent junctional escape rhythm at rest and during exercise. Electrophysiology study revealed the absence of electrical activity and inability to capture with pacing. Decision to insert an implantable cardioverter-defibrillator.

Case presentation

A 20-year-old male presented with 24 h of pleuritic chest pain associated with nausea and vomiting. He denied any preceding coryza, fever, cough, dyspnoea, or syncope. On examination, he was afebrile with a blood pressure (BP) of 78/57 mmHg, pulse rate of 133 b.p.m., and normal oxygen saturation. Cardiorespiratory examination was unremarkable.

The patient was born in India and migrated to Australia at age 6. Past medical history included ulcerative colitis treated with oral mesalazine for the past 4 years. He denied smoking or recreational drug use, and consumed alcohol rarely.

The differential diagnoses included myopericarditis, acute coronary syndrome, pulmonary embolus, and aortic dissection.

Electrocardiogram (ECG) demonstrated sinus tachycardia with widespread ST elevation (*Figure 1*). High-sensitivity troponin T (troponin) was 922 ng/L (normal <14 ng/L). White cell count was elevated at 11.4×10^9/L with neutrophilia (7.1×10^9/L) and eosinophilia (2.2×10^9/L). C-reactive protein was 48.4 mg/L (normal ≤4.9 mg/L).

Computed tomography pulmonary angiogram showed no evidence of pulmonary embolism or aortic dissection. Transthoracic echocardiography (TTE) demonstrated severe left ventricular (LV) impairment and a moderate-sized pericardial effusion (*Video 1*).

The patient was transferred to a cardiac transplant centre, where right ventricular (RV) endomyocardial biopsy revealed severe chronic inflammatory infiltrates comprising prominent eosinophils with lymphocytes and macrophages (*Figure 2*). Bone marrow biopsy demonstrated prominent eosinophilia, and cytogenetics was negative for FIP1L1-PDGFRA and BCR-ABL. A diagnosis of fulminant EM secondary to HES was made and he was treated with intravenous pulse methylprednisolone. There was rapid improvement with normalization of LV function and resolution of pericardial effusion. He was discharged home on a slow-tapering regime of oral prednisolone.

The patient was readmitted to hospital 9 days after discharge with pre-syncope and abdominal pain. Physical examination revealed a BP of 106/63 mmHg, pulse rate of 50 b.p.m., elevated jugular venous pressure, tender hepatomegaly, and mild peripheral oedema. Electrocardiogram demonstrated a junctional escape rhythm (*Figure 3*). Troponin was 2237 ng/L and N-terminal pro-brain natriuretic peptide (NT-proBNP) was 1585 ng/L (normal < 125 ng/L). Repeat TTE showed normal LV function with a trivial pericardial effusion (*Video 2*). RV size and function were normal, with a tricuspid annular plane systolic excursion of 19 mm. Computed tomography abdomen revealed congestive hepatomegaly, dilated inferior vena cava, and bilateral pleural effusions.

The patient was diagnosed with right heart failure and treated with furosemide and pulse methylprednisolone. After consultation with immunology, he was commenced on the interleukin-5 (IL-5) inhibitor mepolizumab, together with cyclophosphamide. The patient's right heart failure resolved; troponin and NT-proBNP decreased to 29 ng/L and 763 ng/L, respectively. However, he remained in a junctional escape rhythm 20 days after readmission. Exercise stress ECG demonstrated low exercise capacity, persistent junctional rhythm, and chronotropic incompetence with a maximum heart rate of 85 b.p.m.

A positron emission tomography scan did not show any active myocardial inflammation. Cardiac magnetic resonance showed late gadolinium enhancement confined to the atria, a small pericardial effusion, and normal ventricular size and function (*Figure 4*).

An electrophysiology study (EPS) was performed to assess the electrical status of the atria in order to identify possible sites for atrial lead implantation, and to exclude inducible ventricular tachycardia. Electroanatomic mapping of the right-sided cardiac chambers

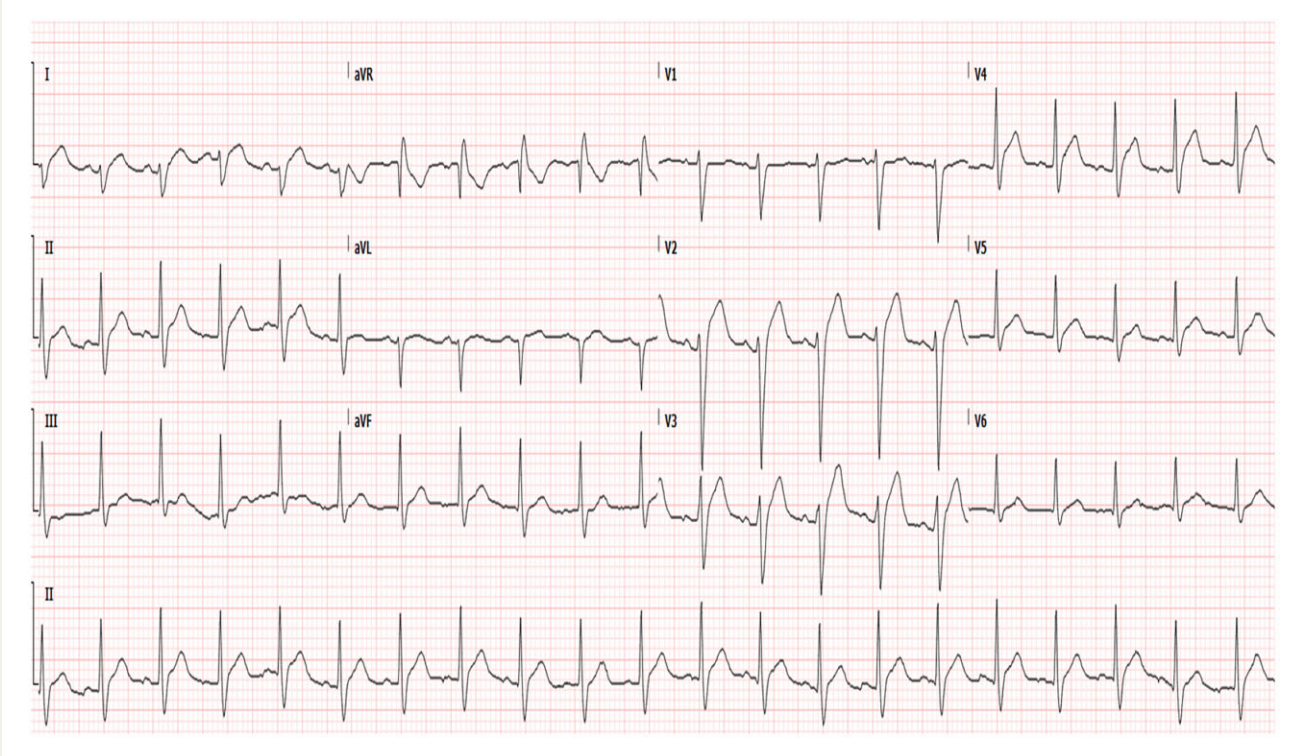
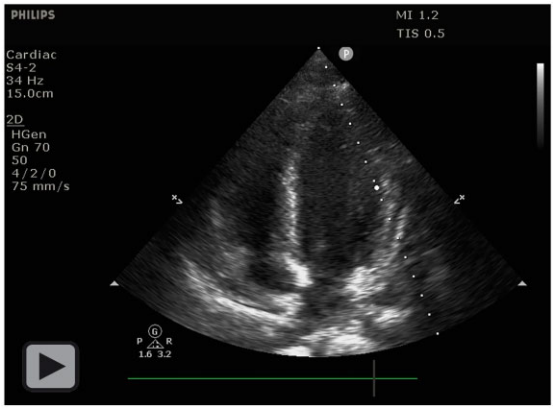


Figure 1 Electrocardiogram at initial presentation. Electrocardiogram performed during initial presentation demonstrating sinus tachycardia and widespread ST elevation.



Video 1 Transthoracic echocardiography at presentation. Apical four-chamber view demonstrating severe left ventricular systolic impairment with moderate-sized pericardial effusion.

revealed absence of electrical activity and inability to capture with pacing (at output of 10 V @ 2 ms) throughout the right atrium and coronary sinus, while there was preserved RV bipolar voltage (*Figure 5*). The H-V interval was normal and there was no inducible ventricular tachycardia. Following atropine (1 mg) and isoprenaline infusion (5 µg/min), there was only mild chronotropic response with a maximum heart rate of 90 b.p.m. After much deliberation amongst the treating physicians, an implantable cardioverter-defibrillator (ICD) capable of cardiac resynchronization (Medtronic Amplia CRT-D) was implanted with a left bundle branch area (LBBA) pacing lead (Medtronic 3830) inserted into the 'LV port', and an apical RV defibrillator lead (Medtronic 6935M). The LV activation time was 80 ms with a paced QRS duration of 120 ms at implant (Supplementary material online, *Figure S1*). An atrial lead was not implanted. The device was set to pace in VVIR 50–150 b.p.m. delivered exclusively via the pacing lead in LBBA. The decision for the ICD was based on the severity of initial LV dysfunction, and the possibility of relapse despite medical therapy. In terms of pacing, an LBBA pacing lead was chosen to reduce the likelihood of pacing-induced dyssynchrony.[3] His-bundle pacing was considered but was not performed because of concerns over potential increase in pacing threshold and the need for lead revision over time.[4] Given the lack of atrial electrical activity, he was commenced on rivaroxaban 20 mg daily for stroke prophylaxis prior to discharge. Other discharge medications included prednisolone 40 mg daily, pantoprazole 40 mg BD, cholecalciferol 1000 units BD, furosemide 40 mg daily, sulfamethoxazole/trimethoprim 800/160 thrice weekly, as well as monthly mepolizumab and cyclophosphamide.

At 6-month follow-up, he remained in persistent sinus arrest with junctional escape rhythm. He was symptom-free and continued on immunosuppressive therapy.

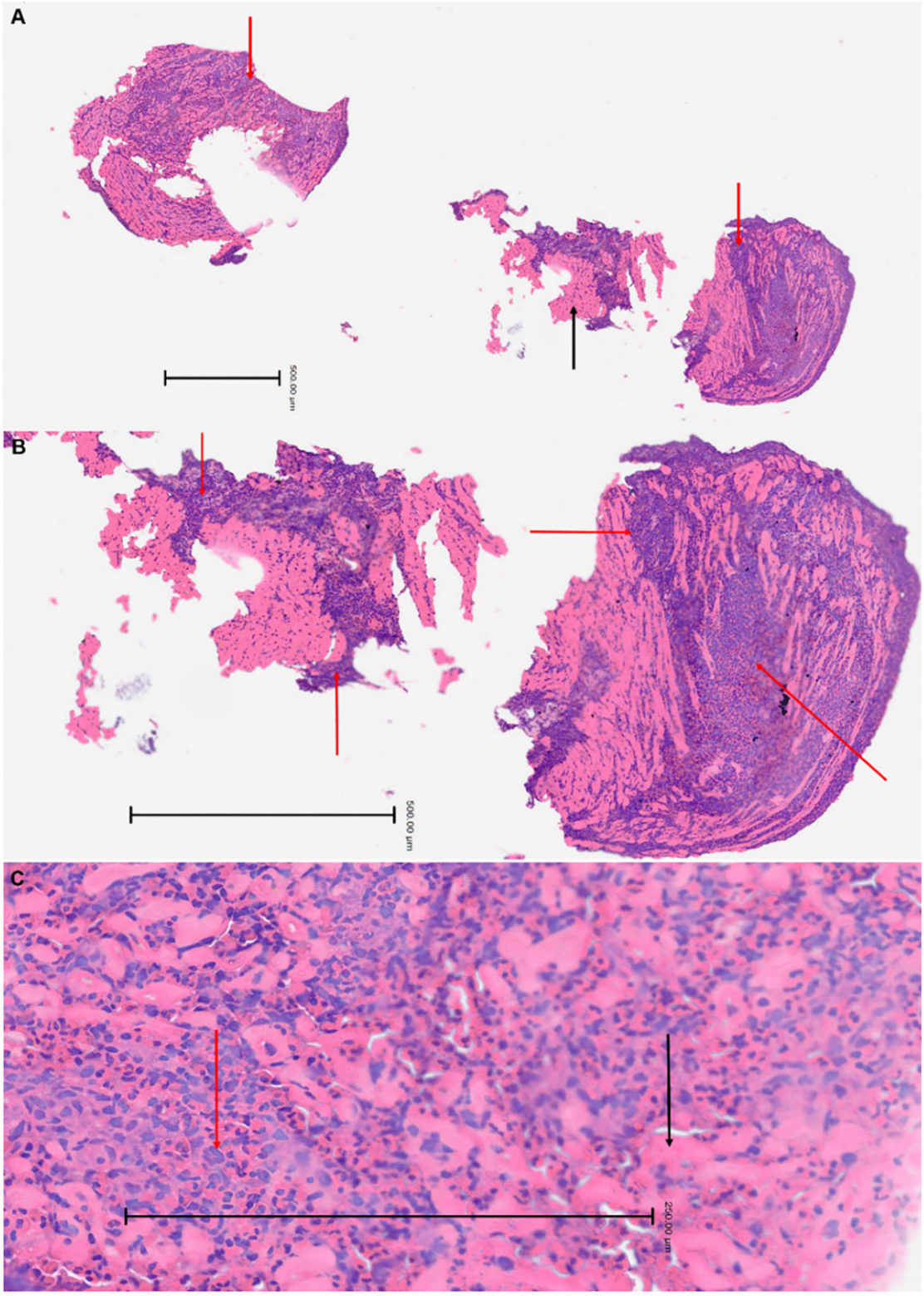


Figure 2 Haematoxylin and eosin stains of endomyocardial biopsy. (*A*) Low power view (40×) shows myocardium (black arrow) and hypercellular areas (red arrows). (*B*) Medium power view (100×) showing cellular infiltrate between and amongst the cardiac myocytes (red arrows). (*C*) High power view (400×) shows that majority of the infiltrating cells were eosinophils (red arrow) with bi-lobed nuclei and cytoplasm containing bright-red eosinophilic granules, adjacent to normal myocytes (black arrow). Morphology was suboptimal due to technical issues with tissue processing.

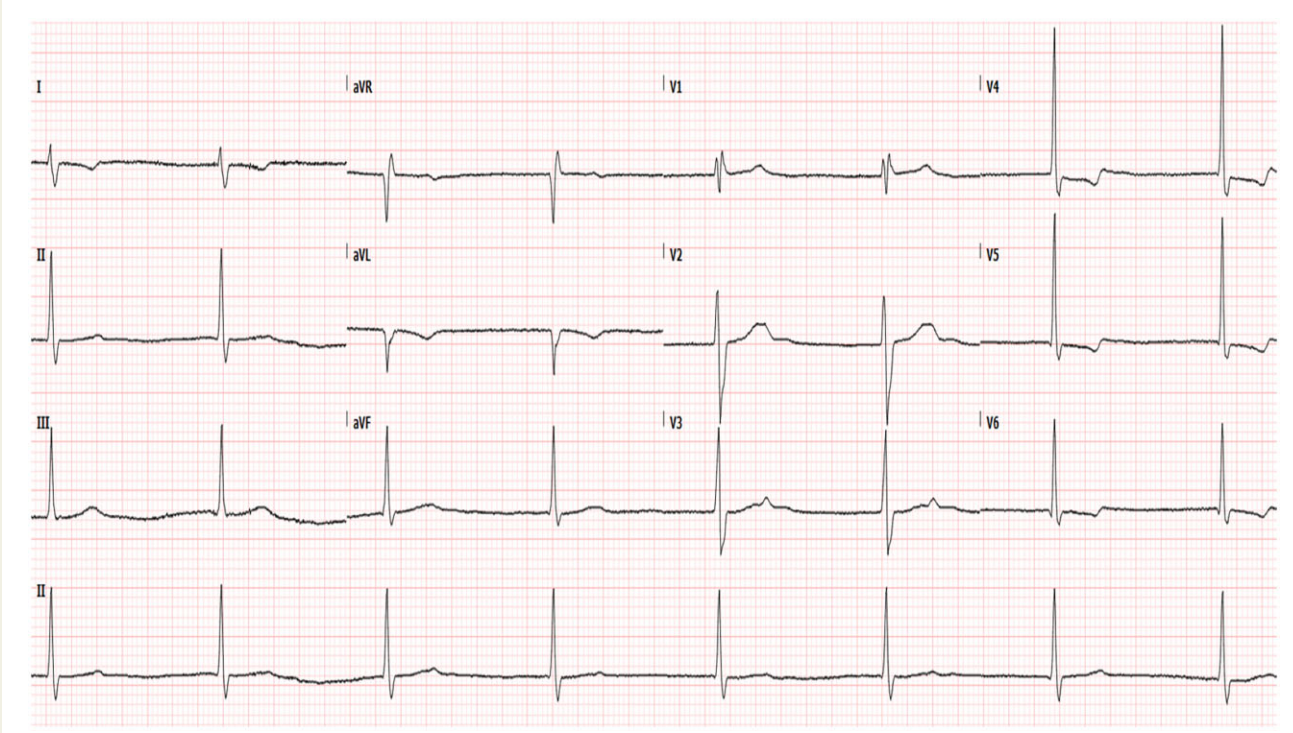
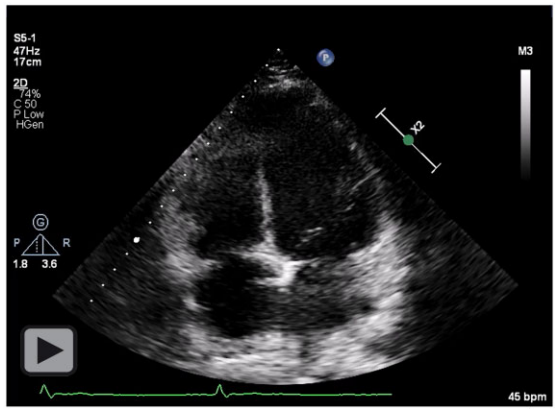


Figure 3 Electrocardiogram at readmission. Electrocardiogram performed during readmission showing junctional escape rhythm with lateral T-wave inversion.



Video 2 Transthoracic echocardiography on readmission. Apical four-chamber view demonstrating normalized left ventricular systolic function with a small pericardial effusion.

Discussion

Eosinophilic myocarditis is rare and unless presenting with fulminant myocarditis, it often goes undiagnosed and is only discovered on autopsy.[1,5] Unselected autopsy studies have reported up to 0.5% prevalence in post-mortem examinations, while epidemiological data reported a lower incidence at 0.036 per 100 000 persons.[1,5] The in-hospital mortality rate is ~22%.[2] Left untreated, the condition may evolve from acute necrosis to a thrombotic, and ultimately fibrotic stage in survivors.[6] A definitive diagnosis of EM is made with endomyocardial biopsy, and immunosuppression is the mainstay of treatment.[1,7,8] High-dose corticosteroids are considered first line therapy with steroid-sparing agents being used as adjunctive therapy in cases of refractory EM.[5] IL-5 is critical to the development of eosinophils in humans. Mepolizumab, an anti-IL-5 recombinant humanized monoclonal antibody, has been shown to be effective in stabilizing eosinophil counts in HES.[9] There have been case reports in the literature describing the successful use of mepolizumab in EM, though there remains a lack of definitive evidence from more robust clinical studies.[8,10] Identification of the underlying aetiology can also lead to further tailored therapies towards EM: cyclophosphamide is used in eosinophilic granulomatosis with polyangiitis; imatinib in FIP1L1/PDGFRA-associated HES; and albendazole in toxocara canis infection.[2]

Here, we present a unique case of relapsing EM with two distinct phases. The first phase was characterized by rapidly progressive fulminant myocarditis leading to severe ventricular dysfunction and cardiogenic shock, with a dramatic response to corticosteroids. The second phase was characterized by isolated bi-atrial myopathy with preservation of ventricular function, culminating in right heart failure and symptomatic persistent junctional bradycardia.

Management of this complex and rare case necessitated multidisciplinary team discussion. There were significant concerns around

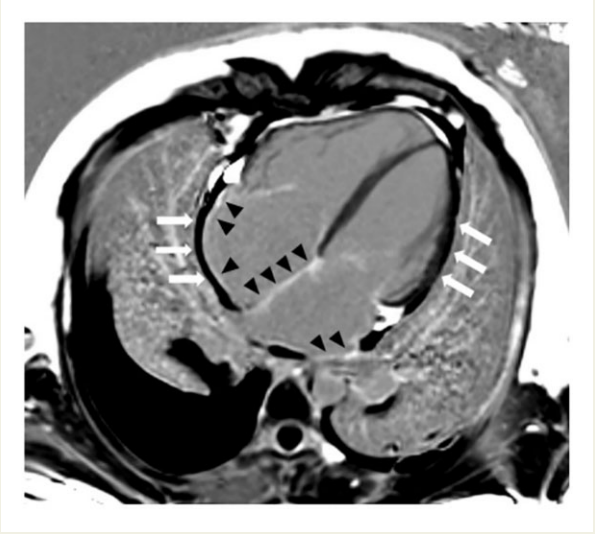


Figure 4 Delayed enhancement cardiac magnetic resonance. Cardiac magnetic resonance demonstrating bi-atrial myopathy with late gadolinium enhancement in the atria and interatrial septum (black arrowheads), a small pericardial effusion (white arrows), and no evidence of late gadolinium enhancement in the ventricles.

implantation of a permanent cardiac device given the patient's young age and the possibility of sinus node recovery. However, given the persistence of bradycardia despite biochemical and imaging evidence of remission, as well as the profound absence of right atrial electrical activity on EPS, a decision was made to proceed with permanent pacing. Another dilemma revolved around the choice to implant a pacemaker or ICD. Although his LV function recovered and no evidence of inducible ventricular arrhythmias was found on EPS, we decided that the safest option was to implant a device with both pacing and defibrillation capacity. This decision was based on the following reasons: first, our patient developed relapsing myocarditis despite the use of high-dose corticosteroids, and there was trepidation regarding the possibility of future deterioration in LV function. Second, EM is historically associated with a high incidence of ventricular arrhythmias, with up to 11% of patients having ventricular tachycardia or fibrillation.[2] Third, malignant ventricular arrhythmias have been shown to occur in myocarditis patients even in the presence of preserved LV systolic function.[11] Ultimately, given the lack of evidence that applies to our patient's specific circumstances, consensus medical opinion amongst the treating physicians was to proceed with ICD, which the patient and his family agreed to after extensive discussion.

We demonstrate a unique case of EM presenting in two distinct phases—initial acute fulminant myocarditis with ventricular involvement and cardiogenic shock, followed by relapse with isolated bi-

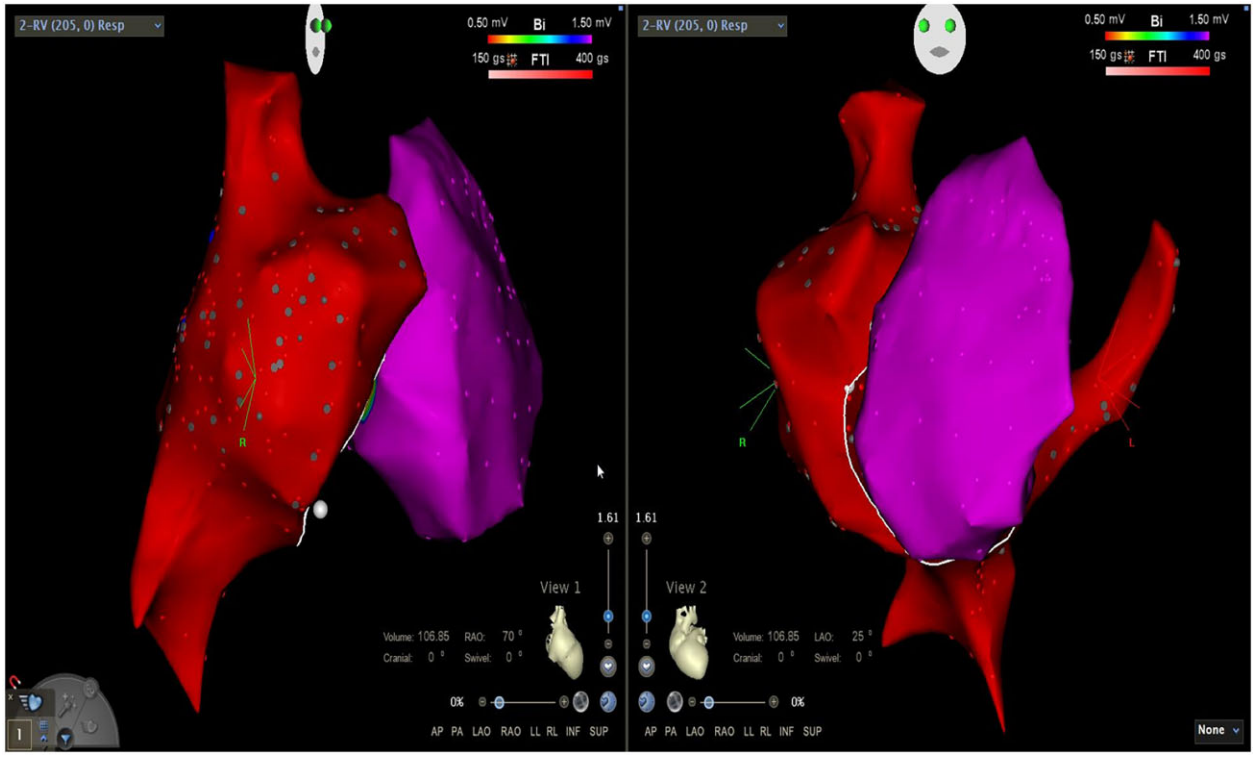


Figure 5 Electro-anatomical mapping of the right atrium and ventricle. Electro-anatomical map showing absence of electrical activity (red = 0.05 mV bipolar voltage; grey dots = inability to capture with 10 V @ 0.2 ms) in the right atrium and coronary sinus, with normal bipolar voltage (purple >1.5 mV) in the right ventricle (left panel = 60° right anterior oblique projection; right panel = 20° left anterior oblique projection).

atrial myopathy, persistent sinus node dysfunction, and right heart failure. This case illustrates the heterogeneous clinical manifestations of EM and the need to remain vigilant during the follow-up of patients with this rare but devastating condition.

Lead author biography

Dr Ronald Huynh completed his medical studies at the University of Notre Dame, Australia in 2013, and his Cardiology Advanced Training at Concord Repatriation General Hospital, Australia in 2020.

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: None declared.

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