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CASE REPORT
Heart failure

A case report of isolated right ventricular lymphocytic myocarditis

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Background Lymphocytic myocarditis is an uncommon condition with a variety of clinical presentations. Isolated involvement of the right ventricle (RV) is very rare. We present a case of a young woman who developed right ventricular dysfunction and arrhythmias as a consequence of this condition, which appeared to be chronic at diagnosis.

Case summary A 26-year-old lady was admitted to hospital following routine echocardiography, requested for screening of pulmonary hypertension in the context of known hypersensitivity pneumonitis. This echocardiogram demonstrated severe right ventricular dilatation and impairment. She was also experiencing atrial fibrillation and non-sustained, symptomatic episodes of ventricular tachycardia. Endomyocardial biopsy revealed lymphocytic myocarditis. She was managed with azathioprine and prednisone, as well as sotalol and apixaban for her atrial fibrillation, and has had no complications in the 12 months since discharge.

Discussion Lymphocytic myocarditis isolated to the RV has only been reported in two previous cases, both of which were acute, dramatic presentations. This is the first report of a chronic example of this disease process. Due to her intercurrent immunosuppression, this patient may have been pre-disposed to the condition either by re-activation of a latent viral infection or partial treatment of a true autoimmune lymphocytic myocarditis.

Keywords Lymphocytic myocarditis • Atrial fibrillation • Right ventricle • Cardiomyopathy • Case report

Learning points

- Lymphocytic myocarditis is typically a viral or autoimmune condition of the left ventricle, but in rare cases, may also affect the right ventricle (RV).
- One should not ignore right ventricular dilatation, as it may be a manifestation of several serious conditions. In the setting of unexplained dilatation of the RV, particularly in young patients, always consider right ventricular myocarditis as a differential diagnosis.

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Introduction

Lymphocytic myocarditis typically presents with fulminant left ventricular failure. It has rarely been reported to affect the right ventricle (RV) in isolation, but where described, the disease course is acute and dramatic in nature.[1,2] Lymphocytic myocarditis is typically caused by a viral infection, with the combination of viral cytotoxicity and the subsequent immune response resulting in myocardial dysfunction and arrhythmias. Viral infections associated with the condition include parvovirus B19, adenovirus, and enterovirus.[3] The incidence of myocarditis is estimated to be 22 per 100 000 individuals, with lymphocytic myocarditis accounting for approximately half of these,[4,5] although the true incidence is unknown as endomyocardial biopsy, the gold standard for diagnosis is not a routinely performed procedure. We present a histopathologically confirmed case of lymphocytic myocarditis that presented with chronic right ventricular dysfunction, complicated by arrhythmia.

Timeline

Date	Event
October 2014	• First admission to hospital for investigation of dyspnoea. Lung biopsy revealed hypersensitivity pneumonitis • Echocardiogram demonstrated right ventricular dilatation and impairment • Treated with methotrexate, sulfasalazine, and intermitted prednisone
June 2018	• Routine echocardiogram (first since 2014) shows severe right ventricular dilatation and impairment, with severe tricuspid regurgitation
June 2018–July 2018	• 28-Day hospital stay with multiple investigations performed • A diagnosis of lymphocytic myocarditis was made on myocardial biopsy • Treatment with immunosuppression was initiated
January 2020	• Patient remains well with no deterioration in symptoms or cardiac function

Case presentation

A 22-year-old Caucasian lady presented in 2014 with features of pulmonary fibrosis, chronic cutaneous problems, and symmetrical polyarthritis. She had previously been well without any comorbidities. A high-resolution computed tomography (CT) chest and lung biopsy were performed, with a diagnosis of hypersensitivity pneumonitis being made, in the context of significant mould exposure. Skin biopsies demonstrated spongiotic dermatitis (eczema). Echocardiography revealed right ventricular dilatation with mild tricuspid regurgitation. Left ventricular size and function was normal.

She was discharged and attended as an outpatient to a specialist centre for pulmonary hypertension, as it was assumed at the time that the right ventricular dilatation was a consequence of undiagnosed pulmonary hypertension. Here, right heart catheterization indicated normal pulmonary arterial pressure. Subsequently, no cardiology follow-up was arranged. The patient was treated with methotrexate, sulfasalazine, and intermittent prednisone over the next 4 years, although a single unifying diagnosis to explain her all of her symptoms was not identified.

In 2018, the patient attended a rheumatology clinic. The rheumatologist was concerned that there were clinical signs of pulmonary hypertension detected on physical examination, and thus a routine echocardiogram was performed. This study demonstrated severe right ventricular dilatation (*Figure 1A*). There was now severe tricuspid valve regurgitation (*Figure 1B*). The left ventricular size was normal, as was systolic and diastolic left ventricular function. There was no significant left-sided valvular disease. The patient was experiencing dyspnoea on walking 50 m on a flat surface, or at the top of a single flight of stairs. Additionally, she described four episodes of unheralded syncope, all occurring whilst seated. On physical examination, the blood pressure was 130/70 mmHg, the heart rate 88 b.p.m., and regular, with oxygen saturation of 99% on room air. The jugular venous pressure was elevated with prominent V waves. There was a right ventricular heave and a loud pan-systolic murmur audible at the left sternal edge. Pulsatile hepatomegaly was present. Fine crackles were present in both lung bases. Electrocardiogram demonstrated atrial fibrillation with a right bundle branch block (*Figure 2A*).

Due to the concerning features on echocardiography and the symptoms of dyspnoea and syncope, the patient was admitted to a monitored cardiac ward for further investigation. Telemetry demonstrated non-sustained ventricular tachycardia (VT) at a rate of 150 b.p.m. (*Figure 2B*), of which the patient was symptomatic with palpitations but there was no haemodynamic compromise.

Right heart catheterization revealed normal pulmonary arterial pressures (22/10 mmHg), but elevated right atrial pressures (16/14 mmHg). Cardiac output (5.4 L/min) and pulmonary vascular resistance (88 dynes.s/cm^5) were normal.

The patient underwent transoesophageal echocardiography (TOE) and successful electrical cardioversion, restoring sinus rhythm. The TOE excluded atrial thrombus, any intracardiac left-to-right shunt, and all four pulmonary veins communicated with the left atrium.

Cardiac magnetic resonance imaging (MRI) did not show any late gadolinium enhancement in either ventricle, and congenital anatomical anomalies were excluded. Cardiac positron emission tomography (PET) did not reveal increased metabolic activity to indicate inflammation or features of active cardiac sarcoidosis. A CT chest demonstrated unchanged features of pulmonary fibrosis.

Myocardial biopsy was performed under fluoroscopic guidance. Histopathology revealed a predominantly lymphocytic chronic inflammatory infiltrate (*Figure 3*). A single well-formed small granuloma as well as a second focus of scattered giant cells was noted. Moderate to severe myopathic features were seen, including myocyte necrosis with features of myocytolysis and anisonucleosis, and patchy regenerative interstitial fibrosis. The diagnosis was consistent with

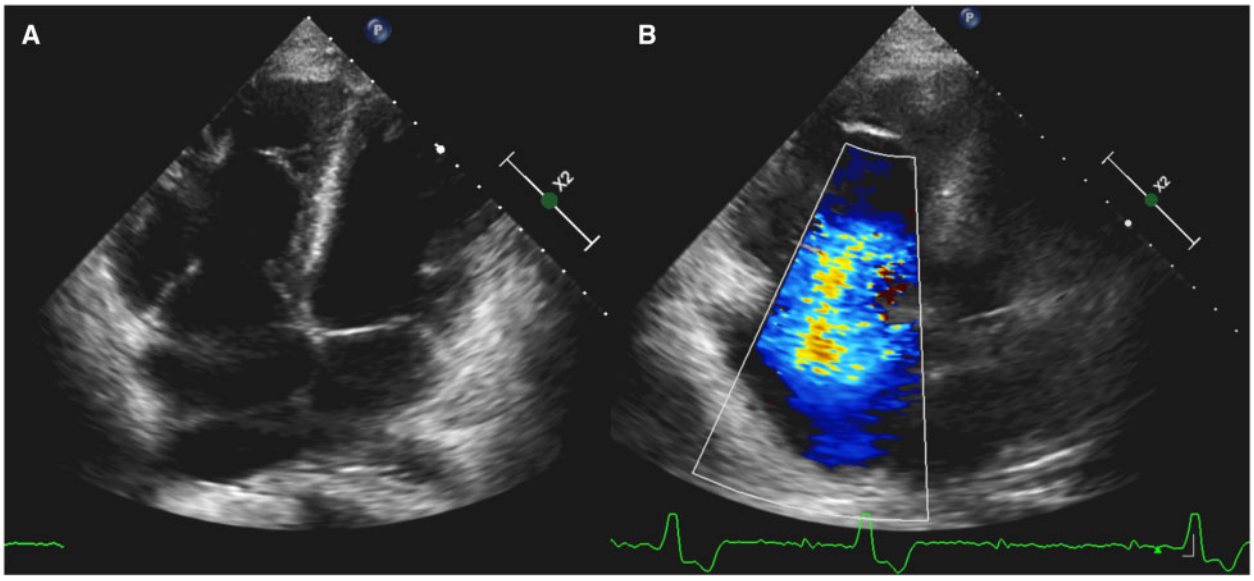

Figure 1 (*A*) Transthoracic echocardiogram demonstrating severe right ventricular dilatation. (*B*) Colour Doppler demonstrating severe tricuspid regurgitation.

lymphocytic myocarditis. The morphological pattern that comprised myocyte necrosis and a widespread lymphocytic infiltrate without predominating giant cells and granulomas was less likely to be consistent with cardiac sarcoidosis or giant cell myocarditis. There was a paucity of eosinophils, making the diagnosis of hypersensitivity myocarditis highly unlikely. The classic features of arrhythmogenic cardiomyopathy (AC) were also not seen, i.e. patchy to diffuse irregular replacement of myocytes by adipose tissue, with associated variable amounts of fibrosis, lack of significant lymphocytic infiltrate, and scattered enlarged degenerate vacuolated myocytes. A broad range of serological investigations had also been conducted, with no significant positive results.

Given the documented symptomatic VT, and the history of syncope, the patient was referred for a cardiac electrophysiology study, which demonstrated inducible VT originating from the RV apex that lasted for over 30 s. Following a multidisciplinary discussion, the patient consented to the implantation of an automated implantable cardioverter-defibrillator (AICD).

The patient was commenced on prednisone 25 mg daily, as well as sotalol 80 mg twice daily and apixaban 5 mg twice daily, prior to discharge. Since discharge, her prednisone has been ceased after being systematically weaned following commencement of azathioprine 100 mg daily. She has been stable thereafter, with no further arrhythmias and has returned to work. Occasional episodes of decompensated mild right heart failure have been treated successfully with oral diuretics, without the need for intravenous therapy or inpatient admission. An echocardiogram performed 12 months after discharge revealed a marginal improvement in right ventricular function, with residual severe tricuspid regurgitation. As the overall clinical condition of the patient has remained stable, repeat myocardial biopsy was not performed.

The process is considered chronic based on the first detection of right ventricular abnormalities 4 years prior. In addition, the chronic inflammatory infiltrate and interstitial fibrosis supports this conclusion.

Thus, we describe a case of an immunosuppressed young lady who was suffering from a chronic low-grade lymphocytic myocarditis of the RV resulting in dilatation of the chamber, severe functional tricuspid regurgitation, and arrhythmic complications including atrial fibrillation and VT. All cardiac imaging modalities demonstrated normal left ventricular size and function, suggesting this process demonstrated a preponderance to the RV.

Discussion

Myocarditis comprises a large variety of clinical syndromes mediated by viruses, toxins, and autoimmune aetiologies. Isolated right ventricular myocarditis is a rare syndrome. In young people particularly, the clinical presentation may mimic that of AC, previously known as arrhythmogenic right ventricular dysplasia. Sarcoidosis isolated to the RV has been described in case reports,[3,4] but examples of lymphocytic myocarditis causing the same are exceedingly rare with only two published cases identified in the literature. Crudele *et al.*[1] describe a case of acute RV myocarditis, which presented with a flu-like illness, followed by sudden death at 3 weeks, the diagnosis being confirmed on autopsy. Hawatmeh *et al.*[2] describe a similar case with a dramatic presentation that included cardiogenic shock and third-degree atrioventricular block. Lymphocytic myocarditis is most commonly caused by a viral infection, but can also be an autoimmune process.[5,6] Of the viruses, parvovirus B19, adenovirus, and enterovirus have been identified as the three most commonly involved

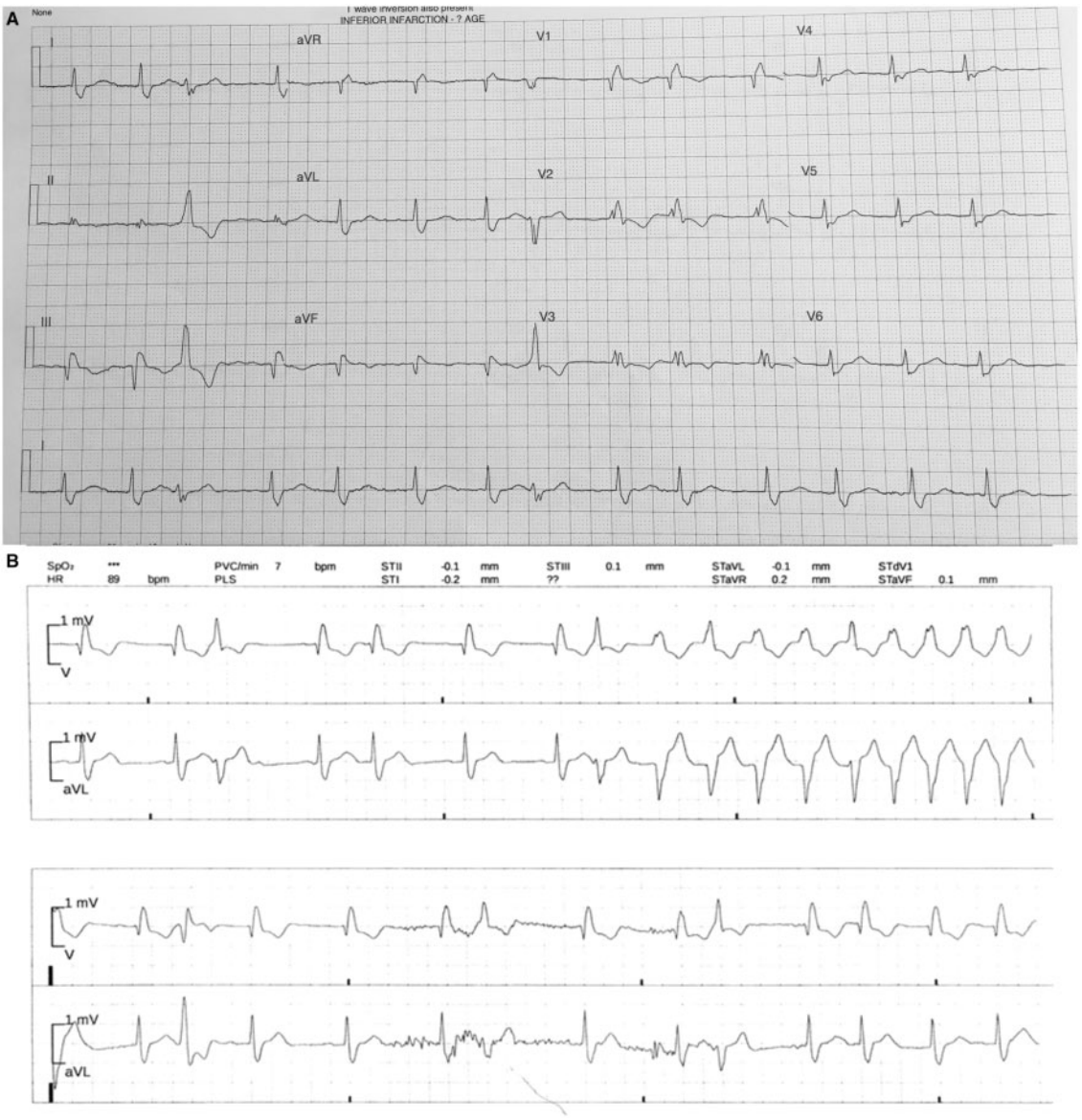

Figure 2 (*A*) Electrocardiogram demonstrating atrial fibrillation and a right bundle branch block. (*B*) Telemetry demonstrating onset of ventricular tachycardia.

pathogens.[6] A disease course of a more chronic and insidious nature as experienced by our patient has not previously been described. The fact that this patient was receiving concurrent immunosuppression may be an explanation for this. Assuming an infectious cause, immunosuppression may have led to a failure of viral clearance and a persistent low-grade inflammatory state eventually resulting in clinically apparent disease. Alternatively, if the myocarditis in this case was due to an autoimmune aetiology, the concurrent immunosuppression may have slowed the disease progression, preventing a sudden fulminant presentation as was seen in the two other reported cases in the literature.

Isolated right ventricular myocarditis presents a different clinical challenge to that of left ventricular myocarditis. First, the relatively thin wall of the RV may make diagnosis using non-invasive imaging modalities more difficult, as was acknowledged during interpretation of this patient's cardiac PET and MRI scans. It is considered, however, that when the RV is clearly affected, transvenous biopsy may be of higher yield, although this has not been formally studied.

Standard guidelines relating to the diagnosis of myocarditis do not consider isolated RV syndromes[7] ; however, it is an important differential diagnosis in the case of a patient with a dilated or impaired RV, particularly where no other cause can be identified.

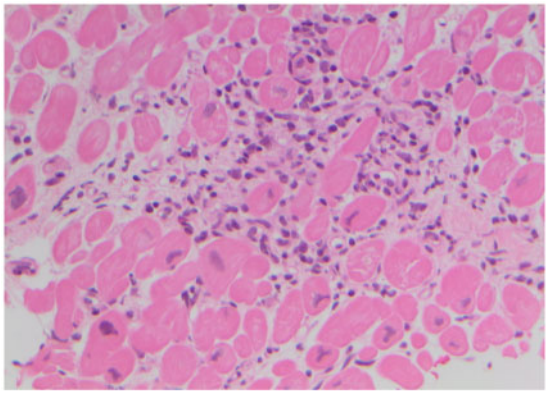

Figure 3 Histopathological specimen of biopsied myocardium demonstrating myopathic features (haematoxylin and eosin stain)—namely loss of architecture with interstitial fibrosis, anisonucleosis (morphological manifestation of nuclear injury characterized by variation in the size of the cell nuclei), and myocytolysis (prominent cytoplasmic vacuoles reflecting cell damage/necrosis). There is a prominent lymphocytic infiltrate (centre) with accompanying myocyte loss and fibrosis.

Lead author biography

Dr Praveen Indraratna completed cardiology training at the Prince of Wales and St. George Hospitals in Sydney, Australia in 2018. He is currently undertaking a PhD in Digital Health at the Prince of Wales Hospital and University of New South Wales. He is the recipient of a postgraduate research scholarship, co-funded by the National Health and Medical Research Council (NHMRC) and the Heart Foundation. He was recently awarded the inaugural Reg Inglis Award presented by the Prince of Wales Hospital Foundation (2018), the Bryan Yeo Best Teacher Award (2019), and won the ESC Asia Young Cardiologists Clinical Case Competition in 2019.

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 author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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