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CASE REPORT
Cardiac imaging

Endomyocardial fibrosis of the right ventricle in a patient with schistosomiasis: a case report

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Background Endomyocardial fibrosis (EMF) is a rare and underdiagnosed cause of restrictive cardiomyopathy. Its aetiology is not yet defined and could be caused by the influence of different clinical factors that seem to combine with genetic aspects of individuals susceptible to an inflammatory process that leads to formation of fibrosis.

Case summary We describe a case of a 50-year-old man from the northeastern region of Brazil, where there is high prevalence of schistosomiasis. He presented to our centre with symptoms of right heart failure. The echocardiogram showed normal left ventricular ejection fraction. Right ventricular had normal systolic function but in the apical region was filled with a homogeneous and hypoechoic image causing obliteration and restriction of the apex. The late gadolinium enhancement with cardiac magnetic resonance showed diffuse and heterogeneous subendocardial fibrosis in the right ventricle apex consistent with EMF, but declined endocardiectomy.

Discussion This report presents an interesting case of EMF and schistosomiasis simultaneously. The hypothesis of parasitosis as a probable cause of EMF was raised by helminth-induced hypereosinophilia. Complementary imaging tests such as magnetic resonance imaging and echocardiography, in addition to clinical and epidemiological suspicion, are essential for its diagnosis. Early surgical resolution becomes crucial for long-term survival.

Keywords Cardiomyopathy • Endomyocardial fibrosis • Heart failure • Hepatopathy • Schistosomiasis • Case report

ESC curriculum 2.1 Imaging modalities • 2.3 Cardiac magnetic resonance • 6.7 Right heart dysfunction • 6.5 Cardiomyopathy • 6.3 Heart failure with preserved ejection fraction

Learning points

- Endomyocardial fibrosis (EMF) is a neglected and underdiagnosed cause of restrictive cardiomyopathy.
- In some tropical countries, EMF and schistosomiasis are endemic diseases with systemic clinical presentation.
- Transthoracic two-dimensional echocardiogram (TTE) is crucial for EMF diagnosis. One or both ventricles can be affected. On TTE, the apical region of one or both ventricles can be filled with a homogeneous and hypoechoic image causing obliteration and restriction.
- The overall prognosis remains poor and treatment options remain limited.

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Introduction

Endomyocardial fibrosis (EMF) is a neglected and underdiagnosed cause of restrictive cardiomyopathy.[1] Its aetiology is not yet defined, but many factors such as protein malnutrition, parasitosis, environmental aspects, and infectious diseases may play a role in its pathophysiology combined with genetic aspects in susceptible individuals. These elements combined can lead to an inflammatory process, damage to the endomyocardial layers, and the formation of fibrosis.[2] This report presents an interesting case of association of EMF and schistosomiasis, either as cause in the development of the disease or an incidental finding.

Timeline

Three years before referral	Symptoms of right heart failure, atrial fibrillation (AF), arterial hypertension, liver disease, hypothyroidism.
At admission	Signs and symptoms of right heart failure (lower limb oedema, significant ascites, jugular vein distention, pansystolic murmur suggestive of tricuspid regurgitation).
Initial transthoracic two-dimensional echocardiogram (TTE)	Right ventricle (RV) with reduced volumes, normal systolic function, and apical region filled with a homogeneous and hypoechoic image causing obliteration and restriction.
Three months after initial evaluation	Cardiac magnetic resonance confirmed the diagnosis of RV EMF. Patient decided against undergoing endocardiectomy.
Six months after initial evaluation	The gastroenterology team confirms that the liver disease is secondary to schistosomiasis.
Eight months after initial evaluation in heart team meeting	The patient was diagnosed schistosomiasis-associated EMF and treated with praziquantel, but declined endocardiectomy. He started medical treatment.
Current clinical status (4 years after initial evaluation)	Patient was asymptomatic after diuretics dosage optimization. Surgery is currently contraindicated due to surgical technical difficulties.

Case presentation

A 50-year-old man was referred to our institution with several years of right heart failure symptoms, AF, and liver disease of unknown aetiology. He was a fisherman and had contact with contaminated water in the past. He had lower limb oedema, significant ascites, jugular vein distention, and 3/6 pansystolic murmur heard loudest at the left lower sternal edge suggestive of tricuspid regurgitation. The patient came from the northeastern region of Brazil, where there is high prevalence of schistosomiasis. Considering the local epidemiology and the presence of hepatosplenomegaly, schistosomiasis was suspected. Due to the symptoms of right heart failure mentioned, cardiac investigations were performed as a primary cause of the liver disease.

The electrocardiogram (*Figure 1*) showed AF rhythm and there was cardiomegaly noted on chest radiograph, with gross enlargement of the right atrial shadow. Blood tests showed thrombocytopenia of 75 000/mm^3 [normal values (NV): 150 000–400 000], normal renal function and liver enzymes, and brain natriuretic peptide of 198 pg/mL (NV ≤ 35). The TTE showed a left ventricle of normal dimensions with a preserved left ventricular ejection fraction (LVEF) (Supplementary material online, *Video S1*). However, the RV cavity was small secondary to a large homogeneous hypoechoic mass with evidence of severe tricuspid insufficiency, secondary to dilatation of the annulus, and severe tethering of the valve leaflets. Besides, the TTE exhibited an intracavitary thrombus adhered to the roof of the right atrium (RA; *Figure 2*; Supplementary material online, *Video S2*). The cardiac magnetic resonance (CMR) imaging showed severe RA dilation. This examination confirmed that RV had small cavity with reduced indexed end-diastolic and end-systolic volumes (38 and 13 mL/m^2, respectively), normal systolic function (EF 65%), and moderate pericardial effusion (*Figure 3*; Supplementary material online, *Video 3*). The late gadolinium enhancement sequence showed diffuse and heterogeneous subendocardial fibrosis in the RV apex (*Figure 4*). The patient was diagnosed with EMF and schistosomiasis by positive IgG ELISA and treated with praziquantel, but declined endocardiectomy. His heart failure symptoms improved on diuretics (furosemide 120 mg/day, spironolactone 50 mg/day, and hydrochlorothiazide 50 mg/day). In addition, the patient was commenced on warfarin with adequate international normalized ratio control for the presence of AF and thrombus.

Discussion

Schistosomiasis is a parasitic disease caused by *Schistosoma mansoni* worms, which has as intermediate host freshwater snails and which could evolve clinically from asymptomatic to severe disease.[3] The parasites lodge in mesenteric vessels, and their eggs produce granulomas and scar nodules in human organs, deposited in the liver and in other parts of the body, which may generate immune responses capable of initiating a trigger for other inflammatory diseases mediated by eosinophils.[3] Endomyocardial fibrosis is characterized by a phase of acute inflammation (pancarditis) with necrosis, a transient phase is represented by endocardium thrombus, and the final chronic phase is characterized by EMF. It is believed this initial acute phase to be triggered by cytokines inflammatory reaction which activates eosinophils; however, this hypereosinophilia is reported inconsistently in EMF.[4,5]

In EMF, the fibrosis extends from the ventricular apex to the subvalvular apparatus with consequent valve dysfunction of the affected ventricle. In the chronic phase, biventricular involvement is the most frequent form of presentation (up to 55%), followed by isolated RV involvement.[5,6] Unexpectedly, BNP was only mildly elevated, perhaps reflecting an aggressive use of diuretics, lack of left ventricular involvement, and a clinically compensated outpatient.[6,7]

Both entities, schistosomiasis and EMF can be the cause of liver disease. The last one can also be secondary to right heart failure and hepatic venous congestion. However, it is worth mentioning that chronic schistosomiasis can lead to severe liver cirrhosis, developing portal hypertension.[5,8,9] Atrial fibrillation occurs in >30% of cases of patients with EMF. Conduction abnormalities, such as first-degree atrioventricular and/or right bundle branch blocks, are common in this disease.[5]

The TTE is routinely used to aid diagnosis of EMF, allowing the evaluation of cardiac morphology and non-invasive haemodynamics. An echocardiographic screening of 1063 subjects conducted in Mozambique showed that EMF was highly prevalent and frequently asymptomatic (78%); obliteration of the right or left ventricular apex,

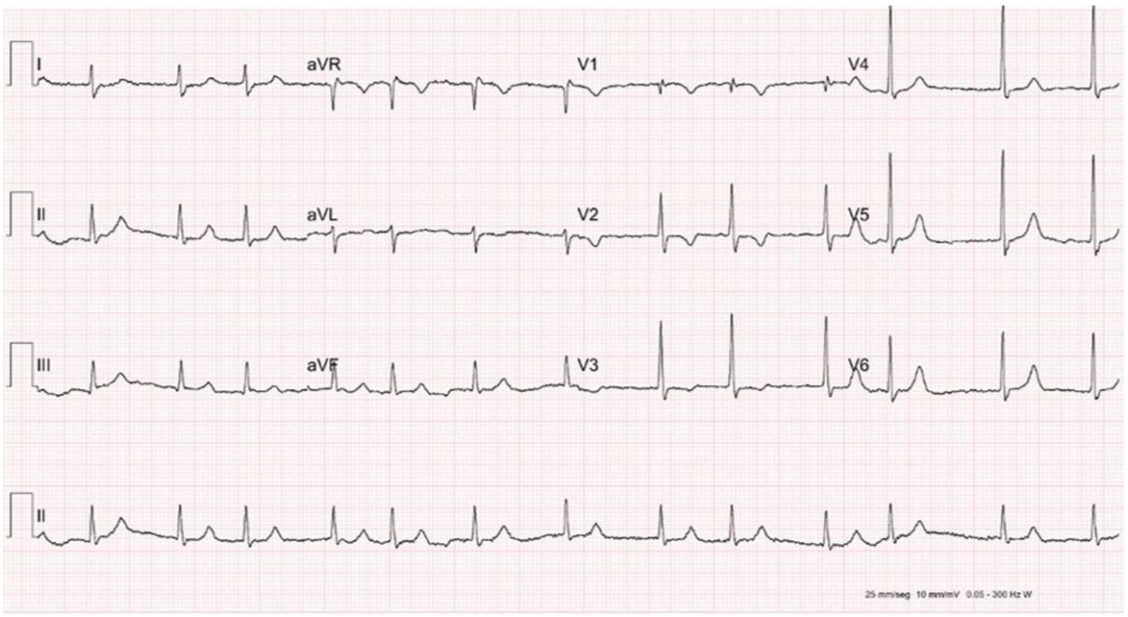

Figure 1 The electrocardiogram showed atrial fibrillation and ventricular repolarization abnormalities in v1–v3.

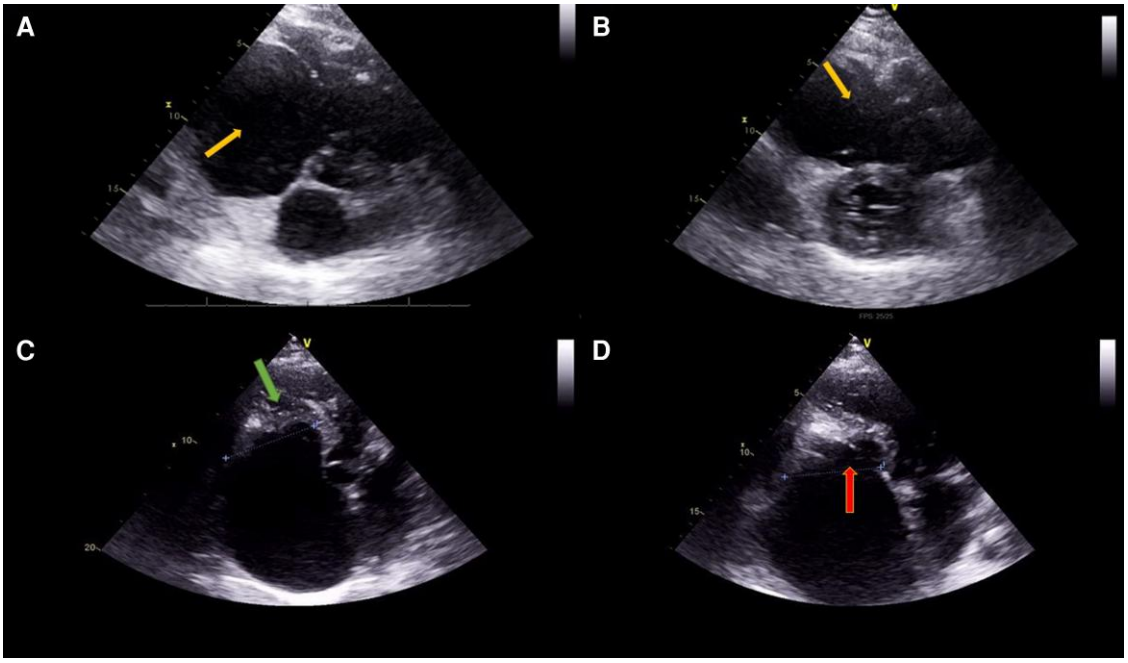

Figure 2 Transthoracic two-dimensional echocardiogram at short-axis view (*A* and *B*) showed severe dilatation of the right chambers (arrows). Apical four-chamber view (*C*) showed the right ventricle apical region with a homogeneous and hypoechoic image causing obliteration (arrow). Apical four-chamber view (*D*) showed dilatation of the tricuspid annulus, and severe tethering of the valve leaflets (arrow).

thrombi in the absence of ventricular dysfunction, and right ventricular apical notch should increase the suspect of this condition.[10]

Cardiovascular magnetic resonance imaging is the gold-standard method for diagnosis and prognosis of patients with EMF, allowing the evaluation of the extension and quantification of late gadolinium enhancement.[11] The main findings in the EMF are obliteration in the LV or RV apical region associated with enlargement of respective atrium, LVEF or RVEF normal or mildly reduced, subendocardial delayed enhancement,

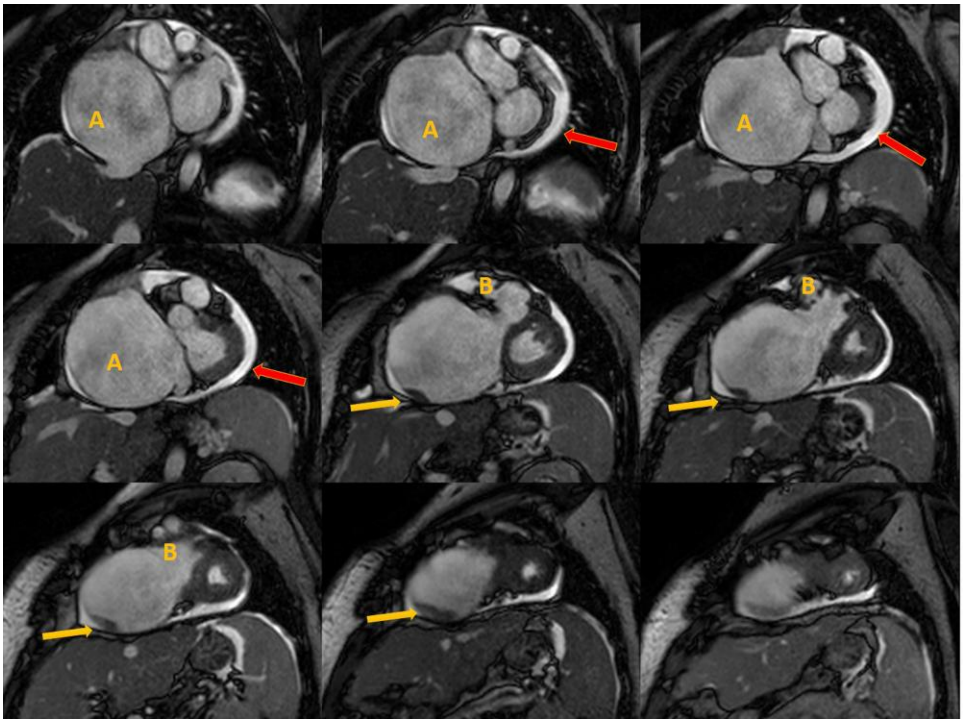

Figure 3 Cardiac magnetic resonance imaging at apical view showed a significant increase in the right atrium (*A*) with associated thrombus (rightward arrow). Thickening and obliteration of the right ventricle apex (*B*), and moderate pericardial effusion without signs of restriction (leftward arrow).

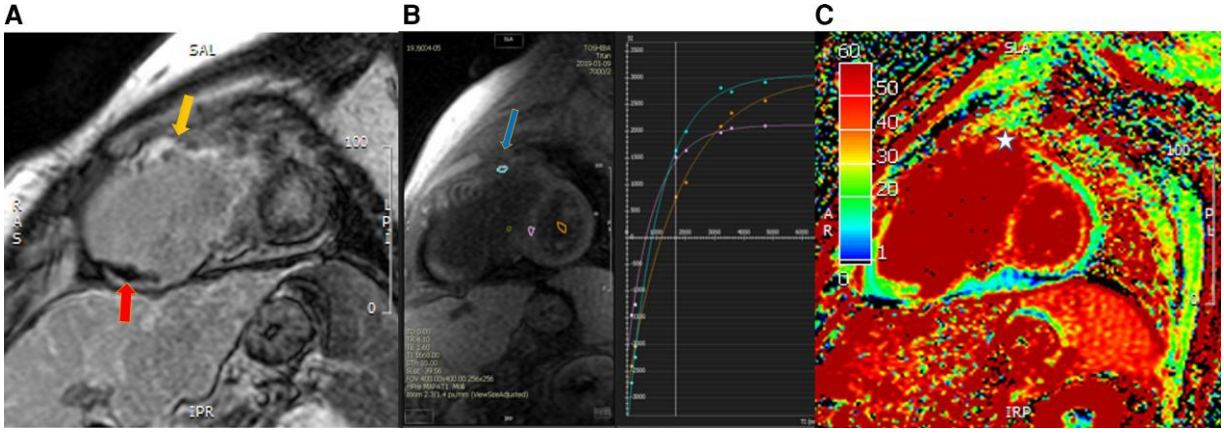

Figure 4 Cardiac magnetic resonance imaging with tissue characterization. (*A*) The late gadolinium enhancement sequence showed diffuse and heterogeneous subendocardial fibrosis in the right ventricle apex (downward arrow) and thrombus in the right atrium (upward arrow). (*B*) The native T_1 value in the right ventricle was increased (1287 ms; downward arrow). (*C*) The extracellular volume was 38% (star).

not restricted to any coronary territory, affecting mainly apex of involved ventricle, and fibrous tissue deposition seen as double V sign at ventricular apex (three-layered appearance of normal myocardium, thickened enhanced endomyocardium, and overlying thrombus).[11,12]

The differential diagnosis of LV EMF includes apical hypertrophic cardiomyopathy, non-compaction cardiomyopathy, and dilated cardiomyopathy with apical thrombus. In addition, in the presence of RV apical obliteration, this could be differentiated from constrictive pericarditis or Ebstein disease.[1] The red flags for EMF diagnosis are shown in *Table 1*.

Despite the fact that the description of EMF was first made 74 years ago, its aetiology still remains unknown. If the determining factor is an infection, as has already been proposed, eradication and prevention of new infections could improve survival and decrease the extent of fibrosis.[9] There is a high rate of in-hospital mortality among most patients

Table 1 Red flags for endomyocardial fibrosis diagnosis

Clinical findings	Signs and symptoms of restrictive heart failure
Echocardiographic findings	Increased of atrium volume and normal ventricle volume
	Atrioventricular valve dysfunction by subvalvular fibrosis
	Apical obliteration of one or both ventricles
Cardiac magnetic resonance findings	Late gadolinium enhancement (LGE) in the endocardium, mainly in the apex of one or both ventricles, not confined to coronary territory
	LGE pattern had a 'V sign' at the ventricular apex, characterized by a three-layer appearance of myocardium, thickened fibrotic endomyocardium, and overlying thrombus.

with EMF.[13] The conditions related to the worst prognosis are NYHA functional Class IV, AF, ascites, predicted VO_2 peak <53%, and degree of fibrosis.[5,14] Clinically treated patients have a mean survival of 97.3 and 87.54% at 5 and 10 years, respectively, while operated patients have a 67% survival in a period of 43 months, as observed in a registry carried out in an institute in India.[15,16] The procedure consists of endocardiectomy as well as subvalvular repair.[17]

Treatment is usually symptomatic (diuretics); prognosis is poor even when cardiac surgery is attempted and stresses that in many places where the disease is highly prevalent it might be difficult to access cardiac surgery. Due to Loeffler syndrome–like pathophysiology, corticosteroids and immunosuppressive drugs would be useful in the early stages of the disease, but with no proved clinical benefit justifying their routine use.[4] It is important to know that surgery should be indicated as soon as the patients present symptoms, because most patients in the terminal stage are no longer eligible for the procedure due to its high risk. During the disease course, in this particular case, fibrosis can no longer be removed by surgical operation due to difficulties caused by calcium deposition. The patient had a good response to diuretic therapy. He also received treatment for schitosomiasis by the gastroenterology team with praziquantel.[18] After initial diagnosis, the patient declined surgery and although he is currently asymptomatic, surgery is contraindicated due to surgical technical difficulties as indicated above. Heart transplantation would be a viable option.[19]

Conclusion

The EMF is a neglected and underdiagnosed cause of restrictive cardiomyopathy and patients who lived in areas considered endemic should always be considered. The TTE was a good screening method in this case, but CMR imaging was the most important examination for diagnosis, considered the gold-standard method. The main findings are obliteration in the LV or RV apical region and subendocardial delayed enhancement, not restricted to any coronary territory. The symptomatic treatment including anticoagulation is the first option and our patient had an adequate response. The surgical treatment is only indicated in patients with refractory symptoms despite optimal clinical management.

Lead author biography

M.D. Cristhian Espinoza is a cardiology resident. He is currently working as a Cardiac Transplant Fellow at the Institute of Heart in Sao Paulo University, Hospital Das Clinicas.

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: The data underlying this article are available in the article and in its online supplementary material.

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