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CASE REPORT
Heart failure

Idiopathic endomyocardial fibrosis in a Western European: a case report

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Background Endomyocardial fibrosis (EMF) is a rare cause of restrictive cardiomyopathy, mainly found in tropical/subtropical country. Endomyocardial fibrosis causes severe congestive symptoms and may lead to end-stage heart failure.

Case summary A French Caucasian 44-year-old man without noticeable medical history and who had never travelled outside of France was hospitalized for a first episode of acute heart failure revealing an atypical appearance of the left ventricle. Cardiac magnetic resonance (CMR) identified EMF, but investigations did not identify any aetiology (no eosinophilia). Despite optimal management of chronic heart failure, functional class declined rapidly resulting in several hospitalizations for heart failure. The patient finally underwent an elective heart transplantation with good results at 6-month follow-up.

Discussion Endomyocardial fibrosis exact physiopathology remains unclear, although association with eosinophilia has been reported. Diagnosis is challenging and is based on multi-modal imagery with a central role of CMR. There is no consensus on optimal management, medical therapy having poor outcomes and rate of peri-operative complications being high. Heart transplantation should be considered for eligible patients.

Keywords Heart failure • Restrictive cardiomyopathy • Endomyocardial fibrosis • Cardiac magnetic resonance • Heart transplantation • Case report

Learning points

- Cardiac magnetic resonance is the non-invasive key exam for the diagnosis of endomyocardial fibrosis (EMF).
- There is no consensus regarding the optimal management of EMF, but in case of permanent severe systolic dysfunction heart transplantation might be the only good therapeutic option.

Introduction

Restrictive cardiomyopathy (RCM) accounts for ∼5% of all cardiomyopathies.[1] Endomyocardial fibrosis (EMF) is a rare cause of RCM, mainly found in tropical and subtropical countries, and with bimodal peaks around ages 10 and 30.[2] Endomyocardial fibrosis is characterized by endocardial fibrosis concerning one or both apices of the ventricles and extending to inflow tract and atrioventricular valves. Fibrosis, chronic inflammatory infiltrates, and neovascularization

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affect all layers of ventricular and atrial walls but are more prominent at sub-endocardium and inner myocardium.[3]

Endomyocardial fibrosis clinical presentation consists of congestive heart failure, thromboembolism, and atrial/ventricular arrhythmias. Cases of EMF in Western Europe are exceptional, and diagnosis is therefore challenging, based on multiple imaging parameters. In addition, there is no consensus about EMF management and medical therapy, surgical endocardectomy or heart transplantation are individually discussed.

Timeline

Weeks before admission	Complains about exacerbation of chronic dyspnoea and swollen ankles
Day of admission (Day 0)	Congestive heart failure, normal electrocardiogram, elevated NT-pro-BNP, atypical appearance of the left ventricle on transthoracic echocardiography
Coronary angiography (Day 4)	No coronary artery disease, left ventricle apical filling on ventriculography. Dip-and-plateau pattern at haemodynamic examination
Cardiac magnetic resonance (Day 13)	Hypo-intense T1/T2 signal circumscribed to the left ventricle apex, without immediate gadolinium enhancement but with late sub-endocardial enhancement, that are typical criteria of endomyocardial fibrosis (EMF)
Hospital discharge (Day 15)	First-line medical treatment, with loop diuretics, beta-blocker, mineralocorticoid receptor antagonist, neprilysin inhibitor, and angiotensin receptor blocker associated with a cardiovascular rehabilitation programme
Six months after hospital discharge	Two hospitalizations for acute heart failure. Pre-transplantation assessment started
Nine months after hospital discharge	Elective orthotopic heart transplantation. EMF confirmed by the anatomopathological examination
Six months heart transplantation	The patient is New York Heart Association Class I. His children have no signs of EMF

Case presentation

A French 44-year-old man without noticeable medical history was admitted for a first episode of acute global heart failure. He was of Caucasian phenotype and had never travelled outside of the north-east region of France. He complained about lower limbs oedema and new-onset New York Heart Association (NYHA) Class III dyspnoea. His vital signs were normal at admission: blood pressure 110/70 mmHg, heart rate 80 b.p.m., respiratory rate 15/min, oxygen saturation of 96% on room air, and temperature at 37°C. Heart sounds were regular, lower limbs oedema up to his knees were noticed without jugular venous distension nor hepatojugular reflux. Bilateral inspiratory crackles were heard on auscultation.

Electrocardiogram was normal, and first-line blood test showed an elevation of NT-pro-BNP [1674 pg/mL (reference range < 300 pg/mL)], with a mild inflammatory syndrome [leucocytes 14.3×10^9/L (reference range 4–10×10^9/L) and C-reactive protein 15.8 mg/L (reference range < 5 mg/L)]. Renal function was normal [93 µmol/L (reference range 59–104 µmol/L), estimated glomerular filtration rate 86 mL/min/1.73 m^2] and we did not notice eosinophilia [eosinophils 0.2×10^9/L (reference range 0.1–0.4×10^9/L)]. Transthoracic echocardiography showed a dilated and hypokinetic left ventricle (left ventricle ejection fraction at 40%). An atypical appearance filled the left ventricular apex (*Figure 1* and Supplementary material online, *Video S1*). No significant valvulopathy was identified, but right and left side pressures were elevated, and right cavities were dilated and hypokinetic. Finally, pericardium had no abnormality. The patient was therefore hospitalized in cardiology ward, intravenous loop diuretics were administered, and early clinical evolution was favourable.

Coronary angiogram was normal, but a left ventricle apical filling was observed during ventriculography (*Figure 2A* and Supplementary material online, *Video S2*). Haemodynamic examination revealed a dip-and-plateau pattern on the left ventricular pressure curve (*Figure 2B*). Cardiac magnetic resonance (CMR) was performed and showed a hypo-intense T1/T2 signal circumscribed to left ventricle apex assessed by balanced steady-state free precession sequence without immediate gadolinium enhancement but with sub-endocardial late enhancement, which are all typical criteria of EMF (*Figure 3* and Supplementary material online, *Videos S3* and *S4*). Second-line blood tests were negative regarding anti-nuclear antibodies. Hepatitis B, hepatitis C, and human immunodeficiency virus serologies were negative, as well as serologies such as schistosomiasis.

At first, medical treatment of chronic heart failure was proposed [namely Bisoprolol 5 mg two times a day (BID), Ivabradine 5 mg BID, Eplerenone 50 mg once a day (OD), Sacubitril/Valsartan 24 mg/26 mg BID, Furosemide 125 mg OD] associated with oral anticoagulation (Warfarin 5 mg OD) because of the increased thromboembolic risk. The patient was discharged after a few days and followed cardiovascular rehabilitation programme.

In the following months, two episodes of congestive heart failure occurred, leading to two unplanned hospitalizations with intravenous administration of loop diuretics and transient inotropic support. In light of unfavourable evolution, low peak VO2 and post-capillary pulmonary hypertension with low pulmonary vascular resistances, a pre-transplantation assessment was started.

The patient had an elective orthotopic heart transplantation 9 months after initial diagnosis. Ventilator-associated pneumonia and acute renal failure needing transient haemodialysis occurred during the post-operative phase. The patient was finally discharged from hospital 3 months after surgery. Macroscopic view and anatomopathological examinations of the explanted heart confirmed endocardial fibrosis, circumscribed to the left ventricle, without valvular lesion (*Figure 4*).

Six months after heart transplantation the patient was NYHA Class I. His medications included Bisoprolol 5 mg OD, Furosemide 20 mg OD, plus antirejection drugs. Echocardiographic follow-up did

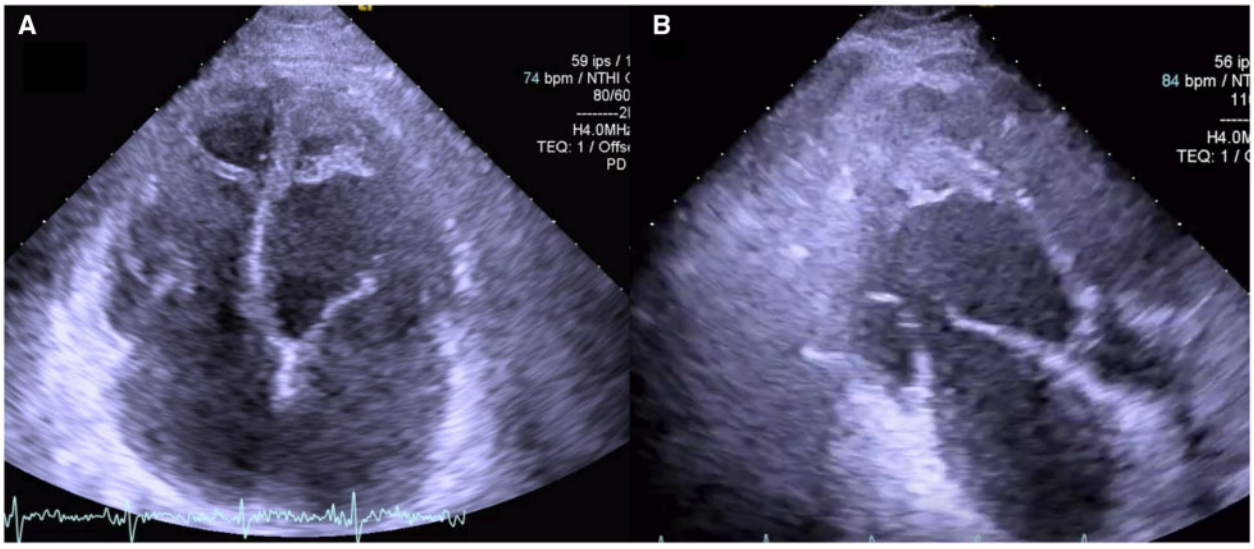

Figure 1 Transthoracic echocardiography showing a heterogeneous mass at the left ventricle apex. (*A*) Apical four-chamber view; (*B*) apical two-chamber view.

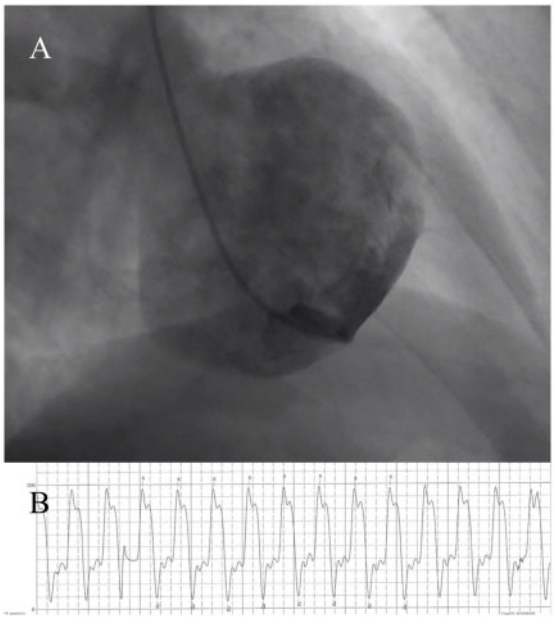

Figure 2 Haemodynamic examination. (*A*) Ventriculography showing a left ventricle apex filled; (*B*) left ventricle pressure measure showing a dip-and-plateau pattern.

not show any sign of fibrosis recurrence, nor transplant rejection. His four children (two boys and two girls) had normal cardiovascular examination, electrocardiogram, and transthoracic echocardiography.

Discussion

Restrictive cardiomyopathy is the less common type of cardiomyopathy, with very different causes.[4] EMF allegedly affects millions of people in tropical countries,[5] mostly children and young adults. However, EMF is an exceptional cause of RCM in occidental countries. Numerous potential causal factors or triggers have been suggested, which may act individually or in combination. Poverty and geographic specificities have emerged as the most consistent risk factors and are related to most proposed aetiologies.[6]

The most frequent association with EMF is eosinophilia, frequently linked to parasitosis. Based on the findings of a Nigerian population with EMF associated with parasitic infections (helminths, schistosomiasis, microfilaria loa-loa, and filariasis), Andy *et al.*[7] stated that EMF endocardial lesions were similar to those found in Hypereosinophilic syndrome. Cross-talk between eosinophils, mast cells, and cardiac fibroblasts could therefore be a key pathogenic factor in defective cardiac remodelling.[8] EMF cases cluster within both families and ethnic groups suggesting either a role of genetic factor in host susceptibility or environmental trigger (shared living locations). The role of human leucocyte antigen (HLA) system was explored in a study that took place in Uganda and Mozambique.[9] EMF patients were more likely than controls to have HLA-B*58 allele in Mozambique and HLA-A*02:02 allele in Uganda. Finally, dietary deficiencies (magnesium)[10] and excesses (vitamin D),[11] ingested toxins (cerium, cyanogenic glycosides, serotonin),[12,13] and herbal preparations[12] have also been proposed as causative.

The diagnosis of EMF can be suspected on transthoracic echocardiography, with RCM abnormalities and endocardial thickening localized to ventricles and/or atrioventricular valves.[14] Concomitant intra-cardiac thrombi are also described. Cardiac magnetic resonance provides detailed information on ventricular morphology and

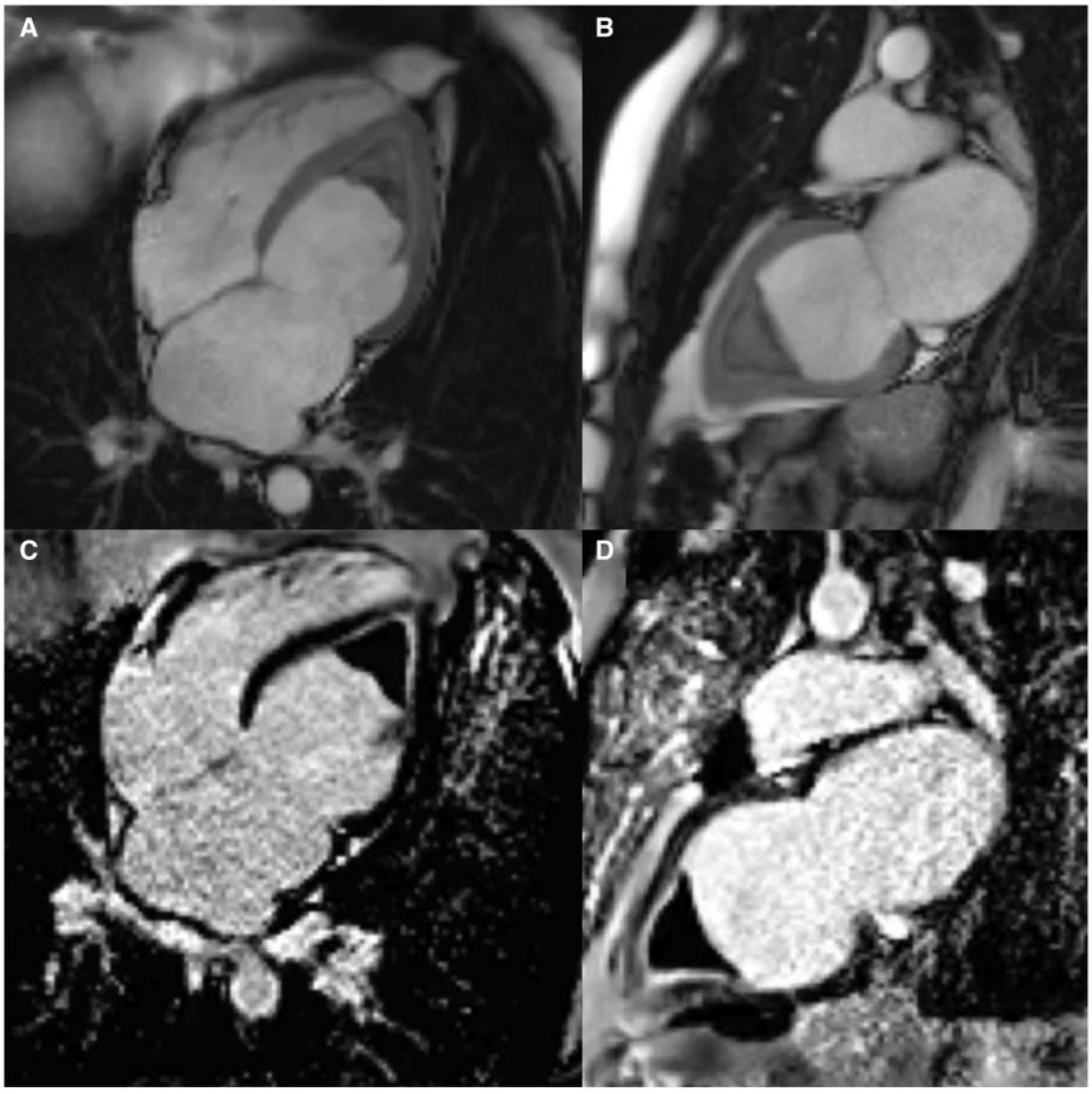

Figure 3 Cardiac magnetic resonance showing a hypo-intense mass assessed by balanced steady-state free precession sequence (*A* and *B*) and late gadolinium enhancement (*C* and *D*) circumscribed to the left ventricle apex without immediate gadolinium enhancement. (*A*) Four-chamber view; (*B*) two-chamber view; (*C*) four-chamber view; (*D*) two-chamber view.

function, including an excellent visualization of the ventricular apex. In addition, CMR allows the identification of myocardial inflammation and fibrosis.[15] Thus, CMR is a key non-invasive exam for EMF diagnosis. Finally, endomyocardial biopsy may provide definitive diagnosis if positive, but exposes to an iatrogenic risk of thromboembolism and pericardial effusion.

There is currently no consensus regarding EMF management. No evidence of efficacy of medical treatment (diuretic, beta-blocker, or angiotensin-converting enzyme inhibitor) is available. The spontaneous embolic risk has led some authors to place surgical endocardectomy as first-line therapy.[16] However, given the important peri-operative mortality (20%),[17] this surgery has to be performed by experienced surgical teams. In addition, post-endocardectomy EMF relapse has been described.[18] In case of permanent severe systolic dysfunction heart transplantation might be the only good therapeutic option, with possible good outcomes. EMF recurrence after heart transplantation has not been described thus far.[19]

Conclusion

Idiopathic EMF is a rare cause of RCM, mainly found in tropical/subtropical countries (association with eosinophilia). Diagnosis of EMF may be challenging and its management remains controversial. We report the case of an idiopathic EMF in Western Europe, with permanent severe systolic dysfunction leading to heart transplantation.

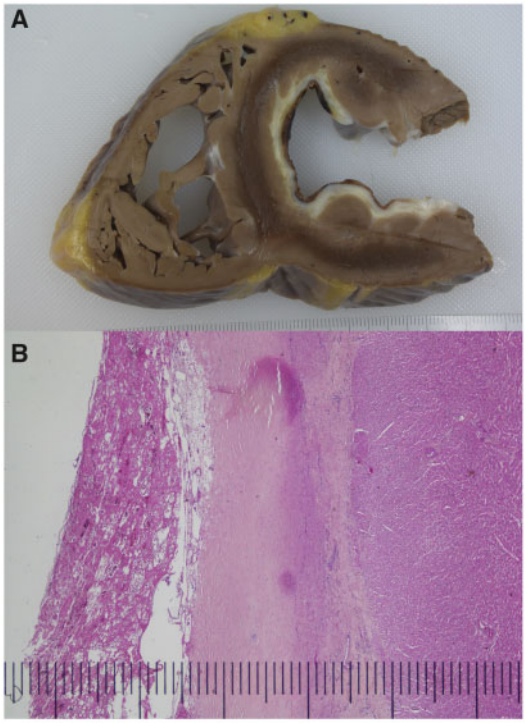

Figure 4 Anatomopathological examination of the explanted heart. (*A*) Macroscopic view of the explanted heart showing a thickened and fibrous left ventricle endocardium, principally on its anterior part. There are fibrin clots on its surface; (*B*) microscopical examination of the explanted heart, showing a fibrotic process localized in the left ventricle endocardium.

Lead author biography

Guillaume Théry, MD, is 27. He is following a residency in Cardiology, and also in Critical Care Medicine, at the Reims University Hospital, France. Moreover, he is completing a master's degree concerning Heart and Circulation Biology, Physiopathology, and Pharmacology at Paris-Est Créteil University, France. His academic interests include cardiogenic shock, extracorporeal life support, and heart transplantation.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

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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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