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CASE REPORT
Heart failure

Case report on heart transplantation in endomyocardial fibrosis: 'do not let your guard down'—suspicion of disease recurrence after heart transplantation

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Background Endomyocardial fibrosis (EMF) is a challenging disease that leads to severe heart failure (HF) due to progressive fibrosis. Diet, parasitic infections, autoimmune disorders, and genetic predisposition have been advocated in EMF pathogenesis, and treatment options for EMF are limited with scarce evidence supporting heart transplantation (HTx).

Case summary A 38-year-old man was diagnosed with EMF with biventricular involvement. The diagnostic work-up ruled out eosinophilia, infections, and autoimmune conditions. The patient rapidly deteriorated, leading to cardiogenic shock with multiorgan failure, and an emergency HTx was performed. Three months later, the graft developed biventricular hypertrophy with atrial fibrosis and the endomyocardial biopsy (EMB) showed extensive inflammation and myocardial damage, compatible with Grade 2R (G3a) cellular rejection. After steroid pulses, the follow-up EMB reveals subendocardial fibrosis and microcalcifications, suggesting the possibility of an EMF recurrence. Nevertheless, the patient had a good clinical outcome, remaining asymptomatic with good graft function 2 years after the transplant.

Discussion This is the first reported case of suspected EMF recurrence following HTx. Given the unknown pathogenesis of EMF, close monitoring is crucial, though HTx appears to be a viable and successful treatment option for these patients.

Keywords Case report • Endomyocardial fibrosis • Heart transplantation • Heart failure • Endomyocardial biopsy

ESC curriculum 7.3 Critically ill cardiac patient • 4.9 Multivalvular disease • 6.1 Symptoms and signs of heart failure • 6.3 Heart failure with preserved ejection fraction • 6.7 Right heart dysfunction

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Learning points

- Recurrence of endomyocardial fibrosis (EMF) post-heart transplantation (HTx): this case highlights the potential for disease recurrence following HTx, emphasizing the importance of vigilant post-transplant monitoring and the possible therapeutic role of immunosuppressive therapy in the early stages of disease.
- Heart transplantation as a viable treatment for EMF: despite limited evidence, this case supports the idea that HTx can be a successful life-saving option for patients with EMF.

Introduction

Endomyocardial fibrosis (EMF) is a life-threatening condition endemic to regions of Africa, Asia, and South America, with an aetiology that remains poorly understood. Contributing factors such as dietary deficiencies, parasitic infections, autoimmune processes, and genetic predisposition have been proposed, but no unified pathophysiological theory has been established. Clinically, EMF leads to restrictive cardiomyopathy with biventricular involvement, extensive myocardial fibrosis, apical obliteration, intracavitary thrombi, and severe valvular dysfunction.[1,2] Treatment options are limited to standard heart failure (HF) therapies and anticoagulation, and surgical resection is associated with a perioperative mortality rate exceeding 20%. Heart transplantation (HTx) has been considered in selected cases, though evidence is limited to a few successful case reports.[3–5]

Summary figure

Endomyocardial fibrosis (EMF) is a life-threatening disease that causes progressive fibrosis of the myocardium and valves.

Diet, parasitic infections, autoimmune disorders, and genetic predisposition have been advocated in EMF pathogenesis.

Treatment options are limited to standard heart failure management and anticoagulation.

The evidence supporting heart transplantation (HTx) in EMF is scarce.

BACKGROUND

A 38-year-old man from Senegal presented with heart failure.

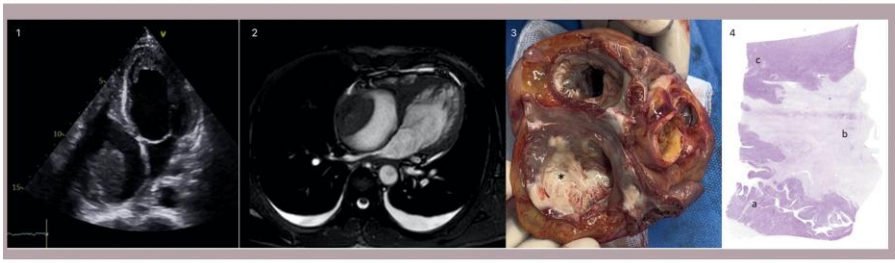
1. Initial TTE: Non-dilated restrictive left ventricle and right ventricle obliteration. Severe atria dilatation with a large thrombus.

2. CMR: Confirmed endomyocardial fibrosis with biventricular involvement.

Diagnostic work-up ruled out eosinophilia, infections, and autoimmune conditions.

The patient rapidly deteriorated, leading to cardiogenic shock with multiorgan failure and an emergency heart transplant was performed.

CASE PRESENTATION

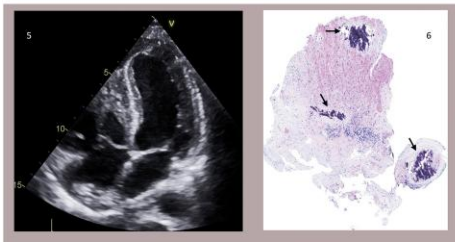


3. Explanted heart with severe endocardial and valvular fibrosis with the tricuspid valve (*) almost obliterated.

4. Hematoxylin-eosin staining of the explanted heart. a. Right ventricle; b. Interventricular septum with severe fibrosis; c. Left ventricle.

- Three months after HTx, transthoracic echocardiogram, cardiac MRI, and endomyocardial biopsy suggested disease recurrence.
- Differential diagnosis included the possibility of cellular rejection, which was treated with steroid pulses.
- The patient had a good clinical outcome, remaining asymptomatic with good graft function two years after the transplant.

CLINICAL COURSE



5. Biventricular hypertrophy, right apex obliteration and roof atria occupation.

6. Hematoxylin-eosin staining of an endomyocardial biopsy with subendocardial fibrosis and dystrophic microcalcifications (black arrows).

- **Heart Transplantation is a viable treatment option for EMF.**
- **Close monitoring is essential, as the possibility of EMF recurrence after HTx cannot be ruled out**

LEARNING POINTS

Clinical case

A 38-year-old man from Senegal presented with severe biventricular HF, including ascites, hepatomegaly, lower extremity oedema, dyspnoea, and cachexia. Cardiopulmonary auscultation revealed a Grade IV/IV systodiastolic murmur in the mesocardium and no rales. The patient had no significant medical history, including the absence of cardiovascular risk factors, no history of substance abuse, and no family history of heart disease. Cardiac magnetic resonance (CMR) revealed extensive EMF with biventricular dysfunction, severe valvular involvement, and a large thrombus in the right atrium. The initial diagnostic work-up ruled out eosinophilia, infections, and autoimmune conditions. He rapidly deteriorated, requiring emergent HTx due to cardiogenic shock (*Figure 1*).

Following HTx, the patient received induction therapy with basiliximab and steroids. An interleukin 2 receptor antagonist was used in order to delay calcineurin inhibitors, given the anticipated high risk of renal dysfunction.

He experienced a complicated post-operative course with primary graft dysfunction, cytomegalovirus (CMV) reactivation, and acute kidney failure, but initial EMB did not show signs of rejection. Three months later, the patient experienced an ischaemic stroke (IS). Although neurological symptoms resolved completely, a CT scan confirmed occlusion of the right vertebral artery. Since he was still hospitalized and under continuous electrocardiographic monitoring, supraventricular arrhythmias were ruled out as the cause of the IS. A transoesophageal echocardiogram showed absence of shunts with diffuse thickening of the atrial endocardium and ventricular hypertrophy with right ventricle (RV) obliteration. EMB revealed Grade 2R (G3a) cellular rejection without humoral rejection, and CMR revealed an increase in extracellular volume (ECV) without evidence of oedema, as well as fibrosis in the roof of both atria and an image suggestive of a thrombus (*Figure 2*). Tacrolimus had been in a low range at the time of the IS due to renal function improvement. He was also treated with mycophenolate 500 mg/12 h and prednisone 10 mg/day. Anti-human leukocyte antigen (HLA) antibody testing resulted negative.

After steroid pulses, the subsequent EMB revealed no signs of rejection, but significant subendocardial fibrosis and dystrophic microcalcifications (*Figure 2*). Although rejection was initially suspected, the findings of the second EMB raised suspicion of EMF recurrence, consistent with published diagnostic criteria.[1] A comprehensive diagnostic evaluation was performed, including serologies for CMV, Epstein–Barr virus, and human immunodeficiency virus, and multiple parasitic infections (Schistosoma, Strongyloides, Fasciola, Trichinella, Taenia, and Plasmodium), as well as faecal and urine parasite screening. This revealed positive serology for *Schistosoma mansoni*, although no parasites or eosinophilia were detected. Praziquantel was prescribed alongside standard immunosuppressive therapy (tacrolimus, mycophenolate, and prednisone), as well as anticoagulation, angiotensin-converting enzyme inhibitors, and sodium–glucose co-transporter 2 inhibitors (SGLT2i). In this case, the use of SGLT2i was considered based on mild signs of HF with high filling pressures and persistent renal dysfunction.[6]

Two years later, the patient remains clinically stable (New York Heart Association Class I) with immunosuppressive therapy within target range. Biventricular hypertrophy and RV apex obliteration persist, alongside atrial fibrosis on CMR, though ECV reduced to 30% (*Figure 2*). Subsequent EMB ruled out cellular rejection but showed mild subendocardial fibrosis persistence and humoral rejection, with negative anti-HLA and anti-major histocompatibility complex class I chain-related protein A antibodies. Additionally, a 1-year coronary angiogram revealed cardiac allograft vasculopathy (CAV) Grade 2. Previous studies on EMF had reported the presence of coronary lesions in both epicardial and microvascular arteries, along with CD68 and complement immunofixation.[7–9] However, both humoral rejection and CAV may be unrelated to the initial episode and EMF, given that both events are not uncommon in transplant recipients.

Discussion

This is the first reported case of suspected recurrence of EMF following HTx. Although ECV and fibrosis can be present in both EMF and rejection, microcalcifications on EMB are characteristic of EMF and not typically seen in cases of rejection.[10] Similar to other conditions that may lead to HTx, such as giant cell myocarditis, EMF is characterized by an unclear aetiology. However, while myocarditis is usually characterized by an acute course and benefits from immunosuppression, EMF follows a more insidious progression and the role for immunosuppression remains uncertain. Nonetheless, given the poorly understood pathogenesis of both conditions, the potential for recurrence after HTx should always be carefully considered.[11] In this case, we hypothesized that rejection may have triggered disease reactivation, based on the

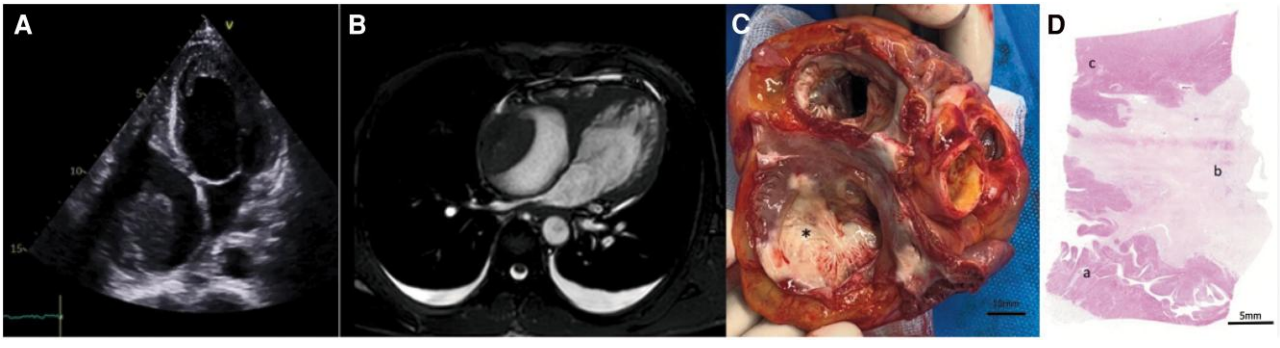


Figure 1 Endomyocardial fibrosis diagnosis on explanted heart. (*A*) Pre-heart transplantation transthoracic echocardiogram showing a non-dilated spherical and restrictive left ventricle and right ventricle obliteration with severe atria dilatation and large thrombus. (*B*) Pre-heart transplantation cardiac magnetic resonance showing endomyocardial fibrosis with biventricular involvement. Severe right ventricle and left ventricle lateral wall fibrosis with severe dilatation of both atria and presence of a large thrombus adhered to the right atrial wall and bilateral pleural effusion. (*C*) Macroscopic view of the explanted heart with severe fibrosis of the endocardium and the atrioventricular valves with the tricuspid valve (*) almost obliterated. (*D*) Haematoxylin and eosin staining of a myocardium section of the explanted heart. a Right ventricle, b interventricular septum with severe fibrosis, and c left ventricle.

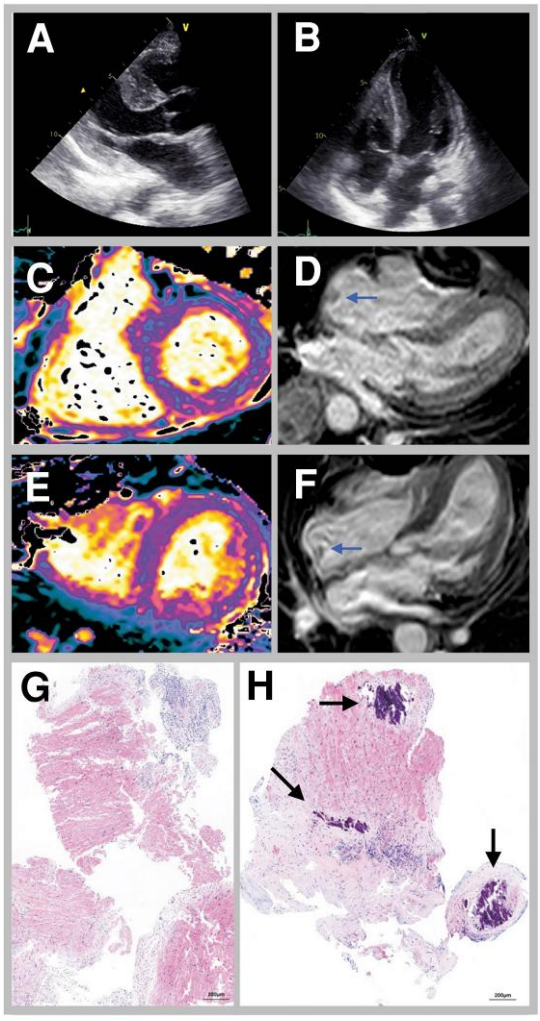


Figure 2 Endomyocardial biopsies, echocardiogram, and cardiac magnetic resonances performed during and after cellular rejection episode. Images (*A* and *B*): Transthoracic echocardiogram with parasternal long-axis and four-chamber views during acute cellular rejection episode showing moderate biventricular hypertrophy and atrial endocardium thickening. Images (*C* to *F*): Cardiac magnetic resonances performed during cell rejection episode (*C* and *D*) and 12 months after the cell rejection episode (*E* and *F*). Native T_1 mapping shows interstitial fibrosis during cell rejection episode (extracellular volume 40%, image *C*) which regresses on the subsequent cardiac magnetic resonance (extracellular volume 30%, image *D*). Images of late gadolinium sequences (*D* and *F*). Inability to properly null the myocardium suggestive of infiltrative disease and presence of fibrosis in atrial roof during the cell rejection episode (image *D*). Small filling defect on right atria roof suggestive of atrial thrombus vs. surgical material (arrows in images *D* and *F*). Images (*D* and *F*) also show an artefact on the right ventricular wall attributed to pericardial calcification. Image (*G*): Three months post-heart transplantation endomyocardial biopsy. Haematoxylin and eosin staining showing marked lymphocytic cellular infiltrate with polymorphonuclear cells and evidence of myocyte damage. Image (*H*): Subsequent endomyocardial biopsy performed after steroids pulses. Haematoxylin and eosin staining showing interstitial lymphocytic infiltrate in resolution without myocyte damage. Marked fibrosis and microcalcifications (arrows) are observed.

understanding that autoimmunity and inflammation are frequently associated disease triggers. Antiparasitic therapy was administered due to positive Schistosoma serology, which may indicate a low-burden active infection despite the absence of parasites in blood samples, and given the low risk of treating. We therefore recommend comprehensive screening and treatment of EMF triggers before HTx to minimize recurrence risk. As EMF is typically diagnosed at advanced stages, its usual progression timeline remains poorly understood, and the potential for reversibility in its early stages has not been thoroughly explored. However, a similar case of EMF in the context of a specific trigger such as pregnancy, with reversibility of the fibrosis after immunosuppressive treatment, has been described in the context of idiopathic hypereosinophilic syndrome.[12]

Conclusion

Given the incomplete understanding of the mechanisms underlying EMF, maintaining a high level of suspicion and rigorous post-HTx surveillance is crucial, as the risk of EMF recurrence cannot be entirely excluded. Nonetheless, HTx appears to be a viable treatment option for patients with EMF.

Lead author biography

Lorena Herrador graduated from the University of Barcelona in 2016. She completed a fellowship in Advanced Heart Failure and Heart Transplantation at Bellvitge University Hospital in Barcelona, where she currently works as an attending physician. Her main areas of interest include mechanical circulatory support and HTx.

Consent: The authors confirm that a written consent for submission and publication of this case report including images and text was obtained from the patient in line with COPE guidance.

Conflict of interest. None declared.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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