Multimodality Imaging in Endomyocardial Fibrosis: An Unusual Etiology of Heart Failure

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INTRODUCTION

Endomyocardial fibrosis (EMF) is a condition that was first reported in 1948 in Africa,[1] and its geographical distribution is strongly related to socioeconomic, cultural, and environmental status. More than half of the cases are reported in countries in sub-Saharan Africa[2]; however, this condition has been described in various parts of the world. The associated factors have been previously described and include malnutrition, parasitic infection, noninfectious systemic diseases, and genetic conditions.[3]

The presence of fibrotic thickening of the endocardium secondary to inflammation generates functional alterations, which are detected by noninvasive methods such as echocardiography,[4] with characteristic findings of a restrictive syndrome and an alteration of the ventricular chamber in the presence of dilated atria.[5] We describe the case of a patient with decompensated heart failure and imaging findings consistent with EMF.

CASE PRESENTATION

An 85-year-old female patient with chronic obstructive pulmonary disease associated with biomass smoke exposure, diabetes mellitus diagnosed 6 years ago, allergy to iodinated contrast media, coronary artery disease that started 15 years ago, and stent implantation in the right coronary artery experienced progressive deterioration of heart failure functional class for the past 5 years. She was in outpatient management with carvedilol 12.5 mg every 12 hours, enalapril 5 mg every 12 hours, and atorvastatin 40 mg/day.

She presented with an exacerbation of her symptoms for 6 days, consisting of dyspnea at rest and edema in the lower limbs, which were classified as symptoms of decompensated heart failure. Electrocardiography showed normal sinus rhythm and QRS duration with repolarization abnormalities in the inferior-lateral leads. Complete hematology studies and biochemical tests were carried out without significant alterations. Additionally, cardiac images were taken, with transthoracic echocardiogram showing the presence of severe left atrial enlargement (volume indexed, 69 mL/m^2) and right atrium enlargement (volume indexed, 46 mL/m^2) with obliteration of the apex by hyperrefringent calcified plaques (Video 1).

Regarding the functional evaluation, the findings were diastolic dysfunction with a restrictive pattern (Figure 1), moderate mitral regurgitation, and moderate decrease in left ventricular ejection fraction (31%) in relation to an important segmental alteration at the level of the apex in the evaluation of longitudinal strain (Figure 2).

With these findings, a clinical diagnosis of idiopathic EMF was made because of the presence of three major and two minor criteria, with a score of 13 that classified it as moderate disease. This diagnosis was complemented with cardiac magnetic resonance imaging showing biatrial dilatation, mild tricuspid insufficiency with 15% regurgitant fraction, trivial mitral regurgitation with 2% regurgitant fraction, minimal pericardial effusion predominantly posterior without hemodynamic impact, and compromised biventricular function and apical obliteration visualized in the steady-state free precession (SSFP) cine sequences in the different views (Videos 2 and 3). Furthermore, extensive subendocardial late gadolinium enhancement was observed, mainly apical-septal and in the three segments of the lateral wall of the left ventricle; the transmural index was <25%, and a thrombus in the apex was visualized. Extensive subendocardial late gadolinium enhancement was also observed in the three segments of the free wall of the right ventricle. These findings were observed in late enhancement sequences without compromise in the intramyocardial and subepicardial regions (Figure 3).

Pharmacological compensation for heart failure was continued, and parasitic infection and systemic or hematological disease was ruled out. The patient did not accept a surgical intervention because of her high surgical risk. After adequate improvement, she was discharged with outpatient follow-up in the heart failure clinic; however, 6 months later, the patient died due to respiratory complications associated with severe acute respiratory syndrome coronavirus-2 infection.

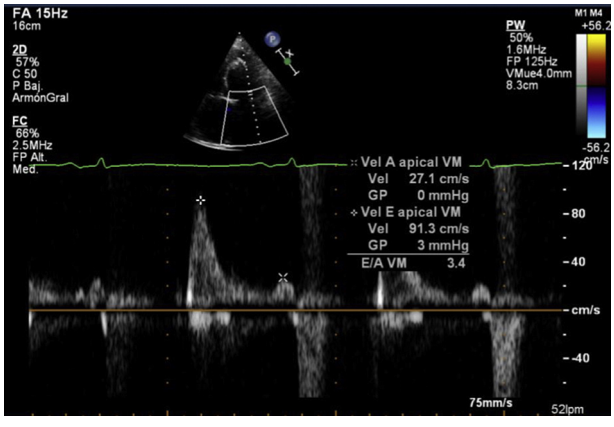

Figure 1 Diastolic evaluation study with evidence of a restrictive pattern; E/A ratio = 3.4.

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Conflicts of Interest: None.

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VIDEO HIGHLIGHTS

Video 1: Transthoracic echocardiogram four-chamber apical window showing the presence of a hyperrefringent image in the distal two-thirds of the left ventricle, with obliteration of the apex.

Video 2: Cardiac nuclear magnetic resonance, SSFP cine sequences in four-chamber view showing biatrial dilation, mild tricuspid insufficiency, trivial mitral regurgitation, minimal pericardial effusion, and mild compromised biventricular function (44% of left ventricular ejection fraction and 45% of right ventricular ejection fraction).

Video 3: Cardiac nuclear magnetic resonance, SSFP cine sequences in two-chamber views showing left atrial dilation, mild compromised left ventricular function, and apical obliteration.

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DISCUSSION

Endomyocardial fibrosis is a rare etiology of heart failure, and the different prevalence worldwide indicates a greater prevalence in African countries, such as southern Nigeria and the coast of Mozambique, and in Asia, in states such as Kerala in India, reaching a prevalence of up to 15%-20%.[6] However, there have been sporadic reports in Latin America in patients with cardiovascular disease.[7] Despite the absence of population-based studies, the global prevalence suggests a global decrease in EMF; however, changes in incidence or prevalence cannot be supported because there is a lack of studies on the subject.[2]

The theories of etiopathogenesis involve eosinophilia associated with infectious parasitic diseases as triggers to the immune response, which stand out in the early phases of the disease. However, nutritional factors have generated hypotheses related to a diet rich in cassava and low consumption of proteins in patients with genetic susceptibility.[3]

It seems that intercurrent episodes of inflammation and hypereosinophilia are independent risk factors for physiopathology and natural history during the early phases of EMF.[3] However, the need to combine several causal pathways independent of the role of eosinophils has been suggested, such as chronic inflammation triggered by infections in patients with genetic predisposition, systemic changes in patients with hematological diseases, or the presence of paraneoplastic syndromes.[8] The three phases of this disease have been previously described: the first is characterized by necrosis and acute carditis, which is usually difficult to diagnose, followed by a subacute phase that predisposes patients to the formation of thrombi in the compromised endocardium, and finally the fibrosis phase, which is characterized by progressive endocardial scarring, resulting in a restrictive pattern with atrioventricular dysfunction and valvular dysfunction.[9] In the chronic phase, biventricular involvement is the most common presentation, occurring in up to 55% of patients, followed by the isolated form with involvement of the right side of the heart or, in rare cases, only the left side of the heart. Atrial fibrillation occurs in more than 30% of cases as do conduction disorders, such as atrioventricular blocks or intraventricular conduction disorders.[3]

Echocardiography is necessary for the diagnosis of EMF. The findings include the presence of areas of fibrosis at the endocardial level with subsequent formation of calcium plaques with obliteration of the apex, a restrictive diastolic pattern as a result of fibrosis, biatrial enlargement, dilation of the inferior vena cava, pericardial effusion, and, in very advanced cases, fibrosis that can spread to the myocardium and atria. The functional changes include the restriction of the movement of the posterior mitral valve and severe regurgitation.[10]

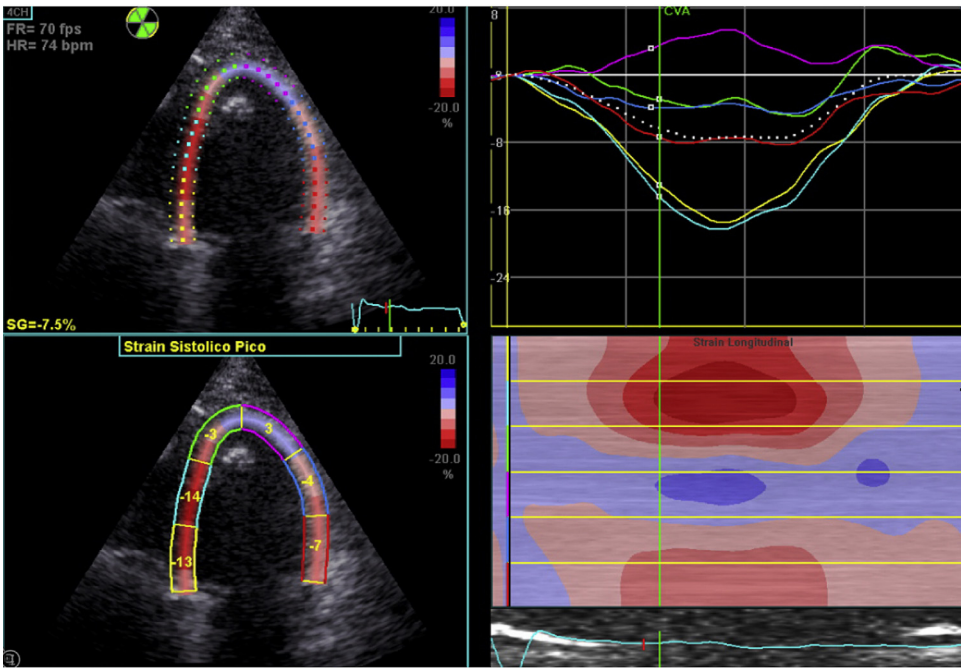

Figure 2 Four-chamber apical longitudinal strain study shows a functional compromise of –7.5% and a predominant compromise in the apical segments, more evident in the curved anatomic M mode with a severe compromise of the apical segments.

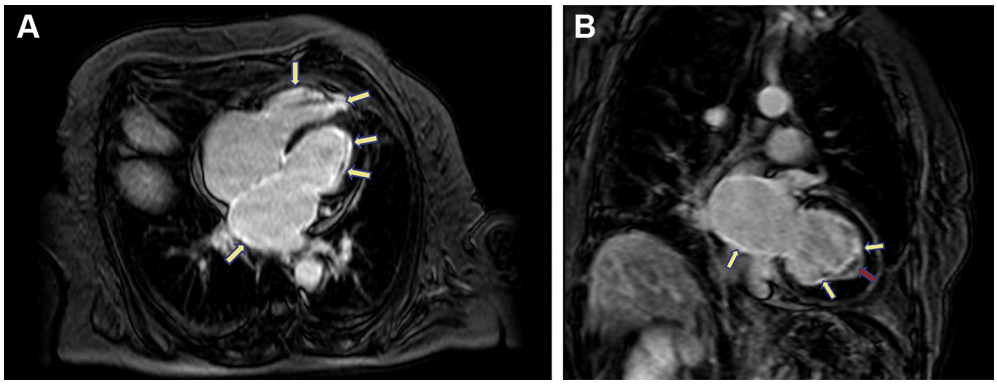

Figure 3 **(A)** Cardiac magnetic resonance imaging, four-chamber image showing biatrial dilatation and the presence of severe subendocardial fibrosis (*yellow arrows*) in the late gadolinium enhancement sequences. **(B)** Two-chamber image showing left atrial dilatation and the presence of subendocardial fibrosis (*yellow arrows*) in the late gadolinium enhancement sequences and small hypointense lesions (*red arrow*) consistent with a thrombus at the apex.

Table 1 Criteria for diagnosis and assessment of the severity of EMF*

Criterion	Score
Major criteria:	
Endomyocardial plaques >2 mm in thickness	2
Thin (≤1 mm) endomyocardial patches affecting more than one ventricular wall	3
Obliteration of the right ventricular or left ventricular apex	4
Thrombi or spontaneous contrast without severe ventricular dysfunction	4
Retraction of the right ventricular apex (right ventricular apical notch)	4
Atrioventricular valve dysfunction, which is due to adhesion of the valvular apparatus to the ventricular wall	1-4†
Minor criteria:	
Thin endomyocardial patches localized to one ventricular wall	1
Restrictive flow pattern across mitral or tricuspid valves	2
Pulmonary valve diastolic opening	2
Diffuse thickening of the anterior mitral leaflet	1
Enlarged atrium with normal-size ventricle	2
M movement of the interventricular septum and flat posterior wall‡	1
Enhanced density of the moderator or other intraventricular bands	1

Reprinted from "A population study of endomyocardial fibrosis in a rural area of Mozambique" by Mocumbi AO, Ferreira MB, Sidi D, Yacoub MH, 2008, N Engl J Med. Jul 3;359(1):43–9.

*A definite diagnosis of EMF is made in the presence of two major criteria or one major criterion associated with two minor criteria. A total score of <8 indicates mild EMF; 8-15, moderate disease; and >15, severe disease.

†The score is assigned according to the severity of atrioventricular regurgitation.

‡M movement of the interventricular septum refers to a pattern of movement observed on M-mode echocardiography that is thought to be due to obliteration or restriction of the left ventricular apex combined with mitral regurgitation.

To make the diagnosis according to these findings, major and minor criteria were established with a scoring system[11] (Table 1). According to this classification, EMF is diagnosed with the presence of two major criteria or one major criterion with two minor criteria. Moreover, the use of ventricular function assessment techniques such as the strain method can help to estimate the functional compromise and segmental alterations secondary to the degree of fibrosis and calcification. Cardiac magnetic resonance imaging is not available in most countries, but this method provides a large amount of information for diagnosis, including the potential of evaluating the disease at an early stage. The degree of chamber distortion and thrombosis extension can be outlined by cardiac magnetic resonance imaging. Additionally, fibrosis and thrombus can be detected by late gadolinium enhancement images, and hypoperfused cardiac areas can be mapped with perfusion studies. Taken together, this suggests that cardiac magnetic resonance should be used to monitor spatial and temporal changes during treatment and before major surgical cardiac procedures.[3,12]

Medical treatment includes pharmacological therapy for heart failure in combination with anticoagulation in cases of intracardiac thrombi. Paracentesis offers only short-term relief because ascites often accumulates again quickly. Corticosteroids and immunosuppressive drugs may be helpful in the early stages, but there are no randomized clinical trials to support their routine use. Cardiac surgery for specific conditions suggests an increase in survival compared with medical treatment; however, significant experience is required to perform the endocardectomy and, when required, valve repair or replacement.[3]

Although early postoperative mortality can be up to 20%, variable rates of recurrence have been reported after surgery; however, prompt surgical treatment appears to be the only option at present to improve clinical outcomes. Patients with end-stage EMF may no longer be candidates for this intervention, even those with clinical signs of advanced disease such as macroscopic and prolonged ascites, chronic pulmonary embolism, extensive endocardial fibrosis, extreme cachexia, or right ventricular fibrosis.[3]

The 10-year survival rate of EMF in most recent publications is 37%.[13] Longer survival can occur in patients with mild disease and early diagnosis; however, biventricular involvement (moderate-severe), right ventricular fibrosis, and the presence of mitral and tricuspid

regurgitation are associated with higher mortality rates[14] of up to 75% at 2 years in advanced stages despite pharmacological treatment.[15]

The study of the etiology of heart failure must include an appropriate analysis of the most likely causes. The identification of very rare diseases presents a challenge in the approach of these patients. The detection of structural alterations in the echocardiogram, such as endocardial fibrosis and obliteration of the apex, and the presence of restrictive diastolic dysfunction are key aspects in the diagnosis of EMF.

CONCLUSION

Endomyocardial fibrosis is a rare disease; therefore, its recognition in echocardiographic studies is essential for a diagnostic approach and the search for possible associated factors. Complementing multimodality studies with cardiac magnetic resonance imaging is of great help to establish the degree of severity. However, this condition has a prognosis limited to 5 years.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2021.06.002.

REFERENCES

1. Davies JNP. Endomyocardial fibrosis in Uganda. East Afr Med J 1948;25:10.
2. Mocumbi AO, Stothard JR, Correia-de-Sá P, Yacoub M. Endomyocardial fibrosis: an update after 70 years. Curr Cardiol Rep 2019;21:1-10.
3. Grimaldi A, Mocumbi AO, Freers J, Lachaud M, Mirabel M, Ferreira B, et al. Tropical endomyocardial fibrosis. Circulation 2016;133:2503-15.
4. Mocumbi AO, Carrilho C, Sarathchandra P, Ferreira MB, Yacoub M, Burke M. Echocardiography accurately assesses the pathological abnormalities of chronic endomyocardial fibrosis. Int J Cardiovasc Imaging 2011;27:955-64.
5. Vijayaraghavan G, Sivasankaran S. Tropical endomyocardial fibrosis in India: a vanishing disease!. Indian J Med Res 2012;136:729-38.
6. Williams A, Ball J, Davies JN. Paper: endomyocardial fibrosis in Africa: its diagnosis, distribution and nature. Trans R Soc Trop Med Hyg 1954;48:290-311.
7. Bukhman G, Ziegler J, Parry E. Endomyocardial fibrosis: still a mystery after 60 years. PLoS Negl Trop Dis 2008;2:1-7.
8. Rutakingirwa M, Ziegler JL, Newton R, Freers J. Poverty and eosinophilia are risk factors for endomyocardial fibrosis (EMF) in Uganda. Trop Med Int Heal 1999;4:229-35.
9. Sato T, Matsuyama TA, Seguchi O, Murata Y, Sunami H, Yanase M, et al. Restrictive myocardium with an unusual pattern of apical hypertrophic cardiomyopathy. Cardiovasc Pathol 2015;24:254-7.
10. Hassan WM, Fawzy ME, Al Helaly S, Hegazy H, Malik S. Pitfalls in diagnosis and clinical, echocardiographic, and hemodynamic findings in endomyocardial fibrosis. Chest 2005;128:3985-92.
11. Mocumbi AO, Ferreira MB, Sidi D, Yacoub MH. A population study of endomyocardial fibrosis in a rural area of Mozambique. N Engl J Med 2008;359:43-9.
12. León D, Martín M, Corros C, Santamarta E, Costilla S, Lambert JL. Usefulness of cardiac MRI in the early diagnosis of endomyocardial fibrosis. Rev Port Cardiol 2012;31:401-2.
13. Gupta PN, Kunju SM, Rajan B, Koshy AG, Vishwanathan S, George PS, et al. Geographical variation in the clinical presentation of endomyocardial fibrosis in India? Indian Heart J 2018;70:56-65.
14. Barretto AC, da Luz PL, de Oliveira SA, Stolf NA, Mady C, Bellotti G, et al. Determinants of survival in endomyocardial fibrosis. Circulation 1989;80(3 Pt 1):I177-82.
15. D'arbela PG, Mutazindwa T, Patel AK, Somers K. Survival after first presentation with endomyocardial fibrosis. Br Heart J 1972;34:403-7.