

Clinical Case Report

Endomyocardial fibrosis and myocardial infarction leading to diastolic and systolic dysfunction requiring transplantation



Monica De Gaspari^a, Giuseppe Toscano^a, Lorenzo Bagozzi^a, Marco Metra^b, Carlo Lombardi^b, Stefania Rizzo^a, Annalisa Angelini^a, Martina Perazzolo Marra^a, Gino Gerosa^a, Cristina Basso^{a,*}

^a Department of Cardiac, Thoracic, Vascular Sciences and Public Health, University of Padova, Padova, Italy

^b Cardiothoracic Department, Spedali Civili di Brescia, Brescia, Italy

ARTICLE INFO

Article history:

Received 17 September 2018

Received in revised form 16 October 2018

Accepted 19 October 2018

Keywords:

Endomyocardial fibrosis

Endomyocardial biopsy

Heart transplantation

Ischemic heart disease

ABSTRACT

Endomyocardial fibrosis (EMF) is an endemic disease in tropical areas, characterized by restrictive physiology due to endocardial fibrous thickening of the ventricular chambers. We report the case of a 25-year-old man of African origin who presented with end-stage heart failure due to both diastolic and systolic dysfunction and extensive endocavitary thrombosis as proven by echocardiography and cardiac magnetic resonance. EMF diagnosis was confirmed by endomyocardial biopsy and the patient had eventually cardiac transplantation. The explanted heart revealed, besides features consistent with EMF, transmural post-myocardial infarction scarring, in the absence of significant coronary artery disease, most probably thromboembolic in origin.

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1. Introduction

Endomyocardial fibrosis (EMF) is one of the commonest forms of restrictive cardiomyopathy worldwide, caused by fibrous thickening of the endocardium, involving one or both ventricles and the atrioventricular valves [1,2]. Its first description dates back to 1948 in Uganda [3]. Epidemiological studies report endemic prevalence in Sub-Saharan Africa and other tropical areas (up to 20% in selected populations), with typical relationship with low socio-economic status. Despite the investigations on different hypotheses for EMF etiology, no certain causative factor can be appointed. Infectious, autoimmune, dietary and genetic factors have been proposed and they all likely contribute to the disease pathogenesis [1]. The association with hypereosinophilia has been inconstant and the relationship between EMF and Loeffler's disease is still debatable [4,5]. The clinical history of EMF is well defined in two classical stages: the acute phase with typical signs of inflammation, when hypereosinophilia and myopericarditis can

occur, and the advanced form of the disease, more frequently presenting to the clinician's attention, with cardiac restrictive physiology eventually leading to heart failure and death [1,4,6]. Diagnostic major and minor criteria and a severity score system have been proposed [2]. Cardiac magnetic resonance (CMR) can provide additional information to echocardiography, mainly tissue characterization [7]. Management of heart failure is the mainstay of EMF treatment nowadays. Surgical approach to advanced stage of EMF consists in open heart endocardectomy and/or valve replacement, or even cardiac transplantation, although access to these therapeutic options is limited in the endemic areas [2,8].

2. Case report

2.1. Index patient clinical history

A 25-year-old man (height 180 cm, weight 54 kg) of Gambian nationality was referred to our center for end stage heart failure. Patient's history was negative, habitual consumption of Cassava, an edible root linked to neuronal and cardiac toxicity, was reported. One month before he has been admitted to another hospital for abdominal pain, vomiting and diarrhea. He reported progressive asthenia and marked limitation of physical activity in the last six months. Blood tests revealed sickle

* Corresponding author at: Department of Cardiac, Thoracic, Vascular Sciences and Public Health, University of Padua Medical School, Via A. Gabelli, 61 35121, Padova, Italy.
E-mail address: cristina.basso@unipd.it (C. Basso).

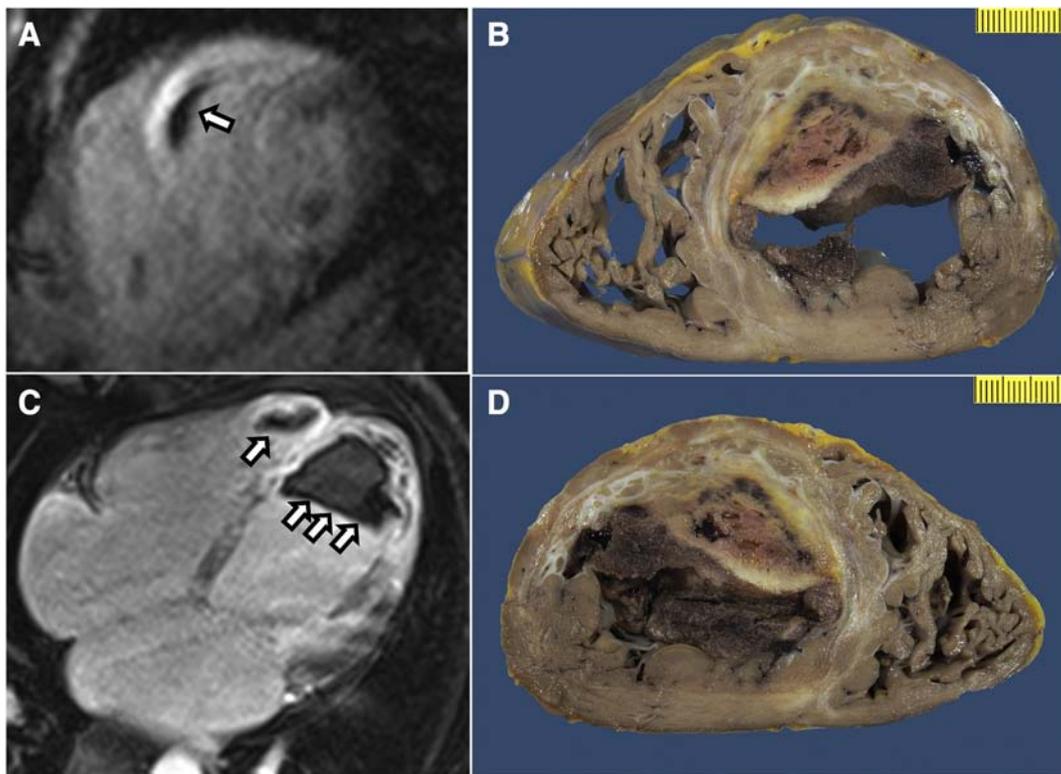


Fig. 1. Correlation between cardiac magnetic resonance (CMR) and explanted heart. A) CMR post-contrast injection: short axis view at mid level showing the endocavitary thrombosis in correspondence of the antero-septal wall of the left ventricle (white arrow). B) Macroscopic view of the explanted heart, transverse cut: mural thrombosis of the left ventricle at different stages of organization associated with marked thinning of the antero-septal and antero-lateral walls. White thickening of the endocardium of both the ventricles can be seen. C) CMR post-contrast injection: 4-chamber view demonstrating transmural late gadolinium enhancement (LGE) of mid and apical antero-septal and antero-lateral regions of the left ventricle, doubtful enhancement of the right ventricular apex and of the endocardium of the basal septum on both right and left ventricular side. The apex of the left ventricle is completely obliterated by a black non-contrast enhanced mass corresponding to a thrombus (white arrows); a thrombus in the right ventricular apex is also detectable (single white arrow on C). D) Apex of the explanted heart, with complete obliteration by a huge thrombus. Some smaller thrombi are present also among the right ventricular trabeculae.

cell trait. Severe left ventricular dysfunction due to hypokinesia (ejection fraction 20%), associated with mitral and tricuspid regurgitation, was found by transthoracic echocardiography. A huge apical left ventricular thrombus, without aneurysm, and thrombosis within the right ventricular trabeculae were also noted. The patient was then put on inotropic support and anticoagulation therapy. During hospitalization he suffered a thromboembolic stroke, rapidly treated with thromboaspiration with neurological recovering. CMR demonstrated mid-apical antero-septal and apical circumferential late gadolinium enhancement (LGE) with no clear LGE of right ventricular wall, and filling defects at the apex of both ventricles, compatible with endocavitary thrombosis (thrombus size left ventricle 2,7 x 3,8 cm; right ventricle 2,6 x 0,5 cm) (Fig. 1). Coronary computed tomography angiography (CCTA) ruled out calcific atherosclerotic plaques or significant stenosis. Right heart catheterization showed a restrictive pattern and endomyocardial biopsy was carried out, with histological demonstration of fibrous thickening of the endocardium and mild inflammatory infiltrates, in the absence of myocyte necrosis, compatible with EMF (Fig. 2). Molecular analysis for detection of cardiotropic viruses or parasites resulted negative. Heart transplantation was eventually performed.

2.2. Explanted heart examination

Examination of the explanted heart revealed a massive endocavitary thrombosis of the left ventricle with apical

obliteration, associated with a marked thinning of the antero-septal and antero-lateral walls due to scarring (Fig. 1). A diffuse endocardial white lining of both ventricular cavities was also present. Coronary artery tree examination revealed only a subcritical stenosis of the left anterior descending branch, due to an eccentric fibro-atheromatous plaque, not complicated by hemorrhage or thrombosis (Fig. 3). Histology confirmed the presence of thrombosis at different stages of organization and the transmural extension of the replacement-type fibrosis at the level of the antero-septal and antero-lateral walls of the left ventricle. The white layer bordering the ventricular cavities was consistent with endocardial fibrous thickening (Fig. 3), matching the endomyocardial biopsy diagnosis of EMF.

3. Discussion

EMF is generally considered a tropical disease with very few cases occurring in Western industrialized countries [8,9]. Gambia is not included among the list of endemic countries [5]. The first review of 32 necropsies by Davies and Ball [10] lists many features that are still considered as the cornerstone for EMF diagnosis and perfectly match our case, such as the demonstration at histology of three zones of the endocardial fibrous thickening, (i.e. the superficial zone usually acellular and often hyalinized; the intermediate zone of loosely-textured fibrous tissue with occasional inflammatory cells and a deep granulation tissue layer), with the

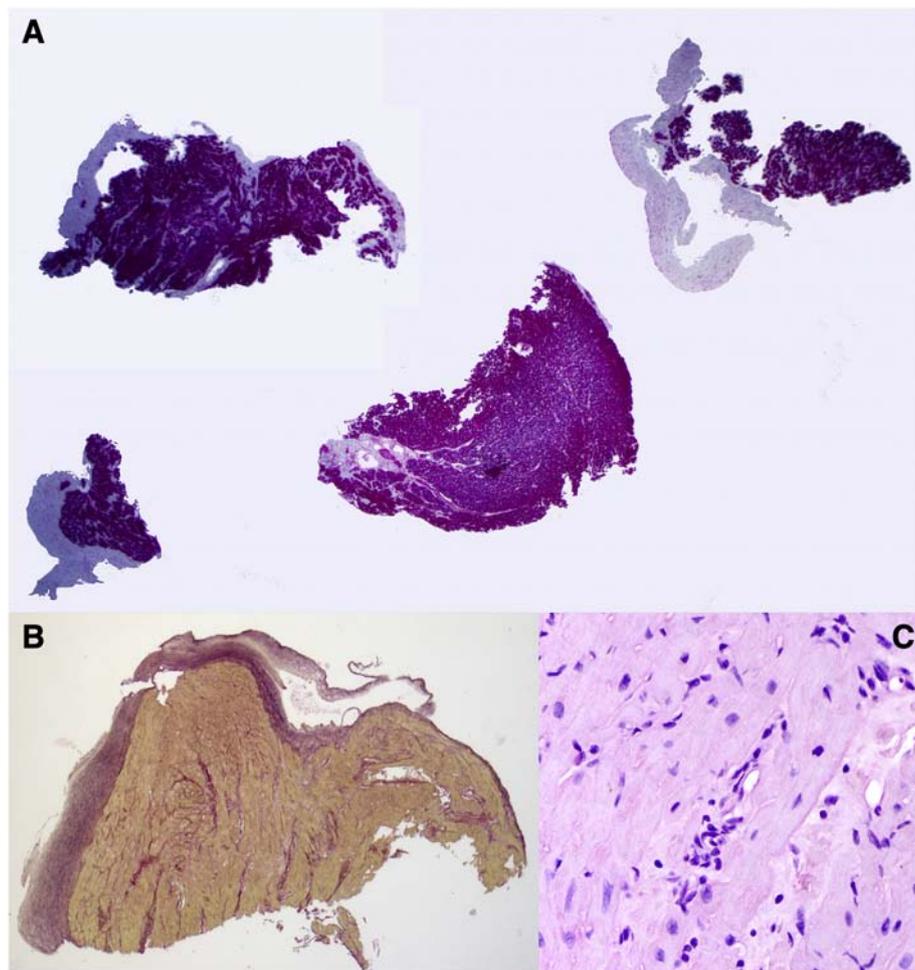


Fig. 2. Endomyocardial biopsy specimens. A) In three small fragments the marked endocardial fibrous thickening is evident (Heidenhain trichrome stain, panoramic view). B) Scanty irregular elastosis is present at the level of the endocardial fibrous thickening (Veigert van Gieson stain, original magnification $\times 25$). C) Mild inflammatory infiltrate without necrosis (Hematoxylin-eosin stain, original magnification $\times 250$).

superimposed mural thrombosis at different stages of organization. Moreover, our case shows biventricular involvement and the presence of mild focal inflammatory infiltrates, as documented both in endomyocardial biopsy and surgical samples from the explanted heart [6,11]. Eosinophilia or eosinophilic infiltrates at histology were not found. CMR findings were in keeping with EMF [7]. The role of viral or parasitic infection in EMF pathogenesis is still controversial [11]. Anyhow, molecular analysis for cardiotropic viruses and parasites from endomyocardial biopsy and explanted heart turned out negative in the case herein reported. Based upon the anamnestic data of prolonged ingestion of tuber (cassava), we can assume a role of diet deficient in protein in disease pathogenesis [12].

In the case herein reported, the main diagnostic challenge is the coexistence of EMF and previous myocardial infarction and the possible cause-effect relationship. Coronary artery disease was ruled out by CCTA, which is known to have a lower detection rate of significant coronary artery disease compared to coronary angiography. However, it was used as a screening modality because of the low pretest risk of coronary atherosclerosis in our young patient. On the other hand, the pathology finding of a stable atherosclerotic

plaque with subcritical stenosis of the proximal tract of the left anterior descending artery does not explain the transmural scarring of the antero-septal and antero-lateral walls of the left ventricle. In the setting of massive endocavitary left ventricular thrombosis, the most reasonable hypothesis is coronary thromboembolism leading to myocardial infarction, as supported by the concomitant thromboembolic stroke successfully treated with thromboaspiration. Noteworthy, pulmonary and systemic embolism are seldom reported in EMF, although they are unusual in the original series by Davies [3].

In conclusion, we presented a rare case of concomitant diastolic and systolic heart dysfunction requiring heart transplantation caused by EMF and ischemic heart disease probably embolic in origin. A definitive diagnosis was reached only through a multidisciplinary approach, including pathological evaluation of the endomyocardial biopsy and explanted heart.

Conflicts of interest

None declared.

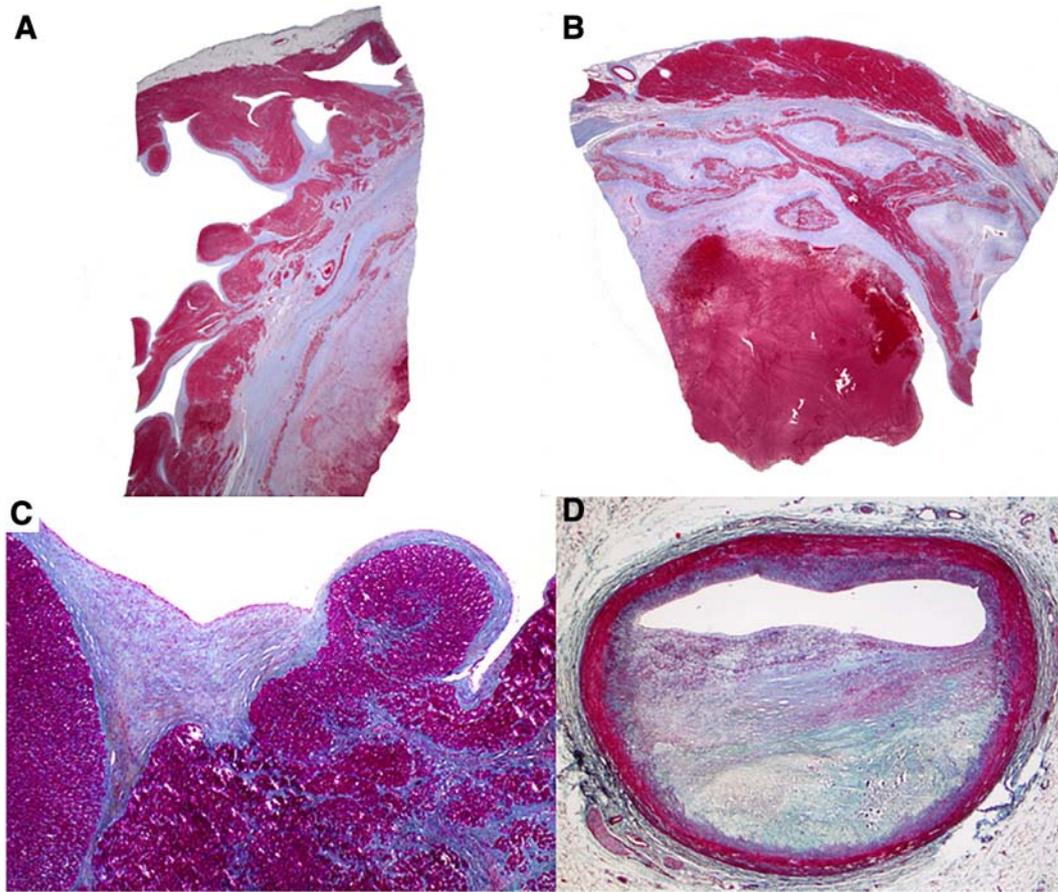


Fig. 3. Explanted heart specimen. A) Evidence of transmural replacement-type fibrosis at the level of the antero-septal wall, coupled with fibrous thickening of the endocardium and organized mural thrombosis of the left ventricle (Heidenhain trichrome stain, panoramic view). B) Thrombosis at different stages of organization and diffuse endocardial fibrous thickening in the anterior wall is visible (Heidenhain trichrome stain, panoramic view); C) The endocardial fibrous thickening is focally deepening into the myocardium, which is showing replacement-type fibrosis (Heidenhain trichrome stain, original magnification $\times 25$). D) Proximal tract of the left anterior descending coronary artery with a subcritical stenosis due to an eccentric fibro-atheromatous plaque, not complicated by hemorrhage or thrombosis (Heidenhain trichrome stain, original magnification $\times 15.6$).

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