Endomyocardial Fibrosis: Viewpoint

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Abstract

Endomyocardial fibrosis (EMF) is a restrictive cardiomyopathy of unknown origin, affecting mainly young people from tropical countries. EMF is considered to be the most restrictive cardiomyopathy in the world. The main risk factors for EMF appear to be age, gender, ethnicity, social vulnerability, and eosinophilia. The deposition of fibrotic tissue in the endocardium, myocardium, and heart valves leads to a decrease in the ventricular cavity and dysfunction in the diastolic filling of the ventricles. In this article we will express our point of view on this pathology, which is relatively unknown and with limited treatment options.

Introduction

Endomyocardial fibrosis (EMF) is a restrictive cardiomyopathy of unknown origin, affecting mainly young people from tropical countries.[1] This condition was first described in Uganda, in 1947, by the pathologist Jack N. P. Davies, who also give this disease the name of Davies.[2]

EMF is considered to be the most restrictive cardiomyopathy in the world.[3] Nevertheless, the doubt surrounding all cases of EMF having the same root cause continues to be one of the greatest mysteries in cardiology, even more than 70 years after its first description.[2] Efforts to understand their mechanisms are hindered by the incapacity to detect EMF in its initial stages in endemic areas, mainly due to health professionals' lack of knowledge and to a general lack of access to health systems.[4] For this reason, to date, no provenly effective therapy has been discovered for this condition.[3]

Epidemiology

The main risk factors for EMF appear to be age, gender, ethnicity, social vulnerability, and eosinophilia.[3] It is a disease that appears markedly in developing countries in both tropical and subtropical regions. Half of the described cases come from Sub-Saharan Africa, with one fourth of these coming from Uganda alone.[2] One echocardiographic study showed a prevalence of nearly 20% in one rural community in Mozambique.[5] In addition, a high prevalence of EMF has been documented in India and China. In South America, EMF has been reported mainly in Brazil and Colombia.[6]

In Uganda, a bimodal pattern of the disease was registered, with peaks in the age group of 10 to 30 years. In this country, a two-fold greater prevalence was documented in women, although this pattern has not been repeated in other studies.[2,5]

Etiopatogenesis

The etiopathogenesis behind the emergence of EMF is still relatively unknown. However, many theories have been postulated concerning the theme. The concentration of the disease in the tropics has led to a search for environmental, nutritional, and infectious causes.[2] The etiopathogenesis of EMF is summarized in Figure 1.

The main thesis deals with a possible relation with a hypereosinophilic syndrome. This theory is corroborated by the observation that EMF is similar to the late stage of Loeffler's syndrome, both characterized by a fibrotic state.[2,6] However, also linked to this theory is the fact that the eosinophilia is limited to the initial stages of EMF, in addition to the geographic inconsistencies in the prevalence of parasitic infections.[6]

The investigation of nutritional factors has been focused on in a possible connection with toxicity stemming from the excessive consumption of cassava root. Cassava is a tuber widely consumed as the main nutritional staple of developing countries, and contains a toxic cyanogenic glycoside. A diet poor in proteins can compromise the detoxification of this metabolite, resulting in an accumulation of cyanide, which is toxic to heart tissues.[6]

One genetic predisposition has also been proposed as an attempt to explain the high prevalence of EMF in specific

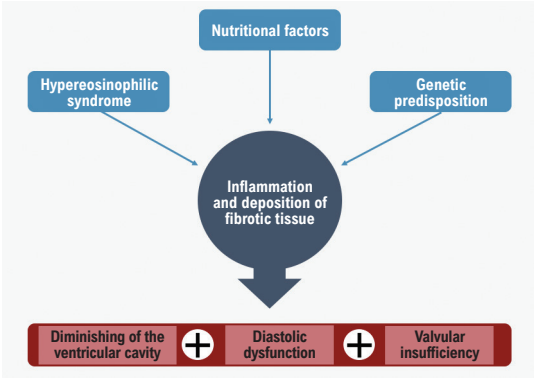

Figure 1 – *Physiopathological mechanisms of endomyocardial fibrosis.*

Keywords

Fibrosis; Endomyocardial; Cardiomyopathy; Ventricles

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areas. One association in families has been described in some studies.[5,6] However, it is not clear if this is due to the environmental factors that they share, to genetic causes, or to both.

Physiopathology

The deposition of fibrotic tissue in the endocardium, myocardium, and heart valves leads to a decrease in the ventricular cavity and dysfunction in the diastolic filling of the ventricles.[1,7] In addition, a serious valvular insufficiency is also developed, mainly in the tricuspid valve. Healing of the endocardium also compromises the systolic function, in variable degrees. With this, a medical condition of heart failure is also generated.[1] Consequently, there is an important dilation in the atrial cavities.[3] This atrial increase can lead to the development of arrythmias, as well as the formation of thrombi and a predisposition to pulmonary thromboembolism.[3,4]

Clinical picture

The clinical evolution of EMF consists of three stages/forms: active stage (inflammatory), transitory progressive stage, and chronic stage.[6]

In the active and initial stage, the EMF is associated with fever, pancarditis, dyspnea, periorbital edema, pruritis, and eosinophilia. Nonetheless, eosinophilia cannot be considered a specific biomarker for EMF, since its occurrence varies from 0 to 70% of the cases. The ECG is unspecific, but in the echocardiography it is possible to observe a pericardial effusion and homogeneous infiltrates on the walls of the heart.[6,8]

The transitory stage of EMF mainly takes place due to the repetition of an active episode, which facilitates the evolutionary path toward the chronic stage of the disease. During evolution, systemic inflammation is not common, nor is the presence of inflammatory markers. Radiology does not normally show specific signs of EMF, but typical linear calcifications on the endocardium can sometime appear.[6] In the echocardiogram, by contrast, it is possible to see areas of endocardial scars, due to the regression of myocardial thickness. With these scars, a restrictive heart disease may occur, with atrial dilation and distortion of the heart chamber.[6] From this, heart failure develops and the patient begins to present acites and edema.

The chronic stage tends to present a biventricular involvement, given that this is present in at least 55% of the cases, but, in addition this pathology, right cardiac involvement, and more rarely, left cardiac involvement, are common.[5,6] In the cases of right ventricular dysfunction, a prolonged portal hypertension is generated, evolving with anasarca. By contrast, when biventricular involvement occurs, an acites disproportional to the peripheral edema can be developed. In a general sense, some other signs that can be seen due to heart failure include testicular atrophy, impaired growth, cachexia, and problems in the development of male secondary sexual characteristics.

In radiological studies, one can see pulmonary infundibular dilatation, cardiomegaly, and pre-capillary pulmonary hypertension. By contrast, echocardiography presents findings of low cardiac output and pulmonary artery hypertension.[6,9]

Diagnosis

The suspicion of EMF should occur for patients in endemic areas that have suggestive echocardiographic results and symptoms of heart failure. The analysis of cardiac involvement includes the echocardiogram and serum troponin evaluations.[5]

The diagnosis can therefore be made using a gravity scoring system, which is separated into greater or lesser criteria, upon agreement from two different cardiologists. To confirm the diagnosis, there should be at least two greater criteria, or one lesser criteria and two greater criteria; these criteria are described in Table 1.

Treatment

In general, clinical treatment with diuretics, vasodilators (blockers of the renin-angiotensin-aldosterone system), and betablockers can be tested, evaluating the clinical response in an individualized manner. However, it is common for patients to present the disease in an already advanced stage, and, due to the absence of randomized clinical trials, the benefits of this clinical treatment become uncertain as regards significant outcomes, such as mortality or hospitalization due to heart failure. For individuals who continue in the functional class III/IV, surgical treatment (generally the endocardiectomia with plasty and/or mitral and/or tricuspid valve replacement) can be considered, but there are doubts about its impact on patient survival.[10]

Table 1 – Criteria for the diagnosis of endomyocardial fibrosis

Greater Criteria	Score
Endomyocardial plaques >2 mm in thickness	2
Thin Endomyocardial plaques (≤1 mm) affecting more than one ventricular wall	3
Obliteration of the right or left ventricular apex	4
Thrombi or spontaneous contrast with no severe ventricular dysfunction	4
Retraction of the right ventricular apex (apical notch of the right ventricle)	4
Atrioventricular valve dysfunction due to adherence of the valvular apparatus to the ventricular wall	1-4
Lesser Criteria	
Thin Endomyocardial plaques located on a ventricular wall	1
Restrictive flow pattern through the mitral or tricuspid valves	2
Diastolic opening of the pulmonary valve	2
Diffuse thickness of the anterior mitral leaflet	1
Increased atrium with normal sized ventricle	2
M movement of the interventricular septum and posterior flat wall	1
Increased density of the moderator or other intraventricular bands	1

Table adapted from Mocumbi et al.[5]

In patients who present Loeffler's syndrome with endomyocardial disease (subtype of hypereosinophilic syndrome), the additional therapeutic approach consists of measures that seek to achieve the normalization of peripheral eosinophilia, since the damage to the heart is secondary to the toxicity related to the degranulation of the eosinophils. This objective can be achieved with corticotherapy. Hydroxyurea, interferon-α and imatinib are possible alternatives.[11]

Author Contributions

Conception and design of the research and Critical revision of the manuscript for important intellectual content: Durães AR; Acquisition of data and Writing of the manuscript: Rêgo LOS, Vilas-Boas GS; Analysis and interpretation of the data: Rêgo LOS, Vilas-Boas GS, Durães AR.

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This article does not contain any studies with human participants or animals performed by any of the authors.

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