Autopsy Case Reports

Image in Focus

Endomyocardial fibrosis

Paulo Sampaio Gutierrez[a], Fernando Peixoto Ferraz de Campos[b]

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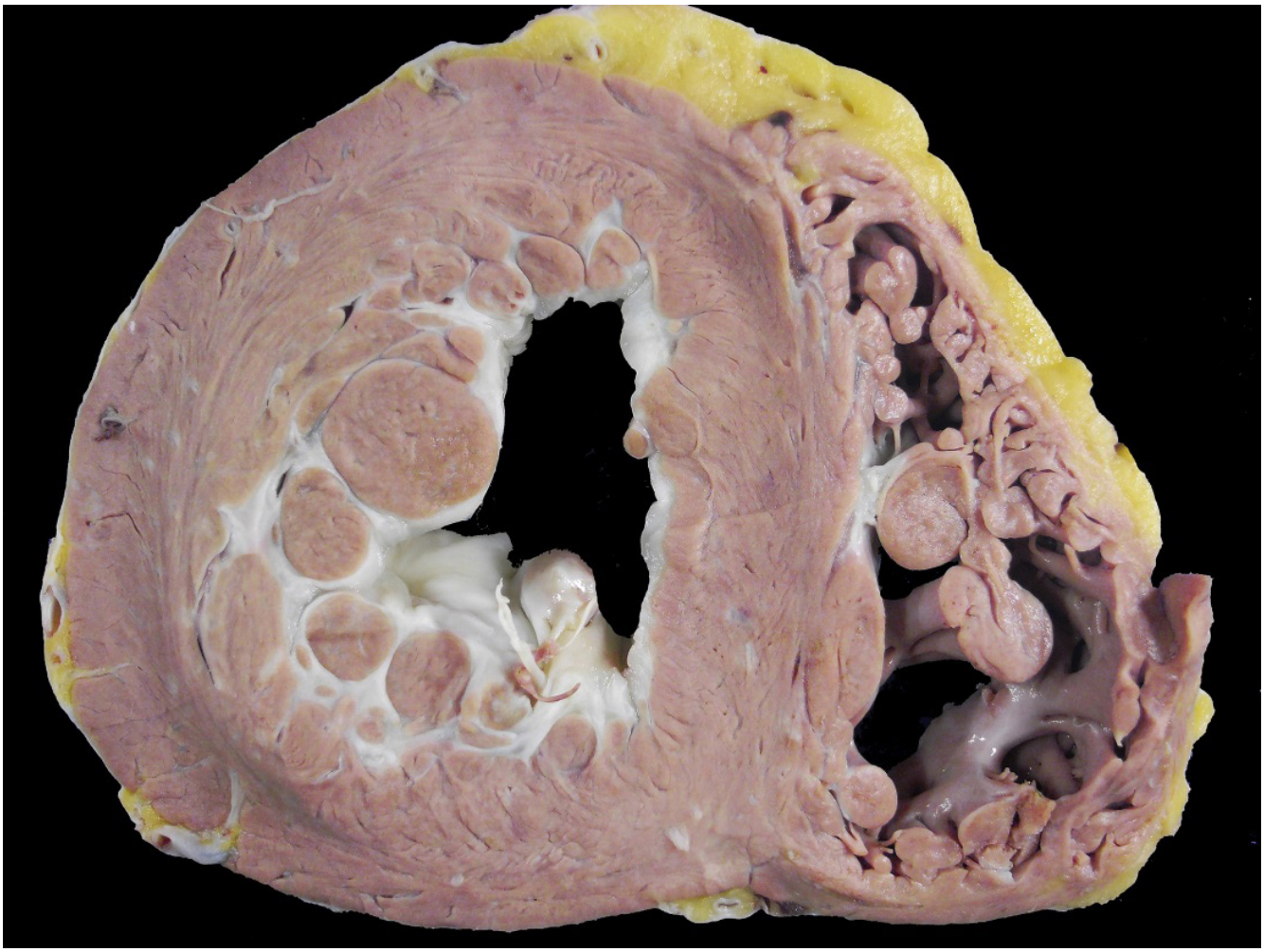

Image courtesy Dr. Paulo Sampaio Gutierrez

Figure 1. Gross view of the mid-ventricular transversal section of the heart showing extensive areas of white fibrosis in the endocardium of the left ventricle that has diffusely thickened the lining of the chamber and involved the papillary muscles. Note the presence of trabeculae that extend across the myocardium.

[a] University of São Paulo, Hospital das Clínicas da Faculdade de Medicina, Heart Institute (InCor), Laboratory of Pathology. São Paulo, SP, Brazil.
[b] University of São Paulo, Hospital Universitário, Internal Medicine Division. São Paulo, SP, Brazil.

The specimen shown in the picture (Figure 1) belonged to a 63-year-old female patient who was referred to the Pulmonologist because of a long-standing complaint of cough and dyspnea. She was a hairdresser and had smoked 8 pack years. The work-up, among other examinations, included echocardiogram, cinecoronarioangiography, and cardiac magnetic resonance imaging (MRI), which disclosed the diagnosis of endomyocardial fibrosis. She was submitted to surgical treatment with partial resection of the left ventricle's endocardium, replacement of the mitral valve by a bioprosthesis, and tricuspid valve repair. Four months later, she was admitted with fever and signs of sepsis, and died soon after. The necropsy and blood culture samples (the results of which were available after death) revealed endocarditis of the mitral prosthesis due to *Streptococcus viridans*.

Endomyocardial fibrosis (EMF)—also called tropical endomyocardial fibrosis—is a restrictive cardiomyopathy of unknown cause. It is characterized by the deposition of fibrous tissue in the endomyocardium, which leads to a restrictive physiology accompanied by a very poor prognosis without a specific management. This results in demise, which is usually due to heart failure, arrhythmias, and thromboembolism. The disease is endemic in Africa, where the first case was described in 1948 (Uganda),[1] but also has a high frequency in Asia (India[2,3] and China[4]) and South America (Brazil[5] and Colombia[6]). Grimaldi et al.[7] called it a disease of poverty, since it afflicts the rural populations of low-income countries. Genetic, environmental, and socioeconomic factors may explain the persistent particular geographic distribution, as well as the decline of prevalence in other areas that have shown social and economic improvement. EMF presents a bimodal distribution peaking at 10 and 30 years of age. Gender seems to lack any predominance, and varies according to the series and the country of the study.

The etiopathogenesis of EMF remains in the field of hypotheses and far from exact knowledge; therefore, it demands systematic research with the aid of current technologies. The seemingly implicated factors, besides ethnicity, poverty, eosinophilia, autoimmunity, and serotonin, are related to: (i) the excessive immune response against certain parasitic infections; (ii) dietary scarcity (malnutrition); (iii) herbal preparations; and (iv) the use of improperly processed or cooked cassava as the primary source of carbohydrate (because of the ingestion of toxic levels of cyanogenic glycoside).[8-12] The occurrence of familial cases supports the participation of genetic predisposition.[7] Although not yet a consensus, the high prevalence of anti-heart antibodies detected in patients with EMF somehow suggests the involvement of autoimmunity in the pathogenesis.[13] Similarly, the usual association of hypereosinophilia with EMF has led some authors to consider this entity as the tropical variant of hypereosinophilic syndrome, which is found in temperate climates with the overproduction of interleukin-5 and fibrotic lesions identical to those seen in EMF.[14]

Typically, EMF presents an insidious onset, usually associated with fever, pancarditis, and eosinophilia, which are morphologically abnormal. This initial active form also presents dyspnea, itching, and periorbital edema.[15] The clinical features of EMF will depend on the predominantly affected cardiac chamber and the duration of disease. Lower limbs edema, ascites, and non-specific gastrointestinal complaints (e.g. nausea, vomiting, and anorexia) are characteristic of the right ventricular and tricuspid valve involvement. However, when the left ventricle is affected, dyspnea, exertional dyspnea, orthopnea, nocturnal paroxysmal dyspnea, and fatigue will predominate. Thromboembolic events, angina-like chest pain, arrhythmias, and syncope, may also take part of the clinical features of EMF involving the left chamber. Growth retardation, testicular atrophy, clinical feminization, finger and toe clubbing, and cachexia are the consequence of low cardiac output in a chronic disease.[16] Left ventricular involvement, isolated or in combination with biventricular disease, is most often encountered in the chronic form of the disease, followed by isolated right-side involvement. In the latter, the physical examination shows signs of systemic venous hypertension with multi-visceral congestion, accompanied (or not) by pulmonary hypertension due to pulmonary thromboembolism. Some characteristic signs include central cyanosis, exophthalmos, giant ascites without pedal edema (sometimes accompanied by peritoneal fibrosis), hyperpigmentation of the lips and gums, proptosis, and parotid swelling. Although chest x-ray and electrocardiogram may show several abnormalities, none of them are specific. However, the echocardiogram is the gold standard technique for the

diagnosis of the chronic disease.[17] Dense endocardial echograms along the mural and valvular endocardium, valvular dysfunction, a restrictive filling pattern with shrinkage of the cavity, the presence of thrombus, and the detection of pericardial effusion are the most typical echocardiographic findings.[18] MRI adds precision to the diagnosis, showing hypoperfused fibrotic areas, and confirms the presence of thrombus and calcifications.[19]

The most prominent pathological characteristics of EMF[20] is a massive deposition of granulation tissue and extracellular proteins, mainly collagen type I, but also collagen type III and elastic fibers, at the endocardium of any or both ventricles. This connective tissue surrounds the papillary muscles and covers the walls of the cavities, thickening the walls and causing a stiffness that impairs the expansion of the chamber. The problem is frequently worsened by calcification and/or mural thrombosis. Typically, the boundaries between the thickened endocardium and the myocardium are not clear-cut, and there are tongues of fibrous tissue penetrating the intertrabecular spaces. Apical portions of the cavities (as well as their inlets) are more commonly committed, and the outlets are almost always free. In spite of the relationship with eosinophilia, significant infiltrates by eosinophils are not seen in the majority of cases.

Keywords
Endomyocardial Fibrosis; Diagnosis; Autopsy

REFERENCES

1. Davies JNP. Endocardial fibrosis in Africans: a heart disease of obscure aetiology in Africans. East Afr Med J. 1948;25:10-6.
2. Nair DV. Endomyocardial fibrosis in Kerala. Indian Heart J. 1971;23(3):182-90. PMid:5139971.
3. Kutty VR, Abraham S, Kartha CC. Geographical distribution of endomyocardial fibrosis in south Kerala. Int J Epidemiol. 1996;25(6):1202-7. PMid:9027525. http://dx.doi.org/10.1093/ije/25.6.1202.
4. Yin R. Endomyocardial fibrosis in China. Chin Med Sci J. 2000;15(1):55-60. PMid:12899403.
5. Guimarães A. Natural history and current status in Brazil. In: Valiathan M, Somers K, Kartha CC, editors. Endomyocardial fibrosis. Delhi: Oxford University Press; 1993. p. 37-54.
6. Bukhman G, Ziegler J, Parry E. Endomyocardial fibrosis: still a mystery after 60 years. PLoS Negl Trop Dis. 2008;2(2):e97. PMid:18301727. http://dx.doi.org/10.1371/journal.pntd.0000097.
7. Grimaldi A, Mocumbi AO, Freers J, et al. Tropical endomyocardial fibrosis natural history, challenges, and perspectives. Circulation. 2016;133(24):2503-15. PMid:27297343. http://dx.doi.org/10.1161/CIRCULATIONAHA.115.021178.
8. Mayanga-Kizza H, Gerwing E, Rutakingirwa M, Mugerwa R, Freers J. Tropical endomyocardial fibrosis in Uganda: the tribal and geographic distribution, and the association with eosinophilia. Tropical Cardiology. 2000;26(103):45-8.
9. Rutakingirwa M, Ziegler JL, Newton R, Freers J. Poverty and eosinophilia are risk factors endomyocardial fibrosis (EMF) in Uganda. Trop Med Int Health. 1999;4(3):229-35. PMid:10223220. http://dx.doi.org/10.1046/j.1365-3156.1999.43376.x.
10. Sezi C. Effect of protein deficient cassava diet on cercopithecusaethiops hearts and its possible role in the aetiology and pathogenesis of endomyocardial fibrosis in man. East Afr Med J. 1996;73(5, Suppl):S11-6. PMid:8756020.
11. Sezi C. Effects of cassava diet on cercopithecusAethiops Livers: a case for cassavas the cause of both tropical splenomegaly syndrome (tss) and endomyocardial fibrosis (EMF). East Afr Med J. 1996;73(5, Suppl):S24-8. PMid:8756024.
12. Davies H. Endomyocardial fibrosis and the tuberous diet. Int J Cardiol. 1990;29(1):3-8. PMid:2262213. http://dx.doi.org/10.1016/0167-5273(90)90265-7.
13. Mocumbi AO, Latif N, Yacoub MH. Presence of circulating anti-myosin antibodies in endomyocardial fibrosis. PLoS Negl Trop Dis. 2010;4(4):e-661. PMid:20422043. http://dx.doi.org/10.1371/journal.pntd.0000661.
14. Brockington IF, Olsen EGJ. Loeffler endocarditis and Davies'endomyocardial fibrosis. Am Heart J. 1973;85(3):308-22. PMid:4727268. http://dx.doi.org/10.1016/0002-8703(73)90365-7.
15. Parry EH, Abrahams DG. The natural history of endomyocardial fibrosis. Q J Med. 1965;34(136):383-408. PMid:5862743.
16. Mocumbi AO. Endomyocardial fibrosis: a form of endemic restrictive cardiomyopathy. Glob Cardiol Sci Pract. 2012;11(1):2012. http://dx.doi.org/10.5339/gcsp.2012.11.eCollection. PMid:25610842.
17. 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(7):955-64.

PMid:21110101. http://dx.doi.org/10.1007/s10554-010-9753-6.

18. Venkitachalam CG, Balakishnan KG, Tharakan JM. Echocardiographic findings in endomyocardial fibrosis. In: Valiathan M, Somers K, Kartha CC, editors. Endomyocardial fibrosis. Delhi: Oxford University Press: 1993. p. 153-67.

19. Cury R, Abbara S, Sandoval LJ, Houser S, Brady T, Palacios IF. Visualization of Endomyocardial Fibrosis by Delayed-Enhancement Magnetic Resonance. Imaging Circulation. 2005;111(9):e115-7. PMid:15753221. http://dx.doi.org/10.1161/01.CIR.0000157399.96408.36.

20. Iglezias SD, Benvenuti LA, Calabrese F, et al. Endomyocardial fibrosis: pathological and molecular findings of surgically resected ventricular endomyocardium. Virchows Arch. 2008;453(3):233-42. PMid:18762973. http://dx.doi.org/10.1007/s00428-008-0652-3.

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Correspondence
Fernando Peixoto Ferraz de Campos
Internal Medicine Division - Hospital Universitário - University of São Paulo
Av. Prof. Lineu Prestes, 2565 – Butantã – São Paulo/SP – Brazil
CEP: 05501-000
Phone: +55 (11) 3091-9275
fpfcampos@gmail.com