Endomyocardial disease: a case report

Endomiyokardiyal hastalık: Olgu sunumu

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Endomyocardial disease is a form of restrictive cardiomyopathy of unknown etiology, which occurs most commonly in tropical and subtropical areas. It is characterized by the formation of endomyocardial fibrosis of the apical and subvalvular regions of one or both ventricles. A 29-year-old male patient was admitted with restrictive cardiomyopathy and decompensated heart failure. Telecardiography showed cardiomegaly and right pleural effusion. Transthoracic echocardiography revealed preserved left ventricular systolic functions, biatrial dilatation, apical obliteration of both ventricles, increased endocardial echoreflectivity, and pericardial effusion. The right ventricular outflow tract was dilated. There was no endocardial thickening in this region. Doppler examination showed grade 3 mitral and tricuspid regurgitation. Ventriculograms showed apical obliteration of both ventricles, marked decrease in the size of the right ventricular cavity, significant dilatation of the right ventricular outflow tract and both atria, and severe mitral and tricuspid regurgitation. Laboratory findings showed no hypereosinophilia. Hepatic congestion, splenomegaly, and ascites were noted on abdominal ultrasonography. Following cardiac catheterization, the patient was placed on the waiting list for cardiac transplantation.

Key words: Cardiomyopathies; echocardiography; endomyocardial fibrosis; heart failure.

Endomiyokardiyal hastalık, sıklıkla tropik ve subtropik bölgelerde görülen, etyolojisi bilinmeyen, bir veya her iki ventrikülün apikal ve subvalvüler bölgesinin endomiyokardiyal fibrozisi ile karakterize bir restriktif kardiyomiyopati türüdür. Yirmi dokuz yaşındaki erkek hasta restriktif kardiyomiyopati ve dekompanse kalp yetersizliği nedeniyle hastaneye yatırıldı. Telekardiyografide kardiyomegali ve sağ plevral efüzyon izlendi. Transtorasik ekokardiyografide korunmuş sol ventrikül sistolik fonksiyonları, biatriyal genişleme, sağ ve sol ventrikül apikalinde obliterasyon, artmış endokardiyal ekoreflektivite ve perikardiyal efüzyon izlendi. Sağ ventrikül çıkış yolunda genişleme vardı, endokardiyal kalınlaşma yoktu. Doppler incelemede üçüncü derece mitral ve triküspit yetersizliği saptandı. Ventrikülografide, her iki ventrikülde apikal obliterasyon, sağ ventrikül kavitesinde belirgin küçülme, sağ ventrikül çıkış yolunda, sağ ve sol atriyumda belirgin genişleme ve ciddi mitral ve triküspit yetersizliği izlendi. Laboratuvar incelemelerinde hipereozinofili yoktu. Abdominal ultrasonografide hepatik konjesyon, splenomegali ve assit saptandı. Hasta kardiyak kateterizasyon ile değerlendirildikten sonra kardiyaktransplantasyon listesine alındı.

Anahtar sözcükler: Kardiyomiyopati; ekokardiyografi; endomiyokardiyal fibrozis; kalp yetersizliği.

Endomyocardial disease (EMD) is a form of restrictive cardiomyopathy of unknown etiology, which occurs most commonly in tropical and subtropical areas, and which is mostly seen in young adults with low sociocultural levels. Endomyocardial disease was first defined by Davies[1] in Uganda in 1948. Although it is seen mostly in equatorial belt of Africa, several cases have been reported in South America, Asia, USA and Turkey.[2,3] The disease is characterized by the formation of endocardial and partly myocardial fibrous thickening of the apical and subvalvular regions of one or both ventricles, leading to restrictive physiology by blocking the ventricular filling. Both ventricles are involved in most cases, whereas the left or right ventricle only is affected rarely.[2] In this article, a young male patient with suspected EMD who visited our hospital due to decompensated heart failure was presented.

CASE REPORT

A 29-year-old male patient visited our hospital due to dyspnea for the past 2 years. The patient was diagnosed with restrictive cardiomyopathy by transthoracic

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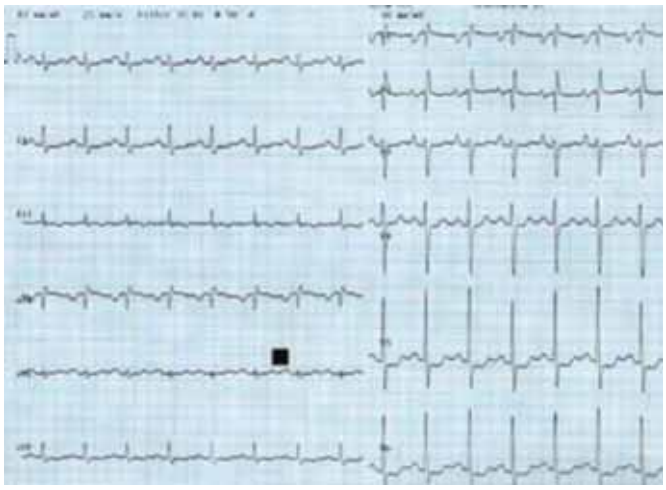

Figure 1. Normal sinus rhythm, biatrial dilatation, partial right bundle branch block and non-specific ST-T changes are seen on the surface electrocardiogram.

echocardiography (TTE) and cardiac catheterization. Treatment with aspirin, digoxin, beta-blocker, diuretics and spironolactone was initiated. The patient was admitted with an increase in dyspnea, swelling in the abdomen and legs lately and was hospitalized with decompensated heart failure. He had no specific characteristics except a history of post-traumatic epilepsy caused by head trauma and chronic diarrhea. His physical examination showed the followings: blood pressure 110/60 mmHg, pulse 84/min, respiration 16/min; venous filling in the neck, decrease in respiratory sounds at the base of the right lung, fine rales at both lung bases, a-2/6-degree pansystolic murmur in left lower parasternal and apical regions, ascites, hepato-splenomegaly and pretibial edema.

Surface electrocardiogram demonstrated normal sinus rhythm, biatrial dilatation, partial right bundle branch block and non-specific ST-T changes (Figure 1). Telecardiography showed cardiomegaly and right pleural effusion. The B-mode images of the transthoracic echocardiography revealed preserved left ventricular systolic functions, imbalanced biatrial dilatation, apical obliteration of both ventricles, increased endocardial echoreflectivity, and pericardial effusion (Figure 2a). The right ventricular outflow tract was dilated; however, there was no endocardial thickening. Color Doppler examination showed grade 3 mitral and tricuspid regurgitation, whereas pulsed wave Doppler revealed diastolic mitral (Figure 2b) and tricuspid regurgitation. In the assessment of diastolic functions, transtricuspid flow sample was found to be consistent with a restrictive type of filling. A diastolic forward flow in pulmonary artery was observed as a finding of restrictive right ventricular physiology (Figure 2c). In the transmitral flow

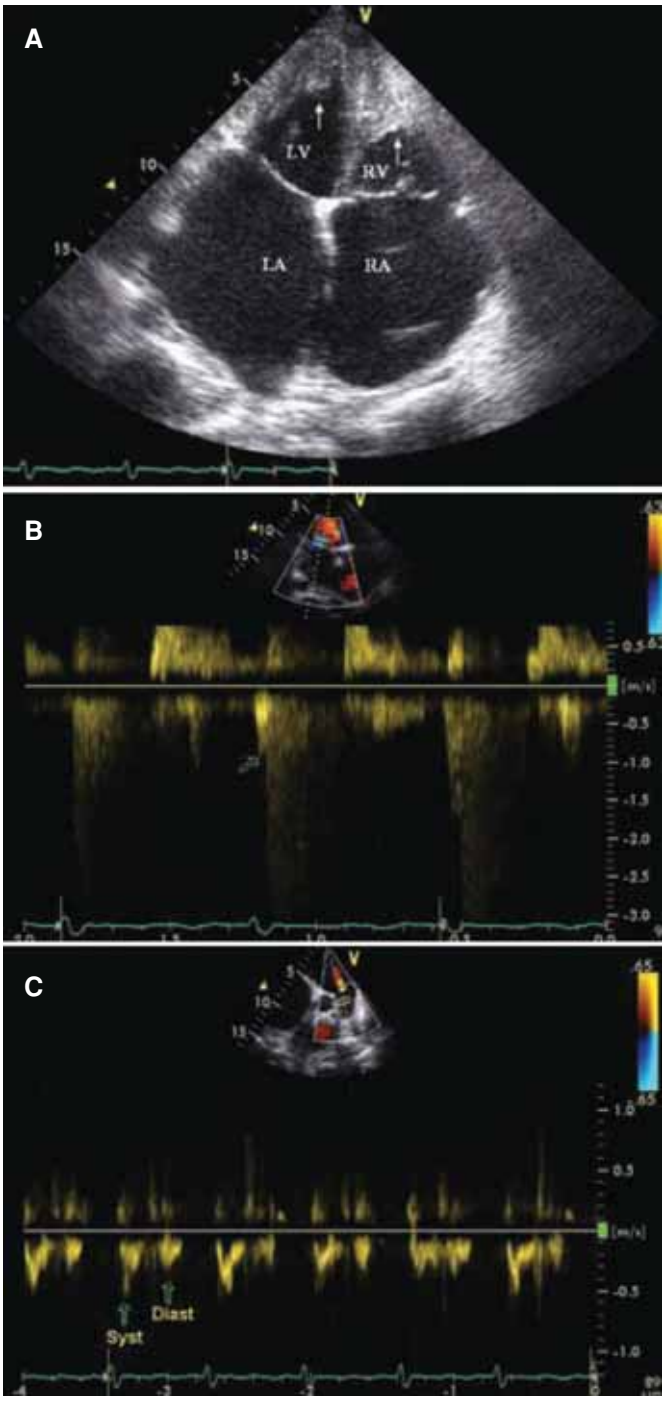

Figure 2. (A) A two-dimensional echocardiogram showing apical obliteration of both ventricles and increased echoreflectivity (arrows) in 4 apical spaces. **(B)** Pulsed wave Doppler showing low rate diastolic mitral regurgitation flow (arrows) immediately at the beginning of mitral regurgitation. **(C)** In addition to the normal systolic forward flow (Syst) monitored by pulsed wave Doppler through the pulmonary artery, a diastolic forward flow (Diast) of restrictive right ventricular filling physiology is observed. RA: right atrium; RV: right ventricle; LA: left atrium; LV: left ventricle.

sample the E/A rate was 2.4, delay time was 98 msc, isovolumic relaxation time was 44 msc, and no change was observed in the rate of E/A with Valsalva maneu-

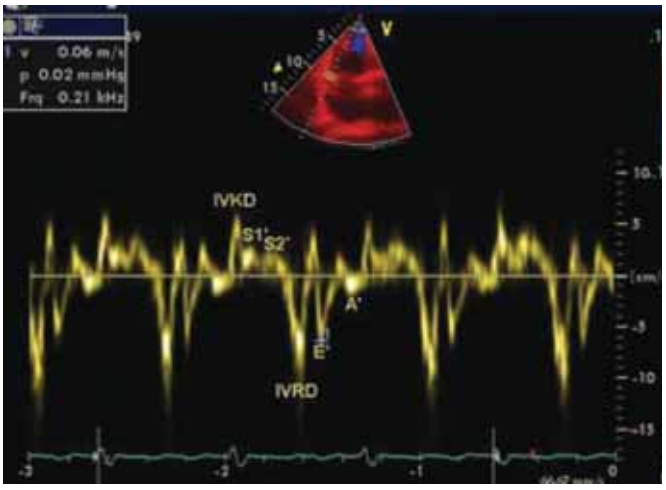

Figure 3. In the tissue Doppler analysis of the lateral mitral annulus, E' velocity was found below 8 cm/sec suggesting the diagnosis of restrictive cardiomyopathy. IVKD: isovolumetric contraction wave; IVRD: isovolumetric relaxation wave.

ver (irreversible restrictive sample). Tissue Doppler imaging showed that lateral mitral annular E' velocity had decreased (6 cm/sec) (Figure 3); E/E' rate was 23 and was thought to be suggestive of an increase in left ventricular end-diastolic volume. Evaluation of the right and left ventriculographies showed apical obliteration of both ventricles, marked decrease in especially the right ventricular cavity, significant dilatation of the right ventricular outflow tract and both atria, and severe mitral and tricuspid regurgitation (Figure 4). Laboratory findings showed mild hyperbilirubinemia (total bilirubin 2.75 mg/dL; normal range 0.00-1.10 mg/dL), increased direct bilirubin (1.27 mg/dL; normal range 0.00-0.30 mg/dL) and hypoalbuminemia (2.5 g/dL; normal range 3.4-5.2 g/dL). The complete blood count revealed white blood cell 8.300/μL (normal range 3800-10.600/μL) and eosinophil rate 0.5% (normal range 0.1-6.0%). No serial increase in eosinophil levels was observed in the peripheral smear and bone marrow analysis. Following the identification of hepatic congestion, splenomegaly, and ascites on abdominal ultrasonography, the diagnosis of carcinoid syndrome, gluten-sensitive enteropathy, parasitosis and inflammatory bowel disease were excluded in the patient's diarrheal etiology. The gingival and duodenal biopsy results were both negative for amyloid. The patient whose findings of heart failure regressed following medical therapy was assessed for cardiac transplantation, and the catheterization performed demonstrated mean right atrial pressure as 13 mmHg (normal range 1-5 mmHg), systolic pulmonary arterial pressure 60 mmHg (normal range 15-30 mmHg) and pulmonary vascular resistance <4 Wood units. The pressure results demonstrated that there was an increase in the end-diastolic volume of

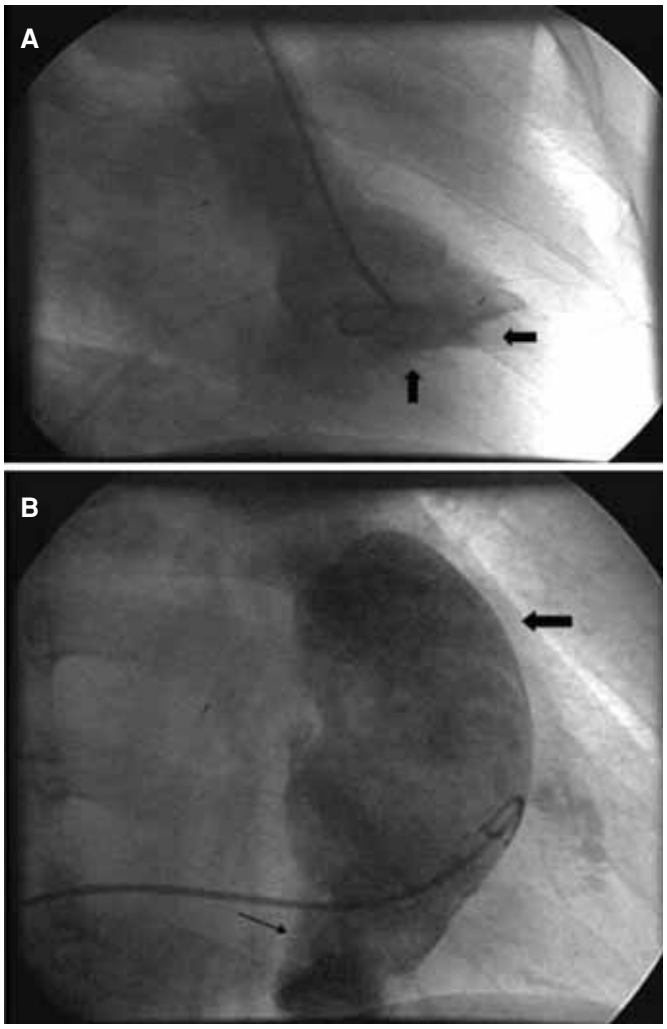

Figure 4. (A) Ventriculography showing significant obliteration in the left ventricular apical region (arrows). **(B)** Ventriculography showing significant shrinkage in right ventricular cavity with dilatation in right ventricular exit pathway.

both ventricles, a >5 mmHg difference between the left and right ventricle end-diastolic pressure and existence of a square root pattern (Figure 5) was observed. The patient was scheduled for cardiac transplantation.

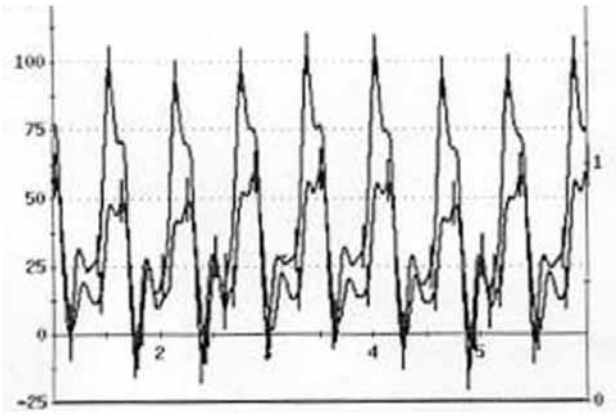

Figure 5. Square root finding in the simultaneous pressures of the right and left ventricle records.

DISCUSSION

It was previously considered that there were two variants of EMD namely endomyocardial fibrosis (EMF) and Loeffler endocarditis. Endomyocardial fibrosis is a condition which is most commonly seen in tropical areas, often affects children and young adults, and which is not always accompanied by marked eosinophilia. On the other hand, Loeffler endocarditis is a condition with a more aggressive clinical presentation, characterized by hypereosinophilia, thromboembolic events and disseminated arteritis, and is predominantly seen in the male gender and in those living in temperate climates. The common characteristics of both variants are histologically confirmed endocardial fibrosis and the presentation of eosinophilia in some cases with EMF.[4] In later years, these findings led to an hypothesis suggesting EMF and Loeffler endocarditis incorporated in a single disease with different stages, whose bases is formed by the toxic effects of eosinophils.[5] This hypothesis suggested that the initial hypereosinophilia with toxic effects led to myocardial necrosis and disseminated arteritis (necrotic stage), and later on to a thrombotic stage in which endocardial thickening and thrombus formation were more apparent following regression of eosinophilia and myocarditis, and the process eventually ended with a fibrotic stage in which fibrosis was more apparent. Currently, however, this process is considered only for cases with EMD living in a temperate climate, whereas endemic EMF is deemed a separate disease associated with different etiologic factors (for example, high cerium and low magnesium levels).[2] Findings of our case support the diagnosis of EMD in the fibrotic stage due to its presence in temperate climate and the abscence of hypereosinophilia.

The differential diagnosis of endomyocardial disease includes rheumatic valve disease, constrictive pericarditis, other causes of restrictive cardiomyopathy, apical hypertrophic cardiomyopathy, dilated cardiomyopathy, Ebstein's anomaly of the tricuspid valve, and apical thrombus.[6] Increased endocardial thickness and echoreflectivity, apical fibrothrombotic obliteration, atrioventricular valve regurgitation due to papillary muscle involvement, biatrial dilatation and normal-small sized ventricle observed in TTE are generally sufficient for the diagnosis of EMD.[7] Visualization of both systolic and diastolic obliteration in the apical region of the involved ventricles revealed by ventriculography in suspected cases may help in the diagnosis. As reported in many cases, an additional finding in our case was the dilated right ventricular exit pathway which was preserved from the fibrotic process.[8] The diagnostic characteristics of EMD, namely endocardial thickening with collagen, fibrosis and thrombus would clearly be displayed if the endomyocardial biopsy material is collected properly; however, biopsy is not generally considered to be obligatory for diagnosis.[6]

Clinically, the most distinguished characteristic of EMD is invisible pretibial edema, despite ascites being very apparent. This imbalanced ascites is explained by a hypothesis suggesting that systemic fibrosis also involves peritoneum.[9] Patients with pretibial edema should be investigated for exudative enteropathy and hypoalbuminemia. In our case, invisible ascites was explained by chronic diuretic treatment, while unapparent pretibial edema was associated with hypoalbuminemia.

There is no definitive treatment for endomyocardial disease and the prognosis of the disease is poor. In addition to the treatment of conventional heart failure, it was shown that corticosteroids relieved the symptoms and prolonged the life span in patients with hypereosinophilia.[2] Hydroxurea, interferon-alpha, imatinib mesylate and mepolizumab can be used in patients resistant to steroids.[3] Surgical endocardectomy (alone or together with valve replacement) is another alternative for patients in the fibrotic stage.[10,11] With promising short-term results, cardiac transplantation can also be performed successfully in selected patients.[12]

REFERENCES

1. Davies JN. Some considerations regarding obscure diseases affecting the mural endocardium. Am Heart J. 1960;59:600-31.
2. Wynne J, Braunwald E. The cardiomyopathies. In: Zipes DP, Libby P, Bonow RO, Braunwald E, editors. Braunwald's heart disease: a textbook of cardiovascular medicine. 7th ed. Philadelphia: Elsevier Saunders; 2005. p. 1659-96.
3. Uçar O, Gölbaşı Z, Yıldırım N. Two cases of endomyocardial disease with hypereosinophilia in Turkey. Eur J Echocardiogr 2005;6:379-81.
4. Patel AK, D'Arbela PG, Somers K. Endomyocardial fibrosis and eosinophilia. Br Heart J 1977;39:238-41.
5. Andy JJ, Ogunowo PO, Akpan NA, Odigwe CO, Ekanem IA, Esin RA. Helminth associated hypereosinophilia and tropical endomyocardial fibrosis (EMF) in Nigeria. Acta Trop 1998;69:127-40.
6. Hassan WM, Fawzy ME, Al Helaly S, Hegazy H, Malik S. Pitfalls in diagnosis and clinical, echocardiographic, and hemodynamic findings in endomyocardial fibrosis: a 25-year experience. Chest 2005;128:3985-92.

7. Acquatella H, Schiller NB, Puigbó JJ, Gómez-Mancebo JR, Suarez C, Acquatella G. Value of two-dimensional echocardiography in endomyocardial disease with and without eosinophilia. A clinical and pathologic study. Circulation 1983;67:1219-26.
8. Marijon E, Ou P. Endomyocardial fibrosis in Mozambique. Clin Cardiol 2006;29:375.
9. Freers J, Mayanja-Kizza H, Rutakingi rwa M, Gerwing E. Endomyocardial fibrosis: why is there striking ascites with little or no peripheral oedema? Lancet 1996;347:197.
10. Schneider U, Jenni R, Turina J, Turina M, Hess OM. Long-term follow up of patients with endomyocardial fibrosis: effects of surgery. Heart 1998;79:362-7.
11. Mocumbi AO, Sidi D, Vouhe P, Yacoub M. An innovative technique for the relief of right ventricular trabecular cavity obliteration in endomyocardial fibrosis. J Thorac Cardiovasc Surg 2007;134:1070-2.
12. Korczyk D, Taylor G, McAlistair H, May S, Coverdale A, Gibbs H, et al. Heart transplantation in a patient with endomyocardial fibrosis due to hypereosinophilic syndrome. Transplantation 2007;83:514-6.