

Eosinophilic myocarditis presenting as acute coronary syndrome

Akut koroner sendrom olarak karşılaşılan eozinofilik miyokarditli olgu

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Summary— Eosinophilic myocarditis (EM) is a rare condition that may result from several heterogeneous eosinophilic diseases, including parasite infection, hypersensitivity reaction, vasculitis, and hypereosinophilic syndrome. Regardless of etiology, the disease may present with various cardiac conditions, such as acute coronary syndrome, heart failure, or arrhythmia. Irreversible endomyocardial fibrosis, which causes restrictive cardiomyopathy, occurs in the late phase of the disease. Early diagnosis and treatment is crucial to prevent disease progression. Presently described is a case of EM presenting as acute coronary syndrome that was treated with steroids.

Özet— Eozinofilik miyokardit parazit enfeksiyonu, aşırı duyarlılık reaksiyonu, vaskülit ve hipereozinofilik sendrom gibi heterojen etkenlerin neden olabileceği nadir bir hastalıktır. Etiyolojik faktörden bağımsız olarak akut koroner sendrom, kalp yetersizliği ve aritmi gibi farklı kardiyak durumlar olarak karşımıza çıkmaktadır. Geri dönüşüm-süz olarak gelişen endomiyokardiyal fibroz hastalığın geç dönemlerinde restriktif kardiyomiyopatiye yol açmaktadır. Hastalığın ilerlemesini önlemek için erken tanı ve tedavi önemlidir. Bu yazıda, akut koroner sendrom olarak karşımıza çıkan ve steroid ile tedavi edilen eozinofilik miyokarditli bir olguyu sunmaktayız.

The most fatal complication of hypereosinophilia is eosinophilic myocarditis (EM). Causes include parasite infection, vasculitis, hypersensitivity reaction, and hypereosinophilic syndrome. Regardless of etiology, the disease may present with various cardiac conditions. EM manifesting as acute coronary syndrome has rarely been reported in the literature. Described herein is a case of EM with non-ST segment elevation myocardial infarction that was treated with steroids. Etiology, pathology, clinical manifestation, diagnosis, and management are discussed.

CASE REPORT

A 68-year-old woman was admitted to emergency department with typical angina and orthopnea symptoms ongoing for 2 days. She had also experienced fatigue for 2 weeks. There was no history of heart disease, but she had history of hypertension, type 2 diabetes mellitus, hyperlipidemia, and asthma for 4 years, as well as several episodes of Hashimoto's thyroiditis. She was taking inhaled steroid/long-acting

β_2 mimetic, oral irbesartan/hydrochlorothiazide, amlodipine, simvastatin, metformin, and montelukast. To reduce acute asthma attacks, she had twice been given omalizumab 150 mg (4 and 2 weeks prior). Physical examination revealed crackles in bilateral lower lungs and apical 3/6 systolic murmur, and bilateral minimal pretibial edema. Electrocardiography revealed sinus rhythm with 1 mm ST segment depression in leads V3 to V6. Troponin T level was 8.3 ng/mL (upper limit: 0.014 ng/mL). Creatinine and hemoglobin values were normal. Patient was diagnosed as non-ST segment elevation myocardial infarction. Echocardiography was performed at time of coronary care admission. Septum and inferior walls were hypokinetic, and ejection fraction was 45% (Figure 1a). Severe mitral regurgitation was observed and systolic pulmonary arterial pressure was 55 mmHg. Oral acetylsalicylic acid, clopidogrel, and intravenous furosemide were added to her other

Abbreviations:

CMR	Cardiac magnetic resonance
EM	Eosinophilic myocarditis
CSS	Churg-Strauss syndrome
HES	Hypereosinophilic syndrome

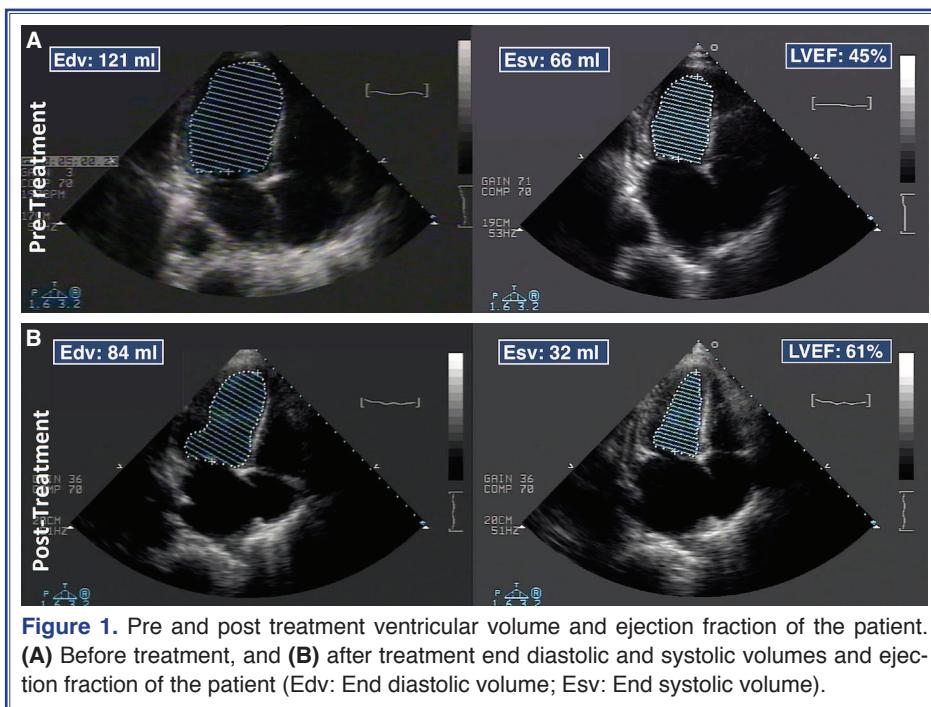
Received: August 30, 2016 Accepted: December 12, 2016

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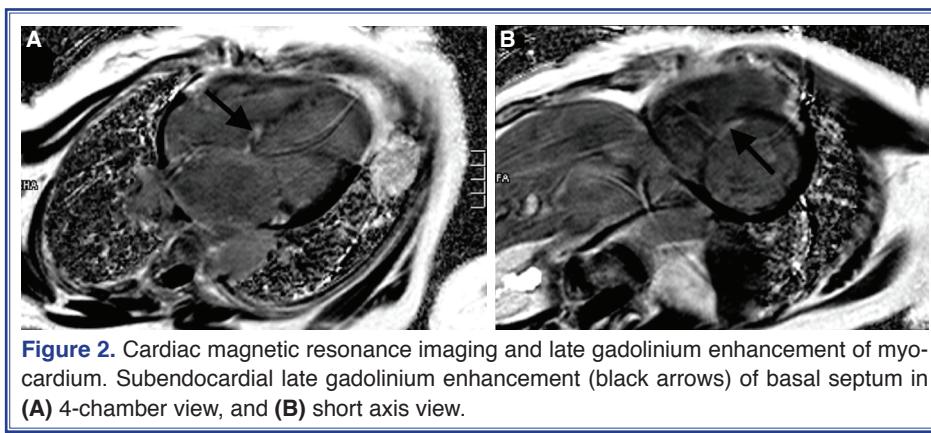
medications. Coronary angiography showed normal coronary arteries. At time of hospital admission, blood count revealed leukocytosis (27,100 cells/ μ L) with 46.2% (12,520 cells/ μ L) eosinophilia.

EM was suspected and cardiac magnetic resonance (CMR) imaging was performed. Left ventricular regional systolic dysfunction, severe mitral regurgitation, heterogeneously late gadolinium enhancement in subendocardium of septum and inferior walls was observed (Figure 2).

Endomyocardial biopsy was not performed due to risk of ventricular perforation and low sensitivity for EM.

Clinical and imaging findings confirmed our initial diagnosis of EM. Secondary causes of hypereosinophilia were evaluated and bone marrow biopsy showed increased number of eosinophils, but was negative for malignancy. Serology and stool studies for *Toxocara*, *Fasciola*, *Trichinella*, and hydatid cyst were negative. Tests for antinuclear and anti-neutrophil cytoplasmic antibodies were negative, and there were no signs of vasculitis, neuropathy, or pulmonary infiltration.

After excluding malignancy, hypersensitivity, parasite infection, and vasculitis, patient's final diagnosis was hypereosinophilic syndrome (HES).



Methylprednisolone 40 mg intravenous bolus was administered, followed by 32 mg per day oral for 10 days. Patient's clinical condition improved, ST segment depressions returned to isoelectric line on electrocardiography. Control echocardiography showed mild hypokinesia in base of inferior wall and inferior septum. Ejection fraction was 55%, with mild and mitral regurgitation. Eosinophil count had decreased from 12,250 cells/ μ L (45%) to 120 cells/ μ L (1.3%). Steroid doses were tapered after 28 days of treatment. at the end of treatment, ejection fraction was 61% without regional wall dysfunction (Figure 1b).

DISCUSSION

EM is a rare form of myocarditis. EM was reported in 0.5% of unselected autopsy series and recent studies have demonstrated incidence of 2.8% to 7.4% in explanted hearts of transplantation recipients who had EM.^[1-3] It is characterized pathologically by myocardial inflammation with focal or diffuse eosinophilic infiltration, and is often associated with elevated peripheral eosinophil count.^[4]

Several etiological factors are associated with EM such as drug hypersensitivity, vasculitis (such as Churg-Strauss syndrome [CSS]), infection, malignancy, and HES.

Although previous definitions required 6-month persistence of eosinophilia, today HES is defined as elevated peripheral eosinophilia count (>1500 cells/ μ L) with eosinophil-mediated organ damage or disorder in the absence of other possible causes.^[5] No other cause of hypereosinophilia was found in our patient. Cardiac involvement occurs in 50% of patients with HES and has high mortality and morbidity. Estimated 5-year mortality is about 30% and depends on the progression of endomyocardial fibrosis.^[6]

Eosinophilic heart disease has 3 stages: the initial stage is eosinophilic infiltration of the myocardium and apoptosis or necrosis of myocytes.^[4] The second phase is thrombus formation over the affected myocardial sites. The final stage is fibrotic scarring of the endocardium, which results in restrictive cardiomyopathy.^[4,6]

Eosinophils also infiltrate the coronary arteries and cardiac nerves. Eosinophilic basic proteins and other vasoactive cytokines from eosinophils may stimulate coronary smooth muscle spasm. Tissue destruction

caused by eosinophils may also predispose to coronary dissection, aneurysm, and thrombosis.^[7]

EM may cause different types of cardiac conditions: acute coronary syndrome, heart failure, cardiogenic shock, atrial or lethal ventricular arrhythmia, pericardial effusion, or pericarditis. Patients may present with a wide spectrum of symptoms, such as chest pain, shortness of breath, palpitations, fatigue, cardiogenic shock, skin rash, bronchial asthma, rhinitis, or urticaria.^[4]

Echocardiographic findings of EM change in different stages of the disease. At necrotic stage, increased ventricular wall thickness, dilated chamber diameters, valvular pathology and decreased ejection function may be seen, but in early phase of disease, ventricular functions may be normal. Thrombotic stage is second, and intraventricular, most often left ventricular apical, thrombus may be seen. In last fibrotic stage, due to endomyocardial fibrosis, restrictive cardiomyopathy signs may be seen.^[4]

CMR is currently the best noninvasive tool for diagnosis of EM. Diffuse or patchy (unrestricted to coronary arterial territory) subendocardial late gadolinium enhancement with involvement of the papillary muscles is pathognomonic finding of the disease. CMR may also help targeting the affected regions for endomyocardial biopsy.^[8]

Endomyocardial biopsy can definitively reveal eosinophilic infiltration of the myocardium. However, it has sensitivity of 50%, and disadvantages due to the procedural technique of ventricular perforation or pneumothorax (for jugular approach). Endomyocardial biopsy should be reserved for patients who have confusing noninvasive test results with strong clinical suspicion.

Management of EM includes conventional treatment for heart failure, arrhythmia, and immunosuppressive therapy for underlying eosinophilia. Additional treatment for underlying disease is also needed, such as antiprotozoal treatment for parasitic infection or withdrawal of possible drugs that cause hypersensitivity reaction.

Steroids are the mainstay of CSS treatment. For non-CSS EM patients, evidence for steroid treatment is based on case reports, case series, and non-randomized studies. Starting dose of steroid therapy is 1mg/

kg per day of prednisolone or equivalent. When clinical response is achieved (about 1 or 2 weeks), drug dose is slowly tapered down. For more advanced disease, steroid therapy can be combined with azathioprine or cyclophosphamide.^[9] New interleukin 5-targeted therapeutic strategies, such as mepolizumab or benralizumab, have been suggested for hypereosinophilia-associated diseases. Initial study results are promising.^[10,11]

EM is the most lethal cardiac complication of HES. Early diagnosis is crucial; if untreated, it leads to irreversible endomyocardial fibrosis and restrictive cardiomyopathy in advanced stages of the disease. Therefore, determining etiology of eosinophilia and providing treatment in early stages of disease is important in order to improve long-term outcomes.

Conflict-of-interest: None declared.

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Keywords: Acute coronary syndrome; eosinophilic myocarditis; heart failure.

Anahtar sözcükler: Akut koroner sendrom; eozinofilik miyokardit; kalp yetersizliği.