OLGU SUNUMU/CASE REPORT
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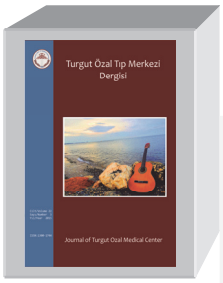

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Myocarditis Associated with Mesalazine: A Case Report

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Abstract
Acute myocarditis is a life-threatening inflammatory disease of the heart muscle. It usually occurs after a viral infection and it is often asymptomatic. Mesalazine is commonly used for the treatment of inflammatory bowel disease. Mesalazine rarely causes acute myocarditis, but the exact mechanism is unclear. A 32-year-old female patient using mesalazine with a diagnosis inflammatory bowel disease was admitted to the emergency department with shortness of breath. The patient showed signs of acute decompansated heart failure. Bedside echocardiography examination showed a reduced left ventricular systolic function. The patient was followed with a diagnosis of fulminant myocarditis and mechanical ventilation and inotropic support was started. The patient has dramatically improved after stopping treatment of mesalazine. Myocarditis due to any drug use should be taken into consideration in patients receiving mesalazine therapy.
Key Words: Mesalazine; Myocarditis; Crohn's Disease.

Mesalazin ile İlişkili Miyokardit: Olgu Sunumu

Özet
Akut miyokardit hayatı tehdit edebilen kalp kasının inflamatuar bir hastalığıdır. Genellikle viral enfeksiyon sonrası gelişir ve sıklıkla asemptomatik seyreder. İnflamatuar barsak hastalıklarında mesalazin yaygın olarak kullanılmaktadır. Mekanizması tam olarak bilinmemekle birlikte mesalazinin akut miyokardite neden olduğu bilinmektedir. İnflamatuar barsak hastalığı tanısıyla mesalazin kullanan 32 yaşındaki bayan hasta, nefes darlığı şikayetiyle acil servise başvurdu. Hastada akut dekompanse kalp yetmezliği bulguları mevcuttu. Yatak başı ekokardiografide azalmış sol ventrikül sistolik fonksiyonları izlendi. Hasta fulminan miyokardit tanısıyla takip edildi, mekanik ventilator ve inotropik destek tedavisi verildi. Hasta mesalazin tedavisi stoplandıktan sonra dramatik bir şekilde iyileşti. Mesalazin tedavisi alan hastalarda ilaç ile ilişkili miyokardit tanısı göz önünde bulundurulması gerekmektedir.
Anahtar Kelimeler: Mesalazin; Miyokardit; Crohn Hastalığı.

INTRODUCTION

Myocarditis is defined as an inflammatory infiltration of the myocardium associated with necrosis or degeneration or both. Although most myocarditis cases are self-limiting, severe cardiac failure may develop, which may rapidly lead to death. Myocarditis may be caused by infections, chemicals, physical agents, toxins, or rheumatological diseases. In addition, myocarditis may be secondary to the use of several drugs as some drugs are already known to cause hypersensitivity myocarditis (1). We present a case of myocarditis arising due to mesalazine use in a patient with Crohn's disease.

CASE REPORT

A 32-year-old female was admitted to emergency service with shortness of breath, she was intubated due to increased hypoxemia and respiratory distress. When the patient was consulted with cardiology department, it was revealed that the patient had no history of cardiovascular disease or any associated risk factors and she had been using mesalasine for 6 months for Crohn's disease. Her physical examination revealed tachycardia, third heart sound, decreased respiratory sounds, bilateral juguler venous distension, and slight peripheral edema. Electrocardiographic examination revealed sinus tachycardia, nonspesific ST segment, and T wave changes. There were leukocytosis (16×10^3), troponin-I levels [5.2 ng/ml, normal reference values 0-1 ng/ml], inflammatory markers such as erythrocyte sedimentation rate [70, normal reference value <10], and C reactive protein [6.3 mg/L, normal reference value 0-0.3 mg/L]. The bedside echocardiography examination showed a decreased ejection fraction (EF) of 20% and the left ventricle was globally hypokinetic (Figure 1a).

Diffuse bilateral pleural effusion and cardiomegaly were detected on the computerized tomography of the thorax (Figure 2). The treatment was maintained for cardiac failure and the patient was supported with positive inotropic agents. Her mesalasine treatment was withdrawn due to possible side effect of cardiac failure of mesalasine. The case was evaluated as fulminant myocarditis and followed up with mechanic ventilation support for 6 days after which the patient was successfully extubated. Viral, bacterial, and inflammatory causes of acute fulminant myocarditis were excluded according to serological markers (Chlamydia, Mycoplasma pneumoniae, Epstein-Barr virus and Cytomegalovirus), anti-nuclear antibody (ANA), anti-

smooth muscle antibody (ASMA), anti-double-stranded deoxyribonucleic acid (Anti-dsDNA), and reumatoid factor (RF). The stool culture, which was positive for vancomycine resistant enterococcus at the time of hospitalization, was considered as nosocomial infection (or contamination). She had an apparent clinical recovery by the tenth day of the hospitalization. Transthoracic echocardiography was repeated and EF was detected to be 60% (Figure 1b). Posteroanterior chest radiograph revealed a normal cardiothoracic index with no pleural effusion and clear cardiophrenic and costophrenic angles (Figure 3). We did not detect ischemia on myocardial perfusion imaging and ischemic cardiomyopathy was, thus, excluded. The patient was discharged with maintainance therapy.

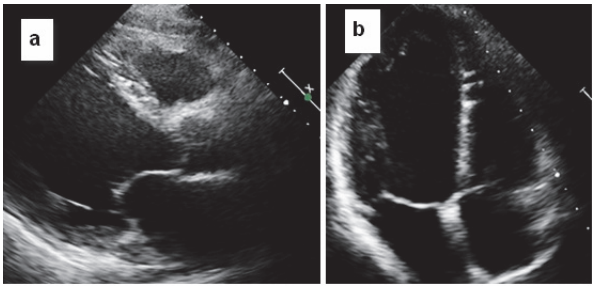

Figure 1a. Increased left ventricle diastolic diameter on parasternal short axis.
Figure 1b. Normal ejection fraction on apical 4-chamber view.

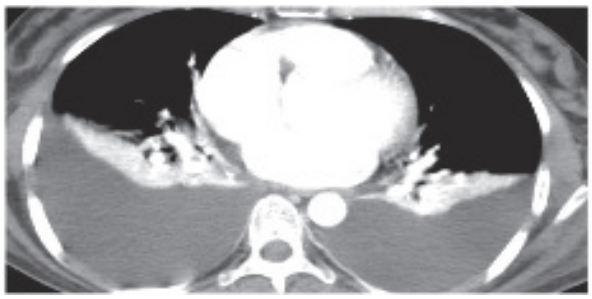

Figure 2. Bilateral massive pleural effusion, increaesed cardiothoracic index.

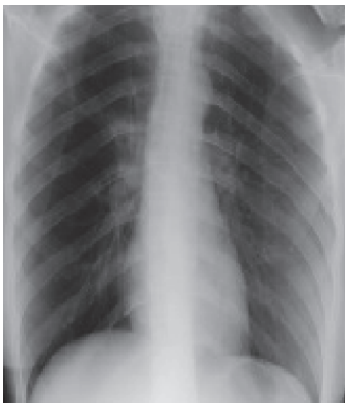

Figure 3. Normal cardiothoracic index; no pleural effusion and clear angles on chest radiograph.

DISCUSSION

Clinical manifestations of myocarditis may indicate a cruise ranging from asymptomatic period to fulminant myocarditis. Patients usually present with acute decompensated heart failure in fulminant myocarditis.

Our patient had no history of any cardiac diseases and she was in a state of acute decompensated heart failure. Complaint of dyspnea had started 5 days ago. The bedside echocardiography showed a decreased EF of 20%. The rapid clinical and laboratory improvement after the withdrawal of mesalazine gave rise to the idea of fulminant myocarditis due to mesalazine use.

The case was considered as myocarditis due to mesalazine use. Heart diseases such as pericarditis (70%) and myocarditis (10%) may accompany the inflammatory bowel disease as extraintestinal manifestations (2). Mesalazine is commonly used for the treatment of inflammatory bowel diseases. Its side effects include fever, rash, renal damage, liverdysfunction, myocarditis, nephropathy, and pancreatitis. The relationship between mesalazine and myocarditis is not clear (3). Kounis et al. explained the possible mechanism of the inhibition of cyclooxigenase-1 enzyme (COX-1) and, thus, overproduction of leucotriens which further promote an initiation of hypersensitivity reaction via eosinophil secreting factor induced by proinflammatory signals and, eventually, causing myocarditis. The relationship between mesalazine and myocarditis is thought to be due to hypersensitivity reaction rather than cytotoxic effects (2, 3). Previous studies showed eosinophilic infiltration of the myocard in mesalazine associated myocarditis in biopsy (4). Although patients with a hypersensitivity disease may develop arteritis, acute myocardial infarction rarely occurs (5). In several studies, development of giant cell myocarditis was shown hystologically in the course of otoimmune disorders such as Crohn's disease (6). Mesalazine associated eosinophilic myocarditis or giant cell myocarditis was considered in our case. Because a provocative test with etiologic agent could lead fatal damage, it was not performed (2-4). Similarly, we did not perfom an endomyocardial biopsy because the patient refused to consent to the biopsy.

In conclusion, drug induced myocarditis is a rarely observed condition. A careful history is of great importance. In a case presenting with chest pain and shortening of breath and receiving mesalazine treatment for inflammatory bowel disease, drug induced myocarditis should be taken into account. Making prior notification to patients receiving mesalazine for inflammatory bowel disease may prevent delay in reaching proper diagnosis.

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