Lamotrigine related myocarditis: case report

Lamotrijin ilişkili miyokardit: Olgu sunumu

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Summary– Myocarditis can develop secondary to several medications. Here, we report a case of myocarditis related to the use of lamotrigine. A 15-year-old boy was admitted to another hospital because of a chest pain that was sustained for 30 minutes. He was transferred to our hospital after detection of cardiac enzyme elevation. He was evaluated in our center, where electrocardiography revealed nonspecific ST elevation at inferior derivations, and the level of troponin T was found to be 0.47 ng/ml (0-0.1), while creatinin kinase MB was found to be 38 ng/ml (0-4.97). Systolic cardiac functions were normal via echocardiography. Cardiac magnetic resonance imaging showed minimal pericardial effusion and a minimal decrease in left ventricular function. He was hospitalized with the diagnosis of myocarditis. Viral and bacterial agents that can cause myocarditis were excluded via serological tests. He had been on a lamotrigine treatment due to epilepsy, and after cessation of lamotrigine, his cardiac enzyme levels returned to normal. Therefore, we diagnosed him with drug related myocarditis due to lamotrigine. If an etiology cannot be found during the evaluation of a myocarditis case, drug hypersensitivity should be considered. Changing the responsible drug for hypersensitivity may be beneficial for these patients.

Özet– Miyokardit birçok ilacın kullanımına ikincil beklenebilir. Bu yazıda, lamotrijin kullanımına bağlı gelişen bir miyokardit olgusu sunuldu. On beş yaşında erkek hastanın 30 dakika süren göğüs ağrısı nedeniyle başka bir hastaneye başvurduğu, kardiyak enzim düzeyinin yüksek gelmesi nedeniyle merkezimize sevk edildiği öğrenildi. Hastanın hastanemizde yapılan değerlendirmesinde elektrokardiyografide inferiyor derivasyonlarda özgül olmayan ST yükselmesi görüldü, kardiyak enzimlerinden troponin T 0.47 ng/ml (0-0.1), kreatinin kinaz MB 38 ng/ml (0-4.97) geldi. Ekokardiyografisinde sistolik fonksiyonlar normaldi. Kardiyak manyetik rezonans görüntülemede minimal perikart efüzyonu ve sol ventrikül işlevinde hafif azalma görüldü. Hasta miyokardit tanısıyla yatırıldı. Seroloji incelemeleri sonucu miyokardite neden olabilecek virüs ve bakteriler dışlandı. Hastanın epilepsi nedeniyle kullanmakta olduğu lamotrijin tedavisinin kesilmesiyle kardiyak enzim düzeyi normale döndü. Hastada lamotrijinin neden olduğu ilaç ilişkili miyokardit düşünüldü. Miyokardit olgusunun değerlendirilmesinde etyoloji bulunamıyorsa, ilaca aşırı duyarlılık dikkate alınmalıdır. İlacın değiştirilmesi aşırı duyarlı hastalar için faydalı olabilir.

Myocarditis is a potentially life-threatening disease with various presentations. Common viral infections are the most frequent cause of myocarditis, but other microbial pathogens, drugs, and systemic diseases have also been implicated. Drugs can cause myocardial inflammation by having either a direct toxic effect on the heart or by inducing hypersensitivity reactions.[1] Medications related with hypersensitivity myocarditis include several anticonvulsants, antipsychotics, and antibiotics. Myocarditis secondary to lamotrigine use had not been previously reported. Here, we report the case of an adolescent boy diagnosed with lamotrigine related myocarditis.

Abbreviations:

ECG	*Electrocardiography*
MR	*Magnetic resonance*

CASE REPORT

A 15-year-old boy was admitted to the hospital because of a chest pain he sustained for 30 minutes. He

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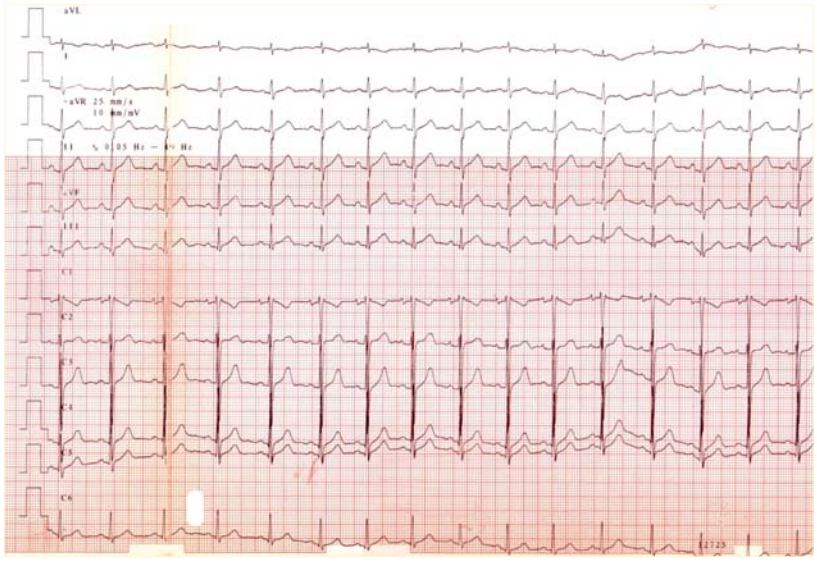

Figure 1. Patients' electrocardiography.

was transferred to our hospital after detection of cardiac enzyme elevation (Troponin I: 4.7 ng/ml, normal range; 0-0.5 ng/ml). His physical examination was normal. Electrocardiography (ECG) revealed non-specific ST elevation at inferior derivations (Fig. 1). His level of troponin T was 0.47 ng/ml (reference range, 0-0.1 ng/ml), myoglobin was 22.6 ng/ml (reference range, 28-72 ng/ml), creatinin kinase MB was 38 ng/ml (reference range, 0-4.97 ng/ml), white blood cell at common blood count was 12700 (no eosinophilia at blood smear), erythrocyte sedimentation rate was 3 mm/hr (0-25), CRP was 0.304 mg/dl (0-0.5). The remaining biochemical tests were normal. Systolic cardiac functions were normal at echocardiography. He was hospitalized with suspicion of myocarditis.

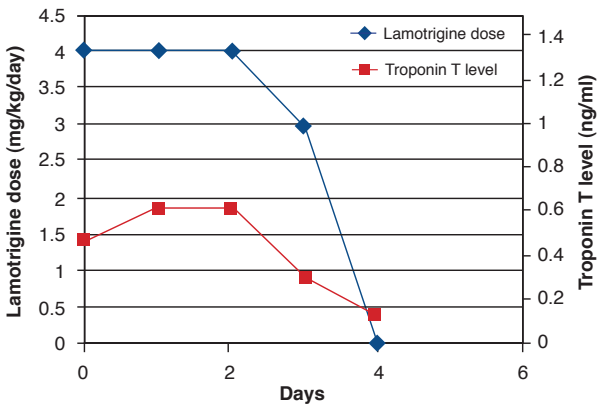

Figure 2. Lamotrigine dose and troponin T level relation.

The following day, his troponin level increased to 0.619 ng/ml. Cardiac magnetic resonance (MR) imaging showed minimal pericardial effusion, and a minimal decrease in left ventricular function. There was no contrast uptake during his MRI. His enterovirus antigens, burucella, salmonella, and borrelia burgdorferia serologies were negative. The patient had been taking lamotrigine (4 mg/kg/day) for one year because of generalized tonic seizures. At the third day of hospitalization, his troponin T level was 0.63 ng/ml. Drug related myocarditis was suspected, so his lamotrigine dose was reduced to 3 mg/kg/day. The following day, his troponin T level was reduced to 0.313 ng/ml. Lamotrigine treatment was stopped and replaced with valproic acid, and the following day his troponin level was further reduced to 0.14 ng/ml (Fig. 2). The patient was discharged with orders to continue valproic acid treatment. Two weeks later, the patient was well, and his cardiac enzyme levels were within the normal range.

DISCUSSION

Clinical presentation of myocarditis in older children includes chest pain, abdominal pain, myalgias, fatigue, cough, and edema.[1] Diagnosis is performed with a combination of clinical, laboratory, and imaging results. Our patient's chest pain, non-specific ECG changes, and elevated cardiac markers suggested a cardiac pathology. An MRI on our patient did not reveal any intensity increase, but MRI can often reveal

the presence of left ventricular dysfunction or pericardial effusion, which provides supportive evidence for myocarditis.[2] There are no specific echocardiographic features of myocarditis, but the most important role of echocardiography during myocarditis evaluation is to rule out other causes that may be affecting the heart.[1] Minimal pericardial effusion was detected via MRI. However, echocardiography did not show any pericardial effusion, so our patient's clinical status was not correlated with pericarditis. Increased serum concentrations of troponin I or troponin T are more common than increased levels of creatinine kinase or creatinine kinase-MB in both adults and children with acute myocarditis. In children presenting with acute myocarditis, troponin T has been reported to have a specificity of 83% and a sensitivity of 71%.[3] Our patient's clinical, laboratory, and imaging results supported the diagnosis of acute myocarditis. We tested the patient for common bacterial and viral causes of myocarditis, but all were negative, and patient's clinical testing did not reveal any autoimmune diseases. Our diagnosis of drug hypersensitivity myocarditis was supported since the patient had a positive response to drug cessation and did not have any other myocarditis etiologies.

Lamotrigine has been approved for use since 1992. It works by inhibiting voltage activated sodium channels, and possibly calcium channels, thereby preventing the release of excitatory neurotransmitters, particularly glutamate.[4] The most common side effect is a skin rash that can progress to Steven Johnson Syndrome.[5] Lamotrigine, like other anticonvulsants, has been known to cause a hypersensitivity syndrome characterized by fever, rash, and lymphadenopathy with internal organ involvement.[6] To our knowledge, there have not been any case reports with lamotrigine related myocarditis, but there are three adverse effect reports presenting as myocarditis at the Drug Information Portal.[7] Development of drug hypersensitivity myocarditis usually occurs within days to weeks of treatment initiation, but may occur within hours to months, and peripheral eosinophilia may or may not be present.[8] Our case developed myocarditis months after initiation without eosinophilia. Drug induced hypersensitivity reactions often respond to withdrawal of the offending medication, as occurred in our case. If a patient treated with lamotrigine presents with symptoms of myocarditis and the etiology cannot be shown, it should be remembered that changing the antiepileptic drug may be beneficial.

Conflict-of-interest issues regarding the authorship or article: None declared

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Key words: Acute disease; cardiomyopathy/etiology; child; diagnostic imaging; heart failure; myocarditis/complications/diagnosis/etiology/therapy; troponin T.

Anahtar sözcükler: Akut hastalık; kardiyomiyopati/etyoloji; çocuk; tanısal görüntüleme; kalp yetersizliği; miyokardit/komplikasyonlar/tanı/etyoloji/tedavi; troponin T.