Statin Induced Myopathy A Patient With Multiple Systemic Diseases

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ABSTRACT

Hydroxymethylglutaryl-coenzyme A reductase inhibitors (statins) are the most successful class of drugs for the treatment of hypercholesterolaemia and dyslipidaemia. However, the popular profile of statins in terms of efficacy has been maligned by their adverse effects. Statin induced myopathy, which can be seen at any time during the course of therapy, is a clinically important cause of statin intolerance and discontinuation. When a patient with multiple systemic diseases who use numerous medications represent with myalgia and muscle cramps, statin induced myopathy may not be remembered at first. We present a patient with multiple systemic diseases, alcohol and morphine abuse in whom myopathy developed. After exclusion of other etiologies, we concluded that myopathy was related to statin therapy.

Key Words: Statins, myopathy, statin induced myopathy, drug induced myopathies.

ÖZET

Çoklu Sistemik Hastalığı Olan Bir Hastada Statine Bağlı Miyopati

Hidroksimetilglutaril-koenzim A redüktaz inhibitörleri (statinler) hiperkolesterolemi ve dislipidemi tedavisinde en başarılı ilaç sınıfıdır. Ancak, statinlerin etkinlik yönünden popüler profilleri yan etkiler dolayısıyla gölgelenir. Tedavinin herhangi bir zamanında ortaya çıkabilen statine bağlı miyopati, klinikte statin intoleransının ve tedavinin kesilmesinin önemli bir nedenidir. Çoklu sistemik hastalığı ve ilaç kullanım öyküsü bulunan bir hasta, kas ağrıları ve krampları tariflediğinde statine bağlı miyopati hemen akla gelmeyebilir. Bu yazıda çoklu sistemik hastalığı bulunan, alkol ve morfin kullanan ve miyopati gelişen bir hasta sunulacaktır. Diğer olası nedenler dışlandıktan sonra, miyopatinin statin ilişkili olduğu kararına varılmıştır.

Anahtar Kelimeler: Statin, miyopati, statine bağlı miyopati, ilaç ilişkili miyopatiler.

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INTRODUCTION

Hydroxymethylglutaryl-coenzyme A (HMG-coA) reductase inhibitors (statins) represent the most successful class of drugs for the treatment of hypercholesterolaemia and dyslipidaemia implicated in the pathogenesis of coronary heart disease and atherosclerosis. However, the popular profile of statins in terms of efficacy has been maligned by their adverse events (1). Statin-related myopathy is a clinically important cause of statin intolerance and discontinuation. The spectrum of statin-related myopathy ranges from common but clinically benign myalgia to rare but life-threatening rhabdomyolysis. Observational studies suggest that myalgia can occur in up to 10% of persons prescribed statins, whereas rhabdomyolysis continues to be rare. The mechanisms of statin-related myopathy are unclear (2). Rhabdomyolysis is a rare but idiosyncratic muscle wasting disorder of different etiologies. Statin-asso-

ciated rhabdomyolysis causes skeletal muscle injury by self-perpetuating events leading to fatal irreversible renal damage through a series of biochemical reactions (1). We present a patient with multiple systemic diseases, alcohol and morphine abuse in whom myopathy developed. After exclusion of other etiologies, we concluded that myopathy was related to statin therapy.

CASE REPORT

A 66-year-old man with a history of chronic obstructive pulmonary disease (COPD) and congestive heart failure of ischemic origin was hospitalized because of dyspnea and peripheral edema. He was thought to have decompensated heart failure and diuretic infusion was performed under close supervision for fluid and electrolyte imbalance. Bronchodilator, steroid and empirical antibiotherapy was planned for exacerbation of COPD. Anticoagulation was also carried out for the management of paroxismal atrial fibrillation. He had no history of diabetes, but fasting blood glucose levels in the follow-up were high and metformin was also added to the treatment. Symptoms of dyspne and peripheral edema regressed and significant electrolyte imbalance didn't occur. He complained about myalgia, paresis, paresthesia and muscle cramps for one year and these symptoms progressed during hospitalization. He had a history of alcohol and morphine abuse for more than 10 years and was using venlafaxine. Therefore we consulted a neurologist by means of alcoholic myopathy. Serum muscle enzymes (creatine kinase, lactate dehydrogenase, aspartat aminotranspherase) and uric acide levels were high. Electrolytes (P, Mg, Na, Cl, K, Ca), serum vitamin B12 and folic acide levels were in normal ranges. An electromyography was performed but no findings suggested motor neuron disease. Thyroid hormones and cortisone levels were also normal excluding an endocrine myopathy. Although laboratory examinations didn't indicate any abnormality about the cause of his muscle cramps, elevation in serum muscle enzymes continued. Upon consultation with rheumatology department with suspicion of sicca and symptomatic artralgia, serum levels of rheumatoid factor, anti-ENA panel, ANA and anti-dsDNA were studied and were reported normal. His muscle cramps were generalized, but sometimes he defined a sharp pain and cramps in the abdomen, so not to overlook a surgical pathology, he was evaluated by general surgery for acute abdomen. His examination and ultrasonographic images didn't make us think a surgical pathology. The physical therapy and rehabilitation clinic also assessed him and suggested a psychiatry consultation. It was advised by psychiatry clinic to increase venlafaxine dose to 150 mg. However his symptoms didn't improve after this dose regulation and finally it was thought to be a statin related myopathy due to the atorvastatin treatment which he was taking for 1-year. After discontuniation of atorvastatin, symptoms of muscle cramps and myalgia improved and serum creatine kinase levels regressed from 954 to 211 IU/ml in the follow-up.

DISCUSSION

Although pharmacokinetic as well as pharmacodynamic interactions have been implicated in pathophysiology of statin-induced muscle wasting, the underlying mechanism is not clearly understood. Besides, pharmacokinetic and pharmacodynamic factors, statin-associated myotoxicity may also implicate pharmacogenomic factors. The pharmacogenomics characterised by CYP polymorphism and other genetic factors are responsible for inter-individual variations to efficacy and tolerability of statins. While difficult to determine prevention strategies, certain risk factors have been identified that may predispose an individual to developing statin induced myopathy. These include older age (with a higher prevalence in females), preexisting liver or renal impairment, hepatic fatty changes (consider this in patients with a history of alcoholism), hypothyroidism, a history of drug abuse, trauma, heavy exercise, ischemic scenarios and concomitant use of fibrates or corticosteroids (3).

After exclusion of other known causes of myopathy, such as substance abuse and hypothyroidism, the general treatment approach is statin discontinuation. Patients experiencing tolerable myalgia however without CK elevation, may continue therapy at the same or reduced doses with careful monitoring. Meanwhile if CK levels increase or myalgia progresses to an intolerable degree, statin use should be discontinued under the physician supervision. Once the patient is asymptomatic, statin therapy may be reinitiated at a reduced dose. This will help to determine causation versus temporal association as well as a possible dose-dependant threshold (4).

It is important to maintain perspective by looking at the impact of statin myopathy relative to the impact of preventing atherosclerotic complications. The potential benefits of therapy must outweigh the risks. In the case of statin therapy the benefit/ risk ratio is overwhelmingly positive (4). The safety and tolerability of the available statins support their use as the first-line treatment of patients at high risk for coronary heart disease, since the clinical benefits greatly outweigh the small risk of myopathy. Nevertheless, clinicians should be aware of the adverse effects possibly related to statin therapy, particularly in patients requiring long-term multiple-drug therapies (4). The interactions of statins with concomitant drugs of different classes merit attention for safety profile of statins (1). Although statin-associated myotoxicity affects compliance, quality of life of patient and discontinuation rate, yet the low incidence of myotoxicity including rhabdomyolysis and less severity of

commonly occurring myopathy and myalgia do not raise doubts about the clinical efficacy and tolerability of statins (4).

Our patient had multiple risk factors for development of myopathy, such as alcohol and morphine abuse, corticosteroid use for exacerbation of COPD and diagnosis of statin induced myopathy was made after exclusion of other diseases. The diagnosis of was further proved by the regression of symptoms and serum markers after cessation of atorvastatin. The history of alcohol and morphine abuse, complexity of clinical status, multiplicity of concomitant chronic diseases, utilization of multiple medications and the fact that he had been taking atorvastatin for 1 year made us to not think statin induced myopathy at first hand. But it should be beared in mind that statin induced myopathy can be seen at any time during the course of therapy. The patient had low serum LDL levels so discontinuation of atorvastatin was the choise, but for the preventive effect of statins for atherosclerosis and cardiovascular diseases, restarting to statin therapy should be assessed by clinical follow-up of symptoms.

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