Düşünen Adam The Journal of Psychiatry and Neurological Sciences 2011;24:243-245
DOI: 10.5350/DAJPN2011240311

Case Reports

A case of Rhabdomyolysis Due to Fenofibrate Use

Tamer Yazar[1], Yusuf Kayran[2], Murat Çabalar[1], Ayla Çulha[2], Vildan Yayla[1]

[1]Neurologist, [2]Resident, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Department of Neurology, İstanbul - Turkey

ABSTRACT

A case of rhabdomyolysis due to fenofibrate use

Fibrates, wide-spectrum fibric acid derivatives, are used for dislipidemia and hypertriglyceridemia treatment. The adverse effects are on striated muscles, kidney, and liver but the most serious and potentially mortal effect is rhabdomyolysis. Rhabdomyolysis is a clinical and biochemical syndrome resulted from acute necrosis of striated muscles and release of these into the circulation due to traumatic (earthquake, road accident etc.) or non-traumatic causes. Clinical course may vary from an asymptomatic syndrome to myopathy, life-threatening hypovolemic shock, cardiac arrhythmias or acute renal failure. Myoglobinuria is the most prominent consequence of muscle cell damage that results with renal failure in 15-33% of patients. In this paper, a case with myopathy and rhabdomyolysis, as a result of fenofibrate treatment is presented.

Key words: Fibrates, rhabdomyolysis, myopathy

ÖZET

Fenofibrat kullanımına bağlı bir rabdomiyoliz olgusu

Fibratlar, dislipidemi ve hipertrigliseridemi tedavisinde sık kullanılan, fibrik asit türevi geniş spektrumlu bir ilaç grubudur. Yan etkileri sıklıkla çizgili kaslar, böbrek ve karaciğer ile ilgilidir. Bu yan etkilerin en ciddi ve potansiyel olarak ölümcül olanı rabdomiyolizdir. Rabdomiyoliz, travmatik (deprem, trafik kazası vs.) veya nontravmatik nedenlere bağlı olarak çizgili kas hücrelerinin akut nekrozu sonucu kas hücre içeriğinin dolaşıma katılmasıyla gelişen klinik ve biyokimyasal bir sendromdur. Klinik seyir asemptomatik tablo, miyopati ile hayatı tehdit eden hipovolemik şok, kardiyak aritmiler ve akut böbrek yetmezliğine kadar değişkenlik gösterebilir. Miyo-globinüri kas hücre yıkımının en belirgin sonucudur ve vakaların %15-33'ünde böbrek yetmezliğine neden olduğu bildirilmiştir. Bu yazıda, fenofibrat kullanan bir olguda ilaca bağlı gelişen miyopati ve rabdomiyoliz gelişimi sunuldu.

Anahtar kelimeler: Fibrat, rabdomiyoliz, miyopati

Address reprint requests to:
Neurologist Tamer Yazar, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Department of Neurology, İstanbul-Turkey

Phone: +90-212-414-7171

E-mail address:
tamer.yazar@yahoo.com.tr

Date of receipt:
December 29, 2010

Date of acceptance:
February 05, 2011

INTRODUCTION

Fibrates are fibric acid derivatives used for treatment of dyslipidemia and hypertriglyceridemia. Fibrates decrease triglyceride-richened lipoprotein levels, increase high-density lipoprotein (HDL) and decrease atherogenic low-density lipoprotein (LDL) levels (1).

Myopathy is a serious adverse effect of fibrates which develops between <3 weeks and 3 months and may cause subsequent rhabdomyolysis and acute renal failure (1,2).

In this report, drug-related myopathy and rhabdomyolysis in a case using phenofibrate is presented which has been consulted in neurological emergency unit with diffuse muscular pain and sudden-onset paraparesis, thought to have clinical symptoms and signs of an inflammatory myogenic disease, acute myelitis syndrome or disc pathology and decided to be presented due to life-saving early diagnosis and intervention.

CASE

Sixty-three year old female patient was admitted to emergency department due to diffuse muscular pain and weakness in legs. She had a history of hypertension, hyperlipidemia (phenofibrate 200 mg/day was started for hyperlipidemia diagnosis approximately ten days before her admission) and ischemic cerebrovascular disease (left hemiparesis 25 years ago). Her physical examination was normal. In neurological examination, muscle strength was found 4/5 in left upper limb and 2/5 in lower limbs and deep tendon reflexes were diminished in both lower limbs.

Urine quantity was normal and there was no darkening in urine color. In urinalysis, red blood cells were +2 (15/HPF) and white blood cells were 30/HPF. Laboratory values at time of admission were as follows; creatine kinase (CPK) 40627 IU/L (normal: 10-172 IU/L),

AST 799 IU/L (normal: 0-35), ALT 247 IU/L (normal: 0-35), LDH 1189 IU/L (normal: 100-245), serum creatinine 1.49 mg/dL (normal: 0.6-1.3), BUN 76 mg/dL, fasting blood glucose 104 mg/dL, serum albumin 3.6 g/dL, hemoglobin 13.9 g/dL, serum potassium 4.3 mmol/L, serum calcium 9.4 mg/dL and erythrocyte sedimentation rate was 29 mm/hr. Thyroid function tests were normal and antibodies (antiTPO, ANA, antidsDNA, anti Jo1) were found negative. Tests for Hepatitis B, C and HIV were all negative. In blood gas analysis, following values were found: pH:7.42; pO_2: 88.6 pCO_2: 31.7, HCO_3: 20.4. Total abdominal and urinary system ultrasonography was normal.

Electromyographic examination of the patient who had paraparesis and diffuse muscular pain was consistent with bilateral chronic neurogenic involvement in L4-L5 innervated muscles. No pathology was found in cervical and thoracic magnetic resonance imaging (MRI). Predominantly subcortical multifocal ischemic-gliotic areas in corona radiata and centrum semiovale were present in cranial MRI. No significant pathological finding was detected in lumbar MRI except bulging into dural sac in L3-4 and L4-5 discs.

Rhabdomyolysis secondary to phenofibrate use and consequent acute renal failure diagnosis was made. Phenofibrate treatment was stopped. Fluid replacement was started. Blood chemistry in her second day of admission was as follows: urea 103, creatinine 2.33 IU/L, AST 555 IU/L, ALT 276 IU/L, LDH 1429 IU/L, CPK 22744 IU/L. Hemodialysis was not needed during her follow-up. Her blood chemistry values regressed (urea 38, creatinine 0.98 mg/dL, CPK 71 IU/L) after this treatment and her neurological examination was normal except hemiparesis sequalae.

DISCUSSION

Rhabdomyolysis is defined as severe myopathy with creatine kinase levels ten times over upper limit and concurrent muscular symptoms. Main risk factors were advanced age, thin body stature, excessive alcohol intake, infections, metabolic disorders, collagen tissue diseases, trauma, hypothyroidism, concurrent use of statins with other risky agents such as fibrates, colchicine, lithium, macrolide group antibiotics, azol group antifungals, verapamil, amiodarone and nicotinic acid. However, there are cases which no clear etiology was found (1-8).

Cholesterol-lowering agents may cause sudden or slowly progressive myopathy. Normal or myogenic electrophysiological findings may be present in rhabdomyolysis. In slowly progressive myopathy, there may be complex repetitive discharges, cramps and even myotonic discharges in spite of spontaneous fibrillation and positive spikes (9). In our case, chronic neurogenic changes which were thought to be related with lumbar disc pathology were detected in EMG and no pathology in favor of myogenic involvement was detected. Absence of myogenic characteristics in EMG was thought to be related with sudden onset of myopathy and early intervention.

Exact mechanism of rhabdomyolysis has not fully been understood but various explanations were made. Related factors causing cell destruction by acidosis and ischemia are also thought to cause rhabdomyolysis and acute renal failure by constriction of renal arteries, tubular cylinder formation and toxicity of myoglobin (2-5,10).

There are few reported cases of rhabdomyolysis due to monotherapy with fibrate derivatives. Among adverse events reported to American Food and Drug Administration, rate of muscle-related symptoms which rhabdomyolysis does not accompany in phenofibrate monotherapy was 8.8 per million prescriptions and 5.5 for rhabdomyolysis (1). In the study of Graham et al. (11) done with 252.460 patients taking lipid-lowering agents, mean annual incidence of rhabdomyolysis per 100,000 people was found 0.44 for statin monotherapy, 2.82 for fibrate monotherapy and 5.98 for statin and fibrate combined therapy and incidence is higher particularly in elderly patients with diabetes (11). Sudden onset of symptoms with medication, excessive increase of creatine kinase levels without any other etiological agent and rapid normalization of clinical and laboratory parameters by cessation of fibrate treatment and by supportive therapy indicate rhabdomyolysis due to phenofibrate use.

We would like to emphasize that rhabdomyolysis

which rapid diagnosis and treatment is life-saving in patients who are admitted to neurological emergency departments with diffuse muscular pain, weakness and having pre-defined risk factors. When phenofibrate is prescribed, potentially fatal adverse events such as rhabdomyolysis and acute renal failure should be kept in mind and utmost care should be given to use this drug in definite indications. Careful follow-up of liver and renal function tests and muscle enzymes are important. Patients should be informed about risks of the drug and possible adverse events such as muscle weakness and muscular pain.

REFERENCES

1. Davidson MH, Armani A, Mckenne JM, Jacobson TA. Safety considerations with fibrate therapy. Am J Cardiol 2007; 99:3-18.

2. Ünal A, Sipahioğlu MH, Tokgöz B, Akçakaya M. Antihiperlipidemik tedavi sonrası gelişen rabdomiyoliz: Üç olgu sunumu. Erciyes Tıp Dergisi 2009; Suppl 1:1-4 (Article in Turkish).

3. Çevik Ç, Çakır M, Soysal D, Avcı A, Gürgör N. Simvastatin ve itrakanazolün birlikte kullanılmasına bağlı bir rabdomiyoliz olgusu. Türkiye Klinikleri Tıp Bilimleri Dergisi 2003;23:150-153 (Article in Turkish).

4. Yıldız G, Uygun Y, Marşan E, Tümuçin M, Candan F. Statin ve fibrat kombinasyonuna bağlı rabdomiyoliz gelişimi ile ilişkili akut böbrek yetmezliği: İki olgu sunumu. Cumhuriyet Tıp Dergisi 2009; 31:2 (Article in Turkish).

5. Yüksel H. Hiperlipidemide fibratlar. Türkiye Klinikleri 2006; 2:73-78 (Article in Turkish).

6. Soysal D, Çevik D, Kırlı A, Avcı A, Tonguç F. Serivastatin, gemfibrozil ve bir makrolid antibiyotiğin birlikte kullanılmasına bağlı rabdomiyoliz olgusu. Türkiye Klinikleri Kardioloji Dergisi 2001; 14: 310-312 (Article in Turkish).

7. Schech S, Graham D, Staffa J, Andrade S, La Granade L, Burgess M , Blough D, Stergachis A, Chan KA, Platt R, Shatin D. Risk factors for statin-associated rhaddomyolysis. Pharmacoepidemiol Drug Saf 2007; 16:352-358.

8. Ireland JH, Eggert CH, Arendt CJ, Williams AW. Rhabdomyolysis with cardiac involvement and acute renal failure in a patient taking rosuvastatin and fenofibrate. Ann Intern Med 2005; 142:949-950.

9. Ertekin C. Santral ve Periferik EMG. Meta Basım Matbaacılık Hizmetleri, İzmir, 2006 (Article in Turkish).

10. Gupta P, Singh VP, Agarwal AK. Acute renal failure resulting from rhabdomyolysis following a seizure. Singapore Med J 2010; 51:79-80.

11. Graham DJ, Staffa JA, Shatin D, Abdrade SE, Schech SD, La Granade L, Gurwitz JH, Chan KA, Goodman MJ, Platt R. Incidence of hospitalized rhabdomyolysis in patients treated with lipid-lowering drugs. JAMA 2004; 292:2585-2590.