Simvastatin Induced Rhabdomyolysis of Anterior Compartment of Leg Resulting in Foot Drop

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ABSTRACT

A 65-year-old physically active man presented with sudden onset leg pain and inability to dorsiflex his foot following a trivial fall. There was no tenseness in the anterior compartment and compartment pressure was normal. Three days later he developed erythema with pitting oedema of the leg. Serum creatine kinase was 14000 U/l initially which gradually decreased. Subsequent Doppler scans and MRI showed evidence of myositis involving the entire anterior compartment. The patient reported a history of simvastatin use for the past year. A nerve conduction study confirmed common peroneal nerve palsy. This case report highlights a rare complication of simvastatin use presenting with foot drop resulting from muscle damage and nerve palsy.

Key Words:
Rhabdomyolysis, Simvastatin, Foot Drop

INTRODUCTION

Rhabdomyolysis from simvastatin use is well known [1], can present with varied clinical pictures and is sometimes obscured by other distracting signs or symptoms such that the actual aetiology is not easily ascertained. This case report describes a rare presentation of common peroneal nerve palsy resulting from rhabdomyolysis subsequent to simvastatin use.

CASE REPORT

A 65 year old non-smoking male presented to the emergency ward with pain in his left leg and back after a trivial fall while walking down a slope. He complained more of back pain than leg pain along with generalised malaise. Radiographs taken on admission showed severe degenerative changes in his lumbar spine. Clinically he had patchy paraesthesia of the left leg over L4 distribution. Power of knee extension was grade 4 and ankle dorsiflexion was grade 0. Weakness of the peroneal group of muscles was also noted and the left knee jerk was depressed. There was no erythema, swelling or tenderness over the anterior compartment or overlying the neck of the fibula. Examination also revealed preserved flexor compartment muscle power and function. The initial diagnosis was left lumbar root canal stenosis with resultant foot-drop.

The patient had a past medical history of hypercholesterolemia, stable ishaemic heart disease, coronary angiography 4 years earlier and hypertension. He had a revision total hip replacement on the opposite side 5years earlier and also had ipsilateral total knee replacement 6 years prior. He suffered from contralateral long standing sciatica pain and degenerative spinal disease. He was prescribed Simvastatin (40mg daily), perindopril, fluoxetine, atenolol, isosorbide mononitrate, etodolac, and ranitidine.

On admission, blood tests showed normal white blood cell count (WBC), platelets, C-reactive protein (CRP), and serum electrolytes but an elevated ESR of 23 mm/hr. Compartment pressure measurement was normal (19 mmHg). Three days later his pain was worse with erythema involving the anterior compartment of leg with pitting ooedema; however, the anterior compartment was not tense. He was stared on intravenous flucloxacillin and benzylpenicillin. Auscultation of the lower lateral part of the leg revealed moderately loud hissing arterial flow. At this time a working diagnosis of chronic compartment syndrome was made with a suspected aetiology of compression of common peroneal nerve resulting in foot drop. At this stage his serum creatine kinase level was 14,000U/l (Figure 1) and serum CRP was 196. He was started on intravenous fluids and was catheterised to monitor renal function.

A Doppler scan done on the same day showed hypoechoic areas involving the anterior compartment muscles notably, tibialis anterior and long extensors (Figure 2). There were dilated veins in the leg with normal venous flow with normal augmentation with calf compression, normal respiratory variation and easy compressibility with no signs of deep vein thrombosis. Venous Doppler findings were identical to the other leg. Arterial flow in the anterior tibial artery showed

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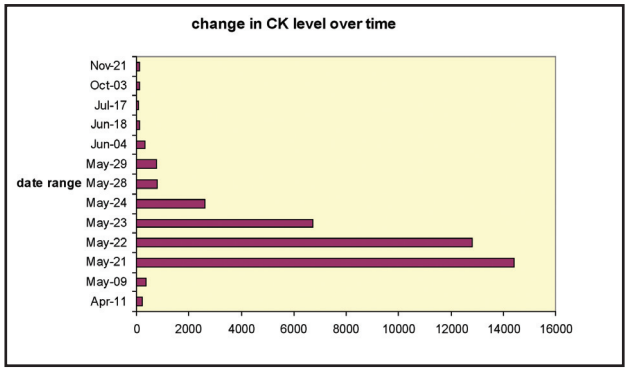

Fig. 1: Change in Creatine Kinase (CK) level over time.

Fig. 2: Ultrasound scan showing hypoechoic muscles in the anterior compartment.

Fig. 3: MRI (T1W) images of anterior compartment showing extensive muscle damage

normal triphasic waveforms with no clutter, dampening or evidence of any aneurysm. The area overlying the fibular neck did not show any lesion compressing the nerve.

Over next two days, the patient developed mild confusion and started to have auditory hallucinations, sweating and distressing hiccoughs. His vital signs were normal and urine was dark coloured and scant in quantity. Blood culture was normal but he still had erythema and pitting oedema. His serum creatine came down to 100 μmol/L, serum urea was 12.7 mmol/L and arterial blood gases were normal. On the next day, serum urea decreased to normal but the hiccoughs and auditory hallucination persisted and leg pain was resolving. A liver function test performed on the same day revealed total serum bilirubin of 16 Ìmol/L and a serum alanine transferase (ALT) 156 U/L signifying mild hepatic dysfunction. On the following day the erythema started to resolve and the patient had a WBC count of 6.6x $x10^9$/L, haemoglobin of12.4g/dl ,and a platelet count of 196$x10^9$/L. Inflammatory markers were resolving with an ESR of 23 and a CRP of 196mg/L. Serum electrolytes were normal with serum sodium 133mmol/L, serum potassium 4.6mmol/L, serum creatine 87 μmol/L and serum urea of 8.1 mmol/L. Serum albumin was low (22 g/L) and a serum creatine kinase(CK) level decreased further to 2593 U/L. Four days later his hiccoughs stopped. Thereafter the patient reported no further leg pain while the erythema, hallucination and confusion resolved. The urine gradually became clearer and of adequate volume and vitals signs were normal. Eventually urinary catheter was taken out. Later on blood results showed improving renal and liver function with serum creatine kinase of 795, serum alkaline phosphatase of 193, serum ALT of 76 and a total serum bilirubin of 12. However, the foot drop persisted.

MRI scan of the leg showed extensive oedema involving the tibialis anterior and extensor digitorum longus and peroneus longus muscles (Figure 3). These muscles contained diffuse but heterogeneous areas of high T1 Weighted signal with a serpiginous geographical outline with a tiny focus in the proximal aspect of the peroneus brevis, adjacent to the common peroneal nerve. The signal characteristics were those of subacute haemorrhage, presumably secondary to myositis.

After three days, the patient's haemoglobin dropped to 6.2g/dl.and he was transfused with four units of packed red blood cells. At this point, consultant rheumatologists examined the patient and ordered an Extractable nuclear antigen (Scl70, Jol, Ro, La, Sm and RNP) screen; results were negative. A clinical diagnosis of Simvastatin induced rhabdomyolysis was made. On repeat neurological examination, the knee jerk and sensation on the lateral aspect of leg below knee were normal. Initial weakness of the leg was attributed to pain and the paraesthesia was probably due to involvement of the superficial peroneal nerve. Both findings became normal over time. Based on improving neurological findings along with radiological and biochemical evidence of muscle damage, a spinal cause for patient symptoms was excluded. In recent follow-up, the foot drop persists, but there is no recurrence of other symptoms.

DISCUSSION

As of 18th August, 2009 there are no case reports published regarding foot drop resulting form rhabdomyolysis. Rhabdomyolysis resulting from prolonged Simvastatin use can result in renal failure [1], may be precipitated by physical exertion [2], and can cause compartment syndrome, which may require four-compartment fasciotomy [3]. In this case report, the patient was on other medications, none of which are known to cause rhabdomyolysis save simvastatin.

Several studies have suggested that HMG-CoA reductase inhibitors such as statins can increase liver transaminase and myopathy. The myopathy ranges from simple soreness to fatal rhabdomyolysis [4]. Drug interactions with fibric acid derivatives, antifungals, protease inhibitors (anti-retrovirals), verapamil, and diltiazem causing severe rhabdomyolysis have been previously reported. Gemfibrogel and statin –induced compartment syndrome is well described in literature. Myocardial depression is another recognised complication of statin administration [5].

Our patient initially presented with foot drop with back pain rather than symptoms of acute compartment syndrome. This is probably due to involvement of the common peroneal nerve damage and gradual muscle damage. The diagnosis of chronic compartment syndrome was made retrospectively only after three days. The leg pain also settled following commencement of antibiotics within another couple of days. Acute presentation along with ultrasound and MRI findings suggested damage to muscles, which in turn resulted in common peroneal nerve damage confirmed with nerve conduction study. Clinical presentation of both renal and hepatic derangement along with muscle damage points towards simvastatin as the cause of the clinical condition presented in light with the available evidence. However, clinical presentation with foot drop as a result of rhabdomyolysis resulting in local damage of common peroneal nerve from a chronic compartment syndrome is unique.

Rhabdomyolysis induced common peroneal nerve palsy is rare and can be easily missed if presents with distracting false localising signs. Utmost care should be taken to preserve renal function with intravenous fluids. Fasciotomy is needed to decompress compartment syndrome but it could spread an overlying infection into the already inflamed underlying muscle compartments. Supportive care with foot drop splint should be used and a risk benefit analysis should be undertakedn to determine the need for fasciotomy.

REFERENCES

1. Najafian B, Franklin DB, Fogo AB. Acute renal failure and myalgia in a transplant patient. *J Am Soc Nephrol,* 2007; 18(11): 2870-4.
2. Marie I, Delafenêtre H, Massy N, Thuillez C, Noblet C. Tendinous disorders attributed to statins: A study on ninety-six spontaneous reports in the period 1990-2005 and review of the literature. *Arthritis Rheum,* 2008; 59(3): 367-72.
3. Webber MA, Mahmud W, Lightfoot JD, Shekhar A. Rhabdomyolysis and compartment syndrome with coadministration of risperidone and simvastatin. *J Psychopharmacol,* 2004; 18(3): 432-4.
4. Wooltorton E. Rosuvastatin (Crestor) and rhabdomyolysis. *CMAJ,* 2004; 171(2): 129.
5. 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(11): 949-50.