STATIN-INDUCED RHABDOMYOLYSIS: A CASE REPORT

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Statins are first-line lipid-lowering therapy for reducing low-density lipoprotein (LDL) cholesterol and are the mainstay agents in the primary and secondary prevention of atherosclerotic cardiovascular disease. Rhabdomyolysis is one of the rare adverse effects of statin therapy, the incidence of which increases in the presence of risk factors such as concurrent use of CYP3A4-inhibiting medications, male gender, and over 60 years old.[1] In this report, we present a case of statin-induced rhabdomyolysis diagnosed and managed at Hanoi Medical University Hospital. Patient was treated with aggressive hydration and statin was withdrawn. Subsequently, the patient recovered gradually with no residual deficit. Statin-induced rhabdomyolysis is a rare but potentially life-threatening adverse effect requiring timely management. This case highlights the importance of early recognition and appropriate management of statin-induced rhabdomyolysis to prevent complications, particularly given the widespread use of statins among elderly patients and those with multiple comorbidities.

Keywords: Statin; Rhabdomyolysis.

I. INTRODUCTION

Rhabdomyolysis is a complex degradative condition characterized by rapid dissolution and necrosis of damaged skeletal muscle, leading to the sudden release of intracellular components into the systemic circulation.[2] Approximately 85% of all rhabdomyolysis results from traumatic injury to muscle tissue, typically related to crush-related mechanical forces, whereas the remaining 15% are of nontraumatic origin, such as due to alcohol or drug abuse, side effects of certain medications, prolonged immobilization or hospitalization, infections, and endocrine disorders.[3,4]

Elevation of serum creatine kinase (CK) together with increased urinary myoglobin represents the most sensitive approach for identifying skeletal muscle injury and confirming the diagnosis of rhabdomyolysis. Treatment of rhabdomyolysis primarily includes IV fluid and electrolyte replacement to prevent dehydration and the development or progression of acute kidney injury (AKI), accompanied by physical rehabilitation to restore muscle function.[2]

Statins, widely prescribed for dyslipidaemia, are a recognized drug-related cause of rhabdomyolysis.[5] Their muscular adverse effects range from myalgia and stiffness to myopathy and, rarely, rhabdomyolysis. Although uncommon, rhabdomyolysis remains clinically important because of its potential severity.[3]

We present a rare case of rhabdomyolysis presenting with fatigue, muscle weakness, extremity pain, and dark urine after treatment with simvastatin 40 mg.

II. CASE REPORT

A 62-year-old hypertensive male presented with fatigue, muscular weakness, pain in

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extremity and dark urine for 1 week. He was hypertensive for 5 years on Captopril/ Hydrochlorothiazide (HCTZ) 12.5mg/25mg. After being diagnosed with dyslipidaemia, the patient had been taking simvastatin 40 mg daily for one month. There was no history of trauma, fever, rash, joint pain, or excessive strenuous exercise. On examination, he was conscious and oriented, with blood pressure of 130/90 mmHg, he appeared underweight with a BMI of 18.0, and presented tenderness of the thigh, calf, and upper arm muscles. Proximal myopathy was noted with weakness in hip flexion and extension (Medical Research Council scale - MRC Grade 3/5) and in shoulder abduction and adduction (MRC Grade 3+/5), while distal muscles were relatively spared. Deep tendon reflexes were present but depressed. Atypical peripheral seventh cranial nerve palsy was observed. No sphincter dysfunction was noted, and both Babinski and Hoffmann signs were negative. No ophthalmoplegia, no ptosis and no rash were observed. Other organ systems showed no abnormality. His laboratory findings showed a marked elevation in creatine kinase (CK) levels (*Figure 1*), while renal function remained normal (*Figure 2*). Transaminases were elevated (AST 571 U/L and ALT 1308 U/L), with negative HBsAg and anti-HCV.

Arterial blood gas (ABG) analysis showed no evidence of metabolic acidosis with a pH of 7.4; bicarbonate 21.8 mmol/L, partial pressure of carbon dioxide 35.7 mmHg, and lactate level of 2.8 mmol/L. Urine pH was within the normal range. C-reactive protein (CRP) was negative, serum calcium, phosphate and potassium levels were within the normal range. Thyroid function tests, including FT4 and TSH, were also normal. These findings helped exclude electrolyte or endocrine disorders as potential causes of rhabdomyolysis.

Nerve conduction study showed no evidence of extremity axonal sensory-motor neuropathy. Electromyography showed a myopathic pattern of involvement, suggested statin-induced immune-mediated necrotizing myopathy, and anti-HMG-CoA reductase antibody testing should be performed. Although the patient presented with an acute onset of muscle weakness, a comprehensive myopathy panel, including anti-HMGCR antibodies, was obtained to exclude autoimmune myopathies and all tested antibodies returned negative.

Chest CT was performed to assess for interstitial lung disease and revealed no abnormalities (*Figure 3*)

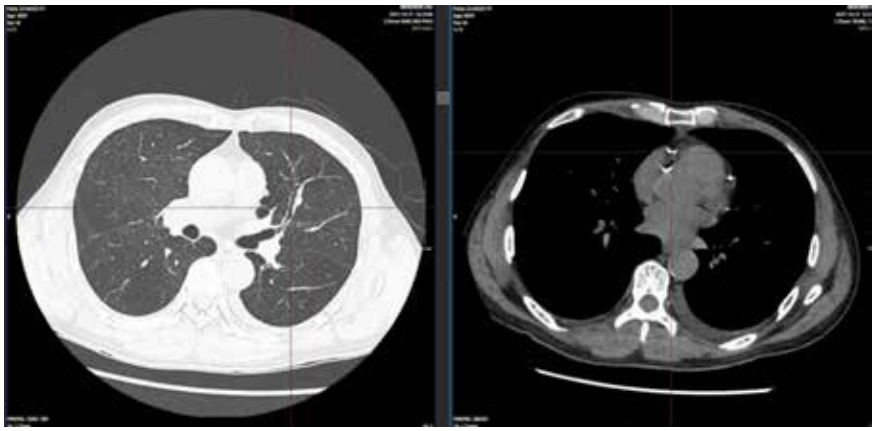

Figure 3. Chest CT

(Source: Le Xuan B. - 62 years old, Medical record ID: 2510184031)

A brain MRI was performed to exclude ischemic or hemorrhagic intracranial pathology, which revealed a few chronic pontine microhemorrhages (<5mm) - (*Figure 4)*.

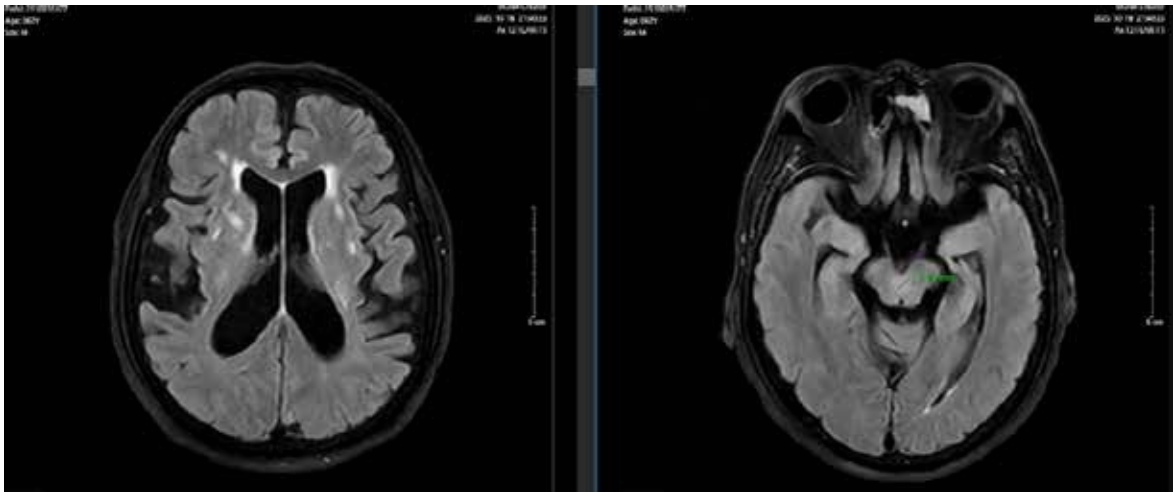

Figure 4. Brain MRI

(Source: Le Xuan B. - 62 years old, Medical record ID: 2510184031)

Therefore, following comprehensive investigations to identify the etiology of CK elevation and the exclusion of alternative causes, statin was considered the most likely causative factor in this patient.

The patient was hydrated intravenously, and the statin was discontinued. Although the CK level continued to rise rapidly during the first six days of hospitalization-peaking at roughly 90960 U/L on Day 6 (*Figure 1*), his renal function remained stable (*Figure 2*), with no evidence of hematuria or urinary acidosis. With ongoing intravenous fluid therapy, the CK level gradually decreased. By Day 12, at the time of discharge, the CK had fallen to 1104 U/L. His myalgia and muscle weakness also improved significantly with physiotherapy, and he was able to ambulate independently by discharge. At one-month follow-up, his muscle enzyme levels had improved, with CK decreasing to 811 U/L, AST and ALT subsequently returned to normal levels and he had no residual muscle weakness.

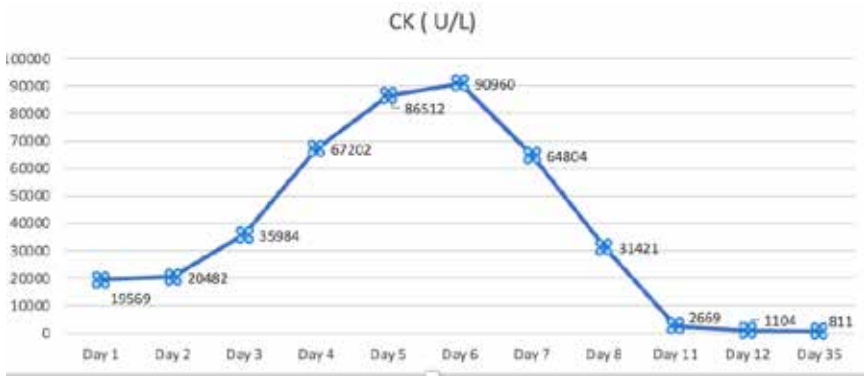

Figure 1. Creatine kinase (CK) levels

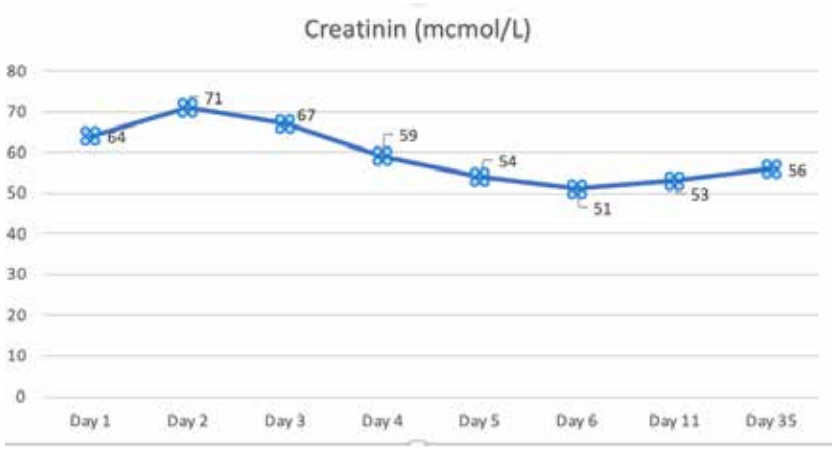

Figure 2. Creatinin levels

III. DISCUSSION

Rhabdomyolysis is a medical condition characterized by the rapid breakdown of damaged skeletal muscle, resulting in the release of intracellular components into the bloodstream and extracellular fluid. The clinical spectrum of rhabdomyolysis ranges from asymptomatic elevations of CK to severe, life-threatening manifestations such as extreme CK elevation, disturbances in electrolytes such as sodium, potassium, calcium, and phosphate, acute renal failure, and disseminated intravascular coagulation.[6,7]

Rhabdomyolysis has a wide range of etiologies that can be grouped into three major categories based on the underlying mechanism of muscle injury: (1) traumatic or compression-related causes; (2) non-traumatic exertional causes, including strenuous or unaccustomed exercise, hyperthermia, and metabolic or inherited myopathies; and (3) non-traumatic non-exertional causes, such as medications, toxins, infections, endocrine disorders, etc. Regardless of etiology, rhabdomyolysis commonly presents with muscle weakness, myalgia, swelling, and dark-colored urine from pigmenturia.[7,8] Several factors increase susceptibility to rhabdomyolysis, including gender (male), race (black), age <10 or >60 years old, obesity (BMI >40 kg/m²), a history of heat-related illness, low baseline physical fitness, chronic use of lipid-lowering medications, and dehydration.

Statins are widely prescribed for dyslipidaemia by inhibiting HMG-CoA reductase, the rate-limiting enzyme in cholesterol synthesis, and they are a well-recognized drug-related cause of rhabdomyolysis, with their main adverse effects affecting the liver and skeletal muscle.[5] Statin-associated muscle injury is thought to result from membrane destabilization, impaired ion pump activity, mitochondrial dysfunction due to reduced coenzyme Q10, and inhibition of the mevalonate pathway, which decreases isoprenoids essential for muscle cell survival. Together, these mechanisms contribute to increased susceptibility of muscle fibers to injury and necrosis. The risk of myopathy and rhabdomyolysis is higher with lipophilic statins (e.g., atorvastatin, fluvastatin, pitavastatin, and simvastatin compared to hydrophilic statins (e.g., pravastatin and rosuvastatin). Among these drugs, simvastatin was associated with a more than twofold higher risk of rhabdomyolysis compared with other statins.[9]

In this case the patient was prescribed 40mg of simvastatin daily - a relatively high dose and had no risk factor for statin-induced myopathy except for male gender and advanced age (>60 years).

According to most studies, the patients with induced rhabdomyolysis experienced muscle weakness, myalgia, fatigue and myoglobinuria. There are no specific clinical feature that distinguish statin-induced rhabdomyolysis from rhabdomyolysis caused by other etiologies.[2] In this case, the patient exhibited all of these clinical manifestations.

The clinical studies were very heterogeneous with regard to the definition of rhabdomyolys. When rhabdomyolysis is associated with the use of lipid-lowering drugs, the CK level cutoff is considered 10 times the upper limit of normal. The definition of severity of rhabdomyolysis varied among studies, some defining “severe rhabdomyolysis” based on different CK cutoff values (>5000 U/L up to >15,000 U/L).[12]

In our case, the patient presented with a markedly elevated CK level exceeding 90,000 U/L, raising significant concern for acute kidney injury. Such an extreme elevation was atypical for uncomplicated statin-associated rhabdomyolysis. Moreover, electromyography suggested a possible autoimmune myopathy, specifically immune-mediated necrotizing myopathy. However, the diagnosis was ultimately excluded, as the comprehensive myopathy antibody panel—including anti-HMGCR—returned negative.

The treatment of rhabdomyolysis is largely supportive. Key principles include preventing heme pigment-induced acute kidney injury, correcting fluid and electrolyte disturbances, and addressing underlying causes to halt ongoing muscle injury. Management primarily involves aggressive intravenous fluid resuscitation, with close monitoring and correction of potentially life-threatening electrolyte abnormalities. Renal replacement therapy may be required if acute kidney injury develops.

In this case, the patient received aggressive hydration during the first 6 days. Daily urine output remained adequate, and close monitoring showed no sign of fluid overload, metabolic acidosis, or acidic urine. Although the creatine kinase (CK) level continued to rise markedly during the first six days, adequate hydration successfully prevented acute kidney injury. From Day 7 onward, CK levels began to decline steadily (*Figure 1*), and intravenous fluids were then reduced while maintaining adequate oral hydration. By Day 11, when CK had decreased to 2669 U/L, intravenous hydration was discontinued and replaced with oral fluids alone. On Day 12, CK further improved to 1104 U/L, and the patient was discharged. Muscle strength gradually recovered throughout the hospitalization. At 1-month follow-up, he was able to stand independently and perform light exercise. He has since demonstrated ongoing clinical improvement without any residual neurological or functional deficits.

IV. CONCLUSION

Statin-induced rhabdomyolysis, although uncommon, remains a clinically significant adverse effect due to its potential severity. There is the importance of early recognition of symptoms such as muscle weakness, myalgia, and dark urine in all patients receiving statin therapy. Prompt laboratory evaluation and timely initiation of treatment are essential to prevent complications, particularly acute kidney injury. Clinicians should carefully assess individual risk factors when prescribing statins, and continued vigilance is necessary to ensure their safe and effective use, particularly among elderly patients and those with multiple comorbidities.

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