## Recurrent statin-induced rhabdomyolysis: Commonly overlooked drug

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### ABSTRACT

Statin-induced muscle pain and myopathy are common. However, statin-induced rhabdomyolysis causing severe nephropathy is somehow uncommon. Here, we present the case of a 68-year-old patient on statin therapy after percutaneous coronary intervention. We want to highlight the fact that physicians should differentiate muscle pain without biochemical derangement and with severe rhabdomyolysis leading to acute kidney injury and hyperkalemia. Patients should be made aware of this commonly overlooked drug causing severe complications.

Key words: Rhabdomyolysis, Statin, Statin-induced nephropathy

Statin is a commonly used drug for cardiovascular health. Statins are lipid-lowering agents that act by inhibiting the 3-hydroxy-3-methylglutaryl coenzyme-A (HMG-Co-A) reductase enzyme essential in the cholesterol synthesis pathway [1]. Among all adverse effects, a maximum (almost 72%) are related to muscles. These can present as myalgia, myopathy, myositis with elevated creatinine kinase, or, at its most severe, rhabdomyolysis, with some people reporting additional joint and abdominal pain [1]. Rhabdomyolysis causes either direct myocyte injury or failure of energy supply to the myocyte [2]. Statin metabolism results in increased exposure of skeletal muscle to statins, which can lead to altered mitochondrial function, calcium signaling, and cell cycle pathways [1].

#### CASE REPORT

A 68-year-old woman presented to the emergency department with complaints of generalized weakness, inability to walk properly, and abdominal pain since 5 days. The patient underwent percutaneous coronary intervention 4 months back for which she was on antiplatelet and statin rosuvastatin 40 mg once a day.

On physical examination, muscle power was 3/5 in the bilateral lower limb. On arrival, vitals were as follows: Blood pressure was 78/48 mmHg, pulse rate was 66/min, respiratory rate was 20 cycles/min, and oxygen saturation was 98% on room air. She was shifted to the intensive care unit.

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Initial laboratory workup showed a raised total leukocyte count of 15000/dL, creatinine of 5.38 mg/dL, and potassium of 6.03 mmol/L. Aspartate aminotransferase and alanine aminotransferase were raised to 247/285 U/L, respectively. Creatine phosphokinase was 21479 U/L (normal: 0–170 U/L). Urine routine showed a granular cast with protein+, blood+++, and sugar+. Hence, urinary myoglobin was sent, which was very high: 43277 ng/mL (normal: <85 ng/mL). There was no history of exercise, heat stroke, or muscle injury. The patient was in septic shock.

Rosuvastatin was withheld, and she was managed with intravenous fluid, renal replacement therapy, anti-hyperkalemia measures, and physiotherapy. Gradually, the patient's weakness improved and she started to walk with support. Laboratory parameters were improved, and the patient was also improved clinically. Hence, the patient was shifted to the ward and discharged. The graphic presentation shows trends in creatinine (Fig. 1) and creatine phosphokinase (Fig. 2) levels.

#### DISCUSSION

As compared to other statins, rosuvastatin has a greater number of binding interactions with HMG-CoA reductase and has a high affinity for the active site of the enzyme [2]. Rosuvastatin is a newer molecule with hydrophilic solubility, 20% bioavailability, 20 h of half-life, 63% hepatic excretion, and 10% renal excretion. Statins are metabolized by the liver and minimally cleared by the kidney with the exception of the hydrophilic statins pravastatin and rosuvastatin [3].

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Figure 1: Serial level of creatinine



Figure 2: Serial level of creatine phosphokinase

Statins have high efficacy but some serious complications such as rhabdomyolysis and renal failure. Various causes of rhabdomyolysis are trauma, drugs and toxins, hypo/hyperthermia, exertional, infection, mitochondrial myopathies, electrolyte abnormalities, endocrine disorders, and idiopathic [4].

The patient was readmitted due to unknowingly starting the statin therapy. The patient again developed renal dysfunction and elevated creatine phosphokinase levels. In controlled clinical trials with comparator statins, 5–40 mg of rosuvastatin

showed an adverse event profile similar to those for 10–80 mg of atorvastatin, 10–80 mg of simvastatin, and 10–40 mg of pravastatin [2]. The risk factors for the development of statininduced rhabdomyolysis include high dosages, advanced age, female sex, renal or hepatic insufficiency, and diabetes mellitus [5]. The FAERS documented that rhabdomyolysis rates were the lowest for pravastatin (1.63 cases) and highest for rosuvastatin (13.54 cases) [6,7].

#### CONCLUSION

Statin is a commonly used drug in cardiovascular health that can cause some serious complications, such as rhabdomyolysis and renal failure. Awareness should be generated regarding this commonly overlooked drug and its severe complications.

#### REFERENCES

- Ward NC, Watts GF, Eckel RH. Statin toxicity: Mechanistic insights and clinical implications. Circ Res 2019;124:328-50.
- Rubba P, Marotta G, Gentile M. Efficacy and safety of rosuvastatin in the management of dyslipidemia. Vasc Health Risk Manag 2009;5:343-52.
- Omar MA, Wilson JP. FDA adverse event reports on statin-associated rhabdomyolysis. Ann Pharmacother 2002;36:288-95.
- Torres PA, Helmstetter JA, Kaye AM, Kaye AD. Rhabdomyolysis: Pathogenesis, diagnosis, and treatment. Ochsner J 2015;15:58-69.
- Davidson MH, Clark JA, Glass LM, Kanumalla A. Statin safety: An appraisal from the adverse event reporting system. Am J Cardiol 2006;97:32C-43.
- Ruscica M, Ferri N, Banach M, Sirtori CR, Corsini A. Side effects of statins: From pathophysiology and epidemiology to diagnostic and therapeutic implications. Cardiovasc Res 2022;118:3288-304.
- Zhang H, Plutzky J, Skentzos S, Morrison F, Mar P, Shubina M, *et al.* Discontinuation of statins in routine care settings: A cohort study. Ann Intern Med 2013;158:526-34.

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