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Rhabdomyolysis Following Addition of Ezetimibe to Chronic Rosuvastatin Therapy in an Elderly Female with Chronic Kidney Disease: A Case Report

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Abstract

Background: Statins are often the most used lipid-lowering therapy for the prevention of atherosclerotic cardiovascular disease. Usually statins are well tolerated, but occasionally, statin associated muscle toxicity can rarely progress to severe rhabdomyolysis with acute kidney injury and multiorgan dysfunction. Advanced age, female sex, diabetes mellitus, and chronic kidney disease are recognized risk factors for statin-associated muscle injury. **Case Presentation:** An 89-year-old Asian female with a history of type 2 DM, chronic kidney disease stage 3A, coronary artery disease, hyperlipidemia, osteoporosis, and glaucoma presented with progressive bilateral lower extremity weakness and inability to ambulate approximately one month after ezetimibe was added to the chronic rosuvastatin therapy. Laboratory evaluation revealed severe rhabdomyolysis with a creatine kinase (CK) level of 12,851 U/L, acute kidney injury with serum creatinine of 2.3 mg/dL, and marked transaminitis with AST 454 U/L and ALT 403 U/L. Both medications were discontinued and IV hydration was started on the patient. The patient demonstrated progressive clinical improvement with declining CK levels and recovery of renal and hepatic function. Follow up laboratory studies demonstrated a return to baseline of liver enzymes and renal function. Lipid management was subsequently transitioned to a PCSK9 inhibitor without recurrence of symptoms. **Conclusion:** This case highlights the potential for severe statin-associated rhabdomyolysis in elderly patients with chronic kidney disease receiving combination lipid-lowering therapy. Prompt recognition, medication discontinuation, and

aggressive fluid resuscitation remain critical to preventing permanent organ injury.

Keywords

Rhabdomyolysis, Rosuvastatin, Ezetimibe, Statin-Associated Muscle Symptoms, Acute Kidney Injury, Transaminitis, PCSK9 Inhibitor

1. Introduction

Hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, commonly known as statins, remain the common lipid lowering therapy for both primary and secondary prevention of atherosclerotic disease. Their widespread use has resulted in the decrease in cardiovascular morbidity and mortality. However, statin induced muscle symptoms remain the most commonly reported adverse effect. This adverse effect from statins is usually the reason for treatment discontinuation. Clinical manifestations range from mild myalgias and asymptomatic creatine kinase elevations to severe rhabdomyolysis with acute kidney injury and multiorgan dysfunction [1] [2].

Rhabdomyolysis is characterized by skeletal muscle breakdown leading to the release of intracellular contents, such as creatine kinase, myoglobin, electrolytes, and aminotransferases, within the systemic circulation. Statin induced rhabdomyolysis is a life-threatening condition associated with significant morbidity and mortality [3] [4]. Risk factors include advanced age, female sex, chronic kidney disease, diabetes mellitus, high-intensity statin therapy, and concomitant use of lipid-lowering agents [1] [2] [5].

Ezetimibe is frequently added to statin therapy in patients who fail to achieve recommended low density lipoprotein cholesterol targets. Combination therapy is generally considered safe and effective; however, rare cases of severe myopathy and rhabdomyolysis have been reported, particularly among patients with multiple predisposing risk factors [5] [6].

We present a case of severe rhabdomyolysis complicated by acute kidney injury and marked transaminitis following the addition of ezetimibe to chronic rosuvastatin therapy in an elderly female with multiple predisposing risk factors.

2. Case Presentation

An 89-year-old Asian female with a past medical history significant for type 2 DM, chronic kidney disease stage 3A, coronary artery disease, hyperlipidemia, osteoporosis, and glaucoma presented to the office with progressive bilateral lower extremity weakness and inability to ambulate.

Her outpatient medications included aspirin 81 mg daily, vitamin D3 2000 IU daily, empagliflozin 10 mg daily, rosuvastatin 20 mg daily, and ophthalmic timolol. During a cardiology follow up visit in November 2025, lipid studies demon-

strated a total cholesterol of 157 mg/dL, triglycerides of 67 mg/dL, HDL cholesterol of 63 mg/dL, and LDL cholesterol of 81 mg/dL. Because her LDL cholesterol remained above the ideal number, ezetimibe 10 mg daily was added to her chronic rosuvastatin regimen.

Baseline outpatient serum creatinine, liver function tests, and creatine kinase values immediately prior to symptom onset were not available for review. However, the patient had no documented history of statin-associated muscle symptoms while receiving chronic rosuvastatin therapy before the addition of ezetimibe.

Approximately one month later, she developed progressive bilateral lower extremity weakness. She reported severe difficulty walking and inability to lift her feet. Physical examination showed bilateral lower extremity strength of 3/5. Given concern for medication induced myopathy, both rosuvastatin and ezetimibe were discontinued and she was admitted for further evaluation.

Review of the available medical record revealed no documented history of recent trauma, excessive physical exertion, or other readily identifiable precipitating factors for rhabdomyolysis. The temporal association between ezetimibe initiation and symptom onset, together with clinical improvement after discontinuation of therapy, supported medication-induced rhabdomyolysis.

Upon admission, the patient was unable to ambulate or rise from bed. Laboratory testing revealed severe rhabdomyolysis with a creatine kinase level of 12,851 U/L. Additional laboratory abnormalities included AST 454 U/L, ALT 403 U/L, serum creatinine 2.3 mg/dL, estimated glomerular filtration rate of 19.9 mL/min/1.73 m^2, blood urea nitrogen of 28 mg/dL, troponin I of 53 ng/L, and lipase of 93 U/L. Initial laboratory findings are summarized in **Table 1**.

Chest radiography was unremarkable. Abdominal ultrasonography demonstrated a stable hepatic cyst and chronic bilateral renal parenchymal disease without evidence of acute hepatobiliary pathology.

Table 1. Initial laboratory findings.

Laboratory Test Value
Creatine Kinase 12,851 U/L
AST 454 U/L
ALT 403 U/L
Creatinine 2.3 mg/dL
eGFR 19.9 mL/min/1.73m^2
BUN 28 mg/dL
Troponin I 53 ng/L
Lipase 93 U/L

The patient was admitted for four days and treated with aggressive intravenous fluid resuscitation, discontinuation of rosuvastatin and ezetimibe, and serial mon-

itoring of creatine kinase, renal function, liver enzymes, and electrolytes. She demonstrated progressive improvement in muscle strength and laboratory parameters throughout hospitalization and was discharged home after clinical stabilization.

Over the subsequent four days, laboratory values improved significantly. By discharge, CK had decreased to 4633 U/L, serum creatinine improved to 1.6 mg/dL, AST decreased to 233 U/L, and ALT decreased to 300 U/L. Clinically, the patient demonstrated improvement in strength and mobility.

Follow up laboratory testing approximately one month later demonstrated continued recovery with serum creatinine 1.22 mg/dL, estimated glomerular filtration rate 42 mL/min/1.73m^2, AST 23 U/L, and ALT 19 U/L. Because of persistent hyperlipidemia and established coronary artery disease, lipid-lowering therapy was transitioned to a PCSK9 inhibitor. Subsequent laboratory studies demonstrated stable renal function, normalized hepatic enzymes, and no recurrence of muscle symptoms.

At follow-up, the patient tolerated PCSK9 inhibitor therapy without recurrence of muscle weakness or creatine kinase elevation. LDL cholesterol improved from 126 mg/dL after discontinuation of statin therapy to 79 mg/dL while receiving PCSK9 inhibitor therapy, supporting successful long-term secondary cardiovascular prevention.

3. Discussion

Statin associated rhabdomyolysis is an uncommon but serious adverse drug reaction that can result in significant morbidity, among elderly patients with multiple comorbidities. Most patients receiving statin therapy experience either no muscle symptoms or only mild myalgias. However, in severe cases of statin associated muscle toxicity patients will experience severe muscle injury characterized by marked CK elevation, weakness, and acute kidney injury [1] [2].

The patient developed profound bilateral lower extremity weakness, inability to ambulate, CK elevation to 12,851 U/L, acute kidney injury, and marked transaminitis shortly after the addition of ezetimibe to chronic rosuvastatin therapy. Notably, she had previously tolerated rosuvastatin therapy without documented adverse effects. Symptoms began shortly after the addition of ezetimibe to chronic rosuvastatin therapy. There was improvement after discontinuation of both agents which supports that the patient was suffering from a medication induced etiology, with the combination regimen likely serving as the precipitating factor.

Several established risk factors likely contributed to the development of severe muscle toxicity in this patient. Advanced age is among the strongest predictors of statin associated myopathy because of age related changes in muscle mass, pharmacokinetics, and drug metabolism. Female sex has similarly been associated with increased susceptibility to statin induced muscle injury. Furthermore, the presence of diabetes mellitus and chronic kidney disease likely increased vulnerability to drug accumulation and muscle toxicity [1] [2] [5]. The coexistence of multiple

risk factors likely amplified the patient's susceptibility to severe rhabdomyolysis.

Although the precise mechanism of statin-induced rhabdomyolysis remains unknown, there are several pathways that have been proposed. Inhibition of the mevalonate pathway may impair synthesis of downstream metabolites involved in mitochondrial energy production and skeletal muscle integrity. Reduced production of coenzyme Q10, mitochondrial dysfunction, impaired calcium homeostasis, and increased oxidative stress have all been implicated in the development of statin-associated muscle injury [2] [5]. These mechanisms ultimately result in myocyte necrosis and release of intracellular contents into the circulation.

An important feature of this case was the marked elevation of hepatic aminotransferases. AST and ALT elevations are frequently interpreted as evidence of primary liver injury. Significant elevations may occur in severe rhabdomyolysis because skeletal muscle contains substantial amounts of these enzymes [3]. In this patient, the parallel decline in CK, AST, and ALT following discontinuation of therapy and administration of intravenous fluids strongly supports skeletal muscle injury rather than intrinsic hepatocellular disease as the primary source of enzyme elevation.

Acute kidney injury remains one of the most feared complications of rhabdomyolysis and is primarily mediated by myoglobin induced tubular toxicity, renal vasoconstriction, and intratubular cast formation [3] [4]. This patient experienced a significant rise in serum creatinine superimposed on underlying chronic kidney disease. Prompt recognition of rhabdomyolysis and aggressive intravenous hydration likely contributed to recovery of renal function and prevention of permanent renal injury.

Management of statin associated rhabdomyolysis requires immediate discontinuation of the offending agents and aggressive fluid resuscitation [3]. In this case, cessation of rosuvastatin and ezetimibe combined with supportive care resulted in rapid improvement in CK levels, hepatic enzymes, muscle strength, and renal function.

An additional strength of this case is the demonstration of successful long-term lipid management following recovery. Given the patient's history of coronary artery disease and persistent need for aggressive LDL cholesterol reduction, lipid-lowering therapy could not simply be discontinued permanently. After normalization of laboratory parameters, treatment was transitioned to a PCSK9 inhibitor, resulting in improved lipid control without recurrence of muscle symptoms. PCSK9 inhibitors have emerged as an effective alternative for patients with documented statin intolerance and are recommended in high-risk patients who remain above LDL cholesterol targets despite conventional therapy or who are unable to tolerate statins [6]-[8].

This case underscores the importance of maintaining a high index of suspicion for medication-induced rhabdomyolysis in elderly patients presenting with new-onset weakness after initiation or intensification of lipid-lowering therapy. Early recognition, prompt discontinuation of offending agents, and aggressive support-

ive management can lead to complete recovery and prevention of permanent organ damage.

This case has several limitations. Although the temporal relationship between addition of ezetimibe, symptom onset, and clinical improvement following discontinuation strongly supports medication-induced rhabdomyolysis, causality cannot be definitively established because rechallenge was neither clinically appropriate nor ethically justified. In addition, baseline creatine kinase levels prior to symptom onset were unavailable, and formal causality assessment using the Naranjo Adverse Drug Reaction Probability Scale was not performed.

4. Conclusion

Severe rhabdomyolysis remains an uncommon but potentially life-threatening complication of statin therapy. Elderly patients with chronic kidney disease, diabetes mellitus, and multiple cardiovascular comorbidities are particularly vulnerable. This case illustrates the importance of maintaining a high index of suspicion for medication-induced myopathy in patients presenting with new-onset weakness following changes in lipid-lowering therapy. Prompt recognition, discontinuation of offending agents, and aggressive intravenous hydration resulted in complete clinical recovery. Clinicians should carefully monitor high-risk patients receiving combination lipid-lowering therapy and consider alternative treatment strategies, including PCSK9 inhibitors, when significant statin intolerance occurs.

Author Contributions

Imran Sheriff: Clinical supervision, case identification, review of the clinical record, and critical revision of the manuscript. Madeeha Sheriff: Literature review, manuscript drafting, revision, and preparation of the final manuscript. Aayan Sheriff: Literature review and manuscript review. Mohammad Arshad: Literature review and manuscript review. All authors reviewed and approved the final manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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