Understanding Rhabdomyolysis – The Impact of Statin Therapy

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***Abstract*—Statins are widely prescribed lipid-lowering agents with an excellent safety profile, though rare cases of rhabdomyolysis can occur. We report a 65-year-old male who developed severe myalgia, myoglobinuria, elevated creatine kinase (8561 U/L), and acute kidney injury following high-dose atorvastatin after primary PCI. Prompt statin withdrawal and aggressive intravenous hydration led to clinical improvement. This case highlights the need for early recognition of statin-induced muscle toxicity.**

***Index Terms*-Acute kidney injury; Acute coronary syndrome; Atorvastatin; Creatine kinase; Drug-induced myopathy; Myalgia; Myoglobinuria; Percutaneous coronary intervention; Rhabdomyolysis; Statins.**

I. INTRODUCTION

Statins are among the most frequently prescribed lipid-lowering agents worldwide and constitute a cornerstone in the primary and secondary prevention of atherosclerotic cardiovascular disease.[1] By competitively inhibiting HMG-CoA reductase, they effectively reduce low-density lipoprotein cholesterol and significantly decrease cardiovascular morbidity and mortality.[1,2] Owing to their favorable benefit–risk ratio, statins are generally considered safe and well tolerated.

The overall incidence of rhabdomyolysis with statin monotherapy is less than 0.1%,[4] but the risk increases with high-dose therapy, advanced age, comorbid conditions, and drug interactions. Rhabdomyolysis is characterized by extensive skeletal muscle breakdown, markedly elevated creatine kinase levels, myoglobinuria, and the potential development of acute kidney injury.[3] However, statin-associated muscle symptoms represent the most important adverse effect spectrum, ranging from mild myalgia to severe myopathy and, rarely, rhabdomyolysis.[4]

Early recognition and prompt management are critical to prevent irreversible renal damage. This report highlights a case of statin-induced rhabdomyolysis following high-dose atorvastatin therapy after percutaneous coronary intervention.

II. CASE DETAILS

A 65-year-old male, a known case of hypertension and type 2 diabetes mellitus on regular treatment, presented to the emergency department with sudden onset breathlessness of four hours duration. The dyspnea was graded as Modified Medical Research Council (mMRC) grade III. There was no prior history of similar episodes, chest trauma, recent strenuous exercise, seizures, alcohol intake, or use of illicit drugs.

On admission, routine laboratory investigations revealed hemoglobin 13.8 g/dL, total leukocyte count 7,860 cells/mm³, packed cell volume 46%, and platelet count 3.2 lakh/mm³. Fasting blood sugar was 102 mg/dL, postprandial blood sugar 168 mg/dL, and HbA1c 7.2%. Renal function tests were within normal limits with blood urea 18 mg/dL and serum creatinine 0.8 mg/dL. Serum sodium was 138 mEq/L and potassium 4.2 mEq/L. Troponin-T was markedly elevated at 544 ng/L. Two-dimensional echocardiography demonstrated regional wall motion abnormalities.

A diagnosis of acute coronary syndrome was made. The patient received loading doses of aspirin 325 mg, clopidogrel 300 mg, and atorvastatin 80 mg. He underwent primary coronary angiography, which revealed double vessel disease involving the left anterior descending (LAD) and right coronary artery

(RCA). Ad hoc percutaneous transluminal coronary angioplasty was performed, and two drug-eluting stents were deployed successfully. The procedure was uneventful. Post-procedure, he was shifted to the cardiac intensive care unit and continued on aspirin 75 mg once daily, ticagrelor 90 mg twice daily, and atorvastatin 40 mg once daily.

On the fifth day of hospitalization, the patient developed sudden onset generalized myalgia, nausea, low-grade fever, and weakness. By the sixth day, symptoms worsened with decreased urine output and passage of reddish-brown colored urine. On examination, he was febrile with a temperature of 102.1°F, pulse rate 122 beats per minute, respiratory rate 22 cycles per minute, blood pressure 150/80 mmHg, and oxygen saturation 96% on room air.

Repeat laboratory investigations showed rapid deterioration in renal function. Serum creatinine rose from 0.8 mg/dL on day 1 to 2.2 mg/dL on day 5 and further to 4.6 mg/dL on day 6. Blood urea increased from 18 mg/dL to 183 mg/dL. Serum creatine kinase was markedly elevated at 8,561 U/L, and urine myoglobin was positive. These findings confirmed the diagnosis of statin-induced rhabdomyolysis complicated by acute kidney injury.

Atorvastatin was immediately discontinued, and aggressive intravenous fluid therapy was initiated. Over subsequent days, renal parameters showed gradual improvement, with serum creatinine decreasing to 3.8 mg/dL by day 9. Fenofibrate 160 mg was introduced for lipid management as an alternative therapy. The patient demonstrated clinical stabilization with improvement in symptoms and urine output.

III. INVESTIGATIONS

Parameter	Day 1 (Admission)	Day 5	Day 6	Day 7	Day 9	Reference Range
Hemoglobin (g/dL)	13.8	—	—	—	—	13–17
Total Leukocyte Count (cells/mm³)	7,860	—	—	—	—	4,000–11,000
Packed Cell Volume (%)	46	—	—	—	—	40–50
Platelets (lakh/mm³)	3.2	—	—	—	—	1.5–4.5
Fasting Blood Sugar (mg/dL)	102	—	—	—	—	70–110
Postprandial Blood Sugar (mg/dL)	168	—	—	—	—	<140
HbA1c (%)	7.2	—	—	—	—	<5.7
Blood Urea (mg/dL)	18	98	183	162	140	15–40
Serum Creatinine (mg/dL)	0.8	2.2	4.6	4.2	3.8	0.6–1.3
Serum Sodium (mEq/L)	138	—	—	—	—	135–145
Serum Potassium (mEq/L)	4.2	—	—	—	—	3.5–5.0
Troponin-T (ng/L)	544	—	—	—	—	<14
Creatine Kinase (U/L)	—	—	8,561	—	—	20–200

Parameter	Day 1 (Admission)	Day 5	Day 6	Day 7	Day 9	Reference Range
Urine Myoglobin	—	—	Positive	—	—	Negative
2D Echocardiography	RWMA present	—	—	—	—	—
Coronary Angiography	Double vessel disease (LAD, RCA)	—	—	—	—	—

IV. MANAGEMENT

Upon suspicion of statin-induced rhabdomyolysis, atorvastatin was immediately discontinued. The patient was managed with aggressive intravenous isotonic fluid administration to enhance renal perfusion, promote myoglobin clearance, and prevent further deterioration of kidney function. Strict monitoring of urine output, renal parameters, and electrolytes was undertaken. Supportive care included antipyretics and symptomatic management for myalgia. Nephrotoxic agents were avoided. Serial measurements of serum creatinine and creatine kinase were performed to assess progression and response to therapy. Over the following days, renal function showed gradual improvement. For continued lipid management, fenofibrate 160 mg once daily was introduced as an alternative agent.

V. DISCUSSION

Rhabdomyolysis is a potentially life-threatening syndrome characterized by acute skeletal muscle breakdown and release of intracellular contents, particularly creatine kinase (CK) and myoglobin, into the circulation.[3] Although statins are generally safe and remain the cornerstone of secondary prevention after acute coronary syndrome, high-intensity therapy can rarely precipitate severe muscle toxicity.[2,4] In the present case, a 65-year-old male developed classical features of rhabdomyolysis—generalized myalgia, fever, oliguria, reddish-brown urine, markedly elevated CK (8561 U/L), positive urine myoglobin, and acute kidney injury—within days of initiating high-dose atorvastatin following percutaneous coronary intervention. The temporal association, absence of alternative causes such as trauma, strenuous exertion, or sepsis, and subsequent improvement after statin withdrawal strongly support statin-induced rhabdomyolysis.

The pathophysiology involves inhibition of the mevalonate pathway, leading to reduced coenzyme Q10 synthesis, mitochondrial dysfunction, and myocyte membrane instability[4]. Risk factors include advanced age, diabetes mellitus, renal impairment, high-dose statin therapy, and drug–drug interactions, particularly with CYP3A4 inhibitors.[4] Although our patient was not on interacting drugs, advanced age and high-intensity statin exposure likely increased susceptibility.

From a preventive perspective, baseline risk stratification is essential before initiating high-dose statins. Clinicians should evaluate renal function, comorbidities, and concomitant medications, and consider hydrophilic statins in high-risk individuals. Patient education regarding early symptoms such as muscle pain and dark urine is critical for prompt reporting. Periodic monitoring of renal parameters and CK in symptomatic patients facilitates early detection. Timely discontinuation of the offending agent and aggressive hydration remain the cornerstone of

management,[3,5] significantly reducing morbidity and preventing irreversible renal failure.

VI.CONCLUSION

Statins are widely prescribed lipid-lowering agents and form the cornerstone of secondary prevention in acute coronary syndrome.[1] High-intensity statin therapy significantly reduces cardiovascular morbidity and mortality but is rarely associated with severe muscle toxicity, including rhabdomyolysis.[2] Statin-induced rhabdomyolysis results from skeletal muscle breakdown with marked elevation of creatine kinase and myoglobinuria, which may precipitate acute kidney injury.[3] Risk increases with advanced age, comorbidities, high doses, and drug–drug interactions involving CYP3A4 inhibitors.[4] Early recognition, prompt discontinuation of the offending agent, and aggressive intravenous hydration remain the mainstay of management.[5]

VI. TAKE HOME MESSAGE

• Statin-induced rhabdomyolysis, though rare, should be suspected in elderly patients receiving high-dose statins who develop acute myalgia, weakness, or dark-colored urine.
• Perform baseline renal function assessment and review comorbidities and potential drug interactions before initiating high-intensity statin therapy.
• Educate patients to report muscle symptoms early, especially within the first week of therapy escalation.
• Promptly evaluate symptomatic patients with serum creatine kinase and renal function tests.
• Immediately discontinue the offending statin if rhabdomyolysis is suspected.
• Initiate aggressive intravenous hydration and close monitoring to prevent or limit acute kidney injury.

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