Acute Onset Significant Muscle Weakness in a Patient Awaiting Liver Transplantation: Look for Statins

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Statins are commonly used drugs in patients with liver and cardiac disease. Statin-induced severe myopathy is a very uncommon presentation and rhabdomyolysis may occur in extreme cases which leads to renal failure. Patients with comorbidities like diabetes, hypothyroidism, and liver disease have higher chances of development of statin-induced myopathy. We describe a case of Child's C cirrhosis wherein the patient had acute onset significant muscle weakness and improved on statin discontinuation. (J CLIN EXP HEPATOL 2017;7:66–67)

A 57-year-old male presented with history of generalized weakness and inability to walk for 4 days. He also felt fatigue of jaw muscles on chewing. There was no history of fever or sensory symptoms. He was diagnosed as a case of cryptogenic (possibly NASH related) cirrhosis with decompensation three and half years back when he developed jaundice and ascites. His co-morbidities included diabetes mellitus and hypothyroidism for 4 years. In addition, he also had morbid obesity (body mass index 34.08 kg/m²). He was worked up for deceased donor liver transplantation. His child's score was 11 and MELD score was 20. He had normal electrolytes, 25(OH)D 34 ng/ml (<20 taken as deficient) and thyroid function test (TSH 3.9 µu/ml, T3 2.6 pg/ml, T4 1.6 ng/dl). His lipid profile revealed low values of total cholesterol (51 mg/dl), low-density lipoprotein (30 mg/dl), high-density lipoprotein (8 mg/dl), and triglycerides 67 (mg/dl). During his pre-transplant workup, he was diagnosed to have 95% stenosis of left anterior descending coronary artery during cardiac evaluation. He underwent coronary stent placement for the same and was started on low dose Atorvastatin as per post-coronary stenting cardiac protocol 19 days before the current admission. He presented with marked generalized weakness and inability to walk for 4 days. His other medications at the time of admission included Aspirin 75 mg, Clopidogrel 75 mg, Furosemide 20 mg, Spironolactone 50 mg, L-ornithine and L-aspartate, Rifaximine, Calcium, Norfloxacin 400 mg once a day (as primary prophylaxis for spontaneous bacterial peritonitis), and Injection Albumin

20% 100 ml intravenous twice a week. At admission, his investigations were as follows: hemoglobin 10.5 g/dl, total leukocyte count 6420/cmm (neutrophils 47%, lymphocytes 27%, monocytes 21%), platelet count 110,000/cmm, serum bilirubin 5.8 (direct 2.8) mg/dl, aspartate aminotransferase 214 IU/L (195 IU/L one month back), alanine aminotransferase 62 IU/L (28 IU/L one month back), normal Alkaline Phosphatase and Gamma-glutamyl Transpeptidase, albumin 2 g/dl, globulins 3.6 g/dl, INR 1.82, creatinine 0.6 mg/dl, magnesium 1.9 (1.6–2.3 mg/dl), calcium 8.2 (8.4–10.2) mg/dl, potassium 4.6 mmol/l, and phosphate 3.7 (2.5–4.5) mg/dl; these levels remained within normal values at the time of symptom improvement also. A thorough neurology evaluation was done which revealed muscle power of 3/5 in lower limbs and 4/5 in upper limbs. He had normal sensory examination and plantar reflex was normal. His further workup revealed raised creatine phosphokinase [4072 U/L (normal 55–170)], raised lactate dehydrogenase [1066 (normal 313–618)], and an electromyography (EMG) which was suggestive of recent onset acute myopathy; muscle biopsy was not done. A diagnosis of statin-induced myopathy was made and Atorvastatin was stopped. He improved gradually over the next week and his creatine phosphokinase levels improved to 744 U/L after 4 days. Statins were subsequently not reintroduced. He underwent a liver transplantation after 6 weeks. The explant liver revealed mixed nodular cirrhosis. The patient had no muscle symptoms before liver transplantation. He died on 28th post-op day due to sepsis and multi organ failure.

Keywords: statin, cirrhosis, muscle, myopathy

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Abbreviations: TSH: thyroid function test; EMG: electromyography; CK: creatine kinase

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DISCUSSION

Statin-induced myopathy is a collective term that includes asymptomatic elevation of creatine kinase (CK), myalgia (muscle pain), myositis (muscle injury with elevation of CK), and rhabdomyolysis (myoglobinuria and renal impairment).¹ It is the most common cause of statin discontinuation.^{2,3} Harper et al. concluded placebo-corrected

incidences of minor muscle pain as 190, myopathy (significant elevations of CK) as 5, and rhabdomyolysis as 1.6 per 100,000 patient years.⁴ The prospective observational data estimates muscle complaints in approximately 10% of patients, while rhabdomyolysis is rare.^{3,4} Symptoms are more in patients on high-dose statins.¹ The risk factors for statin-induced myopathy include higher age, female gender, viral infection, genetics, co-morbidities (diabetes, renal failure, liver disease), multiple medications, perioperative period, and concomitant therapy with certain medications.¹⁻³ Patients with genetic variants of CYP3A4 or on concomitant medications that inhibit activity of this enzyme may result in higher statin levels and thus have higher risk of statin-induced myopathy. These medications include azole antifungals, cyclosporine, clarithromycin, other lipid lowering agents, protease inhibitors, calcium channel blockers, and amiodarone.¹⁻³ Alcohol abuse also predisposes to statin-induced myopathy.^{2,3} Role of exercise in increasing statin-induced myopathy is not well defined.⁵ Exact mechanism of statin-induced myopathy is not clear; possible mechanisms include CYP3A4, vitamin D deficiency, mitochondrial inhibition, changes in intracellular system (due to cholesterol deficiency), and disruption of calcium metabolism of myocytes.^{1,6} Statins should be discontinued if muscle symptoms are intolerable or creatine phosphokinase levels >10 times or in presence of renal impairment. Rhabdomyolysis requires hospital admission and intravenous hydration, urinary alkalization to prevent acute renal failure.⁶ Management options for statin-intolerant patients include statin switching, especially to low-dose, non-daily doses, and other non-statin lipid-lowering agents, such as ezetimibe and colesvelam. Role of coenzyme Q10 and vitamin D supplementation has not been shown to be effective conclusively.^{1,7-9} Statins are considered safe in cirrhosis and several studies have shown reduction of portal hypertension, lower rates of decompensation, risk of hepatocellular carcinoma, and mortality in patients on statins.¹⁰⁻¹² As patients with liver disease are more prone for statin-induced myopathy, statins should be kept in differential diagnosis of muscle-related symptoms in these patients. It should be used judiciously in these patients with

close clinical monitoring for any muscle related symptoms, and checking of creatine phosphokinase as needed.

CONFLICTS OF INTEREST

The authors have none to declare.

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