

Rosuvastatin Induced Rhabdomyolysis and Acute Renal Failure

Deepak Sane¹, Anil Jawahirani²

ABSTRACT

We report a case of Rosuvastatin induced rhabdomyolysis, acute renal failure and quadriparesis. A 54 years aged man, a known diabetic, and with a history of acute myocardial infarction a month back admitted with, h/o quadriparesis, breathlessness, and generalized oedema, and had raised serum creatinine, total creatinine phosphokinase, and urinary myoglobin. He also had pulmonary oedema. Rosuvastatin was stopped. He was treated with supportive treatment and hemodialysis. He responded to hemodialysis and ultrafiltration. Patient gradually recovered, from quadriparesis and renal function improved. Patient was discharged with diet restriction for lipid control. He recovered completely and had normal renal function and controlled lipid levels on follow up of six months and one year after discharge. Thus prompt diagnosis of rhabdomyolysis due to Rosuvastatin in absence of other etiology and multidisciplinary management can save patient from renal injury and pulmonary edema.

Key Words : Rhabdomyolysis, Statin

Introduction :

3 hydroxy, 3 methyl coenzyme A (HMGCOA) reductase, inhibitors, i.e. statins are main stay treatment of ischemic heart diseases for lowering LDL cholesterol level and in management of dyslipidemia for primary and secondary prevention of cardiovascular diseases. Statin use demonstrated 30% reduction in atherosclerotic end points without serious morbidity.¹

Rosuvastatin has higher efficacy than other statins as a competitive inhibitor of the enzyme HMGCOA reductase.² Rosuvastatin is more superior than other statins across its dose range 10 mg to 40 mg although the safety profile is similar.^{3,4,5} Rosuvastatin is associated with a spectrum of adverse effect ranging from mild to threatening. Most severe adverse event is severe myopathy, which can cause acute renal failure.

In this report we present a case of rhabdomyolysis induced by high dose of Rosuvastatin in a 54 year aged man.

Case Report :

A 54 year aged man, was admitted with the complaint of weakness in both lower limbs and swelling over both lower limbs since 2 days. He had inferior wall Myocardial infarction, thrombolysed with streptokinase a month ago and was on antiplatelets, beta blocker, angiotensin converting enzyme inhibitors, oral hypoglycemic and Rosuvastatin 40 mg per day. After physical examination, he was found to have edema lower limb, lower motor neuron quadriparesis (grade III power in upper limb and grade II power in lower limb). Laboratory investigations revealed high serum creatinine level (7.2mg/dl), hyperkalemia (6.1 meq/liter), very high total serum creatinephosphokinase level (18877 U/L). His urine examination showed myoglobinuria, elevated liver enzymes- SGOT (AST) 885 U/L; SGPT (ALT) 665 U/L, ECG (electrocardiogram) was normal, 2D Echo showed mild left ventricular hypertrophy, left ventricular ejection fraction 60%; and ultrasonography of abdomen revealed bilateral renoparenchymal disease. Nerve conduction study showed moderately reduced conduction velocity EMG was normal. His clinical picture & laboratory findings were suggestive of acute kidney injury due to rhabdomyolysis. Various causes of rhabdomyolysis like trauma, thermal injury, toxins & infection were ruled out and statin was thought to be etiology. His Rosuvastatin was stopped and

^{1&2}Consultant Cardiologist and Associate Professor
JNMC, Sawangi

Address for Correspondence -

Dr. Deepak Sane

E-mail : sane_ds@rediffmail.com

hemodialysis was initiated along with supportive treatment. In between patient developed pulmonary edema twice, and was treated with hemodialysis & ultrafiltration. He showed gradual improvement clinically, with increased urine output, improvement in power, reduction of weight. After eleven days patient was mobile and discharged. He recovered completely. On follow up his serum creatinine was 1.48 (after one and half year). Presently he is on aspirin, clopidogrel, antihypertensive, oral hypoglycemic agents and diet restrictions for lipid control.

Discussion :

Many cases of rosuvastatin induced rhabdomyolysis have been reported in Canada and United States.² Rosuvastatin like other Statins can cause, life threatening rhabdomyolysis. The incidence of rosuvastatin induced rhabdomyolysis is not known exactly but it is presumed to be low.⁶ The rosuvastatin induced rhabdomyolysis is probable by CVP2Cg enzyme saturation.⁷ Use of high potency statins is associated with an increased rate of diagnosis for acute kidney injury in hospital admission compared with low potency statins. The effect seems to be strongest in the first 120 days after initiation of statin treatment.⁸ Different mechanisms are associated with acute kidney injury due to rhabdomyolysis such as hypovolemia, intraluminal obstruction by myoglobin, uric acid casts, direct myoglobin toxicity, renal ischemia secondary to muscular vaso constrictors and production of free radicals.^{9,10,12}

Elevated serum CPK levels are enough to establish the diagnosis of rhabdomyolysis. Five times higher

than normal CPK value confirms the diagnosis of rhabdomyolysis.¹⁰

The relative absence of abnormal spontaneous activity and myopathic Motor Unit Potentials in patients with severe weakness and extremely high CK levels was previously noted in rhabdomyolysis and constitute a dissociation between clinical and electrophysiological findings. Also patients with rhabdomyolysis are less likely to show abnormal EMG results when compared with patients with polymyositis.¹²

Treatment should be instituted immediately in order to modify the factors that cause acute kidney injury, such as volume depletion, tubular obstruction injury, aciduria and release of free radicals.⁹ After 3-30 days of withdrawal of Statins, the muscular symptoms usually decrease and the CPK normalizes.¹³

Similar cases of Rhabdomyolysis are reported in Literature, caused by rosuvastatin.

Brijesh Patel et al reported a case of rhabdomyolysis with simvastatin.¹⁴

K.S. Suthar et.al also reported a case of rhabdomyolysis, acute kidney injury and Quadriplegia due to rosuvastatin in a diabetic patient after angioplasty.¹⁵

Christopher-Stine et al. discovered a novel antibody directed against proteins weighing 200 and 100 k Da in the patients with statin induced myopathy.¹⁶ The antibody was eventually found to target the HMGCR (3 hydroxy, 3 methyl coenzyme A reductase).¹⁷ It was proposed that statins cause increased expression of HMGCR protein and an aberrant antigen recognizing process leading to the production of this autoantibody.¹⁷ Despite withdrawal of the statin, the overexpression of HMGCR in regenerating muscle cells sustains the immune response, further propagating the myopathy until immunosuppressive therapies are used to break the vicious cycle. In our case, patient improved after dialysis, hydration and supportive measures.

Table showing serial investigations -

No. of Days	Urea mg/dl	Creatinine mg/dl	Hb% gram%	WBC cells/cmm	Total CPK unit/litre
1	198	7.2	12.2	20,300	188770
3	169	6.4	9.9	11800	
7	157	5.8	10.8	19600	
9	109	4.2	9.7	17500	
12	104	4.1	10.2	22700	
1 year	51.7	1.82			14
1.5 year	48.6	1.71			

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