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SEVERE RHABDOMYOLYSIS AND ACUTE GRAFT DYSFUNCTION DUE TO THE CONCOMITANT USE OF STATIN IN A RENAL TRANSPLANT PATIENT

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ABSTRACT

Rhabdomyolysis is a condition of muscle cell death, resulting in acute to chronic kidney injury. Statins are known to be more safe, tolerated and the most effective drugs for treating hypercholesterolemia **[1]**. Rhabdomyolysis is a severe and rare adverse effect of statins, potentially leading to acute renal failure, promulgative intravascular coagulation, and gradually to death. According to the FDA, the mortality rate of Rhabdomyolysis is 0.15 per 1 million statin users **[2]**. Statins work by inhibiting the conversion of HMGCoA enzyme to Mevalonate by HMGCoA reductase. The exact mechanism of statin-induced Rhabdomyolysis is not known, but the occurrences are known to increase with the dose or their concentrations. The most common reasons for the myopathies associated with statin use are: cholesterol deficiency leading to renal membrane abnormalities, co-enzymes Q10 deficiency leading to abnormal mitochondrial respiratory function, or prenylated protein abnormalities leading to electrolytic imbalances **[3]**. The clinical spectrum of statin-induced myotoxicity includes a group of signs and symptoms, which ranges from asymptomatic elevations in serum Creatinine Phosphokinase (CPK) to more rare and severe myopathies and rarely, fatal Rhabdomyolysis **[4]**. This case describes a case on Rosuvastatin-induced Rhabdomyolysis with a fatal outcome in a patient receiving concurrent Everolimus and Statins for the past few years.

Keywords: HMG-CoA, CK, Allograft, MVA, CPK, CMV

INTRODUCTION:

Among the various antilipidemic agents, the 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors are the most commonly used class of drugs **[5]**. Statins acts by converting HMG-CoA to mevalonate (MVA) bt inhibiting HMGCoA reductase enzyme, which is a rate determining step in the cholesterol biosynthesis. Increases in serum transaminases of hepatic origin are dose dependent and occur approximately 1%. In India, myotoxicity or myalgias and elevated serum CPK levels (>10 times from the normal limit), occurs in 0.1% of patients. Myopathy, defined as a serum creatine kinase level of more than 10 times than the normal, has been estimated to occur in 0.1% to 0.5% of patients treated with statins during randomized clinical trials **[6]**. This is a rare case report of a 43-year-old male hospitalized in October 2023, for profound tiredness, pedal edema (both), right limb pain, and hyperintense lesions on arms and ® neck areas. He has a past history of Type II Diabetes Mellitus (3 yrs), Dyslipidemia (3 yrs), and CKD (Allograft recipient). He had a surgical history of right lobectomy (3 years back) of the lungs for fungal pneumonitis, which is detected pretransplant.

CASE REPORT:

A 43-year-old male patient admitted with chief complaints of pedal oedema, tiredness, right limb pain, itching red scaly lesions on arms and intense itching on the right side of the neck. He was an allograft recipient who underwent a transplant 20 years ago (2003). He has a past medical history of Type II Diabetes Mellitus, Systemic hypertension and Dyslipidemia. He had a surgical history of right lobectomy of the lungs for fungal pneumonitis, which was detected in 2002. His past medicines include T METFORMIN 1gm BD, T PREDNISOLONE 7.5mg OD, T ROSUVASTATIN 10mg HS and T EVEROLIMUS 1mg OD. He has been taking steroids for the past 10 years.

Admission examination showed: Normal body temperature, respiratory rate, pulse rate and blood pressure. Elevated parameters include ESR, CRP indicating the incidence of any form of infections. Other elevated parameters were HbA1C, SGOT, SGPT, Serum urea and Creatinine. Serum calcium, phosphorus, potassium and bicarbonate are within the normal limits. Serum sodium showed a slight decline on admission (132mmol/L). PT INR of the patient was normal and it was monitored daily, as was the renal function test **(Table 1)**. The laboratory parameters showed a greatly elevated creatine phosphokinase (CPK) level (39,557 U/L), which was monitored every other day **(Table 2)**. The peripheral smear study showed dimorphic anemia and mild neutrophilic leukocytosis

with a haemoglobin count of 7.2%. Abdomen and pelvis ultrasonography was done, revealing known complaints of chronic renal parenchymal disease. The transplanted kidney showed elevated cortical echotexture. Sigmoidoscopy did not show any abnormalities except for haemorrhoids. A Truenat-cartridge based nucleic acid amplification test was carried out on the serum, yielding a negative result. CytoMegalo Virus (CMV) was found in the serum (720 copies/ml). To investigate swelling on the right neck, an MRI spine with whole screening was performed, which incidentally detected a Vagal Schwannoma **(Figure 1)**.

Table 1: Daily monitored Renal Function Tests

Parameters (mg/dL)	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13
UREA	108	116	154	178	201	224	192	157	190	243	167	208	301
CREATININE	3.9	4.1	5.0	5.9	6.8	7.1	8.0	6.6	5.6	6.1	5.8	4.7	4.6

Table 2: Creatine phosphokinase (CPK) monitored on alternative days

Parameter (U/L)	D5	D7	D9	D11	D13
CPK	39557	6286	1170	435	214

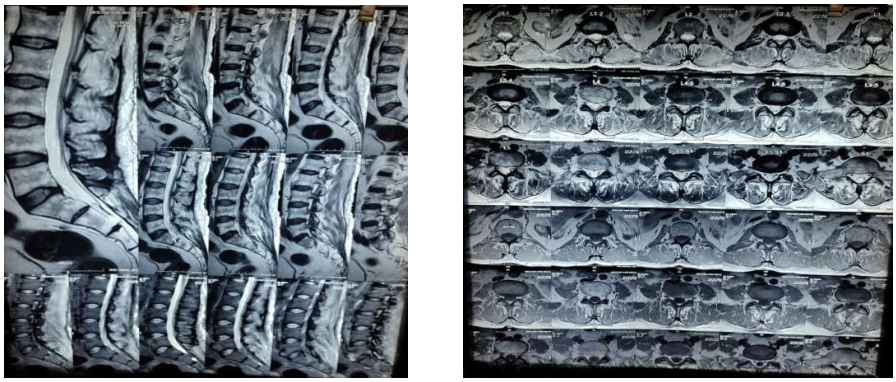

Figure 1: MRI Lumbo-Sacral spine with whole spine screening

After the findings of elevated levels of CPK, Rosuvastatin was suspected as the offending drug and stopped by the physician. All other past medicines were continued. The patient was treated with antibiotics, antihypertensives, iron supplements, urine alkalinizers, antihistamines, antifungals, hepatoprotectants, and nutritional supplements. The patient was given T TORSEMIDE 20mg TDS, T METOLAZONE 2.5mg OD, T IRON PYROPHOSPHATE 30mg OD, INJ ERYTHROPOIETIN 4000IU once weekly, T EBASTINE 20mg HS, LULICONAZOLE CREAM 1%w/w BD, INJ CEFOPERAZONE-SULBACTAM 1.5gm BD, INJ ACETYL CYSTEINE 600mg BD, T URSODEOXYCHOLIC ACID 300mg BD, NUTRITIONAL SUPPLEMENT 30gm BD, T DOXYCYCLINE 100mg BD, INJ METHYL PREDNISOLONE 4mg OD, and T SODIUM BICARBONATE 500mg TDS.

The patient's muscle weakness persisted despite the correction of elevated CPK, hyponatremia and discontinuation of Rosuvastatin. He expired in the hospital on day 14 without regaining his muscle strength. His discharge medicines are **(Table 3)**.

Table 3: Discharge medicines

S. No.	BRAND NAME	GENERIC NAME	DOSE	FREQUENCY
1	TAB OMNACORTIL	PREDNISOLONE	7.5mg	1-0-0
2	TAB CERTICAN	EVEROLIMUS	1mg	0-0-1 (10 pm)
3	TAB FERISOME	IRON PYROPHOSPHATE	30mg	1-0-0
4	INJ EPOSIS	ERYTHROPOIETIN	4000IU	Once weekly

DISCUSSION:

Statins are known to be effective for treating Dyslipidemia. They can also have various side effects, including rhabdomyolysis, which is potentially a fatal condition. Both lipophilic and hydrophilic statins may cause Rhabdomyolysis on concomitant use. Although the incidence was less, there are chances of getting these types of adverse effects. Rhabdomyolysis is caused by damaging the skeletal muscles and leads to the accumulation of muscle components (creatine kinase, myoglobin, lactate dehydrogenase, aldolase and various electrolytes) in the body [7, 8]. Skeletal muscle damage can lead to subsequent loss of muscle integrity. Here is a case report of an allograft recipient with elevated creatine kinase (CK), who was taking taking statins for 3 years and steroids for 10 years respectively. He presented with chief complaints of profound tiredness, pedal oedema, pain in the right limb, hyperintense red scaly lesions on the right side of the neck and arms.

In cases of drug-induced diseases, the prompt aim was to identify the offending drug and its sudden withdrawal. Here, the first step put forward by the physician when the CPK rises was the sudden stoppage of statins. Rhabdomyolysis induced acute graft dysfunction involves various mechanisms like: hypovolemia, intraluminal obstruction by myoglobin accumulation, uric acid casts, myoglobin toxicity, renal ischemia secondary to muscular vasoconstrictors, and production of free radicals [9, 10, 11]. The risk of Rhabdomyolysis or myopathies is higher in patients who are receiving concurrent gemfibrozil, erythromycin, itraconazole, niacin or any other immunosuppressants like cyclosporins, or everolimus. The use of concurrent statin and everolimus is not absolutely contraindicated.

CONCLUSION:

Concomitant use of statins and drugs that inhibit cytochrome P450 (CYP3A4) increases the risk of rhabdomyolysis in patients having renal or hepatic impairments. The efficacy of statins for

lipid-lowering is well tolerated; a small proportion of patients may develop myopathy. Selecting a suitable lipid-modifying agent that is efficacious at low doses and with minimal risk of myopathies helps to maximize the benefit-risk ratio of therapy. Here, the patient was presented with complaints of pedal oedema, tiredness, red scaly lesions over arms and neck, and limb pain. Several laboratory tests were performed and showed an elevation in CPK levels. Thus, the offending agent was identified as Rosuvastatin and later the drug was stopped. Subsequently, the CPK levels began to normalize. An MRI of the spine incidentally detected a Vagal Schwannoma which was managed by giving corticosteroids. The patient was then treated with antibiotics, BP lowering agents, nutrients, hepatoprotectants, steroids, and antifungals. The patient was treated according to the therapeutic guidelines.

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CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest.

REFERENCES:

[1] Schreiber DH, Anderson TR. Statin-induced Rhabdomyolysis. The Journal of emergency medicine. 2006 Aug 1; 31(2):177-80.

[2] Kashani A, Phillips CO, Foody JM, Wang Y, Mangalmurti S, Ko DT, Krumholz HM: Risks associated with statin therapy:a systematic overview of randomized clinical trials. Circulation, 2006, 114, 2788-97.

[3] Antons KA, Williams CD, Baker SK, Phillips PS. Clinical perspectives of statin-induced rhabdomyolysis. The American Journal of medicine. 2006 May 1; 119(5):400-9.

[4] Sathasivam S. Statin induced myotoxicity. Eur J Intern Med. 2012; 23:317-24.

[5] Maron DJ, Fazio S, Linton MF.Current perspectives on statins, Circulation 2000; 101:207-13.

[6] Shek A, Ferrill MJ. Statin-fibrate combination therapy. Annals of Pharmacotherapy. 2001 Jul; 35(7-8):908-17.

[7] Parker BA, Thompson PD. Effect of statins on skeletal muscle: exercise, myopathy, and muscle outcomes. Exercise and sport sciences reviews. 2012 Oct; 40(4): 188.

[8] Torres PA, Helmstetter JA, Kaye AM, Kaye AD. Rhabdomyolysis: pathogenesis, diagnosis, and

treatment. Ochsner Journal. 2015 Mar 20; 15(1); 58-69.

[9] Vanholder R, SU M, Erek E, Lameire N. Rhabdomyolysis. Journal of the American Society of Nephrology. 2000 Aug 1; 11(8): 1553-61.

[10] Rosa EC, liberatori Filho AW, Schor N, Lopes AC. Rhabdomyolysis and acute kidney failure. Revista da Associacao Medica Brasileira (1992). 1996 Jan 1; 42(1): 39-45.

[11] Holt S, Moore K. Pathogenesis and treatment of renal dysfunction in Rhabdomyolysis. Intensive care medicine. 2001 May; 27: 803-11.