CASE REPORT

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Life-threatening side-effect of a popular treatment – case report

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Abstract

Statins are the first-line therapy in the prevention of cardiovascular diseases. One of the most commonly used statins is rosuvastatin. Its main properties include reducing cholesterol and triglyceride levels. However, it can cause side-effects, the most serious of which include rhabdomyolysis and acute kidney injury (AKI). The case is presented of a 91-year-old male with rhabdomyolysis, AKI, anuria, fluid overload and liver injury. Prior to admission to hospital, the patient reported progressively worsening pain in the lower limbs and sensory disturbances. He had undergone a contrast-enhanced imaging study in another hospital, which further aggravated kidney disfunction. The patient had been taking rosuvastatin without dose monitoring, suggesting that statinrelated rhabdomyolysis had caused his condition. This case demonstrates that advanced age, polypharmacy and contrast agents increase the risk of severe statin-related adverse events, and highlights the importance of proper monitoring during therapy.

Key words

acute kidney injury, rhabdomyolysis, rosuvastatin, myopathy

INTRODUCTION

Statins remain the first-line therapy in lipid-lowering treatment for both primary and secondary prevention of cardiovascular disease. These medications not only reduce low-density lipoprotein cholesterol (LDL-C) via inhibition of 3-hydroxy-3-methylglutarate attached to CoA reductase, the key rate-limiting step in the cholesterol biosynthetic pathway, but also upregulate expression of the low-density lipoprotein receptor, improving serum clearance [1]. Mechanisms for statin's demonstrated other benefits, including protection of cerebral arterial vessels from subacute damage due to hypertension, diabetes, and other harmful agents due to their systemic anti-inflammatory and endothelium-protective effects [2].

Despite its favourable safety profile, rosuvastatin – particularly at higher doses or in patients with predisposing risk factors – can be associated with muscle-related adverse events, including myopathy and rhabdomyolysis. Rhabdomyolysis is a complex medical condition involving the rapid dissolution of damaged or injured skeletal muscle [3]. Rhabdomyolysis should be suspected in patients presenting with the triad of muscle pain, weakness, and dark-coloured urine, but few patients have all three classic symptoms [4]. Following muscle injury, the serum CK begins to rise within 2 – 12 hours, and reaches its maximum within 24 – 72 hours [4].

A recent study reported the incidence of rhabdomyolysis with currently available statins in the ranges of 0.6–1.2 per 10,000 person-per year [5]. Its most serious complication is acute kidney injury (AKI), which results from myoglobin-induced nephrotoxicity, intratubular cast formation, and haemodynamic and electrolyte disturbances. The development of AKI in this context significantly increases the risk of multi-organ failure and constitutes a major determinant of prognosis.

OBJECTIVE

The aim of the case report is to present the severe complications of rosuvastatin therapy, and to discuss additional risk factors associated with statin treatment, as well as the importance of its proper recognition in clinical practice.

CASE REPORT

A 91-year-old male patient was admitted to the county hospital's geriatric ward initially due to severe pain, lower limb paralysis, and increasing weakness. The patient had a history of NSTEMI heart attack with PCI LAD DES angioplasty (03.2023), PCI LAD/DIA 2xDES (08.2022), and PCI LAD DES with lithotripsy and DES stent implantation (08.2022). The patient had chronic hypertension with associated lipid disorders and was advised to take rosuvastatin. The patient was taking Zaranta 40mg irregulary at home without regular medical check-ups. For diagnostic purposes, a contrast-enhanced CT scan was performed, and pain and anti-inflammatory treatment initiated. Due to a rapid decline in kidney function and anuria, which may have been induced by exposure to the contrast agent, the patient was transferred to

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At the time of admission, the patient was in a very severe condition with massive rhabdomyolysis, acute kidney damage, liver damage, over-hydration, anuria, and lower limb paralysis. The patient was qualified for renal replacement therapy due to clinical condition, anuria, and high azotemia parameters (creatinine – 8.57 mg/dL; urea – 282.00 mg/dL). In laboratory tests, the current features of water intoxication and electrolyte disorders (HGB – 12.0 g/dL; RBC – 3.61 mln/mm3; haematocrit – 35.2%; BNP – 751.2 pg/ml; hyponatraemia – 130 mmol/l; hypocalcemia – 7.7 mg/dL; hyperphosphataemia – 6.6 mg/dL) and massive rhabdomyolysis (CK – 11270.0 U/L; myoglobin >1000.0 ng/ml; ALT – 412 U/L; AST – 359 U/L; troponin I – 101 ng/L; creatine kinase cardiac isoenzyme – 209.2 U/L). Elevated inflammatory parameters (CRP – 20.958 mg/l; ESR – 26 mm/h; ferritin – 555 ng/ml; fibrinogen and procalcitonin) were within reference ranges. A general urine test was performed which showed the presence of fresh erythrocytes densely covering the field of view.

In the patient's subsequent hospitalization days, a gradual decrease in the values of some parameters was observed. The following data were obtained in laboratory tests: CK – 319.0 U/L; myoglobin – 352.9 ng/ml; creatinine – 5.63 mg/dL; B-type natriuretic peptide – 718.1 pg/ml; troponin I – 41 ng/L. Progressive normocytic anaemia and elevated inflammatory parameters persisted. A previously scheduled neurological and cardiological consultation was performed. In the nerve conduction and EMG study, severe sensory-motor demyelinating polyneuropathy with features of myopathy in the course of rhabdomyolysis was demonstrated. The cardiological consultation and echocardiography showed good contractile function of both ventricles, a Grade I diastolic dysfunction, and mild insufficiency of the atrioventricular and aortic valves. Myocardial ischemia was excluded.

A total of 6 haemodialysis treatments were performed. The applied treatment (pharmacotherapy, dialysis therapy) gradually improved the patient's condition. Laboratory tests showed a decrease in azotemia parameters (creatinine – 1.20 mg/dL; urea – 41.0 mg/dL) and liver enzymes (ALT – 48 U/L; AST – 36 U/L), as well as stabilization of the water-electrolyte balance (potassium – 4.35 mmol/l; sodium – 140 mmol/l; calcium – 9.3 mg/dL, inorganic phosphorus – 2.9 mg/dL). There were no signs of previously present rhabdomyolysis (CK – 29.0 U/L; myoglobin – 76.2 ng/ml; troponin I – 28 ng/L; cardiac CK isoenzyme – 8.9 U/L). Gradual improvement in limb mobility was achieved (symptoms were caused by rhabdomyolysis) and diuresis returned.

The patient was advised to temporarily discontinue taking the previously prescribed rosuvastatin. Consistent care from the Cardiology Clinic and check-ups at the Clinic of Nephrology were also recommended.

RESULTS

During hospitalization, the patient underwent six hemodialysis sessions due to massive fluid overload and severe azotaemia. The treatment, which included pharmacotherapy and renal replacement therapy, led to a significant improvement in the patient's clinical condition. A systematic reduction in markers of rhabdomyolysis was observed, followed by their eventual normalization, which correlated with an improved general condition and resolution of muscle symptoms. Concurrently, a marked improvement in renal function was observed, manifested by a decrease in azotaemia parameters and return of normal diuresis. Additional tests revealed no evidence of acute myocardial ischaemia, with preserved left ventricular systolic function. NT-proBNP levels remained elevated, reflecting chronic heart failure. Despite the observed clinical improvement, anaemia and elevated inflammatory markers persisted. Ultimately, the patient's general condition stabilized and the acute phase symptoms significantly resolved.

DISCUSSION

In the presented case, the complexity and the probable risks associated with the use of statins in elderly patients are shown. This concerns people particularly burdened with many coexisting diseases. Rosuvastatin, despite many beneficial pharmacokinetic factors, such as limited hepatic metabolism and little influence on cytochrome P450, can still cause severe adverse effects, especially in individuals in high-risk groups. In the presented patient factors such as age over 90 years, polypharmacy, chronic cardiovascular disease, possible malnutrition, dehydration, and exposure to a contrast agent were present, which additionally deepened the impairment of kidney function.

In the literature, the risk of statin-induced myopathy increasing with the patient's age, especially above 80 years, has been mentioned many times. This results from physiological changes such as impaired glomerular filtration, reduced muscle mass, various drug interactions and increased susceptibility to electrolyte disorders. The incidence of rhabdomyolysis with currently available statins in the ranges of 0.6–1.2 per 10,000 person-per year [5]. All statins are associated with SAMS. Fluvastatin and pravastatin are least likely to be associated with myopathy followed by rosuvastatin. Atorvastatin, lovastatin, and simvastatin in order with the increasing association of myopathy [6]. Studies conducted to compare the effects of statins and their correlation with rhabdomyolysis showed that among 10,657 reports with rhabdomyolysis with statins, simvastatin was the highest risk statin in comparison with others: ROR = 2.20 (2.11–2.29). The risk was higher in men, older than 74 years and in cases of drug interactions [7]. Additionally, it is worth emphasizing that in geriatric patients there is often a lack of supervision over taking medications. This was the case in the presented 91-year-old patient, who had been taking rosuvastatin for a long time without medical supervision or laboratory testing me.

In the discussed case, the key role was played by the accumulation of several risk factors, namely long-term statin use, deterioration of general condition, simultaneous use of anti-inflammatory drugs, dehydration and nephrotoxicity of the administered contrast agent. The combination of these elements led to massive rhabdomyolysis, which in turn caused acute kidney failure with anuria. It is worth emphasizing that in this case, liver damage also occurred which, together with rhabdomyolysis, may indicate intense muscle breakdown in combination with multi-organ dysfunction. Aggressive fluid therapy, correction of metabolic derangement and, when warranted, renal replacement therapy, formed the mainstays of treatment [8].

In geriatric medicine, the importance of an individualized approach to the patient, the treatment, taking into account anticipated benefits relative to risks, as well as using the lowest affective dose and regular monitoring of necessary parameters, is increasingly emphasized.

The most important element of this case is the presentation of the problem of taking stating by patients without any medical supervision. These drugs are widely used and considered safe, which may consequently lead to their self-administration without medical control and laboratory tests. The lack of monitoring of parameters such as creatine kinase activity, kidney function or liver function may result in late recognition of adverse effects and lead to very severe complications, such as acute kidney injury or rhabdomyolysis. It is worth warning patients about this issue so that in the future they do not unknowingly cause such adverse consequences of the uncontrolled use of statins.

CONCLUSIONS

1. Rosuvastatin, despite its high effectiveness, can lead to severe and even potentially fatal adverse effects. This is particularly important in patients with risk factors.
2. The most serious complications of rosuvastatin are definitely rhabdomyolysis and acute kidney failure.
3. Risk factors for statin-induced myopathy and rhabdomyolysis include advanced age, polypharmacy, metabolic disorders, dehydration, malnutrition, and exposure to nephrotoxic agents.
4. The key element in treating complications from uncontrolled statin use is early recognition of rhabdomyolysis and quick implementation of intensive treatment. This reduces the risk of multi-organ damage.
5. In geriatric patients, fluvastatin and pravastatin are the most preferred statins. However, it is important to remember that all statins have a significant association with myopathy.
6. Coordination of activities of specialists from different fields is necessary to improve treatment outcomes.
7. The education of patients and their caregivers regarding medication use, regular medical check-ups, and the absolute prohibition of independently modifying treatment is essential.

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