Case Report

Myoglobinuric renal failure due to long-standing lovastatin therapy in a patient with pre-existing chronic renal insufficiency

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Introduction

Atraumatic rhabdomyolysis with consecutive acute myoglobinuric renal failure due to lipid-lowering drugs is a rare complication. In earlier years fibrate-associated rhabdomyolysis was observed more commonly in patients with renal insufficiency [1]. There are relatively rare case reports concerning rhabdomyolysis and renal damage due to therapy with HMG-CoA reductase inhibitors; in most of the cases, however, patients had had renal insufficiency or had received other nephrotoxic drugs [2]. We describe a case ofLovastatin-induced myoglobinuric renal failure after 4 years ofLovastatin therapy in a patient with pre-existing renal insufficiency.

Case report

This 67-year-old male patient had a history of epimembranous glomerulonephritis with nephrotic syndrome of 6 years duration. Though the patient was treated initially with prednisolone and cyclophosphamide (i.v. bolus) and later with cyclosporin, the progression of renal disease could not be attenuated. Cyclosporin therapy was stopped when serum creatinine increased to 5 mg/dl. Since 1991 the patient had receivedLovastatin also (20 mg daily) for treatment of hypercholesterolaemia (total serum cholesterol >470 mg/dl) as a result of the nephrotic syndrome (>7.5g protein/24-h urine). In July 1995 the serum creatinine level was 9.0 mg/dl, but dialysis was not initiated because the patient had no symptoms of uraemia. The following drugs were administered at this time: furosemide, marcoumar, dihydroxycholecalciferol, carvedilol, erythropoietin (s.c.), and Lovastatin. Two weeks later the patient was admitted to the hospital with pain in the legs and darkly discoloured urine.

Blood pressure at admission was 160/90 mmHg and heart rate 80/min. Laboratory data at onset included elevated enzyme levels (CK-NAC 9470 U/L, CK-MB 380 U/L, SGOT 309 U/L, SGPT 142 U/L, LDH 1280 U/L and serum myoglobin 19,000 μg/l) and positive evidence of myoglobin in urine (without erythrocytura). Serum creatinine was 9.8 mg/dl, BUN 85 mg/dl, serum sodium 140 mmol/l, serum potassium 6.1 mmol/l, serum calcium 2.01 and phosphate 3.05 mmol/l. According to the drug history and the laboratory data the diagnosis of 'Lovastatin-induced rhabdomyolysis' was made.

On admission diuresis was normal, but decreased to 400 ml urine/day during the next 2 days. In parallel, serum creatinine increased to 11 mg/dl and BUN to 90 mg/dl. Therefore haemodialysis was initiated in the patient. Within the next 10 days elevated enzyme levels returned into the normal range. Under furosemide infusion diuresis increased only to a maximum of 1000 ml/day, as a result the patient had to remain on chronic haemodialysis treatment (Figure 1).

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Discussion

In patients with chronic renal insufficiency, lipid-lowering therapy is able to reduce the high cardiovascular risk [3] and retard the progression of the renal disease [4]. In several studies therapy with lovastatin or other HMG-CoA reductase inhibitors was well tolerated and showed few side-effects in patients with nephrotic syndrome [2,5]. Non-traumatic rhabdomyolysis with consecutive acute renal failure due to administration of HMG-CoA reductase inhibitors is a rare complication. In most cases other nephrotoxic factors played an additional causal role. Some patients reported received nephrotoxic drugs such as cyclosporin [2], e.g. when lovastatin was administered after cardiac transplantation [6]. Probably there is also a higher risk of myopathy and rhabdomyolysis in patients receiving gemfibrozil in addition to lovastatin [7].

Drug-induced non-traumatic rhabdomyolysis occurs usually within the first few weeks after the initiation of drug administration [8]. This complication has a good prognosis despite severe hypercatabolism [9]. In our case non-traumatic myoglobinuria occurred after a long-lastingLovastatin therapy, and necessitated initiation of chronic dialysis requirement. Our patient received 20 mg lovastatin daily, which is the recommended dosage in renal insufficiency when creatinine clearance is below 30 ml/min [10]. Creatinine clearance in our patient was 8 ml/min per 1.73 m² at this point. BothLovastatin and its beta-hydroxyacid metabolite are bound (>95%) to plasma protein. Following an oral dose only 10% of the dose will be excreted in urine and 83% in the faeces. But in a study of patients with severe renal insufficiency (creatinine clearance 10–30 ml/min) the plasma concentrations of total inhibitors after a single dose ofLovastatin were twice those in healthy subjects [11].

We conclude (i) that non-traumatic rhabdomyolysis may occur even after long-standingLovastatin therapy, and (ii) that the recommended dosage of 20 mgLovastatin/day should be reduced in patients when GFR is below 10 ml/min.

References


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