Rhabdomyolysis and Acute Renal Failure in a Heart Transplant Recipient Treated with Hypolipemiant

E. Enrique de Alava  
J.J. Jesús J. Sola  
M.D. Dolores Lozano  
F.J. Javier Pardo-Mindán

Dear Sir,

Rhabdomyolysis is becoming a major cause of acute renal failure (ARF). Its main causes are traumatisms and alcohol or drug abuse such as cocaine or methadone [1]. Over the last years hypolipemiant like lovastatin and gemfibrozil are increasingly recognized as a cause of rhabdomyolysis and ARF [2]. We report a case of a hyperlipemic heart transplant recipient that developed rhabdomyolysis and ARF when treated with gemfibrozil and lovastatin because of his hyperlipidemia.

A 48-year-old man with a history of hypertension and type II diabetes mellitus underwent an orthotopic cardiac transplantation because of ischemic myocardiopathy in February 1989. Postoperatively, he received immunosuppressive therapy. In April 1990 the patient had hypercholesterolemia (346 mg/dl) and hypertriglyceridemia (268 mg/dl) and was treated with lovastatin and gemfibrozil. Thirty-six hours after the beginning of therapy he complained of general malaise, muscular aches, and marked weakness. At the onset of ARF the medical regimen consisted of cyclosporine 3 mg/kg/day, azathioprine 100 mg daily, prednisone 15 mg 3 times a day, gemfibrozil 300 mg 3 times a day, and lovastatin 40 mg daily. Biochemical data at this moment were serum creatinine 6.2 mg/dl, proteinuria 967 mg/day, CPK 14,100 U/l, and serum cholesterol 161 mg/dl. Kidney and muscular biopsies were performed.

Muscle biopsy showed many swollen, hyalinized, eosinophilic muscle fibers without any inflammatory infiltrate. Histochemical study of muscle ATPases and DPNH showed that necrotic fibers were mainly of the type II (fig. 1), suggesting a toxic damage. Renal biopsy displayed widened necrotic tubules filled by eosinophilic, granular, PAS-positive material. An immunohistochemical study using antimyoglobin antibodies identified it as myoglobin (fig. 2). A diagnosis of acute tubular necrosis with myoglobinuria was made. Therapy was discontinued and hemodialysis was required. The patient improved and was discharged in excellent condition after 4 weeks.

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Lovastatin inhibits cholesterol synthesis and gemfibrozil controls hypertriglyceridemia when diet is unsuccessful [2, 3]. Both drugs have a low rate of side effects [2]. However, the combined therapy among lovastatin, gemfibrozil, and cyclosporine has been associated with rhabdomyolysis and acute renal failure which resolved after discontinuation of therapy [2, 4, 5]. Up to now 4 such cases have been described in cardiac transplants.

Both cyclosporine and gemfibrozil appear to inhibit hepatic metabolism of lovastatin, resulting in higher circulating levels of the active drug [2]. A direct toxic effect has been suggested, either destabilizing the sarco-lemmal membrane [2] or damaging mitochondria by influencing the electron transport system of the inner mitochondrial membrane [6]. This toxic effect would lead to myofibrillar degeneration, releasing of myoglobin and filtration by the glomeruli. The mechanism of tubular damage is a combination of mechanical obstruction and toxic injury by either myoglobin or another substance released to blood in muscle damage [7].

References