Rhabdomyolysis and Acute Renal Failure Associated with Lovastatin

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Dear Sir,

Lovastatin is an inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase with known efficiency [1] and few adverse effects, usually mild [1, 2]. Rhabdomyolysis is exceptional and is nearly always associated with other drugs that increase lovastatin levels or can produce rhabdomyolysis by themselves: cyclosporine A [3-5], gemfibrozil [4,6-8], ery-thromycin [9], nicotinic acid [10]. We present a case of severe rhabdomyolysis with acute renal failure (ARF) and hepatopathy during low-dose lovastatin treatment without known drug interactions.

A 65-year-old woman with hyperlipide-mia, hypertension, coronariopathy and mild renal insufficiency was receiving aspirin (125 mg/day), nitrites (20 mg/8 h) and quinapril (20 mg/day). Later, lovastatin (20 mg/day) was added. Two weeks later, she noticed diffuse myalgias and progressive strength loss as well as dark urine. A week later, after no improvement with nonsteroidal anti-inflammatory drug and vitamins, she came to our center with anuria and immobility. There was no history of other drugs, toxics or alcohol ingestion, violent exercises or infectious or systemic symptomatology. Exploration showed blood pressure 150/80 mm Hg, central venous pressure 0 cm of water, dehydrated skin and mucoses and no fever. Muscular masses were painful at palpation with generalized decrease in strength. The rest of the neurological exploration was normal. Laboratory data were: urea 28.02 mmol/l (168 mg/dl), Cr 371 µmol/l (4.2 mg/dl), K⁺ 6.5 mmol/l (6.5 mEq/l), Ca²⁺ 2.44 mmol/l (9.8 mg/dl), P 1.9 mmol/l (6.1 mg/dl), glucose 5.78 mmol/l (105 mg/dl), uric acid 463.94 µmol/l (7.8 mg/dl), bicarbonate 18.7 mmol/l (18.7 mEq/l). Maximal enzyme values were: cre-atine kinase > 1,667 µmol/l (> 100,000 U/l), CK-MB 5%, myoglobin > 41,000 pg/l (> 41,000 ng/ml), aldolase > 4,167 nkat/l (> 250 U/l), aspartate aminotransferase 22.43 µkat/l (1,346 U/l), alanine aminotransferase 11.3 µkat/l (678 U/l), γ-glutamyl trans-peptidase 0.88 µkat/l (53 U/l), lactate dehy-drogenase 104.42 µkat/l (6,264 U/l), alkaline phosphatase 2.90 µkat/l (174 U/l), bilirubin 8.55 µmol/l (0.5 mg/dl). Prothrombin-activ-ity was 69%, prothrombin time 16.5/13.9. Ery-throcyte and platelet count were normal, with 11.6 × 10⁷ (11,600 × 10⁶/l) leukocytes. Urine was dark with colorimetric reaction for blood (+ + +), 10-12

erythrocytes/field and myoglobin 1,560 µg/24 h (n < 50). Microbiological, immunological and thyroid function assays were normal. When we saw the patient, she was off her previous treatment and on steroids because of the initial suspicion of polymyositis. The diagnosis was acute rhabdomyolysis with secondary ARF and hepatopathy, initiating energetic volume reposition and infusion of bicarbonate, mannitol and furosemide with no diuretic response. Anuria lasted for 2 weeks and 10 hemodialysis sessions were needed. Severe hypocalcemia and hyperphosphoremia were produced [Ca²⁺ 1.34 mmol/l (5.4 mg/dl), P 3.19 mmol/l (9.9 mg/dl)]. Spontaneous calcemic rebound was observed [2.61 mmol/l (10.5 mg/dl)] though no calcium was added. Two months later, renal function was similar to previously [Cr 106 µmol/l (1.2 mg/dl), creatinine clearance 0.83 ml/s (50 ml/min)]. Steroids were stopped early, showing no benefits. Muscular symptoms

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matology began to improve in the 3rd week; she was able to get out of bed in the 4th week, as enzymes returned to normal values, and she achieved complete recovery 3 months later. An electrophysiology study on the 2nd day was without anomalies. Ten days later, it showed an acute myositis pattern with myogenic and short polyphasic signs in all explored muscles. Muscular biopsy was not carried out due to artefactation caused by steroids.

After discarding other causes of rhabdo-myolysis (alcohol, toxics, effort, infections, ischemia, hypothyroidism), a pharmacological effect was considered. Before beginning with lovastatin, the patient had perfectly tolerated previous drugs. We did not find reports of rhabdomyolysis due to the drugs she received, except for 1 salicylate-associated intoxication case [11], but our patient received only 125 mg/day of aspirin. Otherwise, there are several rhabdomyolysis reports in relation to lovastatin, most of them associated to some drugs that could strengthen or produce by themselves this adverse effect, as we showed before. By contrast, this patient did not receive any of these drugs, and only low doses of lovastatin were used. Due to lovastatin hepatobiliary metabolism, it seems improbable that previous light renal insufficiency could have increased lovastatin seric levels. This severe rhabdomyolysis case with secondary ARF associated to lovastatin, although exceptional, shows the potential risk during lovastatin use, even at low doses.

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484

Fernández Zatarain/Navarro/García/ Rhabdomyolysis and ARF Associated with
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