

Rhabdomyolysis due to combined treatment with lovastatin and cholestyramine

Assistant Professor C CHRYSANTHOPOULOS (Patras Medical School, Patras, Greece) and Professor NICHOLAS KOUNIS (Patras Technological Educational Institute, Patras 26221, Greece) write: We report two cases in which rhabdomyolysis occurred after combined treatment with lovastatin and cholestyramine.

Case 1—A 31 year old male athlete with type IIa hyperlipidaemia was treated with lovastatin 20 mg twice daily and cholestyramine 12 g twice daily. Four weeks later he experienced diffuse muscular pain and generalised weakness and was unable to walk. Clinical examination showed sluggish tendon reflexes and diffuse muscle tenderness. His urine was red-brown, and dipstick testing showed high concentrations of haem. Microscopic examination of urine showed four to eight erythrocytes per high power field and urine myoglobin concentration was 125 000 µg/l. Serum muscle enzyme concentrations were raised (serum myoglobin >200 µg/l), but his renal function remained normal. Drug treatment was stopped, and he was confined to bed and treated with intravenous fluids. Twenty four hours later the myoglobinuria had resolved. The muscle pain and weakness resolved gradually over the next two weeks, and the serum muscle enzyme concentrations returned to normal.

Case 2—A 42 year old man with type IIa hyperlipidaemia had persistently raised serum lipid concentrations despite appropriate diet and drug treatments. He took regular aerobic exercise. His blood urea concentration was 6.7 mmol/l and serum creatinine 88 µmol/l. Lovastatin 20 mg twice daily and cholestyramine 12 g twice daily were started. Two weeks later he experienced aching of his muscles, which gradually worsened, leading to generalised tenderness and weakness. The urine was dark, and dipstick testing showed high concentrations of haem. The urine myoglobin concentration was 115 000 µg/l. Serum muscle enzyme concentrations were increased (serum myoglobin >250 µg/l), and renal function was impaired (urea 26 mmol/l, creatinine 400 µmol/l). Drug treatment was stopped, and haemodialysis was started the next day. This treatment was continued for two months until the laboratory findings returned to normal.

Severe but reversible myopathy has been reported in two patients receiving combined treatment with lovastatin and cholestyramine and in

one patient receiving lovastatin alone.^{1,2} There are at least four reports of rhabdomyolysis and acute renal failure and three of rhabdomyolysis without renal failure in patients undergoing cardiac transplantation receiving both lovastatin and cyclosporin.^{3,5} Rhabdomyolysis and renal failure have been reported in seven patients receiving combined treatment with lovastatin and gemfibrozil, of whom three had pre-existing renal impairment.^{6,8}

Lovastatin probably interferes with muscle metabolism. Both our patients took regular aerobic exercise. Myoglobinuria may be caused by vigorous exercise, and evidence suggests that exercise predisposes to myopathy.² We cannot say whether cholestyramine played a part in the development of rhabdomyolysis, which should therefore be attributed to lovastatin and exercise alone.

All patients receiving lovastatin alone or with other drugs should avoid strenuous muscular work and be monitored for muscular symptoms.

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- 2 Walrvens PA, Greene C, Frerman FE. Lovastatin, isoprenes, and myopathy. *Lancet* 1989;ii:1097-8.
- 3 Corpier CL, Jones PH, Suki WN, Lederer MD, Quinones MA, Schmidt S, et al. Rhabdomyolysis and renal injury with lovastatin use: report of two cases in cardiac transplant recipients. *JAMA* 1988;260: 239-41.
- 4 Norman DJ, Illingworth DR, Munson J, Hosenpud J. Myolysis and acute renal failure in a heart-transplant patient receiving lovastatin. *N Engl J Med* 1988;318:46-7.
- 5 East C, Alivizatos PA, Grundy SM, Jones PH, Farmer JA. Rhabdomyolysis in patients receiving lovastatin after cardiac transplantation. *N Engl J Med* 1988;318:47-8.
- 6 Kogan AD, Orenstein S. Lovastatin-induced rhabdomyolysis. *Postgrad Med J* 1990;66: 294-6.
- 7 Marais GE, Larson KK. Rhabdomyolysis and acute renal failure induced by combination lovastatin and gemfibrozil therapy. *Ann Intern Med* 1990;112:228-30.
- 8 Pierce LR, Wysocki DK, Gross TP. Myopathy and rhabdomyolysis associated with lovastatin-gemfibrozil combination therapy. *JAMA* 1990;264:71-5.

Nifedipine induced gingival abscesses

Drs GABRIELA KOLLER-BENZ, ANDREA FRITZSCHE, and RETO KRAPF (Insel University Hospital, CH-3010 Berne, Switzerland) write: The calcium channel blocking drug nifedipine has been implicated in the development of gingival hyperplasia.^{1,3} Here we describe a woman who developed gingival abscesses after taking nifedipine.

Three days after starting nifedipine (10 mg four times a day) for idiopathic Raynaud's phenomenon a 27 year old woman consulted a dentist with three gingival abscesses. While she

continued to take nifedipine five more abscesses appeared over the next two days. The abscesses were drained by a paradontologist and nifedipine stopped. Three weeks later her gingiva was normal. We restarted the patient on nifedipine at the same dosage. After two weeks she developed a large gingival abscess and stopped taking nifedipine; two days later the abscess was drained. Biopsy of the abscess wall showed pronounced lymphoplasmacellular infiltrates. There was no epithelial hyperplasia or increase in acid mucopolysaccharide concentration (alcian blue staining), and no bacteria or fungi were present in the specimen. No organisms other than *Streptococcus viridans* were cultivated in the drained material. The abscess healed uneventfully and the patient had no further gingival or dental problems after discontinuing nifedipine treatment (follow up seven months).

The temporal association and recurrence on re-exposure suggest that nifedipine was responsible for the development of gingival abscesses in this patient. She was taking no other drugs and we later confirmed that she swallowed the nifedipine and did not hold it in her mouth. The clinical and histological characteristics were different from the gingival hyperplasia previously observed in patients taking nifedipine, which is characterised by epithelial hyperplasia, absence of serious inflammation, and an increase in acid mucopolysaccharide concentrations.^{1,3} Nifedipine should be stopped in a patient with gingival abscesses; discontinuation may eliminate the need for surgical intervention.

- 1 Lucas RM, Howell LP, Wall BA. Nifedipine-induced gingival hyperplasia. *J Periodontol* 1985;56:211-5.
- 2 Van der Wall EE, Tuinzing DB, Hes J. Gingival hyperplasia induced by nifedipine, an arterial vasodilating drug. *Oral Surg Oral Med Oral Pathol* 1985;60:38-40.
- 3 Shaftic AA, Widdup LL, Abate MA, Jackowitz AI. Nifedipine-induced gingival hyperplasia. *Drug Intell Clin Pharm* 1986;20:602-5.

Guillain-Barré syndrome after treatment with streptokinase

Dr D BARNES and Professor R A C HUGHES (Guy's Hospital, London SE1 9RT) write: A few reports have implicated intravenous streptokinase as a precipitant of the Guillain-Barré syndrome.^{1,3} We have recently seen such a case. A 45 year old epileptic man suffered a myocardial infarction in January 1991 and was treated with intravenous streptokinase. He made an uneventful recovery, but three weeks later he noticed pins and needles in his hands and feet and bilateral facial weakness. He also

suffered his first seizure for 10 years and was readmitted to hospital. Over one week his condition progressed to a glove and stocking sensory loss, severe leg and bulbar weakness, moderate arm weakness, and bilateral internuclear ophthalmoplegia. The results of routine investigations, including a porphyrin screen and viral antibody titres, were normal. The protein content of cerebrospinal fluid was greater than 2 g/l with no white cells. Motor conduction velocities were slightly slowed (41 m/s in the forearm segment of the median nerve; 29 m/s in the leg segment of the tibial nerve), distally evoked motor action potentials were small and dispersed, and F waves were unobtainable. These findings suggested a demyelinating neuropathy. He was given six plasma exchanges, during which his neurological condition improved. One month after the onset of symptoms power in his arms had returned to normal and he could walk with a frame. After three months he was walking independently.

Only two cases of the Guillain-Barré syndrome occurring after myocardial infarction not treated by streptokinase have been reported.⁴ Since myocardial infarction is common this association was probably coincidental. Five cases of the Guillain-Barré syndrome after streptokinase treatment have been described, including ours, but only two occurred after myocardial infarction¹; the other indications for streptokinase were axillary vein thrombosis and multiple pulmonary emboli, and the indications were not stated in the third case.^{2,3} It remains unclear whether this association is genuine or coincidental.⁵ Only one such case was recognised in each of 1981, 1982, and 1983 despite a doubling in the annual number of patients treated with streptokinase during this period. In the United Kingdom the Committee on Safety of Medicines has not received any other similar reports. As streptokinase is a foreign protein derived from group C streptococci it might induce the immunological reaction that is presumed necessary for the development of the Guillain-Barré syndrome.

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- 2 Eden KV. Possible association of Guillain-Barré syndrome with thrombolytic therapy. *JAMA* 1983;249:2020-1.
- 3 Cicale MJ. Guillain-Barré syndrome after streptokinase therapy. *South Med J* 1987;80: 1068.
- 4 McDonagh AJG, Dawson J. Guillain-Barré syndrome after myocardial infarction. *BMJ* 1987;294:213-4.
- 5 Arrowsmith JB, Milstein JB, Kuritsky JN, Murano G. Streptokinase and the Guillain-Barré syndrome. *Ann Intern Med* 1985;103: 302.