
Acute cholestaticis during long-term treatment with fluvastatin in a nephrotic patient

Sir,
Pharmacologic therapy of nephrotic hyperlipidaemia is needed in some patients because prolonged hyperlipidaemia is a risk factor for accelerated vascular disease and for progression of renal damage. Hydroxymethylglutaryl (HMG) coenzyme A reductase inhibitors have become the treatment of choice for nephrotic hyperlipidaemia. However, the long-term efficacy and safety in these patients are unknown. Adverse effects such as liver dysfunction and myopathy may occur.

Case. A 71-year-old man with creatinine 98 µmol/l and high LDL-cholesterol (5.6 mmol/l) secondary to a nephrotic syndrome caused by membranous nephropathy started treatment with fluvastatin (20 mg/day) in September 1996. He received prednisone 20 mg once daily. Six months later, hepatic function was normal, and because of persistingly high LDL-cholesterol levels (5.9 mmol/l) the dose was increased to 40 mg/day. In May 1997, anicteric hepatitis with ALT of 210 IU/l (normal <40 IU/l), GGT of 1818 IU/l (normal <40 IU/l) and alkaline phosphatase of 472 IU/l (normal <270 IU/l) was detected. Abdominal ultrasonography was normal. Viral serology was negative. Fifteen days after withdrawal of fluvastatin the patient’s biochemical pattern returned to normal. Fluvastatin was reintroduced (20 mg/day) with a new rise of GGT 532 IU/l, which prompted definitive withdrawal of fluvastatin and substitution for simvastatin (20 mg/day), so far no abnormal liver function has been noted.

Comment. The acute cholestatic hepatitis initially observed appears to be a dose-dependent effect, even though the new rise of GGT at lower doses, not reproduced with simvastatin, suggests idiosyncratic reaction. We are not aware of other reports of hepatotoxicity during treatment with fluvastatin. To our knowledge the adverse hepatic effects have consisted in a slight rise of transaminases, which in no case was over three times the upper normal limit [1].

Fluvastatin is the only entirely synthetic agent in this class, with high hydrophilicity and liver extraction during the absorption phase [2]. The hepatotoxicity profile of fluvastatin is such that liver-enzyme testing, required with all HMG coenzyme A reductase inhibitors, is less frequently needed with this agent than with the other inhibitors [3]. Although this agent has been proven safe in clinical trials [4,5], like any drug, it also carries the risk of adverse effects. A recent study by Marcelino and Feingold [6] suggested that less than half of the patients on a statin had an annual liver panel to monitor for hepatotoxicity. Monitoring of hepatic function in patients on a statin is advisable even when, during the first months, no rise of hepatic enzymes has been detected. Monitoring is particularly indicated when the dose has been increased.

Microscopic polyangitis associated with non-Hodgkin’s lymphoma

Sir,
Some cases of vasculitis associated with malignant lymphoproliferative processes have been described. They tend to be leukocytoclastic vasculitis with cutaneous but no visceral involvement. We observed a case of microscopic polyangiitis [1] with renal, pulmonary and splenic but not cutaneous involvement in the context of non-Hodgkin’s lymphoma.

Case. The patient was a 40-year-old female who was well until December 1990 when monochromat cell lymphoma was diagnosed with involvement of spleen and tonsils and with generalized retroperitoneal and peripheral lymphadenopathy. She was treated with CHOP and remission of the disease was achieved. In February 1992 the disease relapsed and was treated with prednisone, chlorambucil and radiation therapy with good response. In August 1995 she was admitted for evaluation because of another relapse, now with renal insufficiency and microcytic anaemia. Physical examination revealed: BP: 130/70 mmHg, bilateral and multiple supraclavicular, axillary and inguinal lymph nodes (approximately 2 × 2 cm) and palpable spleen. Blood analysis: ESR, 139 mm; creat., 1.7 mg/dl; Hb, 6.4 g/dl; MCV, 72 fl; direct Coombs test positive; polyclonal hypergammaglobulinaemia; total proteins, 7.6 g/dl; albumin, 3 g/dl; cholesterol, 171 mg/dl; LDLH, 262 mg/dl; glucose, 100 red blood cells/field; protein excretion, 3693 mg/24 h. A bone biopsy showed paratrabecular and non-paratrabecular focal infiltration due to small cell lymphoma and presence of the three haematopoietic series in different stages of maturity. The patient was discharged on oral corticoids 30 mg/48 h. Three months later, during follow-up, renal function continued to deteriorate with creat: 2.2 mg/dl and anaemia. Treatment with B2-deoxycoformycin 6 mg/week was started. Three days after the second dose of 2-deoxycoformycin, the patient was admitted presenting with progressive dyspnea and orthopnea without haemoptysis, decreased diuresis and lid oedema. Blood pressure was TA: 160/90 mmHg. The patient was conscious and oriented. She had orthopnea, pale skin and mucous membranes, congested jugular veins, but no malleolar edema. Bilateral basal crackling was noted. Blood analysis: leuko- cytosis 15 100/mm³ (91% GR); Hb, 7.2 g/dl; MCV, 74 fl; platelets, 213 000/mm³; PT, 100%; creat., 11.7 mg/dl; urea, 280 mg/dl; Na⁺, 129 mmol/l; K⁺, 5.5 mmol/l; GOT, 105 U/l. Blood gas analysis (FiO₂: 0.21): pH, 7.37; pCO₂, 30 mmHg; pO₂, 55 mmHg; bicarbonate, 18.2 mmol/l; O₂ sat., 87%. Chest X-ray showed a bilateral interstitial pattern with Kerley B lines. Abdominal sonography: discrete splenomeg-