Successful treatment of hepatitis B-associated polyarteritis nodosa with a combination of lamivudine and conventional immunosuppressive therapy: a case report

Sir, Treatment of hepatitis B virus (HBV)-associated polyarteritis nodosa with immunosuppression is problematic due to possible enhancement of viral replication

[1], which may also possibly worsen the vasculitis by enhancing viral antigenaemia.

Lamivudine has recently been shown to suppress the replication of HBV by >98% [2–5] and could thus allow the use of conventional immunosuppressive agents to control the vasculitis. We report the case of a patient treated successfully in this manner.

The patient, a general surgeon, developed diffuse myalgias in August 1998. The symptoms initially resolved with high-dose prednisone (150 mg daily), but returned 4 weeks later following tapering of the dose. There was also anorexia, lethargy, night sweats and weight loss of 3 kg. A biopsy of the left temporal artery was normal. A biopsy of the left gastrocnemius showed slight lymphocytic perivascular interstitial infiltration. Four weeks later, in October 1998, admission to our unit was prompted by the development of mononeuritis multiplex.

There was a 15-yr history of mild labile hypertension treated with a beta-blocker. No other risk factors for hepatitis B could be elicited apart from his profession. There was a current smoking history (30 pack-yr).

General examination was unremarkable apart from a blood pressure of 140/90 mmHg in both arms. There was slight tenderness of the calves, but no evidence of synovitis. Sensorimotor defects were evident in the distribution of several peripheral nerves, most profoundly involving the left common peroneal nerve, but also involving the right common peroneal, both tibial and the left median nerves. The left ankle jerk was absent.

The laboratory data showed: leucocytes 15.8×10^9/l, C-reactive protein (CRP) 280 mg/l, alanine aminotransferase (ALT) 77 U/l, γ-glutamyltranspeptidase (GGT) 21 U/l, normal renal function tests and urinary microscopy, slight proteinuria (0.13 g/l), positive hepatitis B surface antigen (HBsAg), 'e' antigen (HBeAg) and antibodies to the core antigen (anti-HBc), HBV viral load 1×10^7 genome equivalents (geq)/ml, other viral serology negative, antinuclear antibodies (ANA) negative, p-ANCA borderline.

The liver biopsy showed chronic minimally active hepatitis with slight intralobular lymphocytic infiltration, occasional cell necroses, slight periportal lymphocytic infiltration and scattered piecemeal necroses. The left sural nerve biopsy was, however, unrevealing.

Hepatitis B-associated polyarteritis nodosa was diagnosed and treatment with lamivudine 150 mg daily was started. Three daily pulses of 500 mg methylprednisolone were administered i.v., followed by 80 mg daily in tapering dosage. On discharge from hospital 1 week later on oral prednisone, 40 mg daily, the viral load had reduced to 2×10^5 geq/ml.

Over the next 4 weeks, the patient complained of increasing anorexia, post-prandial epigastric fullness and weight loss of a further 11 kg. The neurological symptoms were unchanged. The blood pressure varied between 140/105 and 150/110 mmHg. The patient was readmitted in November 1998 in a severely cachectic state. The CRP was 161 mg/l. The viral load had rebounded to 4×10^7 geq/ml following cessation of the lamivudine treatment by the patient 4 days previously.

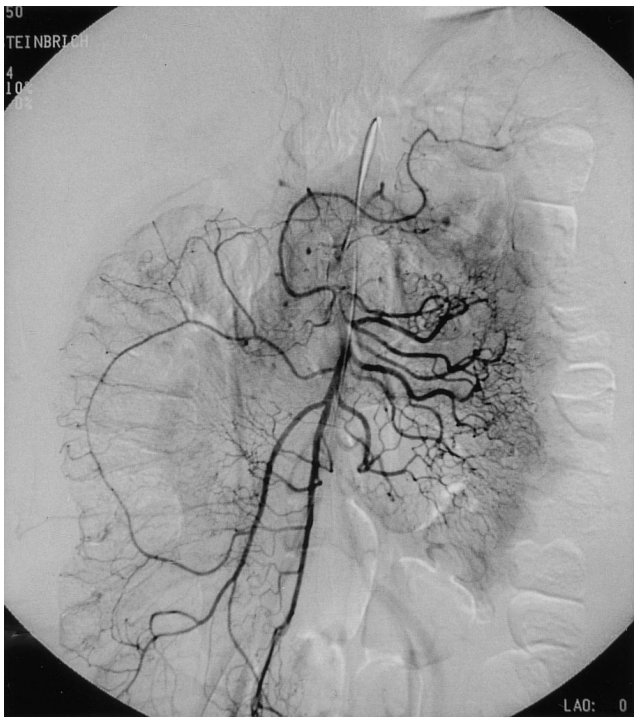

FIG. 1. Visceral digital subtraction arteriography of the superior mesenteric artery showing microaneurysms and irregularities of callibre consistent with polyarteritis nodosa.

Visceral angiography (Fig. 1) performed at this point showed multiple microaneurysmata and calibre irregularities in the arterial supply of the liver, spleen, pancreas, intestine and kidneys.

Cyclophosphamide was commenced, initially 150 mg daily, reducing to 100 mg daily after 2 weeks. Three further daily i.v. pulses of methylprednisolone 500 mg were administered, followed by 80 mg daily i.v. in tapering dose, before changing to oral prednisone. Lamivudine was restarted at a dose of 50 mg twice daily. The hypertension was treated with enalapril, 10 mg daily.

The patient improved rapidly and was discharged 3 weeks later. The cyclophosphamide was reduced to 50 mg daily due to profound lymphopenia. In April 1999, after 4 months of treatment, the cyclophosphamide was stopped and the lamivudine reduced to 50 mg daily due to an unclear asymptomatic increase in the liver enzymes (maximal ALT 754 U/l, GGT 295 U/l), most probably due to drug toxicity however as the HBV viral load remained low and there was no evidence of active vasculitis. The prednisone had been tailed to 7.5 mg daily. The transaminases gradually returned to normal over 3 months. At the last review in June 1999, while on prednisone 5 mg daily and lamivudine 50 mg daily, the patient had regained his previous weight and the weakness in the distribution of the involved peripheral nerves had improved considerably, although there was still marked sensory loss on the soles of the feet and

slight paraesthesiae in the median nerve distribution of the left hand. The CRP was <5 mg/l and the liver enzymes were within the normal range. The viral load was now only 100 geq/ml, but the patient was still HBsAg and HBeAg positive.

This case illustrates successful treatment of hepatitis B-associated polyarteritis nodosa with a combination of lamivudine to prevent increased viral replication and conventional immunosuppression to treat life-threatening vasculitis. We had initially hoped that the reduction of viraemia would be sufficient in combination with high-dose corticosteroids to control the vasculitis, but improvement only occurred when cyclophosphamide was added to the regimen. There was, however, no relapse following the cessation of cyclophosphamide treatment after 4 months, suggesting that the vasculitis was now in remission following almost complete suppression of viral replication.

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