Successful treatment of polyarteritis nodosa related to hepatitis B virus with a combination of lamivudine and interferon alpha

Sir. Hepatitis B virus (HBV) accounts for a substantial number of cases of polyarteritis nodosa (PAN) [1, 2]. Conventional treatment for HBV-related PAN consists of long-term corticosteroids (CS) associated with immunosuppressive agents. We report the case of a patient admitted with severe mononeuritis multiplex due to HBV-associated PAN successfully treated with a combination of lamivudine, interferon alpha (IFN-α) and plasma exchange, after a short course of CS.

In November 1996, a 56-yr-old man was admitted with acute pain and weakness of the lower limbs. In May 1996, routine blood examination revealed elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST). HBV surface antigen (HBs Ag), HBe Ag and viral HBV DNA (3866 pg/ml by the polymerase chain reaction method) were positive; anti-HBs and anti-HBe antibody (Ab), hepatitis C virus, delta agent and human immunodeficiency virus (HIV) were negative. In June, the patient noticed intermittent polyarthritis with bilateral swollen and painful wrists, ankles and knees. In August, he developed paraesthesiae and weakness of the feet. In October, a liver biopsy demonstrated a moderate acute lobular hepatitis without piecemeal necrosis. In November, an electroneuromyography showed severe bilateral mononeuritis multiplex of the lower limbs with left predominance, affecting the tibial nerve and the deep peroneal nerve, with both axonal degeneration and demyelination. The clinical history revealed a recent weight loss of 8 kg, intermittent fever and no drug or alcohol consumption. Blood pressure was 150/90 mmHg, temperature 39°C, and no skin lesions were observed. Tendon reflexes of the upper limbs were depressed without weakness. Plegia and muscular distal atrophy of the lower limbs was present, and ankle reflexes were absent. Laboratory data revealed: ESR 70 mm/h, haemoglobin 11.5 g/dl, haematocrit 35%, WBC 10 600/mm³ (70% of which were neutrophils), CRP 110 mg/l. Liver and renal function tests were within the normal limits. Tests for rheumatoid
factor, ANCA, cryoglobulins, circulating immune complexes, immunoelectrophoresis, antinuclear and anti-DNA Ab were negative. The complement level was within the normal range. A lumbar puncture revealed 0.44 g/l proteins and no pleocytosis. Muscle and left sural nerve biopsy both showed severe segmental vascular lesions with a mononuclear cell infiltrate of the arterial wall with demyelinating lesions of the nerve. The infiltrate consisted of a majority of lymphocytes, mainly CD3+ T cells, but some CD20+ B cells were also present. No fibrinoid necrosis and polymononuclear infiltrate were observed, possibly related to the chronicity of the lesion. Indirect immunofluorescence studies failed to identify IgG, IgM, IgA or C3 deposition at the vascular lesion site. Mesenteric angiography did not show evidence of aneurysms. HBV-related polyarteritis nodosa was diagnosed and the patient was treated with methylprednisolone i.v. 1 g/day during 5 days. Oral prednisone started at 1 mg/kg/day was rapidly tapered within 1 week. Antiviral therapy associating s.c. recombinant IFN-α 2b (Intron A®, Essex) 4.5 million units three times a week and lamivudine 100 mg/day per os was instituted (Fig. 1). Simultaneously, plasma exchanges (PE) (total of 19 PE in 11 weeks) were performed until the emergence of anti-HBs and anti-HBe Ab, and serum clearance of HBs and HBe Ag 2 months after the institution of combination therapy. Response to treatment consisted of regression of fever, myalgias, and the inflammatory syndrome (CRP decreasing from 100 to <3 mg/l in 7 days). By the sixth week of treatment, the HBV DNA level had become undetectable, and a transient 10-fold increase in ALT and AST was interpreted as seroconversion hepatitis. At the fourth month evaluation, the weight gain was 5 kg, pain had disappeared (major analgesics stopped in February 1997), and a slight neurological improvement (sensory modalities) was observed. Treatment with lamivudine and IFN-α was discontinued 4 and 6 months, respectively, after the emergence of anti-HBs and anti-HBe Ab. No evidence of clinical or biological vasculitic recurrence has been observed up to now, 15 months after therapy has been stopped.

In contrast to the conventional therapeutic approach to PAN consisting of immunosuppression (long-term CS and cyclophosphamide), antiviral therapy was instituted in this patient, as proposed by Trépo et al [3] and Guillevin et al [4]. Steroids are known to enhance viral replication, and immunosuppressants alter host autoimmune response to the virus, thus lowering the frequency of seroconversion. These two mechanisms could lead to chronicity of hepatic infection (i.e. cirrhosis) and maintenance of vasculitis symptoms, with relapses being observed more frequently in HBV-related than in HBV-unrelated PAN. IFN-α is the only agent with a long-lasting beneficial effect in chronic hepatitis B [5], and lamivudine has been shown to reduce HBV DNA levels in chronic hepatitis B [6]. Thus, in this patient, the association of two antiviral agents, a short-term course with steroids and PE helped to control the vasculitic process, obviating the use of immunosuppressants. This outcome is consistent with previous data on similar strategies using vidarabine or IFN-α [7] or famciclovir and IFN-α [8] as antiviral drug. Finally, these results point to the possibility of modifying the quality of the immune response involved in immunopathology when an aetiological agent is identified and appropriate therapeutic interventions are available.

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