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CASE REPORT | LIVER

Successful Nucleoside Analog and Corticosteroid Therapy for Chronic Inflammatory Demyelinating Polyneuropathy in a Patient With Hepatitis B Virus Liver Cirrhosis

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ABSTRACT

Here, we describe the case of a 44-year-old man with chronic hepatitis B virus (HBV) infection, who was admitted with progressive muscle weakness and paresthesia in all extremities. He showed slight icterus. Positive HBV e-antigen test, significant HBV-deoxyribonucleic acid load, hypoalbuminemia, hyperbilirubinemia, mild ascites, and demyelinating peripheral axonal lesions in both sensory and motor nerves led to the diagnosis of Child-Pugh class B HBV cirrhosis with chronic inflammatory demyelinating polyneuropathy. Oral lamivudine, intravenous steroids, calcium, and vitamin D therapy led to a significant recovery of muscle strength within 6 weeks and a gradual return to normal after 24 weeks.

INTRODUCTION

Although hepatitis B virus (HBV) mainly affects hepatocytes, extrahepatic manifestations arise in approximately 20% of infected patients.[1,2] These manifestations mostly involve the effects of immune complexes in vascular, renal, dermatologic, arthritic, and neurologic tissues.[2–4] Of these, neurologic manifestations affect nearly 5% of patients with chronic HBV. Peripheral neuropathy is the most common neurologic manifestation of HBV, followed by acute inflammatory demyelinating polyneuropathy.[3] By contrast, chronic inflammatory demyelinating polyneuropathy (CIDP) is rarely reported as an extrahepatic manifestation of HBV. Here, we report a chronic HBV patient with Child-Pugh B cirrhosis and quadriplegia due to CIDP. The latter condition gradually resolved after treatment with lamivudine and methylprednisolone.

CASE REPORT

A 44-year-old man with a 3-month history of progressive bilateral muscle weakness and paresthesia in his extremities was referred from a rural hospital to our center. Initially, he felt tingling sensations in both hands and feet, which worsened over time until he was unable to move his hands and limbs. Finally, he became almost totally bedridden with irritating sensations in his distal bilateral extremities. He had no history of head or back trauma.

On physical examination, his consciousness was fully alert and his other vital signs were normal. He was slightly anemic and mildly icteric. A neurological examination revealed hyporeflexia in all 4 limbs, with Medical Research Council muscle power grade of 3/5 in the upper limbs and 1/5 in the lower limbs. Hypesthesia was noted in all extremities, but pathological reflexes were absent. Laboratory examinations yielded the following data: hemoglobin, 8.5 gr/dL; platelets, 116,000/mm^3; aspartate aminotransferase, 51 U/L; alanine aminotransferase, 56 U/L; total bilirubin, 1.2 mg/dL; prothrombin time, 14.3 seconds with an international normalized ratio of 1.3; albumin, 2.6 gr/dL; total protein, 7.0 gr/dL; and creatinine, 0.59 mg/dL. His electrolyte levels were normal. Repeated viral testing yielded positive results for the HBV soluble antigen (HBsAg) and HBV e-antigen and an HBV-deoxyribonucleic acid (DNA) load of 1.65×10^5 IU/mL, as well as negative hepatitis C virus and human immunodeficiency virus test results. An abdominal ultrasound showed minimal ascites.

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Table 1. Results of nerve conduction studies of the right extremities[a]

Sensory	Latency (ms)	Amplitude (mV)	Velocity (m/s)	
Median	NR[b]	N/A	N/A	
Ulnar	NR[b]	N/A	N/A	
Peroneal/sural	NR[b]	N/A	N/A	
Motor	**Latency (ms)**	**Amplitude (mV)**	**Velocity (m/s)**	**F-waves**
Median	8.8[b]	0.8[b]	28[b]	NR[b]
Ulnar	3.5[b]	1.3[b]	47	NR[b]
Tibial	11[b]	0.2[b]	39[b]	NR[b]
Peroneal/sural	22.2[b]	0.1[b]	21[b]	NR[b]

N/A, not applicable; NR, no response.
[a] Normal values for sensory/motor nerve conduction studies: latency <3.7/< 3.1 ms, amplitude >8.0/>5.5 mV, and velocity >38/>45 m/s.
[b] Abnormal values.

Nerve conduction studies revealed prolongation of the motor distal latency and F-wave latency, and a reduction of the motor conduction velocity, which suggested peripheral axonal demyelination of both the sensory and motoric nerves (Table 1). A cerebrospinal fluid (CSF) analysis revealed a total cell count of 7 lymphocytes/mm^3 and a protein concentration of 135 mg/dL. Serum protein electrophoresis revealed the presence of polyclonal gamma-globulinemia. Brain magnetic resonance imaging (MRI) revealed a lacunar infarction. The patient refused to undergo a biopsy.

Based on these observations, the patient was diagnosed with Child-Pugh class B HBV liver cirrhosis, CIDP, and anemia of chronic disease. Treatment was initiated with once-daily oral lamivudine (100 mg) and intravenous methylprednisolone (125 mg) for 3 days, followed by once-daily oral methylprednisolone (16 mg), an albumin infusion, calcium, and vitamin D supplementation. His muscle strength gradually improved, and he achieved a power grade of 2/5 in the lower-limb muscles after 4 weeks of treatment. At the 6-week follow-up, his lower-limb power grade had increased to 3/5 and he was able to sit independently. Finally, at the 24-week follow-up, he had achieved a grade of 5/5 in all 4 limbs and was able to walk. His HBV-DNA load at that time was 3.29×10^2 IU/mL. The result of the HBV-DNA test repeated at 48 weeks of lamivudine therapy was undetected.

DISCUSSION

CIDP is an acquired peripheral neuropathy caused by damage to the peripheral nerve myelin and subsequent inflammatory demyelination. The condition is characterized by the occurrence of progressive symmetrical paralysis of both the proximal and distal muscles for more than 2 months.[5] Very few cases of CIDP associated with HBV have been reported; only 5 cases have been reported to date (Table 2). Ours is the first report of a full recovery from CIDP in a patient with HBV and decompensated cirrhosis. However, we did not perform the HBV genotype test; the previous cases did not reveal it as well.

Table 2. Baseline characteristics of HBV-related chronic inflammation demyelinating polyneuropathy

	Case 1[7,8]	Case 2[13]	Case 3[12]	Case 4[14]	Case 5[15]
Age (yr)	60	60	39	44	57
Sex	Female	Male	Male	Male	Male
Etiology	HBV	HBV	HBV	HBV	HBV
		HCV		Hantavirus	
Cirrhosis	Compensated	Compensated	No	No	No
HBV-DNA (IU/mL)	N/A	N/A	8.5×10^6	N/A	N/A
Therapy	N/A	IVIG	IVIG	Prednisolone	IVIG
			Tenofovir	Azathioprine	Entecavir
					Methylprednisolone
Outcome	N/A	Improved	Improved	Improved	Improved
Follow-up (wk)	N/A	4	24	32	52

HBV, hepatitis B virus; HCV, hepatitis C virus; IVIG, intravenous immunoglobulin; N/A, not applicable.

Although the exact pathogenic mechanism by which HBV causes CIDP remains unknown, several hypotheses have been proposed. Potentially, cytotoxic T cells might target and damage both HBsAg immune complexes and the myelin sheath.[5,6] Other mechanisms involve direct HBV-mediated myelin damage and progressive polyneuropathy because of the deposition of HBsAg immune complexes in the vasa nervorum.[7,8] In our case, CSF cytology immunofluorescence was not performed owing to the lack of the facility; consequently, the HBsAg immune complexes were unidentified.

Our CIDP diagnosis was based on the clinical, electrodiagnostic, and CSF analysis criteria.[5,9] Specifically, our patient had a chronic onset of progressive, symmetric, proximal-to-distal, and bilateral muscle weakness with sensory abnormalities persisting for more than 2 months, met 3 of the 4 electrodiagnostic criteria, and exhibited an increased CSF protein concentration. Serum protein electrophoresis and MRI were conducted to exclude other differential diagnoses, including type I cryoglobulin-associated vasculitic neuropathy, multifocal motor neuropathy, and the polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes syndrome.[5,10,11] However, type II or III mixed cryoglobulin was not excluded because the cryoglobulin and complement level examination could not be performed in our laboratory. Moreover, the MRI findings did not correlate with the symmetrical muscle weakness.

The patient was administered short-term intravenous and oral corticosteroid therapy and nucleoside analog (NA) treatment, which yielded a gradual recovery after 4 weeks of treatment. Despite high resistance, lamivudine was the favorable NA owing to wide availability and affordability. Based on the consensus of our hospital, lamivudine was preferred for HBV decompensated cirrhosis because tenofovir and entecavir were unaffordable by a majority of our patients. After 24 weeks of NA treatment, his motor functions had recovered and he was able to walk. Aktas et al similarly observed an improvement in muscle strength after 3 months of tenofovir administration in a patient with HBV-related CIDP. The mechanism was the NA reduced nerve tissue expression to HBsAg.[12] Our cases and other cases therefore demonstrate that a combination of prompt NA and immunosuppressive drug therapy can effectively relieve the manifestations of CIDP, even in patients with advanced liver cirrhosis.

DISCLOSURES

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