

Acute-onset chronic inflammatory demyelinating polyneuropathy in hantavirus and hepatitis B virus coinfection

A case report

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Abstract

Introduction: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired autoimmune disorder with progressive weakness. Acute-onset CIDP resembles Guillain-Barre syndrome (GBS), a rapidly progressive disorder, and follows a chronic course. To our knowledge, no case of acute-onset CIDP in hantavirus and hepatitis B virus (HBV) coinfection has been reported previously.

Clinical findings: We report a case of acute-onset CIDP that was initially diagnosed as GBS.

Diagnoses: A 44-year-old male logger complained of acute quadriplegia and dyspnea. Mechanical ventilation was initiated. He was an HBV carrier with mild elevation of hepatic enzyme, and positive for hantavirus antibody. He was diagnosed with GBS and immunoglobulin therapy was administered.

Interventions: After 8 months, quadriplegia and hypesthesia recurred. Immunoglobulin therapy at this time had no effect, but steroid therapy had some effect.

Outcomes: A diagnosis of CIDP was made. After 2 months, severe extremity pain and dyspnea developed again, and steroid pulse therapy was initiated.

Conclusion: Besides GBS, acute-onset CIDP can occur with hantavirus and HBV coinfection. Patients with this coinfection in whom GBS has been initially diagnosed should be followed up for a long time, because of the possibility of relapse or deterioration, and acute-onset CIDP should always be considered.

Abbreviations: CIDP = chronic inflammatory demyelinating polyneuropathy, EP = electrophoresis, GBS = Guillain-Barre syndrome, HBV = hepatitis B virus, HFRS = hemorrhagic fever with renal syndrome, Ig = immunoglobulin, MAG = myelin-associated glycoprotein, MGUS = monoclonal gammopathy of undetermined significance, MRC = medical research council, NCS = nerve conduction studies, TRF = treatment-related fluctuation.

Keywords: case report, chronic inflammatory demyelinating polyneuropathy, hantavirus, hepatitis B virus

1. Introduction

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired autoimmune disorder with relapsing or progressive neuropathy with proximal and distal weakness.^[1] Guillain-Barre syndrome (GBS) is a rapidly progressive disorder showing bilateral and symmetrical weakness of the limbs, usually after

gastrointestinal or upper respiratory infection.^[2] CIDP with an acute presentation resembling GBS followed by chronic or relapsing features is referred to as acute-onset CIDP.^[3]

Hantavirus causes hemorrhagic fever with renal syndrome (HFRS) in Asia and Europe or hantavirus cardiopulmonary syndrome in America.^[4] Neurological complications of HFRS are headache, vertigo, epileptic seizures, and cerebral hemorrhage.^[5] GBS can occur after HFRS.^[6–8] Hepatitis B virus (HBV), although less frequent than hepatitis C virus, is known to cause GBS and CIDP, and the deposition of immune complexes is one possible pathomechanism.^[9] GBS was mainly associated with acute HBV infection^[10,11] and CIDP, with chronic HBV infection.^[12] GBS was also found in chronic HBV infection.^[13] However, there are no studies reporting the relationship between CIDP and hantavirus and the development of acute-onset CIDP after HBV infection. In this paper, we present a case of acute-onset CIDP in a patient with hantavirus and HBV coinfection.

2. Case report

A 44-year-old male logger was admitted to the neurology department because of rapidly progressive quadriplegia and dyspnea. Muscle weakness progressed from distal to proximal muscles, and he needed to use the accessory muscles for breathing. He could not stand without assistance. Manual muscle test

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Table 1**Initial nerve conduction studies.**

Sensory	Right			Left		
	Latency, msec	Amplitude, μ V	Velocity, m/s	Latency, msec	Amplitude, μ V	Velocity, m/s
Median		NR*			NR*	
Ulnar		NR*		3.70*	3.2*	28.4*
Sural	3.45	8.3*	32.2*		NR*	
Motor	Latency, msec	Amplitude, mV	Velocity, m/s	Latency, msec	Amplitude, mV	Velocity, m/s
Median	17.55*	0.5*	N/T†	22.85*	0.2*	N/T†
Ulnar		NR*		4.30*	5.0	44.1*
Peroneal	10.60*	1.1*	38.7*	24.25*	0.6*	47.7
Tibial		NR*		9.25*	0.7*	43.0

NR = no response, N/T = not testable.

* Abnormal values.

† Proximal stimulation showed no response.

revealed medical research council (MRC) grade 2 power in all extremities except ankles, which had grade 1 power. Hypesthesia was also noted. Intubation and mechanical ventilation were started. Brain computed tomography showed no abnormal findings. He was an HBV carrier, and laboratory test showed mild elevation of hepatic enzymes (<100 IU/L). Elevated protein level with no white blood cell was found in the cerebrospinal fluid. Nerve conduction studies (NCS) showed abnormal findings such as no response or delayed latency in all 4 extremities (Table 1).

Fever, malaise, anorexia, and subconjunctival hemorrhage were other complaints. Leukocytosis, decreased plateletcrit, increased C-reactive protein and blood urea nitrogen, hypoalbuminemia, elevated prothrombin time, hematuria, and proteinuria were shown in laboratory tests. The enlargement of both kidneys and splenomegaly were noted in ultrasound imaging. Hantavirus-specific immunoglobulin (Ig) M antibody was detected using the indirect immunofluorescence antibody technique. He was diagnosed with GBS, and intravenous Ig therapy was initiated. Serum protein electrophoresis (EP) showed diffusely increased gamma-globulin fraction, suggesting polyclonal gammopathy. Ig analysis showed IgM in the normal range but increased IgG and IgA levels. After about 1 month of rehabilitation, he had nearly full recovery, evident by MRC grade 4 and independent walking. He was discharged and followed up in the outpatient department thereafter. He took adequate rest and did not continue working as a logger.

After 8 months of initial admission, quadriplegia and hypesthesia recurred. He was admitted to the neurology department. NCS findings indicated worsening. Sural nerve biopsy showed no infiltration of inflammatory cells and no evidence of atrophy or degeneration. With the provisional diagnosis of fluctuating GBS, Ig therapy was started but it had no effect. Steroid and immunosuppressant were administered, following which there was some improvement. Serum EP suggested polyclonal gammopathy. No monoclonal gammopathy was found in immunofixation EP. Anti-myelin-associated glycoprotein (MAG) IgM antibody and cryoglobulin were not detected. He was finally diagnosed with CIDP. After rehabilitation, he was discharged with MRC grade 3 power.

He had no symptoms for 2 months even without medication. However, severe extremity pain and dyspnea developed again, and he was admitted to the intensive care unit. He complained of weakness but the MRC grade was still grade 3. NCS showed further aggravation (Table 2). Steroid pulse therapy was started. Serum and immunofixation EP showed the similar pattern as that during the previous admission. Thereafter, he was transferred to the rehabilitation department with medication (Prednisolone 20 mg and Azathioprine 100 mg per day), and repetitive transcranial magnetic stimulation for 10 days decreased his pain to a tolerable level. He was discharged with MRC grade 4. Written informed consent was obtained from the patient prior to the publication of this case report.

Table 2**Follow-up nerve conduction studies.**

Sensory	Right			Left		
	Latency, msec	Amplitude, μ V	Velocity, m/s	Latency, msec	Amplitude, μ V	Velocity, m/s
Median		NR*			NR*	
Ulnar		NR*			NR*	
Sural		NR*			NR*	
Motor	Latency, msec	Amplitude, mV	Velocity, m/s	Latency, msec	Amplitude, mV	Velocity, m/s
Median	37.60*	0.9*	15.8*	39.40*	0.3*	65.3
Ulnar	21.30*	1.8*	18.4*	16.20*	1.4*	37.8*
Peroneal	23.10*	1.2*	18.4*	33.00*	0.4*	N/T†
Tibial	24.30*	0.8*	30.8*	22.85*	0.3*	42.9

NR = no response, N/T = not testable.

* Abnormal values.

† Proximal stimulation showed no response.

3. Discussion

In the acute phase, CIDP and GBS have many common symptoms and signs, and the time from onset to maximum severity helps differentiate the 2 conditions.^[14] In GBS, disease severity reaches maximum within 4 weeks, but in CIDP, the initial disease progression lasts for more than 8 weeks.^[15] However, 16% of CIDP patients, described as acute-onset CIDP, show rapidly progressive weakness within 4 weeks from onset,^[14,16] and 18% of CIDP patients present with relapsing weakness.^[1] Meanwhile 8% to 16% of GBS patients show one or more deteriorations after initial improvement, described as treatment-related fluctuations (TRFs).^[14] In such cases, it is difficult to distinguish between these 2 conditions.

Some differentiating factors have been suggested in previous reports. The 1st TRF in GBS occurred within 8 weeks from onset, and not more than 2 episodes of TRF were experienced.^[16] Ig and plasma exchange treatment were effective in both CIDP and GBS,^[17] but steroid therapy was effective only in CIDP.^[18] Some CIDP patients, who showed improvement by initial treatment with Ig, relapsed into a chronic stage and improved only after steroid treatment was begun.^[19] In NCS, CIDP showed marked demyelination,^[1] whereas GBS revealed residual axonal loss.^[3] Ventilatory involvement was known as probable in GBS but unusual in CIDP.^[1] But some of CIDP patients needed mechanical ventilation.^[20]

Our patient showed rapid and relapsing weakness. First deterioration after symptom improvement was after 8 months from 1st admission. Although he showed initial improvement with Ig therapy, he responded only to steroid therapy during the 1st deterioration. All these findings suggested acute-onset CIDP rather than GBS. The initial diagnosis of GBS was wrong, and the correct diagnosis was CIDP.

Monoclonal gammopathy of undetermined significance (MGUS) is found in 10% to 20% of CIDP cases.^[1] In MGUS, one of the Ig classes, such as IgM, IgG, or IgA, is selectively elevated.^[21] More than half of the IgM-MGUS patients have anti-MAG IgM antibodies.^[22] The relationship between CIDP and MGUS is relatively established in IgM type but not in the IgG or IgA type.^[21] If the time to peak of neuropathy is less than 6 months and if the course is relapsing, then the diagnosis of MGUS is less likely, and steroid therapy alone is seldom effective.^[21]

Our patient showed not monoclonal but polyclonal gammopathy with elevation of both IgG and IgA. Anti-MAG IgM antibody was not detected. Steroid therapy was effective in the 1st deterioration. Polyclonal gammopathies are usually associated with reactive or inflammatory processes,^[23] and viral infection in this patient might have caused polyclonal gammopathy.

Sural nerve biopsy showed nonspecific findings. A nerve biopsy may be useful in atypical CIDP cases, but it has limited diagnostic value in CIDP with relatively low positive rates.^[1] A negative finding for cryoglobulin could rule out HBV-related cryoglobulinemic vasculitis, which is known to manifest peripheral neuropathy.^[24]

He was an HBV carrier with normal levels of hepatic enzymes. During the 1st admission, hepatic enzyme levels increased mildly and were below 100 IU/L. Before the 1st admission, the patient did not complain of any weakness or sensory change in any extremity. His weakness was not gradual as is generally seen in HBV-related CIDP patients. Clinical and laboratory findings suggested acute HFRS, and the presence of hantavirus-specific IgM antibody confirmed acute hantavirus infection.^[5] The simultaneous symptoms of CIDP brought him to the hospital

in time, and intensive care prevented the further progression of HFRS. Other possible causes of CIDP were ruled out, and we propose that HBV infection can induce CIDP and that hantavirus can cause acute-onset CIDP.

4. Conclusion

Besides GBS, acute-onset CIDP can occur after hantavirus and HBV coinfection. Although the patient was in the HBV carrier state and hantavirus infection was acute, the result of coinfection was rapid and severe enough to need mechanical ventilation. Patients with this coinfection who are 1st diagnosed with GBS should be followed up for a long time, because of the possibility of relapse or deterioration, and acute-onset CIDP should always be considered.

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