Acute Encephalomyelitis Associated with Acute Viral Hepatitis Type B

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Abstract

We describe the case of a 36-year-old woman who developed acute encephalomyelitis after acute viral hepatitis type B. She was admitted to the hospital with a history of general malaise and nausea of 5 days duration. Her serum showed high transaminase levels and positive HBs-Ag and increased IgM HBc-Ab titers. She had urinary dysfunction, myoclonus and postural tremor of her extremities. Several days later, she developed bilateral limb ataxia and alteration of consciousness. The cerebrospinal fluid examinations showed pleocytosis and increased protein. Treatment with high-dose methylprednisolone resulted in a marked improvement of the clinical and CSF examination. Magnetic resonance imaging of the brain and the spinal cord did not disclose abnormal lesions. The symptoms and clinical course were quite similar to those of acute disseminated encephalomyelitis.

Key words: acute disseminated encephalomyelitis (ADEM), acute viral hepatitis, hepatitis B virus (HBV)

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Introduction

Acute disseminated encephalomyelitis (ADEM) is an autoimmune demyelinating disease of the central nervous system that generally develops after acute viral or bacterial infection or vaccination (1-3). ADEM is usually a monophasic disease with acute onset characterized by multiple foci of central nervous system damage, predominantly in the cerebral and cerebellar white matter, although basal ganglia and gray matter may also be involved. Lesions are frequently bilateral, large, and confluent (1-3). Numerous infectious agents have been linked to ADEM. A search of the literature revealed some reports of cases associated with hepatitis A virus infection and hepatitis C virus infection (4, 5). Regarding hepatitis B virus, however, no association of hepatitis B virus infection with acute disseminated encephalomyelitis have been reported despite the fact that some cases associated with hepatitis B virus vaccination have been reported (6-8). Furthermore, the possibility that hepatitis B vaccine may cause or exacerbate multiple sclerosis (MS) stems from several reports of onset or recurrence of symptoms of CNS demyelination shortly after vaccination (9). We describe the case of a 36-year-old woman who developed acute encephalomyelitis after acute viral hepatitis type B, and discuss the pathogenesis of the disturbance.

Case Report

A 36-year-old woman was admitted to the Department of Internal Medicine, Maizuru Kyousai Hospital with a history of general malaise and nausea of 5 days duration. There was no history of toxic substance or drug ingestion. On admission, the serum transaminase (AST; 355 IU/L, ALT; 1,916 IU/L) and γ-GTP (357 IU/L) levels were elevated. WBC level (10,600/μL) in blood was slightly increased. Other routine laboratory examinations including anti-nuclear antibody (ANA), anti-DNA antibody, P-ANCA and C-ANCA were all normal or negative. Hepatitis Bs antigen (48.08) and IgM hepatitis B core antibody (IgM HBc-Ab) were positive. IgMHA-Ab, HCV-Ab, EBV VCA IgG (320), EBV VCA IgM (<10), EBNA (160) were all not significantly increased or negative. She was diagnosed as acute hepatitis B. She showed no signs of neurological deficient. Findings of elec-

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trocardiograph and chest x-ray film examinations were normal. Ten hours later, she developed urinary dysfunction. On the second day of the admission she showed myoclonus on the inside of her thighs and postural tremor of her upper extremities. On the 10th day of admission, she developed bilateral limb ataxia and on the following day she developed alteration of consciousness. The cerebrospinal fluid examinations showed pleocytosis (868/mm³) composed of 760/mm³ mononuclear cells and 108/mm³ polynuclear cells and increased total protein (147 mg/dL). Glucose in CSF was 51 mg/dL. Bacterial, mycobacterial, and fungal cultures from cerebrospinal fluid were negative. Magnetic resonance imaging (MRI) of the brain and the spinal cord revealed no abnormal findings. Gadolinium contrast enhancement MRI was not examined in this patient.

Treatment with high-dose methylprednisolone was followed by a dramatic improvement of the clinical and cerebrospinal fluid findings. The clinical course is shown in Fig. 1. Within a few months the patient recovered completely and there was no relapse during 1 year of follow-up.

**Discussion**

ADEM is a monophasic disease that occurs in the setting of infection or immunization. The pathological characteristics of the condition are perivascular inflammation, edema and demyelination in the central nervous system. After prodromal phase of 1-4 weeks, clinical signs including altered consciousness and multifocal neurological disturbance appear. Moderate pleocytosis in the cerebrospinal fluid is a common feature but, in contrast with multiple sclerosis, oligoclonal bands are rarely observed (10). MRI is considered the diagnostic tool of choice for suspected ADEM (1, 2, 3, 11). In our case, the clinical signs and symptoms combined with the serum and cerebrospinal fluid findings and the clinical marked improvement with corticosteroid therapy were strongly suggestive of ADEM, though MRI could not disclose abnormal findings in the brain or the spinal cord. The incidence of lesions on MRI is variable in ADEM and may depend on the stage of inflammation. Gadolinium enhancing lesions have been described in 30 to 100% of patients. As spinal cord involvement in ADEM has been described in 11 to 28%, spinal cord lesions could be rarely disclosed on MRI (3).

In the present case, apart from the indication of a recent hepatitis virus B infection, laboratory investigation revealed no infection or infectious agent. In recent years, several reports of new cases of central nervous system demyelination or reactivation of multiple sclerosis after hepatitis B vaccination have raised the possibility of a causal link (6-8). In addition, it was reported that hepatitis virus B polymerase shares significant amino acid similarities with the human myelin basic protein (12). However, our search of the literature revealed no previously reported case of ADEM following this infection.

There could be two possibilities, demyelination or vasculitis, for the pathogenetic mechanism of neurological involvement in this case. In general, vasculitis associated with hepatitis viral infection has occurred in the chronic stage, especially in chronic hepatitis type C (13, 14). In some patients with chronic hepatitis type C and B, complicated secondary cryoglobulinemia or polyartilitis nodosa induced damage of the blood vessels, resulting in vasculitic neuropathy (15). The CNS disorders as a complication of hepatitis rarely occur in patients with hepatitis type B, who were also in the chronic stage (15-17). In the present patient, acute onset CNS neurological deficits with CSF pleocytosis occurred shortly after the infection of hepatitis B virus, and steroid therapy showed marked effect for the disturbances. These findings suggest that the pathogenesis in this case could be
due to a demyelinating process, rather than vasculitis.

This case shows that ADEM-like CNS neurological involvement can be associated with hepatitis virus B infection. We emphasize the importance of hepatitis virus B screening in patients with acute encephalomyelitis, since many cases of hepatitis virus B infection remain anicteric or subclinical. Likewise, patients with hepatitis virus B infection should be examined carefully for central nervous system symptoms during follow-up.

References


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