Case Report
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Encephalitis Associated with Acute Hepatitis A

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Encephalitis is caused by multiple organisms, but rarely by the hepatitis A virus. A 27-year-old man visited our hospital because of fever, altered consciousness, and seizures. On physical exam, a stuporous mentality and neck stiffness were found. On laboratory exam, elevated liver enzymes and cerebrospinal fluid abnormalities, including pleocytosis and elevated protein levels were observed. The hepatitis A virus (HAV) IgM antibody was also detected. We conclude that these findings were compatible with encephalitis associated with HAV and discuss the pathomechanisms. **(2011;1:27-28)**

Key words: Hepatitis A virus; Encephalitis

Encephalitis is caused by multiple etiologies, including viruses and autoimmune disorders. The most common symptoms are seizures and alterations of consciousness [1]. Hepatitis A, which is caused by the hepatitis A virus (HAV), induces acute hepatitis but rarely involves the nervous system [2,3]. Here, we present the clinical characteristics of a patient with HAV-associated encephalitis and review and compare these findings with previous reports.

Case Report

A 27-year-old man visited our hospital because of a sudden-onset generalized convulsion. He had been overworking and had slept less than 5 hours a day for the previous month. A week prior to the hospital visit, the patient had developed a fever and generalized myalgia but had not taken any medicine. High fever, anorexia, and generalized malaise appeared. On the day of the hospital visit, he could not be awakened, and he showed no responses to any stimulus. Finally, he developed a generalized tonic-clonic seizure that lasted for about three min and that was accompanied by cyanosis, upward eyeball deviation, and tongue biting.

On physical examination at the emergency department, the patient's body temperature rose up to 38.7℃. He did not show jaundice, hepatosplenomegaly, nor ascites. He was confused and could not follow the examiner's verbal commands appropriately, and he often attempted to run out of the bed while yelling incomprehensible words and abuses. Neck stiffness was found on neurologic examination. Positive or negative myoclonic jerk was not observed.

Brain computed tomography and magnetic resonance imaging showed no abnormalities. Diffuse slowing without epileptiform discharges was observed on electroencephalography (EEG) recordings. The cerebrospinal fluid (CSF) was clear, and its pressure was measured at 16.0 cmH_2O, with 20 leukocytes/μL (95% lymphocytes), protein levels of 70.5 mg/dL, and normal glucose levels (63.0 mg/dL). Blood tests showed that white blood cell counts were increased to 17,230 cells/μL. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and γ-glutamyl transpeptidase levels were increased to 441, 1294, and 460 IU/L, respectively. Total bilirubin and direct bilirubin levels were normal (0.6 mg/dL and 0.2 mg/dL, respectively). Creatine phosphokinase levels were elevated up to 14,500 IU/L. Serum ammonia levels were normal (24 μg/dL).

Seizure did not relapse after 30 min of continuous infusion of 15 mg/kg of phenytoin mixed with normal saline. He regained consciousness on the second admission day and became fully conscious the following day. Intravenous acyclovir was given for two days because of the clinical suspicion of herpes encephalitis, which was discontinued after observing the clinical improvement and the detection of the IgM antibody of HAV. The patient's score on the Korean version of the mini-Mental Status examination (K-MMSE) score was 30 on the fifth admission day. Serum and CSF IgM antibodies of herpes simplex type 1, 2, and varicella zoster were negative. Polymerase chain reaction (PCR) of the CSF for HAV and enterovirus were also negative. AST and ALT levels decreased to 125 and 432 IU/L on the seventh admission day. He was discharged without any sequela. During the year after discharge, he had been seizure-free with normal EEG recordings.

Discussion

HAV, which causes an acute inflammatory hepatitis, is a picornavirus, which is transmitted by the fecal-to-oral route. The clinical spectrum varies from mild flu-like illness to fatality caused by acute fulminant hepatitis. In the anicteric form, diagnosis may be delayed due to the atypical presentation of the disease. In general, the disease is preceded by flu-like prodromes, and the progression of the hepatitis symptoms and liver enzyme elevations is relatively rapid. In a week or so, liver enzymes stop elevating and gradually decrease to normal levels. Diagnosis can be made by the detection of the serum IgM antibody of HAV [4-6].

HAV is rarely associated with neurological diseases, especially encephalitis [2,3]. Seizures may be observed during the period of hepatitis. Common pathomechanisms are attributed to a disturbed detoxification process by the damaged liver and metabolic disturbances, such as fluid electrolyte imbalances. Another possible mechanism is the direct invasion of the central nervous system through encephalitis [7]. Our patient had a seizure in an early stage of the disease, and he showed no specific laboratory abnormalities other than liver enzyme elevations. He showed neck stiffness and a clouding of consciousness that was accompanied by CSF abnormalities that were compatible with encephalitis. These findings support the diagnosis of encephalitis rather than that of toxic-metabolic disturbances due to the hepatitis. CSF PCR results are often negative in an early stage of encephalitis [1].

HAV-associated encephalitis had been rarely reported. The first case was reported in 1982 by Bromberg *et al. [8]*. After reviewing five cases, including the above report, altered consciousness and seizures are commonly manifested. CSF pleocytoses are often observed, but not in all cases. Positive HAV PCR results were reported in one case, of which CSF cells and protein were normal. Imaging abnormalities or specific EEG abnormalities are not observed in all cases. The clinical courses were all benign; all patients improved within a few days to a few weeks with supportive treatment [2,3,8-10].

HAV-associated encephalitis is a very rare disorder, which has not been reported in Korea. No specific radiological or EEG findings are observed. In particular, in the anicteric form of the disease, the diagnosis may be difficult without a clinical suspicion. When progressive liver enzyme elevations are observed in patients with encephalitis, we should consider the possibility of HAV association with the disease.

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