CASE REPORT

Central Pontine and Extrapontine Myelinolysis that Developed during Alcohol Withdrawal, without Hyponatremia, in a Chronic Alcoholic

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Abstract

Central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM) are osmotic demyelination syndrome. A 45-year-old man with a history of alcoholism visited the ER with dysarthria and dysphagia for 2 days. These symptoms occurred 3 days after he had stopped drinking alcohol. The neurological symptoms progressed to anarthria, pseudobulbar palsy and gait disturbance. During admission, the electrolyte studies were within the normal range. Diffusion-weighted images revealed high signal intensities in the pons, thalamus and basal ganglia. Apparent diffusion coefficient image showed low signal intensities in the pontine lesion, but isosignal intensities in the extrapontine lesion. The symptoms gradually improved after 1 month with only conservative treatment. The 1 month-follow-up MRI showed significant reduction of the previous extrapontine lesions. These findings suggest that cytotoxic edema is central to the pathogenesis of CPM, but vasogenic edema plays an important role in the pathogenesis of EPM occurring during alcohol withdrawal.

Key words: central pontine myelinolysis, extrapontine myelinolysis, alcohol withdrawal

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Introduction

Central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM) are osmotic demyelination syndromes (ODS) that were originally described by Adams et al (1). This syndrome has extremely diverse clinical manifestations ranging from a mild tremor or dysarthria to locked-in syndrome and the prognosis can be highly heterogeneous from complete recovery to progression and death (2, 3). The cause and pathogenesis of ODS remain unclear. However, several concomitant chronic diseases predispose patients to developing ODS (4). Among these, the most frequent conditions are chronic alcoholism, rapid correction of hyponatremia and liver transplantation (5, 6). Here, we describe a patient who was a chronic alcoholic and he suffered with ODS without hyponatremia during alcohol withdrawal and the patient eventually had a good recovery.

Case Report

A 45-year-old man visited the ER with progressive dysarthria and dysphagia that he had for the previous 2 days. These symptoms occurred 3 days after he stopped drinking. He had drunk more than one bottle of Soju (Korean gin) daily for 20 years. One year previously, he had been diagnosed with hypertension and hyperlipidemia and he had taken calcium channel blocker and statins to the present time. His vital signs at ER included a blood pressure 140/80 mmHg, pulse 70 beats/minute, respirations 18/minute, and temperature 37.7℃. On the first neurological examination, the patient was alert and well oriented and he had no extraocular movement limitation, nystagmus, limb muscle weakness or gait disturbance, except for dysarthria and dysphagia. The laboratory data at that time showed a mildly abnormal liver function test, according to the following findings; aspartate aminotransferase 39 IU/L (normal range: 5-38 IU/L), alanine aminotransferase 60 IU/L (normal range: 4-43...
IU/L), γ-glutamyl transpeptidase 227 IU/L (normal range: 11-75 IU/L), and total bilirubin 2.4 mg/dL (normal range: 0.2-1.2 mg/dL), but the serum sodium 138 mEq/L (normal range: 135-150 mEq/L), the potassium 4.1 mEq/L (normal range: 3.5-5.1 mEq/L), the osmolality 289 mOsm/kg (normal range: 280-300 mOsm/kg) and the glucose 75 mg/dL (normal range: 70-110 mg/dL) were normal. He was treated with intravenous thiamine and vitamin supplementation. However, two days after admission, the neurological symptoms progressed to anarthria, pseudobulbar palsy and gait disturbance, yet the serum electrolytes, including the sodium and osmolarity, were within the normal range during admission. T2-weighted MRI of the brain revealed high signal intensities in the central portion of the pons, the bilateral caudate nuclei, the lentiform nucleus and the thalamus (Fig. 1A and 1B). Diffusion-weighted image (DWI) showed marked hyperintense lesions corresponding to the areas of high signal intensity lesions on T2-weighted image (Fig. 1C and 1D). Apparent diffusion coefficient (ADC) image showed low signal intensities in the central pons, but isointense signals in the extrapontine lesion (Fig. 1E and 1F).

The symptoms gradually improved, except for mild bilateral facial palsy and slight dysarthria, after 1 month with only supportive treatment and physical therapy. The one month follow-up MRI showed reduced hyperintensities in the extrapontine lesion on FLAIR images (Fig. 2C and 2F). In contrast, the hyperintensities in the pontine on T2/FLAIR image were changed to a cavitary signal lesion on T1- and T2-weighted images (Fig. 2A, 2B, 2D and 2E).

Discussion

CPM and EPM are demyelinating disorders that are caused by osmotic disturbances. Although most of the cases of ODS have been reported in association with rapid correction of hyponatremia (7, 8), ODS has also been reported in cases of hyperosmolarity secondary to severe hyperglycemia and azotemia without significant shifts of the serum sodium (9-11). The prevailing hypothesis for the genesis of ODS implicates a reduced adaptive capacity of the neuroglia to large shifts in the serum osmolarity (12, 13). But this hypothesis cannot exactly explain why many patients who have received rapid sodium correction do not develop ODS and also why patients who had mild hyponatremia slowly corrected can develop ODS (14-16). The underlying chronic diseases may be central to the development of ODS. Chronic alcoholism is the most common predisposing condition for developing ODS (2). In particular, the majority of the cases of ODS with normonatremia were associated with chronic alcoholism (17). For the cases associated with chronic alcoholism, many patients developed ODS during the terminal stage of binge drinking, yet there have been a few case reports of ODS after alcohol withdrawal (18, 19).
Considering that ODS tends to occur in patients with a chronic medical condition such as dialysis, liver failure and transplantation, carcinoma and various types of cachexia from different causes (20, 21), the relative minor osmotic derangement due to the inherent lack of glucose or glycogen may predispose a person to ODS (14). Similarly, the osmotic change due to a decreased intake of food or water that occurs during binge drinking or alcohol withdrawal, as in the present case, may be the cause of ODS development.

DWI with an ADC image is sensitive to cytotoxic and vasogenic edema. Cytotoxic edema is characterized by a marked decreased ADC value and a high signal on DWI. However, on DWI, vasogenic edema can also be visualized as a high signal intensity (T2 shine through effect), but it is characterized by an increased ADC value. And thus ADC map is necessary to differentiate cytotoxic edema from vasogenic edema (24). Although there have been few case reports on DWI for patients with ODS, several reports have shown that DWI and the ADC map showed the presence of cytotoxic edema in the pons irrespective of the change of serum sodium or osmolarity (17, 23, 25, 26), but the signal of the extrapontine lesion was variable. The extrapontine lesions related to the rapid correction of hyponatremia showed cytotoxic edema on the DWI and ADC map (23, 26). One case report associated with alcoholics suggested that the extrapontine lesion occurred due to vasogenic edema (25), but that authors did not obtain the ADC map. In the present case, the initial DWI showed high signal intensity in the pons and extrapontine lesions, but the ADC map showed low signal intensity in the pontine lesion and an isointense signal in the extrapontine lesion. Low signal intensity on ADC map suggested that pontine lesion represented cytotoxic edema and isointense signal on ADC map with a high signal on DWI suggested that the extrapontine lesion occurred due to mixed cytotoxic and vasogenic edema. The one-month follow-up T1 and T2 images showed that the pontine lesion had changed to a cavitary lesion, but the extrapontine lesions had nearly disappeared. These findings are indicative that the pathogenesis of EPM is different according to the predisposing condition. Vasogenic edema may play an important role in the pathogenesis of the EPM that develops during alcohol withdrawal or binge drinking without rapid correction of hyponatremia and the cytotoxic edema may be important for the EPM that is associated with an episode of acute correction of hyponatremia. The precise mechanism by which cellular injury occurs in CPM and EPM is unknown but Norenberg (27) has suggested that osmotic vascular endothelia injury is a pathogenic mechanism for ODS and this causes the release of myelinotoxic factors, production of vasogenic edema and resultant injury to oligodendrocytes. In the present case, although the exact mechanism for the difference in the pathogenesis between CPM and EPM is unclear, it seems that the extrapontine area may be more resistant than the pontine area to osmotic change and the vasogenic edema of the extrapontine area does not progress to tissue necrosis. Thus, EPM has been...
rarely observed in ODS with alcoholism, maybe due to minor osmotic change, in contrast to ODS induced by the rapid correction of hyponatremia (25). This different pathogenesis of EPM is presumed to play an important role in the good prognosis of ODS associated with a history of alcoholism (17).

In conclusion, this is a rare case of CPM/EPM that developed during alcohol withdrawal, and the patient had a good prognosis with only supportive treatment. Physicians should pay attention to the development of ODS during alcohol withdrawal, and DWI and ADC map can be very useful to diagnose and predict the prognosis of ODS.

References