

Osmotic Demyelination Syndrome Associated with Hyponatremia Caused by Lactulose Enema in a Patient with Chronic Alcoholism

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A 44-year-old man with chronic alcoholism presented with seizure and loss of consciousness. He was diagnosed with alcoholic hepatic encephalopathy, and his neurologic symptoms recovered after lactulose enema treatment. His initial serum sodium level was 141 mEq/L. However, his mental state became confused after treatment with lactulose enema for five days, and his serum sodium level increased to 178 mEq/L. After five days of gradual correction of serum sodium level from 178 mEq/L to 140 mEq/L, the patient's mental state recovered, but motor weakness in both limbs remained. Therefore, magnetic resonance imaging of the brain was performed. T2-weighted brain images showed bilateral symmetrical hyperintensities in the central pons, basal ganglia, thalami, hippocampi and unci, which were consistent with central pontine and extrapontine myelinolysis. We report a rare case of osmotic demyelination syndrome that occurred as a result of a rapid increase from a normal sodium level to hyponatremia caused by lactulose enema administered to treat alcoholic hepatic encephalopathy.

Key Words: Central pontine myelinolysis, Extrapontine myelinolysis, Lactulose, Alcoholic, Hepatic encephalopathy

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INTRODUCTION

Severe hyponatremia is defined as a sodium concentration > 160 mEq/L. Pure water loss, hypotonic fluid loss and receipt of hypertonic sodium all can cause hyponatremia¹. Osmotic demyelination syndrome (ODS) is a rare condition caused by osmotic stress². It is often associated with several clinical conditions, such as alcoholism, liver disease, malnutrition, hypokalemia and hypophosphatemia². The most important risk factor for ODS is rapid correction of hyponatremia to normonatremia. However, ODS in patients with normonatremia or hyponatremia has been reported rarely^{3,4}. The pathomechanism of ODS associated with hyponatremia remains poorly understood. Based on

animal study data, a rapid change in sodium level from normal to severe hyponatremia can cause myelinolysis⁵. It has not been fully determined how rapid correction of hyponatremia causes brain injury. In rat experiments, disruption of the blood-brain barrier and shrinkage of endothelial cells might be associated with myelinolysis in rapidly corrected hyponatremia. Blood-brain barrier disruption allows entrance of complement components and other neurotoxic components into the brain. Myelinolysis lesions and complement component localization are related^{6,7}. Other observations suggest that osmotic insult is the mechanism of oligodendrocyte apoptosis in ODS⁸.

We report a rare case of ODS that occurred as a result of a rapid increase from a normal sodium level to hyponatremia caused by lactulose enema administered to treat

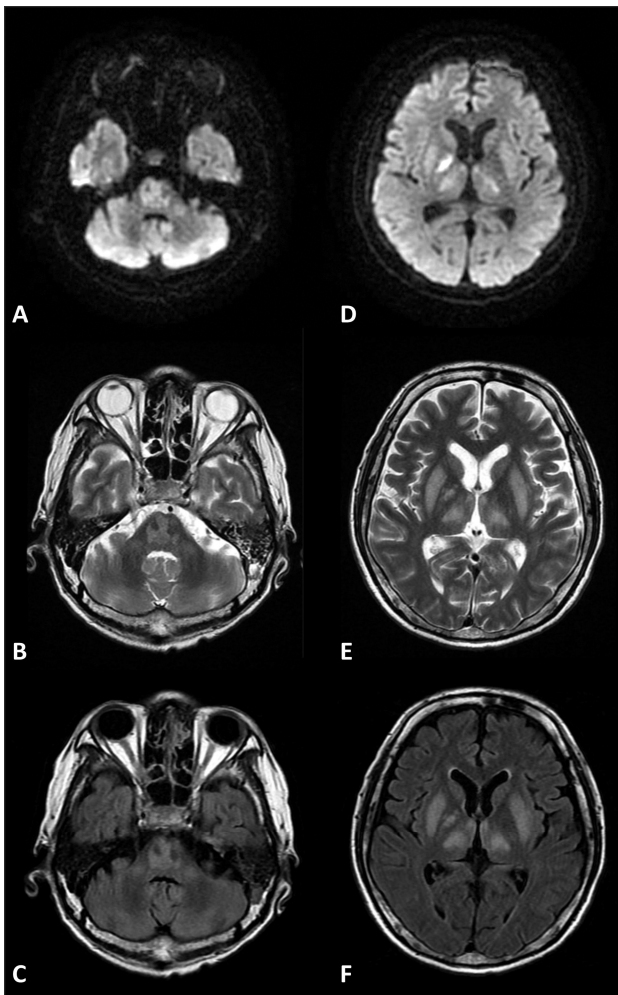


Fig. 1. Findings of brain magnetic resonance imaging (MRI). MRI demonstrates bilateral symmetrical hyperintensities in the central pons, basal ganglia and thalami on DWI (A and D), T2-weighted imaging (B and E) and T2 FLAIR imaging (C and F). DWI: diffusion-weighted imaging, FLAIR: fluid-attenuated inversion recovery.

alcoholic hepatic encephalopathy.

CASE REPORT

A 44-year-old man with chronic alcoholism presented with seizure and loss of consciousness. The laboratory data were as follows: serum creatinine, 0.7 mg/dL; sodium, 141 mEq/L; potassium, 3.8 mEq/L; chloride, 100 mEq/L; total calcium, 9.9 mg/dL; albumin, 4.7 g/dL; hemoglobin, 14.7 g/dL; and ammonia, 206 mg/dL. Computed tomography (CT) of the brain did not show any abnormal findings. The patient

was diagnosed with alcoholic hepatic encephalopathy and was treated with retention enema using lactulose every six hours for five days. His neurologic symptoms initially recovered after treatment, but a stupor mental status developed after five days of lactulose enema.

The patient was transferred to our hospital from a local clinic. His serum sodium level had increased to 178 mEq/L, while his ammonia level had decreased to 88 mg/dL. The patient was treated with mechanical ventilation because his PaO₂ and O₂ saturation values decreased to 61 mmHg and 86 mmHg, respectively. In addition, we began continuous renal replacement therapy (CRRT) because his serum creatinine level increased to 1.7 mg/dL and his urine output decreased to < 30 mL per hour for 12 hours. His serum sodium level gradually decreased from 178 mEq/L to 140 mEq/L after treatment with CRRT and correction of sodium level over five days. Magnetic resonance imaging (MRI) was performed due to persisting motor weakness of both extremities despite recovered mental status. T2-weighted images of the brain MRI revealed bilateral symmetrical hyperintensities in the central pons, basal ganglia, thalami, hippocampi and uncus, which were consistent with central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM) (Fig. 1). The patient was moved to a rehabilitation hospital to continue his recovery from the resulting motor weakness.

DISCUSSION

ODS includes CPM and EPM, which have the same pathology. In ODS, there is symmetric non-inflammatory loss of myelin, but the neuronal bodies and axons are preserved⁹. The most common cause of ODS is hyponatremia. Not every patient who has hyponatremia but those with chronic hyponatremia and correction can develop ODS². In acute hyponatremia present for < 24 hours, there is severe brain edema. Rapid correction of hyponatremia reverses this brain edema and improves symptoms without adverse effects. However, in chronic hyponatremia that persists for > 48 hours, brain edema is minimal. If hyponatremia is rapidly corrected, myelinolysis can develop¹⁰.

ODS has variable clinical manifestations that are correlated with the affected sites, which are differentiated as either pontine or extrapontine. In CPM, patients exhibit vigi-

lance disorders, coma, paresis, dysarthria, dysphagia and ocular disorders. When patients are affected by EPM, akinetic-rigid symptoms, tremor, dystonia, chorea and ataxia can be present. If ODS occurs in the cortex or in the transition between gray and white matter, frontal dysfunction, concentration disorders, psychiatric disorders and epileptic seizure can be observed. Some patients show few or no symptoms²⁾. If the patient has risk factors for ODS, such as electrolyte disturbances, chronic alcohol abuse, malnutrition or history of liver disease, appropriate laboratory tests, a complete medical history and imaging are helpful to confirm ODS²⁾. Since MRI is more sensitive than CT at detecting demyelination lesions correlated with ODS, MRI is the preferred imaging modality. Demyelination lesions exhibit hyperintensity on T2-weighted and T2 fluid-attenuated inversion recovery images, and hypointensity on T1-weighted images. The optimal timing of imaging is not clear. If the lesions are not identified on early (< 7 days) MRI images, follow-up imaging should be performed one to two weeks later¹¹⁾.

There are few data regarding treatment of ODS, which is primarily based on case reports and some case series. Prevention of ODS is better documented than treatment²⁾. In severe hyponatremia (< 120 mmol/L), very slow sodium correction of less than 0.5 mmol/L per hour and < 12 mmol/L per day significantly reduces ODS incidence¹²⁾. In animal studies, rapid sodium correction showed a myelinotoxic-inflammatory component. Some cases of early treatment with dexamethasone or plasmapheresis have been documented^{13,14)}. Minocycline is a drug that is inspected to be used for treatment of ODS. It has anti-inflammatory and anti-apoptotic effects in other demyelinating conditions, such as multiple sclerosis. Minocycline also inhibits microglial cell activation. In animal models, minocycline showed a protective effect against development of ODS after rapid sodium correction for chronic hyponatremia^{15,16)}.

Lactulose is a beneficial laxative for management of hepatic encephalopathy¹⁷⁾. It produces an osmotic effect through a large amount of poorly absorbable solutes in the colon. The diarrhea caused by lactulose contains a low concentration of sodium, and the water loss is larger than the loss of sodium, which can result in hypernatremia when fluid replacement is inadequate¹⁸⁾.

We presented a case of ODS associated with hypernatremia caused by lactulose enema in a patient with chronic alcoholism. Patients with chronic liver disease and alcoholism are at risk of ODS and have a greater chance to undergo treatment with lactulose. Clinicians should monitor these patients for ODS, even when they show normal sodium level.

Conflict of Interest

The authors declare no relevant financial interests.

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