Case Report

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Osmotic Demyelination Syndrome in a High-Risk Patient Despite Cautious Correction of Hyponatremia

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Hyponatremia is a common electrolyte disorder requiring careful management to prevent severe complications. Osmotic demyelination syndrome (ODS) is a serious neurological disorder that can develop from rapid correction of hyponatremia. Herein, is a description of the case of a 61-year-old man with multiple risk factors, including alcoholism, hypokalemia, malnutrition, and alcoholic liver cirrhosis, who developed ODS despite adherence to the recommended correction rate for hyponatremia. The patient presented to the emergency department with generalized weakness, gait disturbance, and decreased muscle strength. Initial laboratory investigations revealed severe hyponatremia, hypokalemia, and dehydration. The patient was treated with cautious correction of the hyponatremia below 8 mmol/L per day. However, on the seventh hospital day, he developed tremors, rigidity, and decreased consciousness and was diagnosed with osmotic demyelination syndrome. Despite receiving general supportive care, desmopressin, and dextrose 5% in water to reduce the serum sodium levels, the patient did not show significant improvement and was transferred to a nursing home for long-term conservative care on day 35 of hospitalization. This case report highlights the challenges associated with the diagnosis and management of osmotic demyelination syndrome and the importance of identifying patients at high risk of developing this neurological disorder.

Key Words: Alcoholism, Hypokalemia, Hyponatremia, Malnutrition, Osmotic demyelination syndrome

INTRODUCTION

Hyponatremia is a common electrolyte disorder requiring careful management to prevent severe complications. Osmotic demyelination syndrome (ODS) is a serious neurological disorder that can occur because of rapid correction of hyponatremia. This condition was first described in 1959[1]. Since then, significant advances have been made in our understanding of its pathophysiology, diagnosis, and treatment. The diagnosis and management of ODS are challenging, and there is a lack of consensus regarding optimal management strategies. However, both American and European guidelines on hyponatremia emphasize the importance of cautious correction of hyponatremia to prevent ODS. The American Expert Panel recommends that the rate of correction should not exceed 8 mmol/L in any 24-hour period for individuals at high risk of ODS[2], while the European Clinical Practice Guidelines recommend a maximum correction rate of 10 mmol/L within the first 24 hours, followed by a maximum of 8 mmol/L every 24-hour period thereafter[3]. The recently published Korean Society of Nephrology recommendation for hyponatremia similarly suggests that serum sodium concentrations should not be corrected above 10 mmol/L per day, with a stricter limit of 8 mmol/L per day for patients at high risk of ODS[4]. As aforementioned, rapid correction of hyponatremia is the primary mechanism underlying the development of ODS. However, certain patient conditions can increase the risk of developing this neurological disorder, in-

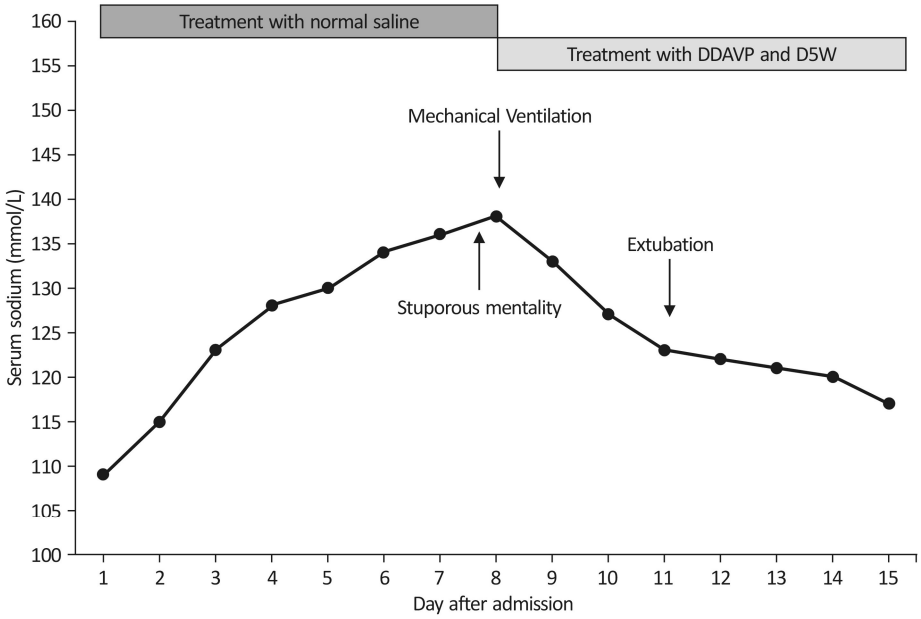

Fig. 1. Clinical course of high-risk patient treated for hyponatremia that later developed Osmotic Demyelination Syndrome.

cluding serum sodium levels <105 mmol/L, hypokalemia, alcoholism, malnutrition, and advanced liver disease[5,6]. In this case report, we present the case of a patient with multiple risk factors who developed ODS despite adherence to the guidelines mentioned above during the correction of hyponatremia.

CASE REPORT

A 61-year-old man presented to the emergency department with symptoms of generalized weakness and gait disturbance that began several days prior to his admittance. He had a medical history of alcoholic liver cirrhosis and hypertension and was taking hydrochlorothiazide 12.5 mg/day. A week prior to admission, he was consuming alcohol daily, without eating any food and only drinking water.

On examination, he appeared systemically malnourished and dehydrated, with a blood pressure of 90/60 mmHg. He was drowsy and confused. The patient had decreased muscle strength in the extremities; however, no other neurological abnormalities were observed.

Initial laboratory investigations revealed a serum sodium level of 109 mmol/L (normal range, 136-145 mmol/L), serum osmolality level of 223 mosm/kg (normal range, 275-300 mosm/kg), serum potassium level of 2.2 mmol/L (normal range, 3.5-5.1 mmol/L), blood urea nitrogen level of 9.1 mg/dL (range, 6-24 mg/dL), serum creatinine level of 0.58 mg/dL (range, 0.74-1.35 mg/dL), urine sodium level of 10 mmol/L (normal range, 40-220 mmol/L), and urine osmolality level of 153 mosm/kg (normal range, 300-800 mosm/kg) (Fig. 1). Based on physical examination findings and abnormally low serum creatinine and urinary sodium levels, it was concluded that his overall nutritional status was poor.

The patient was admitted to the intensive care unit (ICU). Hyponatremia was corrected by discontinuing the hydrochlorothiazide and administering isotonic saline intravenously. The infusion rate was adjusted to correct the sodium levels by no more than 8 mmol/L within the first 24 hours, with a final correction of 6 mmol/L. Subsequently, the correction rate did not exceed 8 mmol/L per day.

On the fifth day of admission, he regained lucidity and mobility and was transferred to the general ward. However, on the seventh day after admission, the patient developed generalized tremors and rigidity. His level of consciousness decreased to a stuporous state and he began to hyperventilate. Upon examination, the patient showed bilateral hyperreflexia, but no Babinski sign or clonus was observed. The patient was transferred to the ICU and required intubation and

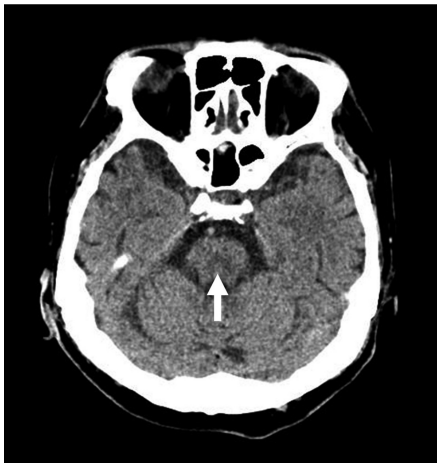

Fig. 2. Initial brain computed tomography of patient being treated for hyponatremia shows ill-defined patch hypodense lesion (arrow) at the pons.

mechanical ventilation.

Further imaging tests revealed hypodense shading of the pontine on computed tomography of the brain (Fig. 2). T2 hyperintense signal in the central pons on brain MRI was indicative of central pontine myelinolysis (Fig. 3). OSD was diagnosed based on the evaluation of clinical and radiological findings.

After diagnosis, he received general supportive care and was treated with desmopressin and dextrose 5% in water to reduce his serum sodium levels. Over the next three days, his serum sodium level decreased by 15 mmol/L, and his breathing stabilized, allowing for the removal of mechanical ventilation and intubation. His level of consciousness improved enough to allow him to follow simple commands; however, the rigidity and tremors remained unchanged. His serum sodium level decreased for three more days, but his condition did not improve. Therefore, relowering therapy was discontinued and he was initiated on rehabilitation and supportive care. The patient was eventually transferred to a nursing home for long-term conservative care on day 35 of hospitalization.

DISCUSSION

During the acute phase of hyponatremia, the brain undergoes a two-step adaptation to hypovolemia. Initially, extracellular fluid moves into brain cells, primarily astrocytes,

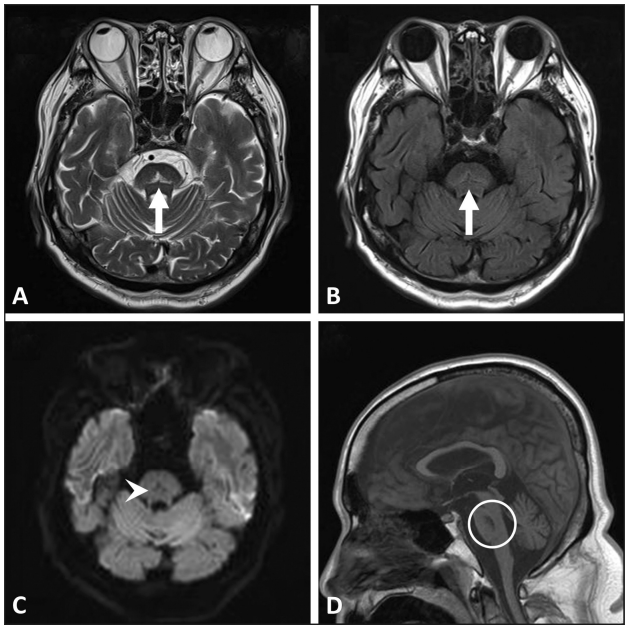

Fig. 3. Brain MRI of the patient being treated for hyponatremia shows triangular high SI lesion that looks like a small lambda symbol (arrow) in the central pons on the T2-weighted image (**A**) and FLAIR image (**B**), and there is diffusion restriction (arrowhead) (**C**). T1-wighted sagittal image reveals low SI lesion (circle) in the pons (**D**). FLAIR: fluid attenuated inversion recovery, MRI: magnetic resonance image, SI: signal intensity.

which raises the hydrostatic pressure in the interstitium and causes the extracellular fluid to move through the cerebrospinal fluid into the systemic bloodstream[7]. If hyponatremia persists for more than three hours, brain cells release intracellular substances such as potassium and organic solutes. If hyponatremia lasts longer, astrocytes release other organic substances (osmolytes), such as phosphocreatine, myoinositol, glutamine/glutamate, and taurine, and the adaptation is completed in approximately 2 days[8]. Through this process, brain cells can eliminate excess water and attain the same tonicity as plasma, preventing a significant increase in cell water, thereby protecting against cerebral edema.

However, once the brain has adapted to hypotonicity, the rate of correction of hyponatremia becomes important, and a rapid correction can lead to ODS. The mechanism underlying ODS is uncertain; however, it has been hypothesized to be related to the downregulation of sodium-coupled amino acid transporters in astrocytes exposed to hypotonicity[9]. This delays the reuptake of osmolytes into as-

trocytes and renders them unable to keep up with changes in the tonicity o the extracellular fluid. This temporal imbalance can lead to brain dehydration, astrocyte and oligodendrocyte death, and subsequent disruption of the blood-brain barrier.

Astrocytes experience hyperosmotic stress during the correction of chronic hyponatremia, as they strive to compensate for increased extracellular osmolality to prevent excessive cell shrinkage, damage, and cell death by transporting myo-inositol and glutamine/glutamate back into the cell. Patients with a history of alcoholism or malnutrition may have chronic deficiencies in substrates, such as phosphate, amino acids, glucose, potassium, and magnesium, which can hinder their ability to mount an adequate compensatory response. Furthermore, these patients are unable to maintain the activity of the Na^+/K^+-ATPase pump because of a decrease in energy supply[10]. Patients with cirrhosis, hepatic encephalopathy, and chronic hyponatremia experience a significant depletion of brain myoinositol stores[11]. This suggests that patients with cirrhosis may be more vulnerable to ODS. Other risk factors related to ODS are serum sodium at presentation below 105 mmol/L and a longer duration of hyponatremia over 2 days.

The patient in this case report had four risk factors for ODS: alcoholism, malnutrition, alcoholic liver cirrhosis, and hypokalemia. Despite following the US and European guidelines, the patient developed ODS and suffered irreversible brain damage. This highlights the importance of not only an appropriate correction rate for hyponatremic patients with multiple risk factors but also a close observation of clinical signs suggestive of ODS. There have been reports of ODS in patients with normonatremia or hypernatremia [12-15], all of whom had at least one of the above risk factors, suggesting that the primary cause of the patient's ODS is related to the underlying conditions rather than the correction rate of hyponatremia.

ODS symptoms can vary widely, ranging from asymptomatic to severe, and include lethargy, dysarthria, ophthalmoplegia, ataxia, confusion, and coma depending on the location of demyelination. Distinguishing these symptoms from those associated with alcohol withdrawal syndrome can be challenging, so close monitoring of patients for the development of neurological symptoms is essential, even if hyponatremia is being corrected at an adequate correction rate.

Although ODS has no known effective treatment and has a high mortality rate, recent research has shown that aggressive supportive care can improve outcomes. A study followed 36 cases of ODS in the ICU for one year and reported that 25 (69%) survived, with 14 (56%) experiencing only minimal neurological deficits[16]. Therefore, aggressive supportive care should be provided during the diagnosis. Several case reports have described the effectiveness of relowering therapy with desmopressin and dextrose 5% in water early after ODS diagnosis[17]. In this case, relowering therapy was attempted, and although the patient did not fully recover, he was successfully weaned off the mechanical ventilation.

In conclusion, although ODS is typically associated with rapid correction of hyponatremia, this case illustrates that it can occur even with slow correction, particularly in patients with multiple risk factors. Healthcare providers should be aware of this possibility and maintain a high index of suspicion of ODS, as prompt diagnosis and aggressive supportive care can improve outcomes. It is important to remember that ODS has a high mortality rate and can cause long-term neurological deficits. Prevention through careful monitoring and management of serum sodium levels is crucial in high-risk patients.

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