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Case Series

Navigating the complexity of osmotic demyelination syndrome in the elderly: insight from three cases

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ABSTRACT

Osmotic demyelination syndrome (ODS) results from rapid shifts in serum osmolality and can be triggered by various factors such as hyponatremia, hyperglycaemia, malnutrition, alcohol abuse, and liver disease. Although hyponatremia prevalence increases with age, ODS typically manifests between ages 30 to 50, indicating a complex age-susceptibility relationship. Its pathophysiology involves brain volume restoration adaptation, with rapid correction of osmolality leading to dehydration and subsequent demyelination. Hyperglycaemia-induced ODS results from rapid correction of hyperosmolar states, overwhelming neuronal compensatory mechanisms. Neuroimaging, usually MRI, is crucial for diagnosis, revealing hyperintense lesions. Clinical manifestations vary widely, from dysarthria and dysphagia to spastic quadriparesis, with poor outcomes, especially in older patients. Below, three cases of ODS in elderly patients are presented, each with distinct clinical presentations and outcomes. Case1 highlights the association between rapid correction of hyperglycaemia and ODS while Case 2 and 3 illustrates the consequences of overly rapid correction of hyponatremia. Diagnosing Osmotic Demyelination Syndrome (ODS) in the elderly poses challenges due to overlapping clinical features with conditions like encephalopathy, delirium, and postictal confusional states, which closely mimic ODS. Further research is needed to better understand the pathophysiology and optimize management approaches, especially in vulnerable populations like the elderly.

Keywords: Case series, Osmotic demyelination syndrome, Elderly, Hyponatremia, Hyperglycaemic hyperosmotic state

INTRODUCTION

Osmotic demyelination syndrome formerly known as central pontine myelinolysis, represents a neurological disorder characterized by the demyelination of nerve cells, primarily occurring within the central pons and other extrapontine locations. This condition arises from rapid shifts in serum osmolality, often stemming from overly aggressive correction of electrolyte imbalances. Initially associated with hyponatremia, ODS has been found to coexist with various other metabolic disturbances, including hyperglycaemia, malnutrition, chronic alcohol abuse, and certain medical interventions like haemodialysis or liver transplantation.[1]

While the prevalence of hyponatremia, a predisposing factor for ODS, increases with age, intriguingly, the mean onset age for ODS falls between 30 to 50 years, challenging the assumption of a direct correlation between age and ODS incidence.[2] In older adults, ODS prevalence results from a complex interaction of physiological changes and comorbidities, affecting diagnosis, presentation, and management. The pathophysiology of ODS involves the delicate balance of osmotic pressures within the brain and the body. Extrapontine myelinolysis (EPM) generally has a better prognosis than central pontine myelinolysis (CPM). EPM is more likely to be reversible with earlier detection on MRI.[3]

This case series aims to explore the intricate mechanisms underlying the development of ODS in elderly, considering its multifactorial etiology and the potential implications for clinical management. By elucidating the interplay between electrolyte disturbances, metabolic insults, and the vulnerability of brain structures, this series seeks to enhance understanding of ODS pathogenesis and improve diagnostic recognition in clinical practice.

CASE SERIES

Case 1

An 81-year-old female with a history of insulin-dependent diabetes mellitus presented with a generalized tonic-clonic seizure followed by postictal confusion. She also complained of polyuria. On examination, she appeared visibly dehydrated with decreased skin turgor. She was conscious, oriented, and had a blood pressure of 132/78 mmHg and a pulse rate of 112 per minute. Her random blood glucose was 686 mg/dl, with no acidosis and normal anion gap. Urine sugars were positive, but ketones were negative in both blood and urine. Initial sodium levels were high (146 meq/l, corrected 155 meq/l).

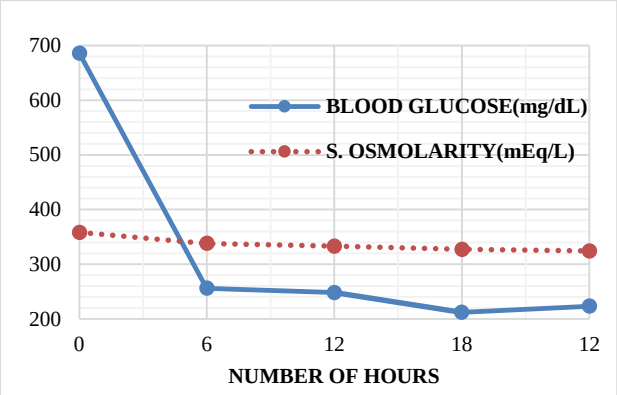
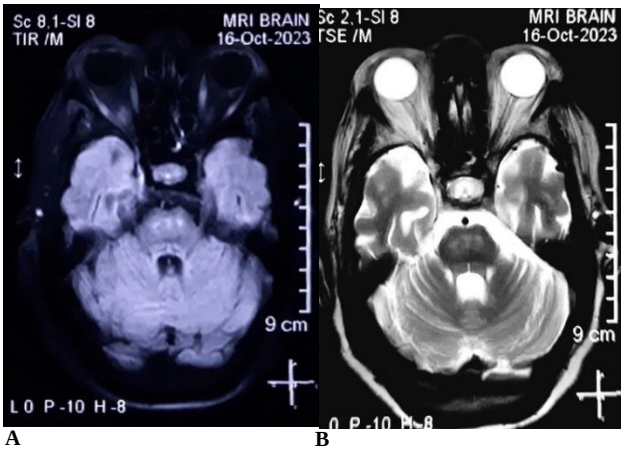


Figure 1: Trend of blood glucose and serum osmolarity levels with time.



A B

Figure 2 (A and B): CE-MRI T2W and FLAIR sections showing pontine hyperintensities.

Treatment included intravenous fluids and insulin. As shown in Figure 1 six hours later, blood glucose levels decreased to 256 mg/d, and sensorium improved. However, 30 hours after admission, the patient became lethargic again with decreased responsiveness, and glucose levels were 245 mg/dl with sodium levels of 142 mEq/l (Figure 4). The pupils exhibited normal reactivity, and both plantar reflexes were bilaterally flexors, with normal muscle tone and reflexes. Cerebrospinal fluid analysis was done which was normal. MRI brain showed periventricular ooze along with hyperintense lesions on T2-FLAIR suggestive of osmotic demyelination syndrome (ODS) in the clinical context (Figure 2). EEG was normal. Antibiotics were added for aspiration pneumonitis.

The patient gradually improved and was discharged after one week in a stable condition.

Case 2

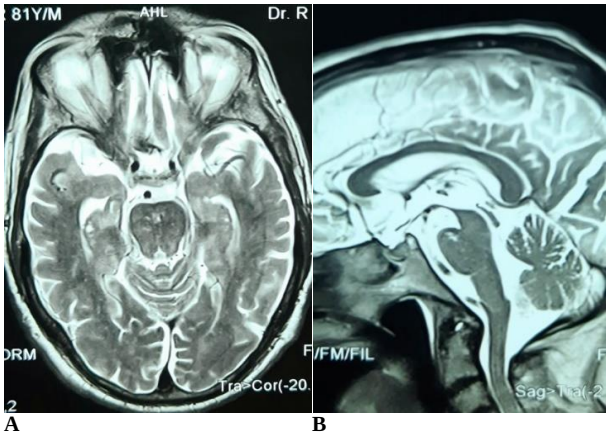
An 84-year-old hypertensive female, on amlodipine and hydrochlorothiazide, experienced multiple loose stools followed by confusion. Initial presentation at a local hospital revealed severe hyponatremia with sodium of 112 mEq/l (Figure 4), corrected with 3% sodium chloride. While initially responsive, she relapsed into altered sensorium after 48 hours after which Upon admission to our department, the patient presented with stable vital signs, normal random blood glucose, and unremarkable physical examination and sodium of 129 mEq/l. Despite this, she experienced a generalized tonic-clonic seizure with associated tongue bite and post-ictal drowsiness. Levetiracetam was initiated for seizure management. Neurological examination revealed normal pupils, flexor plantar reflexes, increased muscle tone, and grade 2+ reflexes. No meningeal signs were evident. Cerebrospinal fluid analysis was done to rule other aetiologies and returned normal. MRI revealed a demyelinating lesion in the pons, indicative of osmotic demyelination syndrome due to rapid correction of hyponatremia. Despite conservative management, her sensorium showed minimal improvement at a 60-day follow-up, with a Glasgow Coma Scale score of E4V5M6, and no focal neurological deficits were observed at discharge.

Case 3

A 70-year-old male with a history of hypothyroidism presented with altered sensorium, decreased verbal output, and limb immobility. Glasgow Coma Score was E2V2M4. Vitals were stable. Pupils were normal in shape and reactive, plantar reflexes were extensor bilaterally, and there was increased tone with spasticity in all four limbs. Muscle power was 2/5. Random blood glucose was 123 mg/dl. Initial serum sodium was 129 mEq/l, and potassium was 3.0 mEq/l. NCCT head was normal. Cerebrospinal fluid analysis reports were non-significant.

History revealed recent administration of 3% saline boluses at a private hospital, with previous records

showing severe hyponatremia (107 mEq/l) as demonstrated in Figure 4, correcting to 121 mEq/l after 24 hours. CE-MRI showed T2 hyperintensities in the pons (Figure 3) consistent with osmotic demyelination syndrome. The patient was managed conservatively with electrolyte and fluid management, but developed ventilator-associated pneumonia and died during the course of illness.



A B

Figure 3 (A and B): Coronal and sagittal T2W sections of CE-MRI showing pontine hyperintensities.

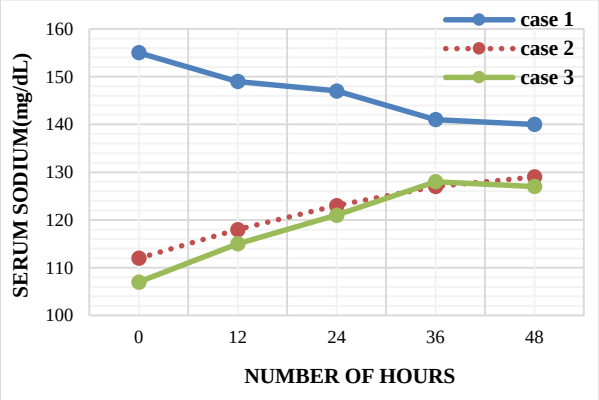


Figure 4: Trend of variation of serum sodium levels with time.

DISCUSSION

Osmotic demyelination syndrome (ODS), consists both central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM).[4] Although originally described in hyponatremia; osmotic demyelination may coexist with hyperglycaemia, hypokalaemia, malnutrition, chronic alcohol abuse, primary adrenal insufficiency, prolonged administration of diuretics, high blood sugar levels, haemodialysis, and liver transplantation.[5]

The largest autopsy series reported a prevalence of 0.25% to 0.5% for osmotic demyelination syndrome in the general population. However, due to limited research on ODS epidemiology, caution is necessary when making conclusions about its incidence.[6] Age is a significant prognostic factor, with increasing age linked to poorer outcomes. The average age in the group with favourable outcomes was 44.7±14.4 years, compared to 52.3±13.6 years in the group with poor outcomes (p=0.006).[7]

In hyperglycaemic conditions like Case 1, osmotic demyelination syndrome (ODS) can occur due to a hypertonic insult, where the serum or extracellular space becomes hypertonic faster than brain cells can adapt. This imbalance damages myelin sheaths in the brain, leading to ODS.[8] Rapid shifts in plasma osmolarity during hyperglycaemia correction also contribute to ODS in such conditions.

In the population based Rotterdam Study, 7.7% of individuals aged 55 or older exhibited hyponatremia (serum sodium <136 mmol/l), with a higher prevalence of 11.6% in those aged 75 and above.[9] Hyponatremia leads to water influx into cells, causing swelling and increased brain pressure. The brain compensates by removing solutes and water within 24 to 48 hours. Rapid correction of hyponatremia can create a hyperosmotic external environment, leading to cell shrinkage as water exits glial cells, potentially resulting in ODS.[10]

In case 2, there was rapid correction of 11 meq/dl sodium in the first 24 hours. The American Expert Panel recommends limiting the correction of serum sodium to 10–12 mEq/l within any 24-hour period and 18 mEq/l within any 48-hour period for patients with an average risk of osmotic demyelination syndrome (ODS). For patients at high risk of ODS, the suggested limit is 8 mEq/l within any 24-hour period.[11]

Moreover, even gradual correction of hyponatremia can lead to osmotic demyelination syndrome (ODS) if hyponatremia is associated with hypokalaemia, alcohol use disorder, liver disease, malnutrition, and initial serum sodium levels of <105 mEq/dl. These factors can be particularly deleterious in the elderly if not vigilantly screened.[12]

In case 3, spastic quadriparesis developed 3 days after patient was given 3% normal saline bolus. When the pons, corticobulbar, and corticospinal tracts are affected, typical symptoms include initially dysarthria and dysphagia, followed by a transition from flaccid paralysis to spasticity and 'locked in' state. In contrast, extrapyramidal movement disorders (EPM) manifest with symptoms such as tremors, ataxia, and various movement abnormalities including mutism, Parkinsonism, dystonia, and catatonia.[13] Hyponatremia may be corrected faster when potassium is administered alongside due to the Na-K-ATPase on cell membranes. As potassium enters cells to replenish depleted stores, sodium is extruded, resulting in a quicker rise in serum sodium.[14]

The typical MRI findings include hyperintensities in the central pons, basal ganglia, and thalamus on T2-weighted

(T2W) and FLAIR images, along with hypointensities on T1-weighted (T1W) images.[15]

Diagnosing osmotic demyelination syndrome (ODS) in the elderly is challenging due to various comorbidities and factors leading to impaired consciousness, including metabolic encephalopathy, delirium, dementia, and postictal states. Symptoms such as encephalopathy, seizures, and psychiatric manifestations like catatonia or hallucinations, combined with delirium, can further complicate diagnosis. Prompt recognition of ODS is crucial in the elderly for effective management and to prevent neurological deterioration.

Managing critically ill individuals necessitates initiating neurorehabilitation while closely monitoring concurrent morbidities. Case 3's demise from sepsis and ventilator-associated pneumonia underscores the importance of addressing secondary complications. To prevent overly rapid correction of hyponatremia, administer 5% Dextrose W/V (252 mOsm/l) and desmopressin. The former, given at 6 ml/kg of lean body weight over 1 to 2 hours, reduces serum sodium by 2 mEq/l. Desmopressin, at 2 to 4 mcg intravenously or subcutaneously, enhances water reabsorption by binding to renal V2 receptors. These interventions aim for a gradual reintroduction of hyponatremia, targeting a correction rate of 8-12 mEq/l per 24 hours.[16]

CONCLUSION

Osmotic demyelination syndrome (ODS) presents a formidable challenge in clinical practice, particularly in elderly patients. Our report outlines three cases of ODS, each with distinct clinical presentations and outcomes. Case 1 underscores the risks associated with overly rapid correction of glucose, while Case 2 and 3 shed light on the potential consequences of rapid correction of hyponatremia with coexistent hypokalaemia in case 3. Advanced age poses additional complexities in the clinical course and prognosis of ODS. Age-related physiological changes, comorbidities, and reduced physiological reserve contribute to the intricacies of managing ODS in older individuals. Moreover, age emerges as an important prognostic factor, with poorer outcomes associated with increasing age. In conclusion, ODS represents a significant clinical dilemma, especially in older patients with close confounders. Diagnosis demands a high index of suspicion, thorough evaluation, and neuroimaging. Treatment strategies should be tailored to individual patients and may involve cautious correction of electrolyte imbalances and supportive care. Further research is warranted to deepen our understanding of the pathophysiology and refine management strategies, particularly in vulnerable populations such as the elderly.

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