Case report

Unusual progression of osmotic demyelination after liver transplantation on MRI brain

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ABSTRACT

Osmotic demyelination syndrome, comprised of central pontine and extrapontine myelinolysis, is an important and potentially fatal complication primarily related to rapid overcorrection of serum sodium leading to devastating neurological symptoms. While traditionally presenting in the pons, we report the case of a 43-year-old female patient who recently underwent a liver transplant and developed extrapontine myelinolysis and subsequently central pontine myelinolysis resulting in irreversible spastic quadriparesis. This rare case highlights the variability of presentation of osmotic demyelination syndrome on imaging.

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Introduction

Patients with liver dysfunction undergoing liver transplant are known to be highly susceptible to changes in serum sodium concentration. When sodium levels rise too rapidly in the setting of chronic hyponatremia, potentially irreversible damage may be done to critical structures within the brain by way of myelinolysis. The neurological manifestations of myelinolysis in this setting are known as osmotic demyelination syndrome. While classically occurring within the central pons, osmotic demyelination syndrome can also arise within extrapontine structures. We present a patient developing extrapontine and subsequent central pontine myelinolysis (CPM) after liver transplantation.

Case report

A 43-year-old female with a history of alcoholic liver cirrhosis presented to her local emergency room with weakness, nausea and vomiting. Initial laboratory findings were significant for serum sodium of 119 mmol/L (136-145 mmol/L) among various other abnormalities. Due to advanced liver disease, she was transferred to a tertiary care center where hepatology and transplant surgery were consulted. She was found to be in acute decompensated cirrhosis and the decision was made to undergo orthotopic liver transplantation. The patients Model For End-Stage Liver Disease (MELD) score was 36 and Child-Pugh score was 13, class C. Preoperatively, the serum sodium value was noted to be 128 mmol/L. Over the next 24 hours, the
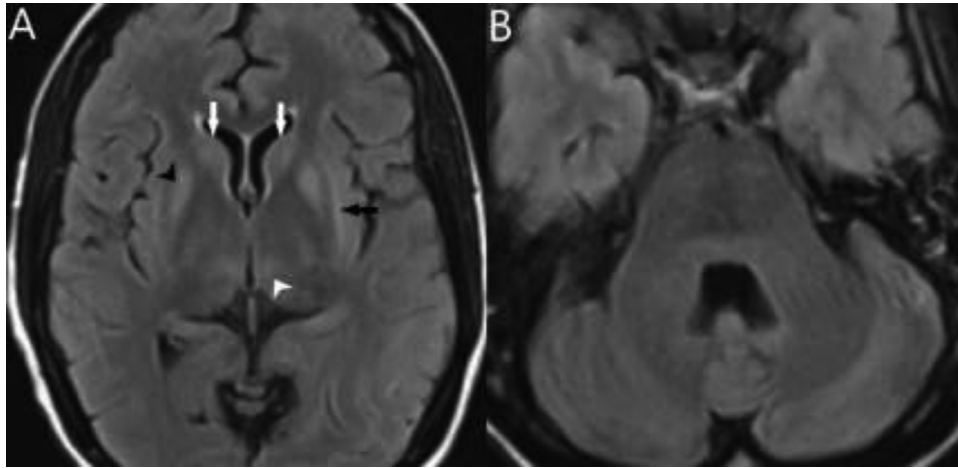
Fig. 1 – MRI performed 8 days postoperatively. FLAIR sequence at the level of the basal ganglia and mid pons demonstrating isolated extrapontine myelinolysis. (A) demonstrates symmetric hyperintense signal within the caudate heads (white arrows), lentiform nuclei (black arrowhead), medial thalami (white arrowhead), and external capsule (black arrow). (B) demonstrates no abnormal hyperintense signal within the central aspect of the pons. Color version of figure is available online.
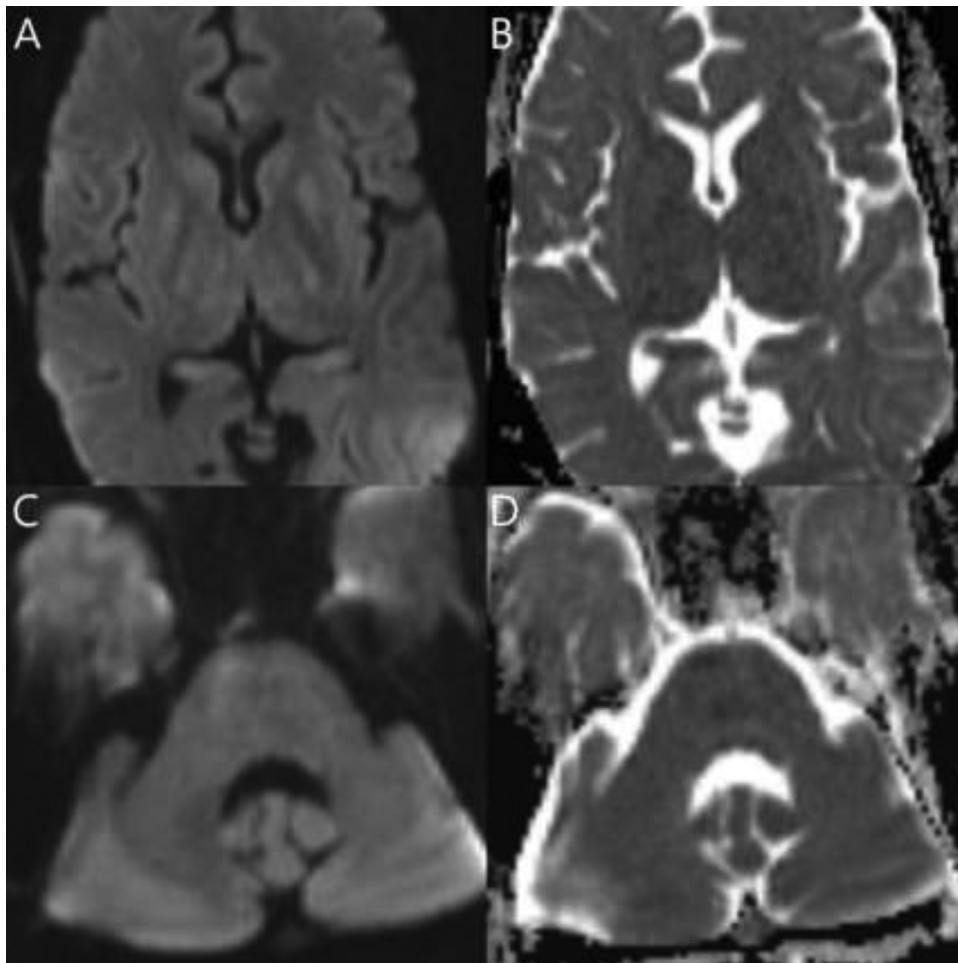

Fig. 2 – MRI performed 8 days postoperatively. High b-value diffusion weighted images (DWI) and corresponding apparent diffusion coefficient (ADC) map at the level of the basal ganglia and pons. (A-D) demonstrate no abnormal restricted diffusion within the basal ganglia or pons.
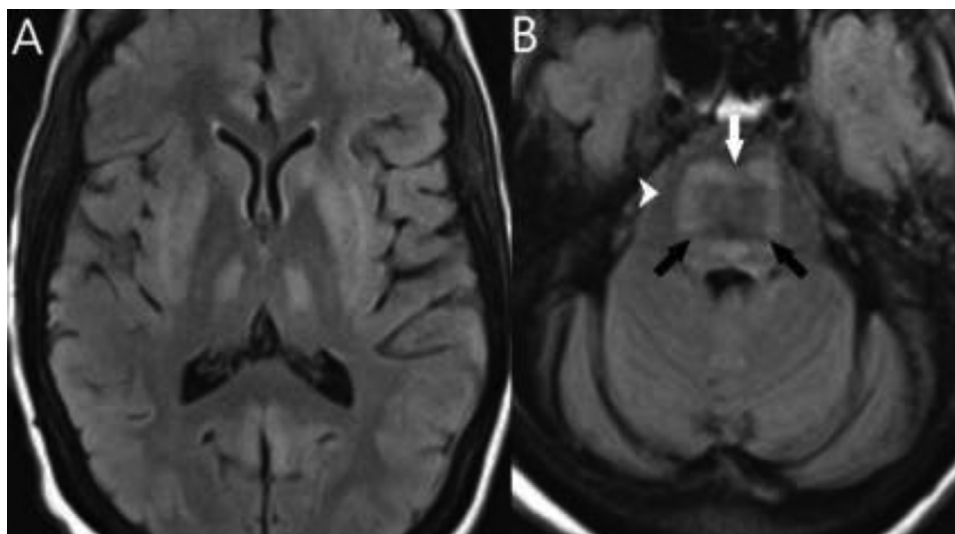
Fig. 3 – MRI performed thirteen days postoperatively. FLAIR sequence at the level of the basal ganglia and mid pons demonstrating central pontine and extrapontine myelinolysis. (A) demonstrates relatively increased and more diffuse hyperintense signal within the basal ganglia, thalamus and external capsule compared to the prior MRI. (B) demonstrates interval development of hyperintense signal within the basis pontis (white arrow) centrally with relative sparing of the periphery (white arrowhead). Note also the relative sparing of the transverse pontine fibers (black arrows). Color version of figure is available online.

serum sodium rapidly increased to 147 mmol/L, a difference of 19 mmol/L. Three days postoperatively, neurology was consulted for possible seizure activity. Neurologic examination was limited in the setting of intubation and sedation, however electroencephalography demonstrated bifrontal seizure activity and was favored to be metabolic in etiology. Eight days postoperatively while still intubated and sedated, magnetic resonance imaging (MRI) of the brain was performed due to continued seizure activity and showed signal abnormality in the deep gray nuclei and external capsule with sparing of the brainstem (Fig. 1 and 2). Follow-up MRI of the brain 5 days later demonstrated increased signal abnormality in the deep gray nuclei and external capsule and new signal abnormality in the central pons (Fig. 3 and 4). After weaning sedation and extubating, neurologically the patient was noted to be awake however demonstrated spastic quadriparesis, mutism, and was nonresponsive. Four months postoperatively, no neurologic improvement was identified.

Discussion

This case illustrates the importance of close evaluation of the extrapontine structures as this may be the initial or only manifestation of osmotic demyelination syndrome. ODS, previously known as CPM, is an important and potentially fatal complication which is most often attributed to rapid overcorrection of chronic hyponatremia. ODS was first reported in 1959 and, as inferred by its former name, was a disorder originally described as involving loss of myelin within the central pons [1]. Since that time, studies have demonstrated these same findings to be present within additional regions throughout the brain, known as extrapontine myelinolysis [2].

ODS is characterized by loss of myelin with sparing of the neuronal bodies and axons with a lack of associated inflammatory findings. This is in contrast to the inflammatory demyelination seen in disorders such as multiple sclerosis. While the exact pathophysiology of ODS remains unclear, it is known to be in part associated with changes in osmolar balances between cells and the extracellular space. In the setting of acute imbalance such as acute hyponatremia, cells can respond appropriately, shifting excess osmolytes inside the cell. In chronic states however, cells undergo adaptation by shifting organic osmolytes (such as glutamine, glutamate, myoinositol, and taurine) into the extracellular space over the course of hours to days to create a new equilibrium [3–5]. Subsequently, when extracellular osmolar levels rise too rapidly, the cells are no longer able to respond appropriately as these organic osmolytes cannot be synthesized or transported quickly enough into the intracellular space. This leads to cellular shrinkage and potentially cell death. Oligodendrocytes, the cells responsible for the generation of the myelin sheath around axons within the brain, are known to be highly susceptible to osmotic imbalance either through breakdown of the blood-brain barrier or by direct injury [3,4,6]. Degeneration of these cells leads to myelinolysis and damage to critical white matter tracts.

Multiple theories have been introduced as to why the pons is classically susceptible to myelinolysis, including high concentrations of oligodendrocytes and tightly packed descending and transverse fiber tracts in gridlike configurations within the centrally located basis pontis [3,7]. Similar findings have been reported within key extrapontine structures including the basal ganglia, thalamus, external and extreme capsule, hippocampus, and cerebellum among others [2,3,7]. As myelinolysis occurs, fiber tracts within these regions become damaged leading various neurological deficits. Demyelination with
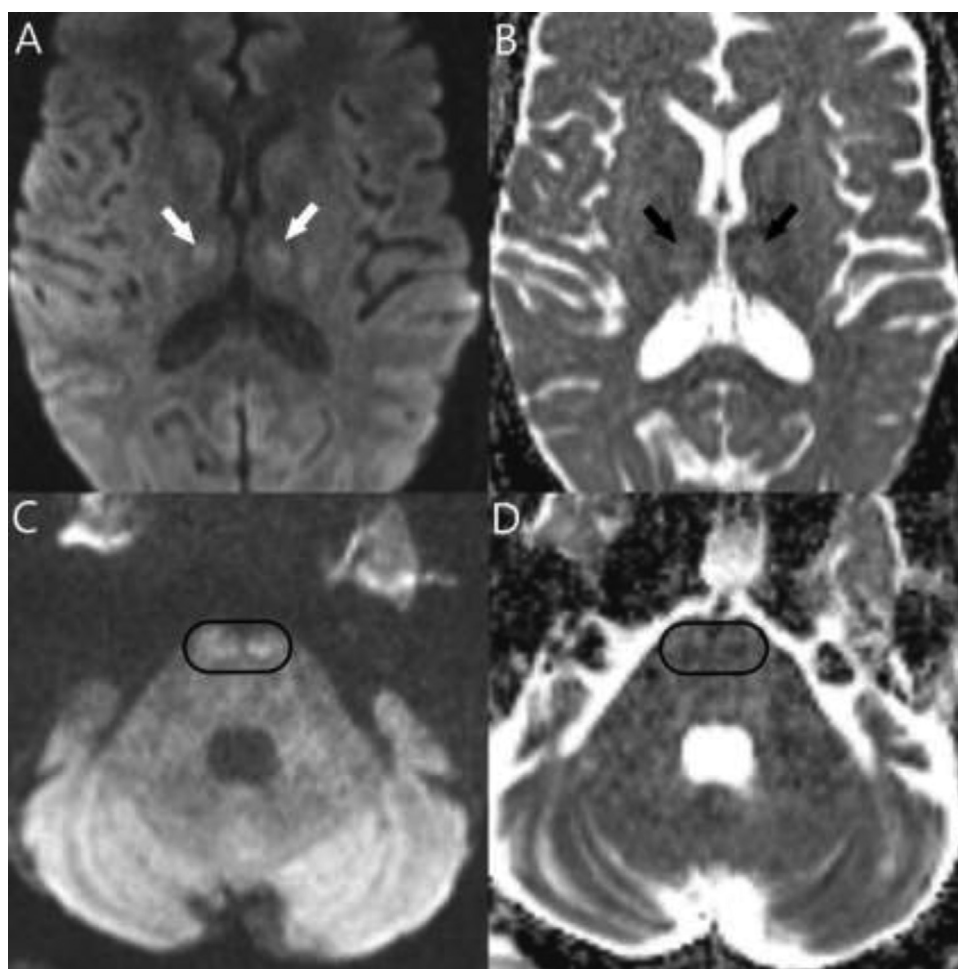
Fig. 4 – MRI performed thirteen days postoperatively. High b-value DWI and corresponding ADC map at the level of the basal ganglia and pons. (A and B) demonstrate increased signal on the DWI (white arrows) without decreased signal on the ADC map (black arrows) in the basal ganglia. (C and D) demonstrate minimal diffusion restriction within the pons anteriorly (black oval). Color version of figure is available online.

the basis pontis causes injury to numerous tracts including the corticobulbar tracts and, in advanced cases, the corticospinal tract. Neurologically, this presents as dysarthria, dysphagia, and spastic quadriparesis. Involvement of the basal ganglia can lead to movement disorder symptomatology [7,8].

Imaging findings in ODS generally manifest after clinical symptoms [10]. As such, a diagnosis of ODS should still be considered in the setting of normal imaging in the appropriate clinical context. Computed tomography has a low sensitivity in the evaluation of ODS and MRI is the preferred imaging modality [2,9]. MRI findings in CPM include hyperintense signal on T2-weighted imaging within the central pons with relative sparing of the peripheral pons and corticospinal tracts. This classically has been likened to the 3-pronged appearance of a trident, coined the "trident sign." There is also traditionally sparing of the transverse pontine fibers. Signs of EPM are similar, with hyperintense T2 signal most seen in the cerebellum with additional sites including the lateral geniculate body, caudate nucleus, putamen, thalamus, hippocampus, external and extreme capsule, and cerebral subcortical white matter [3,7,17]. Less common reported areas of involvement include

the midbrain and medulla, internal capsule, mamillary bodies, as well as the spinal cord [7,9,17].

Restricted diffusion on DWI has been shown to be an early finding of ODS, seen as soon as 24 hours after the onset of paresis, however, is only present in 40-50% of cases [2,10]. Contrast enhancement within the demyelinating lesions is seen variably in approximately 20% of patients [2].

Early autopsy studies demonstrated pontine involvement in the majority of cases, seen in up to 93% [2]. Isolated EPM was present in 6% of cases with combined pontine and extrapontine involvement seen 27% of the time. Newer studies utilizing primarily MRI have demonstrated similar results with isolated or mixed CPM present 87% of the time. Isolated EPM was seen 13% of the time and combined CPM and EPM was seen in 31% of cases [2].

Patients with cirrhosis undergoing liver transplant are known to be at high risk of ODS. Sodium levels are an independent predictor of mortality in cirrhotic patients and are an important marker in evaluation for transplantation, utilized in the MELD score [11]. In cirrhotic patients, chronic hyponatremia is common, with at least moderate hyponatremia

(<130 mmol/L) seen in up to 22% of patients [6]. For patients undergoing transplantation, close monitoring of sodium levels is of critical importance as administration of intravenous fluid and blood products intraoperatively and postoperatively can lead to significant osmotic shifts within the extracellular space [6]. Current guidelines recommend a maximum correction of sodium levels no more than 8-10 mmol/L with a goal of 4-6 mmol/L over the course of 24 hours in critically ill patients [12].

Evidence for the treatment of ODS is limited. Several case reports have been published demonstrating improvement in neurologic symptoms when sodium levels were reduced back to acceptable levels within the first 12 hours from the onset of clinical deterioration [13–15]. However, a review of the literature demonstrated no evidence for lowering of sodium once neurological symptoms have been present for more than 24 hours. Treatment otherwise is primarily supportive.

Prognosis for ODS on an individual basis is difficult to determine acutely as studies have shown that initial severity of symptoms does not correlate with long term outcomes [16]. A study by Graff-Radford et al in 2011 evaluating the location and volume of the demyelinating lesions, diffusion restriction, and lesion enhancement suggested that there is no imaging correlation with outcomes, however the study was limited with only 24 patients [17]. Originally, it was believed that the disease was fatal as ODS was diagnosed by autopsy. Subsequent studies utilizing clinical and radiologic diagnosis have shown that up to 70-80% of patients can survive, with 50%-60% of all patients demonstrating some neurological improvement [2]. Unfortunately, studies focused on ODS in liver transplant patients differ from the general population, with statistics showing significant morbidity and mortality in up to 77% of patients with only 23% of patients showing neurological improvement [2].

Conclusion

We describe a rare case of osmotic demyelination syndrome in a postoperative liver transplant patient initially manifesting as extrapontine myelinolysis with later involvement of the pons. Patients with underlying liver dysfunction undergoing liver transplant are known to be especially vulnerable to rapid changes in serum sodium levels and monitoring of laboratory and clinical symptoms is of vital importance. Once symptomatic patients demonstrate radiographic findings, current evidence shows that while reversibility is not possible, many patients can still improve neurologically. Early recognition of ODS based on imaging, clinical history, and laboratory values can help referring physicians in optimization of supportive treatment in hopes of recovery.

Patient consent

Documented informed consent was obtained from the patient's medical power of attorney.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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