



Case report

Occult central pontine myelinolysis post liver transplant: A consequence of pre-transplant hyponatremia



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ABSTRACT

Rapid overcorrection of chronic hyponatremia can lead to osmotic demyelination syndrome or central pontine myelinolysis (CPM), a diagnosis often triggered by observing the characteristics of neurological abnormalities developed as a result of CPM. However, anyone with chronic hyponatremia and overcorrection of serum sodium is at risk of physiological CPM despite the lack of clinical symptoms. We report an adult patient who presented as post-op delirium, had incidental finding of CPM by magnetic resonance imaging (MRI) of the head after a liver transplant. Despite his non-typical presentation, the patient had the typical risk factors of CPM such as chronic hyponatremia, rapid overcorrection of serum sodium and cirrhosis undergoing a transplant. As hyponatremia and neurological disorder such as encephalopathy simultaneously affect patients with cirrhosis, CPM may be more common than once thought in the chronic liver disease population and inappropriate hyponatremia management has important medical consequences that can go unnoticed.

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1. Introduction

Central pontine myelinolysis (CPM) is a well-known neurologic event that is classically associated with serious, and sometimes catastrophic, neurologic sequelae including spastic quadriplegia, pseudobulbar palsy and locked in syndrome [1]. Cerebellar syndrome and seizures are also reported [1,2]. Classically, CPM is associated with significant hyponatremia as well as its rapid correction and has well-known brain imaging characteristics affecting the pons [3]. CPM is also recognized to be a complication of liver transplantation [2–5] and has been reported to be a consequence of post-operative serum sodium abnormalities including hypo and hypernatremia [3,4] and presumed tacrolimus neurotoxicity [6]. Occasionally, CPM post-transplant has no obvious precipitating events.

Most of the reported cases in the literature describe symptomatic CPM. It is with this in mind that we report an adult patient

who was found to have CPM on MRI imaging immediately post-transplant without any neurological complications or sequelae.

2. Case history

A 55-year-old man with decompensated cirrhosis due to primary biliary cholangitis (PBC) developed acute confusion and memory loss three days after undergoing a deceased donor liver transplant. Prior to transplant, his end stage liver disease was complicated with portal hypertension, diuretic-refractory ascites requiring large volume paracentesis, an episode of spontaneous bacterial peritonitis (SBP), esophageal varices requiring banding, and hepatic encephalopathy. In the three months prior to transplantation, he had required multiple hospitalizations and emergency department visits for the management of refractory ascites requiring weekly paracentesis for the removal of 7–10 L of ascetic fluid. Three weeks before liver transplantation, he was admitted to the hospital with severe hyponatremia, SBP and hepatic encephalopathy. It was during this admission that he was transferred to our transplant center and eventually received a liver transplant. Peri-operatively, he had mild hyponatremia (Na 133 mmol/L), which was corrected appropriately by oral fluid restriction and avoidance of hypo- and isotonic saline infusion.

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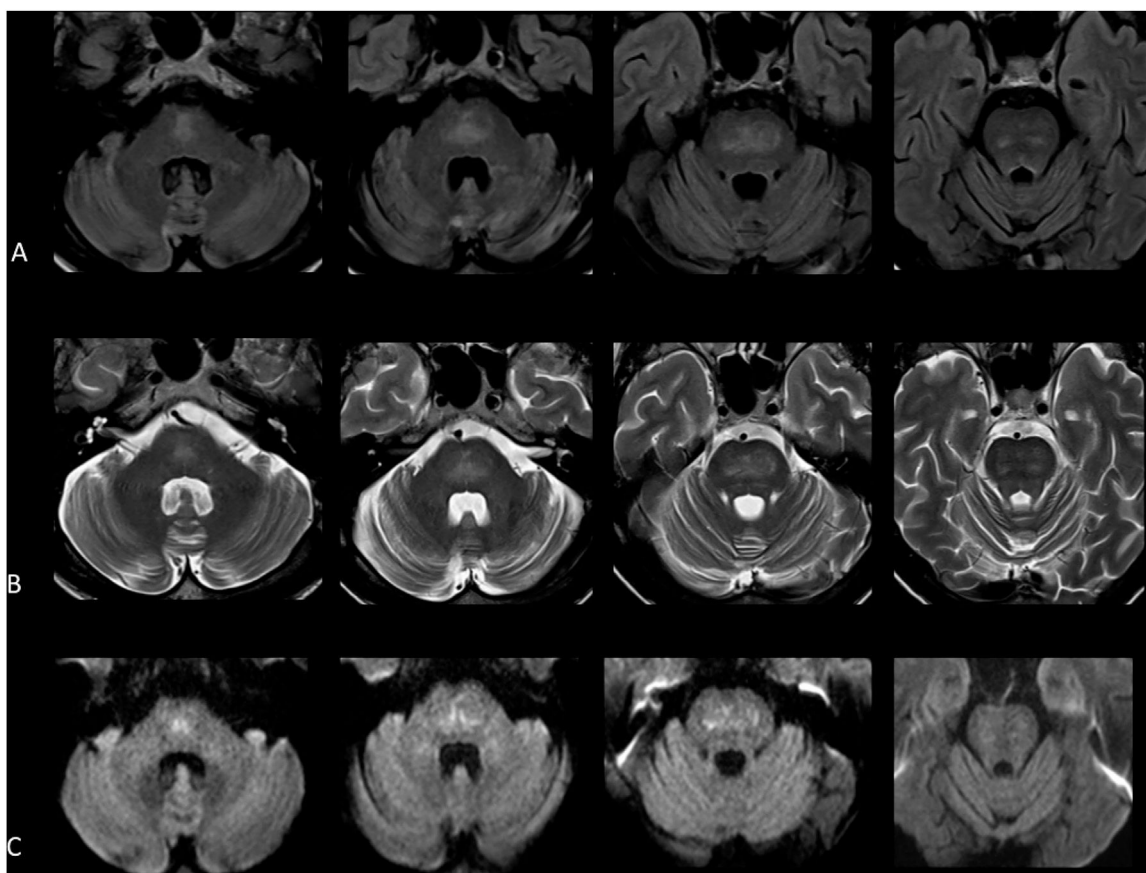


Fig. 1. Axial (A) T2 FLAIR and (B) T2 weighted images demonstrate abnormal high signal in the central pons with sparing of the periphery. (C) Axial B1000 diffusion weighted images demonstrate correlating mildly increased signal without evidence of restricted diffusion on the ADC map (not shown) consistent with T2 shine through.

His other past medical history was significant for mild asthma and dyslipidemia.

The initial immunosuppression regimens were IV methylprednisone taper starting at a dose of 500 mg IV on post-operative day (POD0), tacrolimus induction on POD0, and mycophenolate mofetil on POD0. Tacrolimus dosing was titrated to target a trough level between 5 and 10 $\mu\text{g/L}$. On POD2, he was noted to be mildly confused. This became more pronounced on POD3 when he was not oriented to self, time or place. He was unable to remember his own name, recognize his wife, recall his home address, or identify where he was. Other than memory loss, the patient had an inappropriate affect and general indifference to his condition. The neurology service was consulted to investigate the acute-onset confusion and amnesia. His cranial nerve, cerebellar, motor and sensory exams were grossly normal. Serum sodium was normal between 135 and 145 mmol/L in the post-op period. Septic work up was negative for any infectious etiologies. An initial CT of the head on POD3 was negative for intracranial abnormalities. Based on the clinical presentation and the unremarkable CT scan, a diagnosis of post-operative delirium was made. A follow-up MRI of the head on POD4, however, showed patchy high signal within the central pons on T2 FLAIR and B1000 images with two tiny associated microhaemorrhages, highly suspicious for central pontine myelinolysis. There was also possible mild high T2 FLAIR signal within the caudate and lentiform nuclei which could be related to extra pontine myelinolysis (Figs. 1 and 2). By this time, however, the patient had recovered fully i.e. cognitively normal and fully ambulatory. Post-op delirium was the most likely diagnosis. The patient was discharged home

shortly thereafter. In the following months up to now, he continues to function well.

Given the incidental MRI findings, whose relevance to the clinical presentation was questioned, a retrospective chart review of his outpatient records and his other hospital admissions were undertaken. The records revealed that he had been chronically and persistently hyponatremic in the three months prior to his liver transplant with serum sodium ranging between 113 and 123 mmol/L. However on one occasion, 6 weeks prior to his transplant, his hyponatremia was rapidly corrected, increasing his serum sodium from 119 mmol/L to 138 mmol/L within 24 h.

3. Discussion

Central pontine myelinolysis is also known as osmotic demyelination syndrome although many clinicians still refer to it as CPM and as of 2018, published papers still appear in the medical literature using the term CPM interchangeably with ODS. The other possible differential diagnoses of a demyelination syndrome of the central nervous system in a liver transplant patient are medication-induced demyelination such as from a calcineurin inhibitor, viral and autoimmune demyelination conditions. The patient did not have more invasive investigations such as a lumbar puncture and cerebral spinal fluid analysis to exclude them, mainly because we believe this short-lived presentation was consistent with post-op delirium, therefore an LP was not indicated when a patient rapidly returned to his normal functional baseline. Classic risk factors for CPM are rapid correction of chronic hyponatremia greater

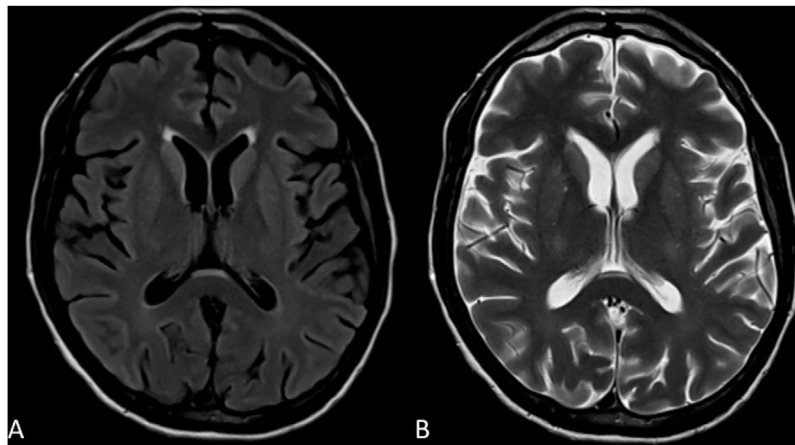


Fig. 2. Axial (A) T2 FLAIR and (B) T2 weighted images demonstrate mildly increased signal in the caudate and lentiform nuclei bilaterally.

than 8 mEq/L/day from a serum sodium concentration less than 120 mmol/L [7]. Rapid correction of hyponatremia is completely avoidable in hospitals, however about 40% of severely hyponatremic (<120 mmol/L) patients underwent rapid sodium correction in hospital as reported in a recently published study [7]. In this study, 9 patients with severe hyponatremia underwent brain MRI, 8 cases of CPM were found and all of these cases except one had undergone rapid correction of hyponatremia. About half the patients with CPM had presentations of encephalopathy while 12.1% had documented seizures, and 7.1% suffered from coma [7]. Less commonly, hemiparesis, ataxia, oculomotor symptoms occurred in less than 10%. In addition to hyponatremia, medical conditions such as cirrhosis, liver transplant, beer-potomania, malnutrition, chronic diuretic use, and alcoholism are well described in association with CPM. In a meta-analytic review [8], liver transplantation and cirrhosis were the second and third most common cause of CPM, comprising 13.7% and 12.5% of the overall diagnosis of CPM based on brain MRI finding. More than half of the patients suffering from symptomatic CPM recovered without residual neurological deficits, however 23.3% had some functional deficits and death was seen in 24.8%, a proportion that seemed particularly high in the liver transplant cohort [9]. It was suggested that over correction of hyponatremia can be effectively reversed by desmopressin with or without hypotonic fluids [9].

Our case is interesting as a short-lived post-op delirium resulted in imaging that revealed otherwise “occult” CPM. Clinically, we believe that the CPM was an incidental finding only and was clinically silent. The delirium was related to the operation and not from CPM. Although asymptomatic post-transplant CPM has been reported in Japan in the pediatric transplant population [10], to the best of our knowledge, this is the first time that clinically incidental CPM has been reported after liver transplantation in adults. The importance of this case lies in the fact that it is a dramatic demonstration that correction of significant hyponatremia associated with decompensated cirrhosis must be performed carefully due to the risk of CPM. We note that hyponatremia is not uncommon in advanced liver disease especially in patients decompensated enough to require liver transplantation as recognized by creation of the MELD-Na as a prognostic formula [11]. Our patient was fortunate as he did not suffer clinical symptoms of CPM. As this case shows, brain lesions caused by CPM may not always result in clinically significant neurological symptoms and MRI head is most sensitive in detecting these lesions despite the fact that they can be clinically latent or silent. We suspect that CPM may be more common than was once thought, especially in clinically asymptomatic

individuals. It is interesting to speculate that neurological symptoms in cirrhotic patients with significant hyponatremia that may be attributed to hepatic encephalopathy may in part be due to unrecognized CPM. Prevention of rapid correction of hyponatremia should be the standard of care and should be practiced in all aspects of medicine including the treatment of decompensated cirrhosis.

Abbreviations

CPM	central pontine myelinolysis
MRI	magnetic resonance imaging
PBC	primary biliary cholangitis
SBP	spontaneous bacterial peritonitis
POD	post-operative day
MELD	model for end stage liver disease

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Conflict of interest

No competing interests to disclose.

Informed consent

Informed patient consent was obtained for publication of the case details.

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