

Case report

Can osmotic demyelination syndrome be a complication of liver failure?

Kaylynn Purdy^a, Dustin Anderson^{a,b}, Richard Camicioli^a, Rachel G. Khadaroo^{b,c,*}^a Department of Medicine (Neurology), University of Alberta, Edmonton, Alberta T6G 2G3, Canada^b Department of Critical Care Medicine, University of Alberta, Edmonton, Alberta T6G 2B7, Canada^c Department of Surgery, University of Alberta, Edmonton, Alberta T6G 2B7, Canada

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ABSTRACT

This case demonstrates that osmotic demyelination syndrome (ODS) can occur in absence of hyponatremia in patients with fulminant liver failure and markedly high bilirubin levels. Extremely high bilirubin levels, such as > 900 µmol/L in the case presented here, may lead to blood brain barrier dysfunction by disrupting blood vessel endothelial cell function as well as increase the release of inflammatory cytokines. As demonstrated in the case here, even small fluctuations in electrolytes may make the brain increasingly more vulnerable to ODS. Clinicians should keep ODS high on their differential even in eunatremic patients with liver failure who have decreased levels of consciousness or coma.

1. Case summary

A 30-year-old male with primary sclerosing cholangitis was admitted to a tertiary hospital awaiting liver transplant. On post-admission day 65, he was found to be non-responsive. He was urgently stabilized and transferred to the intensive care unit.

On examination, he was jaundiced and cachectic. He had extensor posturing to central pain and brainstem reflexes were absent, save for an intermittent cough reflex. His total bilirubin was elevated at 955 µmol/L and had fluctuated between 591 and 994 µmol/L during his admission. Ammonia and electrolytes were normal at the time of the event; however, 11 days prior, sodium had increased by 12 mmol/L over 4 days from 140 to 152 mmol/L. Computed tomography (CT) demonstrated hypoattenuation of internal capsules, thalamus, midbrain, and the pons (Fig. 1A). Magnetic resonance imaging (MRI) demonstrated T2 hyperintensities (Fig. 1B) and T1 hypointensities (Fig. 1C) involving the pons and a number of extra-pontine structures. These abnormalities both diffusion restricted and gadolinium enhanced along their peripheral margins (not shown). Overall, imaging was felt to be most consistent with a diagnosis of osmotic demyelination syndrome (ODS).

ODS typically occurs following rapid correction of hyponatremia and patients classically present with locked-in syndrome [1]. Characteristic imaging findings include T2 hyperintensity and corresponding T1 hypointensity in the pons and extra-pontine structures [1]. Though rare, cases of hypernatremic ODS are well-described within the

literature [2,3].

In human cell culture models designed to mimic the blood brain barrier (BBB), it has been shown that elevated levels of unconjugated bilirubin disrupts endothelial cell homeostasis, as well as causes an increase in release of inflammatory cytokines such as IL-8 and VEGF [4]. This suggests that prolonged hyperbilirubinemia in our patient may have contributed to dysfunction in the patient's BBB as well as inducing a pro-inflammatory environment, making him more vulnerable to small osmotic shifts and, hence, ODS.

A course of high-dose methylprednisolone was initiated, in an attempt to improve the integrity of the BBB by blocking inflammatory mediators [5]. Despite a course of high-dose steroids (1 g IV/day for 5 days), there was no clinical improvement. Case reports have demonstrated that plasma exchange improves clinical outcomes in patients with ODS [6]; however, the family did not wish to pursue plasma exchange, and decided to withdraw all forms of medical care. The patient died 6 days after being admitted to the intensive care unit. The family declined to proceed to autopsy to confirm the diagnosis.

It is known that post-liver transplant patients are at increased risk of developing ODS when they become hyponatremic [7]. Cases in post-transplant ODS patients are often in settings complicated by post-transplant sepsis, organ rejection or hypotension, all of which can lead to elevated levels of bilirubin [8]. The increased rates of ODS in liver transplant patients, and in our patient, may be related to elevations in serum bilirubin, which may in turn create BBB dysfunction leading to greater vulnerability of the brain to mild shifts in serum osmolarity

* Corresponding author at: 2D3.77 Walter Mackenzie Centre, 8440-112th Street, Edmonton, AB T6G 2B7, Canada.

E-mail addresses: kaylynn@ualberta.ca (K. Purdy), dustin3@ualberta.ca (D. Anderson), rcamicio@ualberta.ca (R. Camicioli), khadaroo@ualberta.ca (R.G. Khadaroo).

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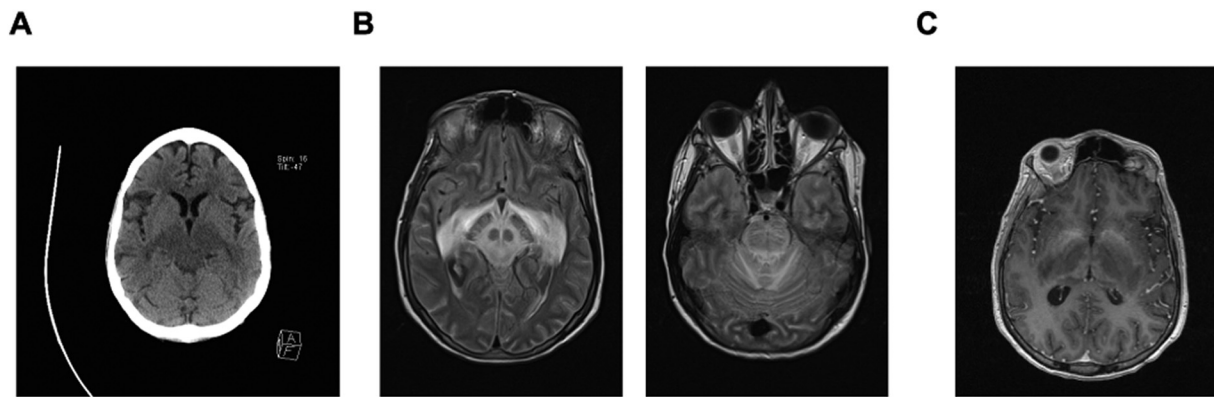


Fig. 1. Imaging findings in osmotic demyelination syndrome. Non-contrast CT (A) showing symmetrical hypoattenuation of the internal capsules, thalami, and midbrain. T2 fluid-attenuated inversion recovery MRI (B) demonstrating symmetrical high signal within the diencephalon, midbrain, and pons. T1 MRI (C) demonstrating extensive low signal throughout the diencephalon and midbrain.

such as the mild hypernatremia documented here. This case highlights that ODS should remain on the differential in patients with liver failure presenting with sudden neurologic deterioration, even in the absence of overt hyponatremia or correction of hyponatremia.

Author contributions

Kaylynn Purdy performed the patient's clinical assessment, drafted the manuscript and created the figure. Dustin Anderson and Richard Camicioli assisted in the patient's clinical assessment and drafted the manuscript and figure legend. Rachel G. Khadaroo provided patient care in the intensive care unit and performed a critical revision of the manuscript for intellectual content.

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Declaration of Competing Interest

Dr. Purdy reports no disclosures. Dr. Anderson reports no

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