Is Central Pontine Myelinolysis Reversible?

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ABSTRACT
Central pontine myelinolysis (CPM) is a rare phenomenon that causes significant morbidity and mortality. Active therapeutic interventions for CPM can have a positive impact on recovery and overall prognosis. This case represents a 34-year-old white man with a chronic history of alcohol abuse who had Parkinsonian symptoms 13 days after rapid correction of his serum sodium in the hospital. Similarly to prior CPM case reports, this patient significantly improved following reinduction of hyponatremia, methylprednisolone, and/or plasmapharesis. This report demonstrates that CPM is potentially reversible when quickly recognized and therapeutic interventions are initiated rapidly.

CASE PRESENTATION
A 34-year-old white man with chronic alcohol abuse came into clinic for follow-up of his hospitalization for alcohol intoxication, hyponatremia, hypokalemia, and hypophosphatemia. Upon admission he had altered mental status with slurred speech in the setting of drinking 15 beers per day for the last 3 weeks and an otherwise normal physical exam. His initial sodium and potassium were 109 and 1.5, respectively. During the first 6 hours of his hospitalization, the sodium corrected to 119 with normal saline. Throughout the hospitalization, his mental status improved. He was discharged at his baseline mental status 4 days later.

Beginning 3 days after his discharge from the hospital, the patient noted new onset numbness in his legs and an unstable gait. Over the next few days, he had worsening jaw tremors, slurred speech, and difficulty swallowing. On review of systems, he had blurred vision in his left eye but denied fever, chills, night sweats, weight loss, bowel or bladder dysfunction, headache, or recent gastrointestinal/upper respiratory illness. He denied alcohol or other drug use since his hospital admission. On physical exam the patient had vertical nystagmus; bradykinesia; a slow, wide-based, unsteady, shuffling gait; a resting, pill-rolling tremor; as well as diffuse coarse tremors in his jaw, mouth, tongue, and legs. Cranial nerves II-XII were intact with 2+ biceps, brachioradialis, Achilles, and patellar reflexes bilaterally. Rapid alternating movements, Romberg sign, and finger-to-nose testing were within normal limits. He had muscle rigidity with passive range of motion, 5/5 strength except for 4/5 strength in his right hip flexor, and normal sensation to light touch, temperature, and pinprick throughout. Further neurological testing was negative for pronator drift, clonus, and asterixis. A basic metabolic panel was within normal limits. Urine and serum drug screens were negative. Magnetic resonance imaging (MRI) of the brain demonstrated a well-defined central pons lesion with a low T1 signal intensity on the sagittal view and high T2 signal intensity on an axial view consistent with central pontine myelinolysis (CPM) (see Figure).

In an attempt to reverse osmotic demyelination syndrome (ODS), induction of hyponatremia was initiated first. The serum sodium was lowered carefully, maintained, and slowly increased over the course of 6 days using a combination of minocycline, hypotonic saline, furosemide, desmopressin, and albumin. Serum sodium was maintained between the following sodium goals as noted: 122-125 mEq/L on days 1 and 2, 125-128 mEq/L on day 3, 128-132 mEq/L on days 4 and 5, and 132-135 mEq/L on day 6. Methylprednisolone was initiated simultaneously with the induction of hyponatremia.

The following day he was transferred to the intensive care unit (ICU) and intubated given concerns of inability to manage his secretions and airway. The patient subsequently required an intermittent norepinephrine drip to maintain his blood pressure.

Plasmapheresis was initiated on hospital day 3; the patient
ataxia, nystagmus, tremor, lethargy, confusion, behavioral disturbances, and/or disorientation. Alternatively, symptoms and radiologic findings may be delayed as long as 16 days. 

A negative MRI cannot rule out ODS and should be repeated in 15 days with diffusion weight imaging, T2-weighted images, and fluid-attenuated inversion recovery (FLAIR) images without contrast if clinical suspicion for ODS remains high. 

Treatment cited in the literature is varied and frequently multifaceted. Reintroduction of hyponatremia following a rapid correction of hyponatremia in murine models reduces neurological manifestations, prevents further myelinolysis, and improves survival by up to 94%. 

Benefit in humans has been demonstrated in 2 case reports but not in a third. However, those reports did not discuss how to best induce hyponatremia. The reintroduction of hyponatremia in this patient was based upon clinical experience only and not on any predefined protocol. We pursued this first as it had the most literature to support its utility and the lowest risk for adverse effects and excessive health care costs. Methylprednisolone was added due its ability to potentially reduce inflammation, which in the setting of no current infections posed a low overall risk, especially when given for only a few days.

Given minimal clinical improvement and data from multiple studies showing an improvement in neurological symptoms in patients with CPM with the use of IV Ig, we initiated this treat-
ament next. IVIg may work by binding to myelinotoxic substances, thereby stopping any further breakdown of myelin. Another possible effect is the immunoglobulins may act as a glue to help bring the myelin together to assist with the repair process, though this is very much speculative. Given small improvements in neurological status with IVIg, we started plasmapheresis as another method to remove possible myelinotoxic substances.

As demonstrated in this case, as well as numerous other cases in the literature, improvement is usually seen early in treatment but may be delayed for up to 4 years. ODS, previously thought to have a dismal prognosis, may yield a meaningful recovery if quickly recognized and appropriately treated.

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**REFERENCES**
