

Is Central Pontine Myelinolysis Reversible?

David Lee Rebedew, MD

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 plasmapheresis. 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

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Author Affiliations: Medical College of Wisconsin Affiliated Hospitals, Waukesha Family Practice Residency Program, University of Wisconsin School of Medicine and Public Health, Monroe Clinic.

Corresponding Author: David Lee Rebedew, MD, W6153 Tucker Rd, Monticello, WI 53570; phone 920.960.9953; fax 262.548.6903; e-mail david.lee.rebedew@gmail.com.

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 asterix. 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

received 3 sessions in total. On hospital day 4, plasmapheresis was followed by intravenous immunoglobulin (IVIg). The next day he was extubated, then transferred out of the ICU 3 days later. Over the next 3 days, the patient's orientation improved from alert & oriented times 1 (A&Ox1) to A&Ox3, speech progressed from 25% to 100% intelligible, and clonus decreased from more than 50 beats to 8 beats bilaterally. Subsequently, he was transferred out of the ICU and discharged home 3 days later, performing all of his activities of daily living. One month later at an outpatient follow-up, the patient had no appreciable neurological deficits.

DISCUSSION

Central pontine myelinolysis, a subset of ODS, was first described in 1959 (coinciding with the introduction of plastic tubing and widespread use of IV fluid therapy) by Adams and Victor. ODS has been cited to account for 0.06% of all admissions to the medical service of a general hospital.¹ A large autopsy series found a prevalence of 0.25% to 0.5% in the general population.² ODS occurs most commonly in men between the ages of 30 and 60 years old, as was the case with this patient.

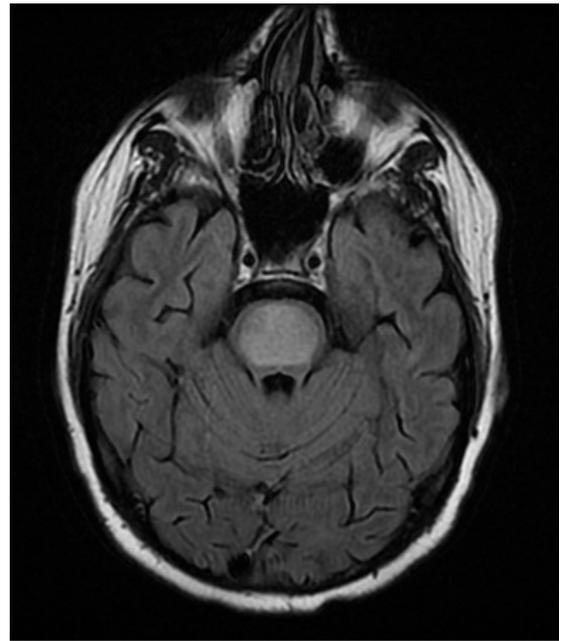
Demyelination typically occurs in areas of the brain that are slowest to uptake osmolytes, which most commonly include the central pons (30%-50%), extrapontine sites (20%-50%), or both the central pons and an extrapontine area (30%-50%).¹⁻³ The most common extrapontine sites in order of decreasing frequency include the cerebellum, lateral geniculate body, hippocampus, cerebral cortex, thalamus, caudate nucleus, internal capsule, mid-brain, and mammillary body.^{1,2,4}

The exact amount of osmotic stress necessary to induce ODS is currently unknown. Rates of sodium correction greater than 10 mEq/L per 24 hours or 18 mEq/L per 48 hours are cited as thresholds—though slower rates of sodium correction in patients at increased risk of ODS also have been associated with its development.^{2,5} Risk factors for ODS include patients with chronic alcoholism, history of liver transplant, rapid correction of hyponatremia, and malnutrition.^{2,6}

Prior to 1994, mortality for ODS at 3 months was described as high as 90% to 100%.^{1,2,7} More recent studies cite that approximately 28% to 40% of patients with ODS recover without any neurologic abnormalities, 25% to 33% remain severely incapacitated, and 6% to 9% die.^{1,2,8,9} Neither clinical nor radiological features are predictive of which category a given patient will fall into.^{1,4} Poor prognostic factors for ODS include low GCS when hospitalized, severe hyponatremia ≤ 115 , hypokalemia, or any pontine involvement.^{8,10} In this case, the patient had 3 poor prognostic indicators.

Approximately 2 to 6 days following a rapid rise in serum sodium levels, patients with ODS present with Parkinsonism (44%-50%), quadriplegia, "Locked-in" syndrome, coma, bulbar palsy, or less frequently with dysphagia, dysarthria, facial paresis,

Figure. T2 FLAIR Image Depicting an Abnormal, Hyperintense Central Pontine Signal With No Associated Restricted Diffusion.



Abbreviation: FLAIR, fluid-attenuated inversion recovery.

ataxia, nystagmus, tremor, lethargy, confusion, behavioral disturbances, and/or disorientation.^{1,2,5} Alternatively, symptoms and radiologic findings may be delayed as long as 16 days.¹ 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.¹

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%.^{11,12,13}

Benefit in humans has been demonstrated in 2 case reports but not in a third.^{8,10,14} 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 IVIg, we initiated this treat-

ment 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.¹⁵ ODS, previously thought to have a dismal prognosis, may yield a meaningful recovery if quickly recognized and appropriately treated.

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