CASE REPORT

Central Pontine Myelinolysis without Rapid Changes in Sodium Level: Possible Association with Malnutrition, Hypophosphatemia and Hypokalemia

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Abstract

Central pontine myelinolysis (CPM) is a rare demyelinating condition most commonly associated with a rapid rise in plasma osmolality, especially during the correction of chronic hyponatremia. The clinical consequences can vary from mild motor weakness to devastating locked-in syndrome (LIS). The condition has also been described in association with other conditions like alcoholism, an acquired immunodeficiency syndrome (AIDS), hepatic failure[1] hypernatremia, hypophosphatemia,[2,3] liver transplantation, and carbamate poisoning.[4] We report a case of a 76-year-old female with carcinoma rectum with acute gastroenteritis, sepsis, and acute kidney injury who developed CPM, not related to rapid correction of hyponatremia, during recovery from the acute illness.

Highlights: Central pontine myelinolysis (CPM), which is part of the osmotic demyelination syndrome (ODS), usually results from the rapid increase in plasma osmolality during the correction of chronic hyponatremia. The clinical consequences vary from mild motor weakness to devastating LIS. ODS has also been described in association with alcoholism, malnutrition, diabetes mellitus (DM), liver transplantation, and electrolyte abnormalities like hypernatremia, hypophosphatemia, and hypokalemia.

A 76-year-old female with rectal adenocarcinoma was admitted with anorexia, prolonged diarrhea due to *Clostridium difficile* infection, malnutrition, and sepsis. She had hypophosphatemia, hypocalcemia, and hypoalbuminemia on admission and persistent hypokalemia due to profuse diarrhea. She developed CPM with no evidence of rapid correction of sodium. We postulate that CPM may have been a consequence of malnutrition, hypophosphatemia, and hypokalemia.

Keywords: Central pontine myelinolysis, Hyponatremia, Hypophosphatemia, Malnutrition.

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Case Description

A 76-year-old female was admitted to other hospital for 2 months with a diagnosis of carcinoma rectum and had received chemo- and radiotherapy preceding a plan for surgery. She developed pancytopenia, fever, and chronic diarrhea, which lasted for 3 weeks. She became progressively drowsy and was diagnosed with sepsis with hypoxia and hypotension, and required vasopressors, endotracheal intubation, and mechanical ventilation. She was subsequently shifted to our hospital.

On admission, she had anemia (hemoglobin 7 gm/dL), thrombocytopenia (platelets 66000/mm^3) with leukocytosis (17.89 cells/mm^3). She also had hypoalbuminemia (serum albumin 2.9 gm/dL) with deranged liver function tests (total bilirubin 7.21 mg/dL, serum glutamic-oxaloacetic transaminase 76 U/L, serum glutamic-pyruvic transaminase 45 U/L, ammonia 100 µmol/L, and alkaline phosphatase 236 U/L). A two-dimensional echocardiogram revealed left ventricular (LV) systolic dysfunction with an LV ejection fraction of 25%. Chest X-ray showed bilateral infiltrates which was considered to be due to pulmonary edema in view of poor LV systolic function, which was treated with diuretics. The patient was conscious and obeying commands but had proximal muscle weakness. Biochemistry revealed hypocalcemia [ionized calcium (Ca) 0.95 mmol/L, serum Ca 5.9 mg/dL], hypophosphatemia (serum inorganic phosphorus 1 mg/dL), hypokalemia [serum potassium (K) 2.67 mEq/L], hypomagnesemia [serum magnesium (Mg) 1.7 mg/dL], and hypoalbuminemia, suggestive of severe malnutrition. Enteral feeds were gradually reintroduced to prevent refeeding syndrome. The stool sample was positive for *C. difficile* toxin, so enteral vancomycin was started. She received octreotide to reduce intestinal secretions. Intravenous (IV) correction of Ca, phosphate, and Mg were done during the first week of intensive care unit admission. Serum sodium (SNa) was 137 mEq/L on admission. It was difficult to wean her from the ventilator. Electromyography/nerve conduction studies showed primarily demyelinating sensorimotor polyneuropathy with axonal loss affecting both upper and lower limbs. The patient was treated with IV immunoglobulin (IVIg) in view of nerve conduction velocity features of demyelinating polyneuropathy. On day

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18 of the hospital stay, the patient became unresponsive and stopped obeying commands. Electroencephalography showed no seizure activity. Magnetic resonance imaging (MRI) brain showed typical signal abnormality (trident sign) in central pons showing restricted diffusion highly suggestive of CPM or ODS (Fig. 1). Careful reexamination showed that she could perform voluntary eye movements on command.

A review of her charts from our hospital and also the hospital where she was admitted earlier showed no marked fluctuation in SNa. SNa on admission was 137 mEq/L. During the hospital course, lowest SNa level was 125 mEq/L and highest was 154 mEq/L, and the maximum change in SNa was 7 mEq/L in any 24-hour period. However, she had recurrent episodes of hypokalemia which was likely due to *C. difficile* infection leading to profuse diarrhea, requiring IV K replacement.

Discussion

Central pontine myelinolysis (CPM) is an acute noninflammatory, demyelinating disorder first described by Adams et al. in 1958.[5] It predominantly affects the pons but may involve extrapontine structures, including the midbrain, thalamus, and cerebellum. MRI is the imaging modality of choice,[6] and the trident sign in the pons (Fig. 1) is a classical feature. The presentation can be catastrophic with pseudobulbar palsy, spastic quadriparesis, and the "LI" syndrome resulting in a fully conscious patient with intact sensory inputs and only voluntary eye movements.[7] CPM is commonly precipitated by rapid correction of chronic severe hyponatremia (defined as SNa <120 mEq/L). The American Expert Panel Recommendations recommend an SNa correction limit of 10–12 mEq/L in any 24-hour and 18 mEq/L in any 48-hour period for patients at average risk of ODS and 8 mEq/L in any 24-hour period for patients at high risk of ODS,[8] whereas the European Clinical Practice Guidelines recommend a daily limit of SNa correction of 10 mEq/L in the first 24 hours and 8 mEq/L during every 24 hours thereafter.[9] ODS can sometimes occur despite adherence to these hyponatremia correction guidelines, especially in patients with SNa <115 mEq/L.[10] Our patient never had SNa <125 mEq/L, and it did not fluctuate by >7mEq/L in any 24 hours period, making this an unlikely cause for the CPM.

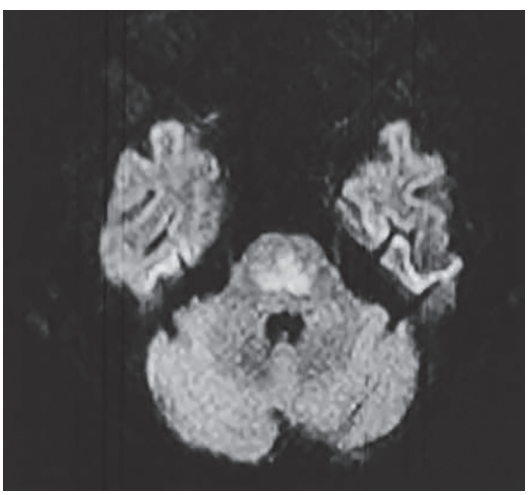

Fig. 1: Magnetic resonance imaging (MRI) of the brain showing the typical "trident sign" of CPM. Note the characteristic "W"-shaped area of hyperintensity due to restricted diffusion in the central pons on the diffusion weighted image corresponding to the localized acute demyelinating changes

Other causes of ODS reported include alcoholism, malnutrition, liver transplantation,[10] hyperosmolar coma in DM, AIDS, hepatic failure,[1] hypernatremia, hypophosphatemia,[2,3] and carbamate poisoning.[4] Our patient had hypokalemia, hypophosphatemia, hypomagnesemia, hypocalcemia, and hypoalbuminemia on admission, suggestive of significant malnutrition. In the absence of severe hyponatremia or its rapid correction, ODS in our case appears to be multifactorial and related to hypokalemia, hypophosphatemia,[2,3] and malnutrition.[10] Rapid correction of severe hyponatremia is frequently implicated as a causative factor, but CPM has been reported in the presence of normonatremia,[1] hypokalemia,[2] and hypophosphatemia.[3] In these cases, a hypothesis based on osmotic trauma must be questioned. Recently an apoptotic hypothesis has been proposed.[4] It is suggested that a depletion of the energy supply to glial cells might limit the function of their Na^+/K^+ adenosine triphosphatase pumps. This could reduce their ability to adapt to relatively minor osmotic stress caused by small changes in SNa concentration and ultimately lead to apoptosis.[3]

Case reports and small observational studies have reported a beneficial response in the form of improved neurological symptoms with corticosteroids, plasmapheresis, and IVIg, but there are no randomized trials to confirm their efficacy.[11] Interestingly, our patient had received IVIg for demyelinating neuropathy a week prior to the development of CPM.

In conclusion, although rapid correction of hyponatremia is the commonest cause of ODS and CPM, other metabolic causes should be kept in mind as causative or contributory factors to this uncommon disorder.

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