

Case Report

Extra Pontine Myelinolysis associated with Hypophosphatemia

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Abstract

We report a unique association of extra-pontine myelinolysis with severe hypophosphatemia developing in a young lady with a prolonged febrile illness and inadequate oral intake. The late identification of severe hypophosphatemia resulted in extra-pontine myelinolysis. Gradual improvement in clinical status was noticed with phosphate replacement and good supportive care.

Introduction

Focal symmetric demyelination in the CNS may be precipitated by aggressive correction of a hyper or hypoosmolar state - osmotic myelinolysis.¹ Since the first descriptions of central pontine myelinolysis (CPM) were put forth in 1959 in alcoholic patients, it has become evident that myelinolysis is not exclusively restricted to the pons. In many cases myelinolysis may share other brain regions, while in still others the pons may not be affected at all - extra-pontine myelinolysis (EPM).² Hence, specific anatomical locations are more susceptible to demyelination than others.

Severe hypophosphatemia ($<1\text{mg/dL}$ or 0.3mmol/L) is a medical emergency and has been correlated with increased mortality³ due to seizures, severe haemolysis, rhabdomyolysis and cardiac failure hence, it is therefore prudent to check and treat dangerously low serum phos-

phate concentrations in susceptible patient groups: alcohol abusers, malnourished patients, critically ill patients; since it places them at an increased risk of developing complications.⁴

We have reviewed the published cases of extra pontine myelinolysis and believe this to be the first report of EPM occurring in the setting of severe hypophosphatemia.

Case Report

A 35 years old previously healthy woman presented with 2 weeks history of high grade fever, malaise and a painful swelling at the introitus. An incision and drainage procedure was performed for an infected Bartholin's cyst. Post-operatively, she was febrile and had vomiting. She was receiving intravenous 5% dextrose with 0.9% saline, amoxicillin-clavulanate and metronidazole. She was referred to the Medical Service on account of hypotension secondary to septic shock. On examination, she was in hypotensive shock, febrile and drowsy but arousable, moving all four limbs equally; there were no signs of meningeal irritation. She had an infected surgical wound. Blood gases revealed metabolic acidosis: pH 7.26, paO_2 86 mmHg, paCO_2 25mmHg, HCO_3 15 and O_2 sat. 93%. Labs revealed WBC $28.9 \times 10^9/\text{L}$, platelet count $96 \times 10^9/\text{L}$, P.T. was 21.3 sec. (control 13.4 sec.) and P.T.T. was 37.4 sec. (control 28.0 sec.), D-dimers 4.0 ug FEU/ml (0.2-4.0 ug

Figure 1. Normal plain MRI scan of the brain (axial section), T1 weighted image.

FEU/ml), serum sodium was 135 mmol/L, serum potassium 3.3 mmol/L, serum lactate 26.5 mmol/L; renal and liver function tests were normal. A diagnosis of septic shock with D.I.C. was made and she was treated with aggressive fluid resuscitation with I.V. 0.9% saline alongwith I.V. cef-tazidime and metronidazole.

Figure 2. Normal plain MRI scan of the brain (axial section), T2 weighted image.

After 4 days, she became alert with improvement in hemodynamic parameters. Serum sodium was 139 mEq/L. Wound and blood cultures grew enterococcus sensitive to ceftazidime. Subsequent biochemical profile revealed serum sodium 142 mmol/L, serum potassium 3.6 mmol/L, corrected serum calcium 2.1 mmol/L, serum phosphorus was profoundly low at 0.11 mmol/L (0.8-1.45 mmol/L), serum magnesium 0.92 mmol/L and CPK 1485 U/L. Phosphorus was replaced via the intravenous route at 0.16 mmol/kg (8.0 mmol) every 6 hours till the serum phosphorus level reached 0.8 mmol/L and then switched to oral therapy (serum phosphorus levels were measured every 6 hours during treatment).

Two days later, the patient complained of dysphagia followed over 48 hours by increasing body rigidity and

Figure 3. Plain MRI scan of the brain (axial section) revealing hypointense signals on T1 weighted image in the head and body of the caudate and putamen bilaterally consistent with extrapontine myelinolysis.

Figure 4. Plain MRI scan of the brain (axial section) revealing hyperintense signals on T2 weighted image in the head and body of the caudate and putamen bilaterally consistent with extrapontine myelinolysis.

altered mental status. Plain MRI scan of the brain was done which was normal (Figures 1 and 2). EEG revealed diffuse slowing. Meticulous nursing care was instituted. After 9 days, improvement in mental status was noticed, but she had become cognitively impaired (e.g. she was unable to recognize her son) and was mute. A repeat MRI scan of the brain was done which revealed abnormal signals in the head and body of the caudate and putamen bilaterally -findings consistent with extra-pontine myelinolysis (Figures 3 and 4).

Despite adequate correction, the late identification of severe hypophosphatemia coincided with the onset of the patients neurological deterioration. With supportive care, the patient made a gradual recovery. She was discharged two months after admission with only a mild residual spastic dysarthria which was improving.

Discussion

Central pontine myelinolysis (CPM) and extra-pontine myelinolysis (EPM) is a distinct clinical syndrome and is characteristically found in malnourished alcoholics

with chronic hyponatremia which is corrected too rapidly. It may be seen in any patient with hyponatremia corrected rapidly.⁵ Episodes not associated with hyponatremia have also been reported as isolated case reports⁶⁻⁸ as well as those occurring in spite of a careful correction of hyponatremia.⁹

The pathophysiology of myelinolysis is not well understood. Conventionally, osmotic stress leads to pontine glial cell swelling through osmosis and eventually to cell death (in CPM). For EPM. It is postulated that in regions of compact interdigitation of white and gray matter, cellular edema, which is caused by fluctuating osmotic forces, results in compression of fiber tracts and induces demyelination. The pitfall of this hypothesis is based on osmotic trauma as it does not account for why certain individuals develop myelinolysis with relatively mild osmotic insults. Recently, an apoptotic hypothesis has been proposed suggesting that a depletion of the energy supply to glial cells might limit the function of their Na⁺/K⁺ ATPase pumps reducing their ability to adapt to relatively minor osmotic stress caused by small changes in serum sodium concentration, and ultimately lead to apoptosis. Hence, individuals predisposed to myelinolysis have inadequate energy provision as well as other factors that result in a proapoptotic drive, which renders them susceptible to brain injury from diverse causes.^{4,10}

Clinical presentation may vary from an asymptomatic condition to a fulminant state. There may be behavioural abnormalities, spastic dysarthria, spastic quadriparesis, pseudobulbar palsy, movement disorders, parkinsonism, seizures or coma.⁵ Neuropsychological deficits do not necessarily diminish spontaneously with the radiological or clinical neurological findings, but may persist for a longer period of time or even become permanent.¹¹ Improvement generally begins 2 weeks after correction and continues up to a year in some patients. Symmetric foci in basal ganglia, thalami, cerebral peduncles and cortico-medullary junctions of cerebrum and cerebellum have been documented.¹²

Spinal fluid analysis is usually normal and may reveal a high myelin basic protein. EEG commonly shows non focal slowing. Brainstem auditory evoked potentials show prolonged 3 through 5 latencies.⁵ MRI is the investigation of choice. MR appearances of lesions on T1 and T2 weighted, and diffusion weighted imaging (DWI) sequences with apparent diffusion co-efficient (ADC) mapping make

MRI superior to CT in depicting lesions in osmotic elinolysis.¹³ Thyreotropin releasing hormone, plasmapheresis and corticosteroids have yielded variable therapeutic results. Immunoglobulins appear to be a promising therapeutic option in CPM¹⁴ and methylphenidate may be useful in the treatment of neuropsychiatric symptoms of CPM and EPM.

EPM is a neurological disorder with a variety of manifestations which may be fatal or result in permanent disabilities. The symptoms of EPM are often masked in critically ill patients. We emphasize the importance of watching for this entity during the management of critically ill patients and recommend early monitoring of serum phosphorus levels in susceptible patient groups and the use of MRI scans to confirm the clinical diagnosis of osmotic myelinolysis. Optimal outcome depends on collaboration by all members of the health care team. The disease has not been described in association with hypophosphatemia before, as in this patient.

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