CASE REPORT

Central pontine myelinolysis: electrolytes and beyond

J V Mascarenhas, E B Jude

Department of Diabetes and Endocrinology, Tameside NHS Foundation Trust, Manchester, UK

Correspondence to

Dr E B Jude,
edward.jude@tgh.nhs.uk

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SUMMARY

Central pontine myelinolysis (CPM), which is a component of the osmotic demyelination syndrome (ODS), is a frequent neurological complication that follows rapid correction of hyponatraemia. However, there are other predisposing risk factors (chronic alcoholism, hypokalaemia) that perpetuate the development of ODS. We report a case of a 39-year-old woman with a history of chronic alcoholism who presented to us with progressive neurological deficits (paraparesis, paresthesias). She was initially detected to have coexisting hypokalaemia which was eventually rectified with potassium supplementation. However, she continued to experience progressive worsening of her neurological symptoms despite adequate potassium supplementation. Therefore, a neurological opinion was sought for and she was diagnosed with CPM based on a background of chronic alcoholism and malnutrition; an MRI of the brain showed a hyperintense signal in the central pontine region. Following the diagnosis of CPM, she was rehabilitated with occupational and physiotherapy.

BACKGROUND

Electrolyte abnormalities are frequently encountered during hospitalisations which are usually followed by aggressive normalisation of the involved electrolyte. The osmotic demyelination syndromes (ODS) comprising central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM) are common neurological complications associated with abrupt osmotic fluctuations. ODS is a non-inflammatory demyelinating disorder affecting the pons and other regions of the central nervous system. Although most of the cases, earlier, were mainly attributed to rapid corrections of hyponatraemia, certain predisposing factors such as chronic alcoholism, malnutrition and even hypokalaemia have emerged as potential instigators of ODS. CPM accounts for majority of the cases as evidenced in nascent studies.^{1–3} However, recently, the incidence of EPM (alone or in combination with CPM) has increased, probably due to better quality MRI.⁴ The first case of CPM was reported by Adams *et al*⁵ in 1959 in an alcoholic patient. We report a case of alcohol-induced CPM in a woman who initially presented with peripheral neuropathy.

CASE PRESENTATION

A 39-year-old woman with a history of chronic alcoholism, chronic obstructive pulmonary disease and depression presented to our emergency

department with vomiting, diarrhoea and paresthesias of all four limbs since 1 week. Since routine workup prior to her admission revealed hypokalaemia (K^+ —1.9 mEq/L), she was later admitted for evaluation of her presenting symptoms and hypokalaemia. Vital parameters and systematic examination were normal except for a bilateral nystagmus on lateral gaze. ECG showed T wave inversion in V4 and V5. She was started on oral and parenteral potassium (K^+) supplements following which the serum K improved to 3.7 after 1 day of therapy, and she was therefore discharged.

After 5 days, she presented to the emergency department due to recurrence of similar symptoms along with perioral paresthesia. Systemic examination was remarkable for abnormal neurological findings which included reduced sensory perception of bilateral hands and feet, paraparesis, hypertonic lower limbs and a wide-based unsteady gait. There was no evidence of cranial nerve dysfunction. Biochemical evaluation detected low folic acid (FA) and magnesium (FA—1.9 μ g/L, Mg—0.49 mmol/L), but normal vitamin B₁₂ levels. Her neurological presentation was suggestive of peripheral neuropathy secondary to ethanol intoxication that warranted further investigations (brain MRI and nerve conduction studies) on an outpatient basis. The nutritional deficits were rectified with oral and parenteral vitamin supplementation, including thiamine and FA; she was discharged after 1 week, although her neurological deficits still persisted.

After a month, she presented to the emergency department with worsening of neurological deficits and sudden deterioration in mobility which is when she came under our care. Biochemical evaluation at admission revealed hypokalaemia (K^+ —2.8 mEq/L), which was treated with parenteral K^+ supplementation. ECG was within normal limits. Neurological examination was significant for absent sensory perception of hands and feet bilaterally, quadriparesis, areflexia, upgoing plantars and impaired coordination of both lower limbs. A neurological opinion was sought for and a diagnosis of CPM was made based on the background of alcohol-induced nutritional deficits and progressive limb weakness and peripheral neuropathy.

The diagnosis was confirmed by MRI (brain) that showed hyperintense signalling in the central pontine region on T2-weighted images, which were suggestive of CPM (figure 1). MRI of the spine was normal. Nerve conduction studies also showed evidence of large fibre sensory neuropathy and sensory ganglionopathy.

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Figure 1 MRI of the brain of our patient showing a hyperintense signal detected in the central pons (encircled) on a coronal flair T2-weighted image.

OUTCOME AND FOLLOW-UP

Our patient reported that her alcohol consumption increased over the past 9 months from the onset of symptoms. Moreover, she regularly took citalopram which was prescribed for her depression. Alcohol induces hyponatraemia and other nutritional deficits. Citalopram, a selective serotonin reuptake inhibitor (SSRI), has been often associated with syndrome of inappropriate antidiuretic hormone secretion. As suggested, chronic alcoholism and SSRI intake could have resulted in hyponatraemia which may have been overlooked. Her recent history of diarrhoea and vomiting may have further compounded the electrolyte deficits which led to rapid fluctuations in plasma osmolality. Following the diagnosis of CPM, she was rehabilitated with occupational and physiotherapy.

DISCUSSION

The ODSs, namely CPM and EPM, are osmotic-driven neurological sequelae that are mostly attributed to overly and rapid correction of hyponatraemia. Approximately 10% of cases with CPM have coexisting EPM.⁶ However, several case studies have repeatedly demonstrated other independent predisposing factors such as chronic alcoholism, malnutrition and chronic liver disease.^{7–8} Over the recent years, other electrolyte abnormalities such as hypokalaemia have also been linked to the development of CPM.^{9–10}

Although rapid osmotic flux commonly inflicts the pontine region, certain extrapontine areas are also affected, namely the thalami, basal ganglia, subcortex, cerebellum, lateral geniculate bodies and the cerebral cortex.

Mechanism of ODS

Physiologically, a fall in serum osmolality is accompanied by entry of water into the cells resulting in cellular oedema. Theoretically, this would result in brain oedema. However, as an initial protective and adaptive mechanism, the interstitial fluid (which is rich in organic and inorganic osmolytes or osmoles) is drawn into the cerebrospinal fluid, thereby sparing the neurons from the osmotic insult. The subsequent depletion in cellular osmolytes is normally replenished by synthesis of newer osmoles.^{11–12}

During rapid correction of hyponatraemia, the sudden rise in serum osmolality may supersede the time required for the

regeneration of cellular osmoles, therefore causing shrinkage of neurons, particularly oligodendrocytes. These osmotic-induced fluid shifts facilitate separation of the axon from the overlying myelin sheaths, resulting in demyelination. In addition, continued neuronal shrinkage from hypertonic stress can lead to apoptosis of oligodendrocytes.

Osmotic fluctuations damage the underlying endothelium of the blood–brain barrier (BBB). A breach in the BBB exposes the susceptible brain regions to myelinotoxic agents such as circulating complements which induce myelinolysis of myelin-rich neurons (oligodendrocytes) and vasogenic oedema.¹³ Vasogenic oedema leads to fibre tract compression in areas composed of white and grey matter.

CPM and EPM have a propensity to affect areas with an admixture of grey and white. The basis pontis is the most common site involved in CPM. In EPM, lesions are predominantly detected in the basal ganglia, thalami, subcortex, cerebellum, lateral geniculate bodies and the cerebral cortex.

Role of risk factors

Chronic alcoholism is frequently associated with malnutrition which is characterised by a deficiency/depletion of essential nutrients. Chronic alcoholism and other malnourished states would, therefore, perpetuate the development of CPM due to delayed regeneration of organic osmoles.¹⁴

Alcohol may exert its toxic effects directly on the pons or indirectly through undocumented hyponatraemia from binge drinking. In such instances, hyponatraemia may occur subsequent to several mechanisms mediated by alcohol toxicity¹⁵:

- Gastrointestinal fluid losses leading to true volume depletion and subsequent hyponatraemia.
- Alcohol-associated hypertriglyceridaemia which induces a state of pseudohyponatraemia due to an increase in the non-aqueous phase of plasma.
- Beer potomania, a phenomenon mostly observed in alcoholic binge drinkers.
- Reset osmostat syndrome—this results from abnormal osmoreceptor activity due to defective cellular metabolism.

Hypokalaemia: In the presence of hyponatraemia, coexisting hypokalaemia increases the risk for the development of CPM. In a case series led by Lohr,⁹ a combination of hypokalaemia and hyponatraemia was reported in 89% of patients with CPM.

Clinical manifestations

Patients with ODS present with an array of symptoms ranging from neuropsychiatric disturbances to flaccid paresis.¹⁶

Cognitive or behavioural disturbances: acute confusion.

Pons: Dysarthria, dysphagia (corticobulbar tracts); quadriplegia, spasticity (corticospinal tracts); locked-in syndrome.

Movement disorders: These are mainly seen with extrapontine involvement and are characterised by mutism, parkinsonism, dystonia and catatonia.

Favourable prognostic factors⁴

- ▶ Absence of coexisting hypokalaemia
- ▶ Less severe hyponatraemia
- ▶ Higher Glasgow Coma Scale at admission and at discharge.

Diagnosis

MRI is the preferred radiological modality compared with CT due to its higher sensitivity for earlier detection of CPM lesions and its superiority in the detection of EPM lesions. The classical radiological finding in CPM is a hyperintense central pons made evident on a T2-weighted image. If CPM is highly suspected but

there is no evidence on imaging, then it is recommended to repeat the MRI after 2 weeks (following the onset of symptoms or correction of hyponatraemia) as inconspicuous lesions may be revealed during this period.¹⁶

Learning points

- We recommend that clinicians have a high index of suspicion for osmotic demyelination syndrome (ODS), especially in patients presenting with cognitive disturbances or neurological sequelae against a background of chronic alcoholism and malnourishment.
- Electrolyte abnormalities other than sodium should be investigated and rectified.
- An in-depth neurological examination is mandated to assess the severity and progression of ODS.
- MRI is the radiological modality of choice for earlier detection of ODS lesions; however, in highly suspicious cases without radiological evidence of central pontine myelinolysis/extrapontine myelinolysis lesions, it is worth repeating the MRI after 2 weeks.

Contributors EBJ was involved in the management of the case in review and chose to prepare this case report in order to enlighten practising clinicians about the nature and progression of central pontine myelinolysis. JVM analysed the case records of the patient and drafted the case report which was reviewed by EBJ.

Competing interests None.

Patient consent Obtained.

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