CASE REPORT

Central pontine myelinolysis with meticulous correction of hyponatraemia in chronic alcoholics

Konark Malhotra,¹ Luis Ortega²

¹Department of Neurology, Drexel University College of Medicine, Allegheny General Hospital, Pittsburgh, Pennsylvania, USA

²Division of Nephrology and Hypertension, Temple School of Medicine, Allegheny General Hospital, Pittsburgh, Pennsylvania, USA

Correspondence to

Dr Konark Malhotra,
konark.malhotra@yahoo.com

SUMMARY

Central pontine myelinolysis is a demyelinating disorder that arises due to osmolar disturbances in the cerebral microenvironment characterised by loss of the myelin sheath of neurons. The diffusion-weighting imaging sequence of MRI is the most sensitive diagnostic imaging modality for myelinolysis. The rapid correction of hyponatraemia by >20–25 mmol/L/48 h has been known for a long time as a prime cause of osmotic demyelination. Various other comorbidities in hyponatraemic patients are well known that can lead to osmotic demyelination such as alcoholism, hypoxaemia, severe liver disease, malignancy, burns, liver transplantation and malnutrition. Chronic alcohol abusers with additional liver disease and malnutrition have altered osmotic equilibrium at baseline that predisposes them to osmotic demyelination. We suggest a more cautious and meticulous approach should be followed in these patients to avoid the dreaded complication.

BACKGROUND

We report a case of Central pontine myelinolysis (CPM) in a chronic alcoholic male even with meticulous correction of hyponatraemia according to textbook and clinical guidelines. While the rapid correction of hyponatraemia has been conventionally known to be an important factor for CPM, our case focuses on the importance of comorbid conditions associated with hyponatraemia, especially chronic alcoholism leading to CPM. We suggest a more cautious approach in this group of patients with sodium correction by <6 mmol/L/day or 0.5–1.0 mmol/L/h without exceeding the sodium levels of 130 mEq/L during the first 48 h. This guideline should be followed in these cases to avoid osmotic demyelination syndrome.

CASE PRESENTATION

A 48-year-old man with a history of chronic alcoholism was admitted due to a syncopal episode with sodium of 107, creatine of 2.02, aspartate transaminase of 241, alanine transaminase of 114, alkaline phosphatase of 251, serum osmolality of 234 and urine osmolality of 97 (measured by an osmolometer). Blood ethanol concentration was not checked during this admission. On clinical examination, patient was found to be malnourished with no evidence of tremors, asterixis or testicular atrophy. He was mildly confused in time while the rest of the neurological examination, including recent and remote memory, was completely intact. His gait was noted to be ataxic while his motor

strength, sensory exam and deep tendon reflexes were completely normal. Abdominal ultrasound showed severe hepatic steatosis without any other liver abnormalities. His low sodium was referred as hypotonic hyponatraemia due to excess fluid and low solute intake. He was treated with fluid restriction and his sodium was corrected at a rate <10–12 mmol/L in the first 24 h. The sodium levels (figure 1) began to normalise at 115 mmol/L on day 2, 123 mmol/L on day 3, 126 mmol/L on day 4, 127 mmol/L on day 5, 132 mmol/L on day 6 and 135 mmol/L on the day of discharge. During his initial hospitalisation, a working diagnosis of hyponatraemia with acute kidney injury was made. He was discharged in a stable condition on day 7 and advised to abstain from alcohol consumption.

Ten days after his discharge, he began to experience generalised weakness and presented with an unsteady gait and slurred speech. On clinical examination, he was noted to have dysarthria and coordination deficits with dysmetria, dystaxia and dysidiadochokinesia. He was noted to be quadriparetic with a motor strength of 4/5 in the upper limbs and 3+/5 in the lower limbs; he had increased tone throughout, as well as an equivocal plantar response, while the rest of the upper motor neuron signs were negative. His cranial nerves, sensations to touch/temperature/vibration/position and deep tendon reflexes were found to be normal. Labs on this admission revealed a serum sodium of 135 mmol/L while his initial serum sodium was 107 mmol/L on prior admission. Following his previous discharge, he resumed alcohol consumption and the blood ethanol concentration was 24 mg/dL during his subsequent admission. A differential diagnosis of ataxia secondary to either alcoholic vermal degeneration or demyelinating lesion related to the recent correction of hyponatraemia was considered. A non-contrast CT scan of the head was non-diagnostic at the time of admission. MRI of the brain (figure 2) showed abnormal signal intensity in the central pons suggestive of CPM with no evidence of extrapontine myelinolysis. His ataxia was most likely secondary to pontine demyelination, which significantly improved during hospitalisation with physical and occupational therapy.

OUTCOME AND FOLLOW-UP

At the time of discharge, the patient had mild motor weakness with 4/5 strength in both the upper/lower extremities, some dysarthria, and improved gait while the rest of the neurological exam was completely intact. Our patient required

To cite: Malhotra K, Ortega L. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-009970

Figure 1 (A) Trends of serum sodium (mmol/L) from the time of admission. (B) Trend of serum osmolality (mosm/kg) from the time of admission.

long-term outpatient rehabilitation for his residual weakness and dysarthria.

DISCUSSION

CPM was first described by Adams *et al*¹ in 1959 as a non-inflammatory demyelinating disorder of pons characterised by loss of myelin with relative sparing of neurons. Around 10% of cases present with extrapontine myelinolysis (EPM) in areas such as the midbrain, thalamus, basal nuclei and cerebellum. It has been proposed that the term 'osmotic demyelination syndrome' (ODS) is better suited than CPM for cases with extrapontine lesions that result from correction of hyponatraemia.² Symptoms usually begin with weakness, confusion and dysarthria and may progress to pseudo bulbar palsy and locked-in-state, arise 1–7 days after overcorrection of hyponatraemia. CPM is a devastating neurological disorder that has been known to develop after rapid correction of chronic hyponatraemia. Over 75% of CPM cases are associated with chronic alcoholism. We present a case of a patient with chronic alcohol abuse admitted with hyponatraemia who developed CPM despite appropriate correction for serum sodium.

CPM is most commonly associated with rapid correction of serum sodium, especially in the chronic hyponatraemic states. During the slow and chronic (>48 h) development of hyponatraemia, brain cells adapt to the osmotic changes by losing

organic solutes aka osmolytes such as myoinositol, glycerophosphorylcholine, phosphocreatine/creatine, glutamate, glutamine and taurine. When chronic hyponatraemia is corrected too rapidly, the concentration of brain sodium increases beyond normal levels and reuptake of organic osmolytes occurs at a much slower rate as compared to sodium. Therefore, overshooting of the optimal sodium concentration in the brain occurs in the context of depleted organic osmolytes.³ Depletion of organic osmolytes leads to shrinkage of brain cells, leading further to ODS. Sterns and Silver⁴ have shown that the exogenous administration of myoinositol, a major organic osmolyte, speeds up the brain's reuptake of osmolytes and reduces demyelination caused by the rapid correction of sodium. It has also been suggested that the rapid correction of sodium shrinks the CNS vascular endothelial cells that are adapted to chronic hyponatraemia, thus disrupting their tight junctions and opening the blood–brain barrier, which allows cytokines and lymphocytes to enter the brain. This hyperosmotic stimulus leads to intracellular hydration of oligodendrocytes in the pons and other susceptible areas leading to apoptosis and demyelination.

MRI is the most sensitive diagnostic imaging modality to detect myelinolysis. MRI typically is normal at the onset of symptoms and may not become positive for as long as 4 weeks after disease onset. Our patient presented with quadriparesis and an MRI-positive demyelinating lesion after approximately

Figure 2 Brain MRI of the patient on readmission. (A) Diffusion-weighted imaging-axial sequence showing trident-shaped hyper intensity within the pons. (B) T1-sagittal sequence showing hypointensity within the basis pontis. (C) Fluid attenuated inversion recovery sequence showing hyperintense focus in the central pons.

2 weeks of sodium correction during his initial hospitalisation. Diffusion-weighted imaging (DWI) is a relatively new MRI technique sensitive to the motion of water. Since the underlying process of CPM is the osmotic imbalance of water and electrolytes, DWI has been found to be a better modality to identify CPM/EPM but it does not regularly precede tissue changes detectable on conventional MRI.⁵

Severe hyponatraemia is defined as sodium concentration <120 mEq/L and its inadequate treatment has been associated with severe neurological damage. In acute (<48 h) hyponatraemia, prompt treatment with hypertonic saline (3%) can prevent seizures and respiratory arrest. For chronic (>48 h) symptomatic hyponatraemia, correction must be rapid during the first few hours (to decrease brain oedema), followed by a slow correction.⁶ Rapid correction of sodium has been shown to improve survival and decrease the brain lesions, if symptomatic hyponatraemia is corrected under the accepted guidelines. Ayus *et al*⁷ reported rapid correction of symptomatic hyponatraemia with an absolute change in serum sodium of >14 and <25 meq/L in the first 24 h allowed 100% of the rats to survive for 5 months without brain lesions, while an absolute change in serum sodium of >25 meq/L in the first 24 h resulted in the development of brain lesions and 12% survival over the next 5 months.

It is well known that chronic alcoholism, cirrhosis and other chronic diseases reduce the ability to generate protective cerebral mechanisms against osmotic stressors.⁸ There have been a few cases in the literature mentioning the association of CPM with Wernicke's encephalopathy.⁹ Alcohol consumption has been associated with upregulation of the aquaporin-4 (AQP4) water channel, leading to brain oedema and osmotic disequilibrium.¹⁰ Katada *et al*¹¹ further observed that ethanol administration significantly reduced sodium concentration in blood especially 24 h after traumatic brain injury. Ethanol, similar to urea but unlike glucose, has ready access to intracellular water and causes a more pronounced hyperosmolar state independent of the osmotic changes caused by its action on the inhibition of antidiuretic hormone (ADH) release.¹² Chronic alcohol abusers with additional liver disease and malnutrition have altered thresholds for ADH secretion at baseline that predisposes them to CPM. ODS can also result from rapid normalisation of serum sodium from brisk free-water diuresis in beer potomania. Treatment of beer potomania with isotonic or hypertonic saline causes brisk free-water diuresis, thereby causing exceedingly rapid sodium correction and thus ensuing osmotic demyelination. Rapid self-correction of serum sodium in beer potomania should be treated with D5W infusion at a rate to match the urine output.¹³

In the presence of conditions posing a high risk for CPM such as chronic hyponatraemia of <110 mEq/L, alcoholism, hepatic failure, orthotopic liver transplantation, potassium depletion and malnutrition, correction of serum sodium should not exceed 6 mEq/L in any 24 h period.¹⁴ Sterns *et al*¹⁵ suggested not to exceed 10 mmol/L/day as a limit for sodium correction and 6–8 mmol/L/day as a goal of therapy to avoid development of serious complications. We suggest a more cautious approach in this patient group with sodium correction by

0.5–1.0 mmol/L/h without exceeding >6 mmol/L/day and maintaining sodium levels <130 mEq/L during the first 48 h. However, it cannot be over emphasised that CPM may occur even with meticulous correction of sodium levels, especially in alcoholics and malnourished patients. Physicians need to manoeuvre their clinical judgement for each respective case to avoid the development of this devastating neurological disorder.

Learning points

- ▶ Central pontine myelinolysis (CPM) in chronic alcoholics is a multifactorial entity.
- ▶ Chronic alcoholics have altered antidiuretic hormone secretion predisposing to CPM.
- ▶ Hyponatraemia in chronic alcoholics should be approached more cautiously.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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