Central Myelinolysis in a Patient with Hyponatraemia
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ABSTRACT
We present a case of a 50-year old man who developed mutism and a flaccid quadriparesis within 48 hours of presentation to hospital with severe hyponatraemia. A diagnosis of central pontine myelinolysis was made based on the clinical features and typical appearances on magnetic resonance imaging.

CASE REPORT
A 50-year old man presented to the University Hospital of the West Indies, Jamaica, with polydipsia of several years duration, loss of appetite for three weeks, vomiting and unresponsiveness for one day. He had been diagnosed with schizophrenia 15 years prior to admission and was being treated with trifluoperazine 5 mg daily and trihexyphenidyl 2 mg daily. His sister reported that for many years he would, on a daily basis, frequently drink large volumes of water. In the three weeks prior to admission, he continued drinking large volumes of water but had stopped eating and began complaining of generalized weakness. Three days prior to admission he was noted to be drowsy. On the day of presentation to the emergency room he reportedly had four episodes of vomiting and was said to be even more drowsy. There was no history of alcohol abuse or head injury.

On examination, he was dehydrated but not in cardiorespiratory distress: BP 128/89 mmHg, pulse 76/minute, respiratory rate 20/minute, temperature 97°F. His respiratory and cardiovascular system and abdominal examinations were normal. He was drowsy and oriented to person only. He gave appropriate but slowed responses in short sentences to questions. Cranial nerve examination was normal with no

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ophthalmoplegia or papilloedema noted. His power was recorded as grade 5 (Medical Research Council) in all limbs with generalized hyperreflexia, normal tone and no gross sensory deficits.

Blood results were as follows: Hb 15.5 g/dL; WBC 15.7 x 10^3/μL; platelets 234 x 10^3/μL; PT 11.9/12; PTT 46.7/31.7 secs; serum sodium, 99 mmol/L; potassium, 2.8 mmol/L; chloride, 74 mmol/L and urea 2.4 mmol/L.

The patient was diagnosed with hypo-osmolar hyponatraemia secondary to psychogenic polydipsia precipitated most likely by recent vomiting and trifluoperazine use. Slow correction of the hyponatremia with 0.9% saline was started, aiming at a correction rate not exceeding 12 mmol/L/24 hours. His serum sodium level reached 125 mmol/L one day after admission. By 36 hours after admission, he was noted to be more responsive and alert. On day 2 of admission, however, the consciousness of the patient deteriorated again, he became mute and required nasogastric tube feeding. His serum sodium level on day 2 was 128 mmol/L. His examination now revealed a flaccid quadriparesis with generalized hyperreflexia. He was reviewed by the psychiatry unit who thought that his acute problem was organic and recommended neurological evaluation. The neurology service suggested an osmotic demyelination syndrome, in particular, central pontine myelinolysis, as the likely diagnosis in view of the history of recent correction of severe hyponatraemia, the subsequent acute deterioration of mental status and the associated quadriaparesis, hyperreflexia and new onset mutism.

A CT brain performed on day 12 revealed mild diffuse cerebral atrophy and a possible small left cerebellar infarct. The pons was unremarkable.

An MRI brain on day 17 showed a well-defined area of increased signal on T2 and decreased signal on T1 weighted sequences in the central pons with an uninvolved outer rim. There was no mass effect. Mild diffuse cerebral atrophy was noted. Extrapontine lesions were not seen. The patient remained mute with minimal spontaneous limb movements until the 21st day of admission when he became more alert and started making direct eye contact. His serum sodium was then 137 mmol/L. He showed continued improvement in mentation and became conversant but with slurred speech by the 30th day of admission. His flaccid paralysis remained unchanged at the time of his discharge to the medical outpatient clinic. The patient at his last known review 5 months post discharge had returned to his baseline mental status, was able to feed himself but was still wheelchair dependent.

**DISCUSSION**

Central pontine myelinolysis (CPM) is pathologically defined by a symmetrical non-inflammatory demyelination of the central basis pontis. Histological examination typically reveals myelinolysis with loss of oligodendroglia, reactive astrocytosis and relative sparing of the axons and nerve cells. The blood vessels are patent and unaffected (1, 3). These features allow CPM to be differentiated from demyelinating disorders such as multiple sclerosis, post infectious encephalitis or acute disseminated encephalomyelitis (ADEM) which have scattered demyelination and inflammatory reaction on histology.

The spectrum of presenting symptoms in CPM is wide, ranging from a lack of clinical symptoms to frank coma (2, 3). Central pontine myelinolysis classically manifests as a rapidly evolving flaccid quadriparesis, mutism, dysphagia, dysarthria and impaired consciousness (1, 2).

Some patients recover with complete reversal of both the clinical and the imaging findings. Disruption of the blood-brain barrier following a marked osmolarity shift, usually by a rapid correction of hyponatremia, may play a critical role in the pathogenesis of CPM. Most reported cases have occurred when chronic hyponatremia was corrected at rates faster than 12 mmol/24h (4, 5). Central pontine myelinolysis has however developed in patients with normal serum sodium levels (6), in spite of careful correction of hyponatremia (7) in patients with acquired folate deficiency, malignancies, malnutrition, as a complication of dialysis and during the management of severe hypoglycaemia (1, 2, 8, 9).

Lamp and Yazdii on review of the literature found that of the cases of CPM reported between 1986 and 2002, 174 (39.4%) have been reported in chronic alcoholics; 95 cases (21.5%) followed the correction of hyponatremia and 17.4% followed liver transplantation, with the development of CPM being attributed to the use of the immunosuppressive agent, cyclosporine (3).

Non-enhanced CT scans may be normal or show non-specific hypodensities on magnetic resonance imaging. There is evidence of prolongation of both T1 and T2 relaxation producing high signal on T2 – weighted sequences and low signal on T1-weighted sequences. The imaging manifestations reflect increased water content in the affected areas. The transverse pontine fibres are most severely affected whilst the descending corticospinal tracts are relatively spared. Enhancement following contrast media varies; some enhance but others do not. The affected area may sometimes have a characteristic “butterfly” shape. There is a characteristic sparing of the peripheral pontine parenchyma with central pontine lesions (10–14).

Cramer performed diffusion weighted sequences on two patients with acute CPM and found restriction of diffusion (15). Computed tomography and MRI results become positive only 6 to 10 days after clinical signs of myelinolysis become manifest and do not necessarily correlate with the clinical features (3, 13, 14).

Absence of contrast enhancement and significant mass effect may help to differentiate CPM from conditions such as tumours, ischaemia, multiple sclerosis and encephalitis which may have similar imaging findings.

Untreated acute severe hyponatraemia (serum sodium less than 115 mmol/L and of duration less than 36 to 48
hours) is associated with cerebral oedema and accompanying confusion, coma or seizures and high rates of morbidity and death. Chronic severe hyponatraemia may present with milder symptoms and no evidence of cerebral oedema. There is some debate as to whether the clinical outcome in CPM is influenced by the severity of neurological deficits, the degree of hyponatraemia and the rate of correction of hyponatraemia (16).

This case report illustrates the difficulty in identification and subsequent management of acute versus chronic severe hyponatraemia. More rapid correction of hyponatraemia is required eg in the setting of acute severe hyponatraemia associated with seizures but there is more evidence supporting the institution of slow rather than rapid correction of chronic severe hyponatraemia. Our patient had symptoms of at least three weeks duration suggesting a chronic severe hyponatraemia (likely secondary to primary polydipsia) and had no clinical or radiological features of cerebral oedema. A slow correction of serum sodium (with isotonic rather than hypertonic saline) is advisable in this setting to prevent the well known complication of CPM seen with a more rapid reversal of serum sodium. Once central pontine myelinolysis develops, there is no proven effective treatment and for cases with significant neurological deficits, the prognosis is usually poor.

In summary, we presented a case of a man with chronic severe hyponatraemia, likely secondary to primary polydipsia who developed mutism, a flaccid paraparesis and diminished consciousness within 48 hours of correction of his serum sodium. The clinical impression of central pontine myelinolysis was supported by typical features on magnetic resonance imaging.

REFERENCES