Central Myelinolysis in a Patient with Hyponatraemia

W West, DT Gilbert, RJ Wilks

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.

La Mielinolisis Central en un Paciente con Hiponatremia

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RESUMEN

Presentamos un caso de un hombre 50 años de edad que desarrolló mutismo y cuadriparesis flácida en el curso de las 48 horas tras presentarse en el hospital con hiponatremia severa. Se hizo un diagnóstico de mielinolisis central pontina, sobre la base de los rasgos clínicos y las apariencias típicas en la imagen de resonancia magnética.

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INTRODUCTION

Central pontine myelinosis (CPM), a demyelinating disease involving the central pons, was first described by Adams *et al* in 1959 (1). Extrapontine myelinolysis involving other parts of the central nervous system has since been recognized, and the term osmotic demyelination syndrome (ODS) encompassing both disorders has been coined. Typical neurological features of isolated central pontine myelinolysis include flaccid quadriparesis, pseudobulbar palsy, changing levels of consciousness and coma. Some patients develop a state of pseudocoma (a locked-in syndrome with mutism, quadriparesis and relatively preserved comprehension and sensation) which may progress to death. Extra-pontine lesions will alter the typical neurological picture, with symmetrical involvement of the thalamus, internal capsule, cerebellum or deep cerebral cortex being described (1, 2). Central pontine myelinosis has been associated with chronic alcoholism, chronic nutritional deficiencies, hepatic failure, chronic renal failure and systemic disorders which result in electrolyte imbalance (1, 3).

Rapid correction of hyponatraemia is an important contributor to the development of CPM and myelinolysis is more likely to occur after the treatment of chronic rather than acute hyponatraemia. The diagnosis of CPM is often clinical and magnetic resonance imaging may support the diagnosis when characteristic imaging features are seen. We report the case of a 50-year old man who presented to the University Hospital of the West Indies, Jamaica, with severe hyponatraemia who subsequently developed clinical features consistent with a central pontine myelinolysis.

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

From: Department of Surgery, Radiology, Anaesthesia and Intensive Care[1], Department of Medicine[2], Tropical Medicine Research Institute[3]. The University of the West Indies, Kingston 7, Jamaica, West Indies.

Correspondence: Dr W West. Department of Surgery, Radiology, Anaesthesia and Intensive Care. The University of the West Indies, Kingston 7, Jamaica, West Indies. E-mail: wayne_west@hotmail.com.

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}/uL; platelets 234 x 10^{-3}/uL; PT 11.9/12; PTT 46.7/31.7secs; 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 demy-elination 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 quadriparesis, 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 hyponatraemia, may play a critical role in the pathogenesis of CPM. Most reported cases have occurred when chronic hyponatraemia 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 hyponatraemia (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).

Lampl and Yazdi 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 hyponatraemia 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

1. Adams RD, Victor M, Mancall EL. Central pontine myelinolysis. A hitherto undescribed disease occurring in alcoholic and malnourished patients. Arch Neurol Psychiatry 1959; **81:** 154–72
2. Leens C, Mukendi R, Foret F, Hacourt H, Devuyst O, Colin IM. Central and extrapontine myelinolysis in a patient in spite of a careful correction of hyponatremia. Clin Nephrol 2001; **55:** 248–53.
3. Lampl C, Yazdi K. Central pontine myelinolysis. Eur Neurol 2002; **47:** 3–10.
4. Strub MU, Steck AJ, Fuhr P. Asymptomatic central pontine myelinolysis Neurology 1999; **53:** 914.
5. Sterns RH, Riggs JE, Schochet SS. Osmotic demyelination syndrome following correction of hyponatremia. N Engl J Med 1986; **314:** 1535–42.
6. Brunner JE, Redmond JM, Haggar AM, Elias SB. Central pontine myelinolysis and pontine lesions after rapid correction of hyponatremia: A prospective magnetic resonance imaging study. Ann Neurol 1990; **27:** 61–6.
7. Mascalchi M, Cincotta M, Piazzini M. Case Report: MRI demonstration of pontine and thalamic myelinolysis in a normonatremic alcoholic. Clin Radiol 1993; **47:** 137–8
8. Perros P, Sellar RJ, Frier BM. Chronic pontine dysfunction following insulin-induced hypoglycemia in an IDDM patient. Diabetes Care 1994; **17:** 725–7.
9. Pirzada NA, Ali IL. Central pontine myelinolysis. Mayo Clin Proc 2001; **76:** 559–62
10. Martin PJ, Young CA. Central pontine myelinolysis: clinical and MRI correlates. Postgrad Med J 1995; **71:** 430–2.
11. Rippe DJ, Edwards MK, D'Amour PG, Holden RW, Roos KL. MR imaging of central pontine myelinolysis. J Comput Assist Tomogr 1987; **111:** 72–726.
12. Ho VB, Fitz CR, Yoder CC, Geyer CA: Resolving MR features in osmotic Myelinolysis (central pontine and extrapontine myelinolysis), AJNR Am J Neuroradiol 1993; **14:** 163–7
13. Koragi Y, Takahashi M, Shinzato J et al: MR findings in two presumed cases of mild central pontine myelinolysis. AJNR Am J Neuroradiol 1993; **14:** 651– 4.
14. Chua GC, Sitoh YY, Lim CC, Chua HC, Ng PY. MRI findings in osmotic myelinolysis. Clin Radiol 2002; **57:** 800–6
15. Cramer SC, Stegbauer KC, Scneider A, Mukai J, Maravilla KR. Decreased diffusion in central pontine myelinolysis. AJNR Am J Neuroradiol 2001; **22:** 1476–9.
16. Menger H, Jorg J. Outcome of central pontine and extrapontine myelinolysis (n = 44). J Neurol 1999; **246:** 700–5.