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Short reports

Central pontine myelinolysis: clinical and MRI correlates

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Summary

Central pontine myelinolysis (CPM) is a rare condition characterised by spastic tetraparesis, pseudobulbar palsy and the 'locked-in syndrome'. It is frequently fatal. We report a patient who developed CPM secondary to profound hyponatraemia and who recovered with no disability. Serial magnetic resonance imaging (MRI) demonstrated characteristic abnormalities within the pons at the onset of the disease, whereas computerised tomography was normal. Clinical improvement was followed six months later by progressive resolution of the MRI changes, with almost complete resolution after 18 months. Clinical and MRI findings correlate early in the course of CPM but clinical recovery predates MRI improvement by several months.

Keywords: central pontine myelinolysis, magnetic resonance imaging

Central pontine myelinolysis (CPM) is an infrequent condition characterised by loss of myelin in the central pons, sometimes accompanied by areas of extra-pontine demyelination. It was originally described in hyponatraemic patients with a history of alcohol abuse[1] but more recently has been documented following liver transplantation[2] and in patients with hypokalaemia.[3] Almost invariably it occurs in the hospital setting in association with correction of the electrolyte disturbance, and it frequently results in death. We report a patient with CPM who made a full recovery and in whom serial magnetic resonance imaging (MRI) showed progressive resolution of the initial characteristic pontine changes.

Case report

A 25-year-old man with a history of alcohol abuse was admitted to a local general hospital having suffered prolonged vomiting following an alcoholic binge. There was no evident neurological deficit, but the serum sodium was 105 mmol/l. There were no other biochemical abnormalities apart from elevated liver enzymes. The hyponatraemia was corrected using a normal saline infusion (0.9%; 130 mmol/l). Over the next 48 hours the serum sodium rose to 122 mmol/l, and it rose further to 138 mmol/l during the ensuing five days. It then remained within the normal range.

Seven days after admission, he developed a progressive spastic tetraparesis with mixed bulbar and pseudobulbar palsy, dysphagia and anarthria. Computed tomography (CT) of the brain was normal. He was transferred to a neurological centre and underwent MRI using standard T1- and T2-weighted sequences at 1.5 Tesla (Magnetom, Siemens). T1- and T2-weighted sagittal sections and T2-weighted axial views revealed extensive signal abnormalities in the pons, consistent with myelinolysis (figure, A). There was no evidence of extra-pontine myelinolysis.

The patient's condition gradually improved over the next four weeks, such that he was able to walk, speak and swallow. Repeat MRI showed appearances similar to the original scan (figure, B). Despite the clinical improvement, there was no significant improvement in the radiological findings. He was discharged to his own home two weeks later.

After a further six months the patient was walking independently and was fully self-caring. Further MRI showed some resolution of the abnormality within the pons (figure, C). One year later, the patient was fully recovered and had returned to work. A further MRI scan showed almost complete resolution of the previous pontine abnormalities (figure, D).

Discussion

Originally, CPM was a clinical diagnosis characterised by the progressive onset of tetraparesis and pseudobulbar palsy, with further progression to a 'locked-in' state. The six-month survival rate of CPM is only between 5 and 10%.[4] Imaging using CT usually fails to reveal any abnormality although sometimes areas of reduced attenuation compatible with myelin loss are apparent.[5] Brainstem evoked potentials may be of some help in localising the lesion, but not in elucidating its character.[5] MRI is now the imaging modality of choice, but despite a number of reports of MRI findings early in the condition,[6–8] there is a paucity of information regarding long-term serial MRI and clinical examinations.[9] This case is unusual in that the patient survived with complete clinical recovery, and in that serial MRI was undertaken.

Usually CPM occurs in association with a rapid rise in serum sodium (more than 12 mmol/l a day) although even cautious rever-

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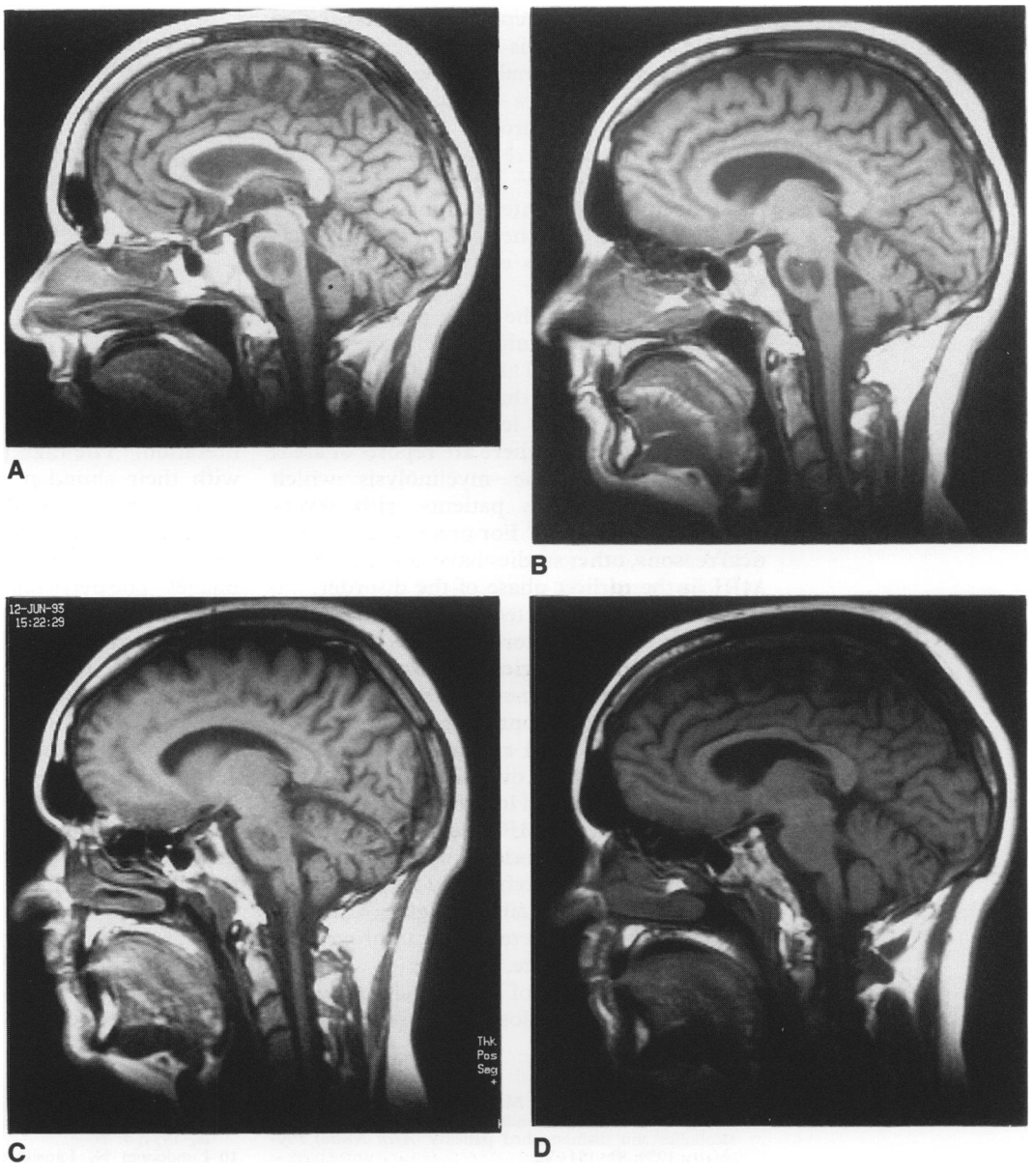

Figure Series of four T1-weighted MRI scans taken in the sagittal plane. The first sequence (A) was taken seven days after the onset of neurological symptoms and shows an extensive hypointensity of the central pons compatible with myelinolysis. One month later (B) the abnormality was relatively unchanged despite improvement in the patient's clinical condition. Six months later (C) there was some resolution of the low signal area within the pons, and the abnormality had almost completely resolved a further year later (D).

Central pontine myelinolysis: clinical features

- tetraparesis: usually spastic although flaccidity has been described especially soon after onset
- pseudobulbar palsy: dysarthria, dysphagia, weakness of tongue and palatal movement, exaggerated jaw jerk and emotional lability
- early depression of conscious level
- progression to 'locked-in' state
- other brainstem features according to extent of myelinolysis; failure of ocular movement, absence of pupil reactions
- cerebellar ataxia if cerebellar peduncles or cerebellar hemispheres are involved
- seizures may occur if associated with hyponatraemic encephalopathy

Box 1

sal of hyponatraemia may be a precipitant.[10] Certainly, it seems that the rate of correction of hyponatraemia, rather than the absolute sodium concentration is the most important factor in its pathogenesis since chronically hyponatraemic patients do not necessarily develop CPM, and CPM can even occur with hypernatraemia. It is unclear what role other factors (such as hepatic dysfunction) might have.

The mechanism of myelin loss in CPM is unclear. Extra-pontine myelinolysis may also be a feature, particularly involving the thalami and the basal ganglia, but there is a particular predilection for the pons. These areas all have a relatively high grey/white matter interface. It is suggested that the rise in serum sodium exerts an osmotic endothelial injury leading to the local release of myelinotoxic factors mainly

derived from more vascular grey matter.[11] The absence of myelinolysis in pure white matter tracts such as the internal capsule supports this view. Autopsy studies in early CPM have shown altered lipid:protein ratios, little inflammatory reaction, relative sparing of the axons, and oedema.[12] This latter element accounts for the hypointense signals seen on T1 MRI sequences and the hyperintense signals seen on T2 sequences early in the course of CPM.

Certain studies in the acute phase of CPM have shown that the clinical deficit may precede the appearance of MRI abnormalities by two or three weeks,[5,13] and that MRI may fail to demonstrate pontine lesions found at autopsy.[14,15] Conversely, there are reports of areas of presumed pontine myelinolysis which remain subclinical in patients with severe electrolyte imbalance.[5] For practical and logistical reasons, other studies have failed to obtain MRI in the earliest phase of the disorder.

In the case reported here, the clinical deterioration was mirrored within days by the marked neuroradiological abnormality. The findings on MRI did not worsen significantly over the following month suggesting little, if any, delay of the MRI appearance behind the clinical picture during disease onset. However, on recovery the clinical improvement preceded the resolution of the MRI findings by approximately six months. Indeed, useful functional recovery was still accompanied by quite pronounced MRI abnormalities (figure, C). Only after 18 months was there a major improvement in the MRI appearance.

The chronic lesion of CPM is characterised by intense fibrillary gliosis with astrocyte proliferation.[6] The high proportion of astrocytes, with their abundant cytoplasm, elevates the water content of the gliotic tissue. This explains the hypointense signals seen on T1 sequences and the hyperintense changes on T2 images. The persistence of gliosis and hence the MRI changes, despite clinical improvement, should provide useful diagnostic information from elective MRI after the acute phase of the disease and may enable studies of the true incidence of pontine myelinolysis in patients with electrolyte imbalance.[16]

MRI is the radiological modality of choice in suspected CPM. It is usually, but not exclusively, abnormal within a few days of symptom onset. Resolution of the MRI changes appears to follow the clinical improvement, although with a delay of several months. The clinical picture probably remains the best guide to prognosis, although MRI can provide useful confirmatory data and may be of diagnostic value at least six months after recovery.

Central pontine myelinolysis: postulated causes and associations

- profound hyponatraemia with rapid correction (>12 mmol/l per day)
- absolute correction of hyponatraemia by >25 mmol/l per day
- reversal of hypokalaemia
- chronic liver disease and following liver transplantation
- chronic alcoholism
- malnutrition

Box 2

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