

Clinics in Diagnostic Imaging (45)

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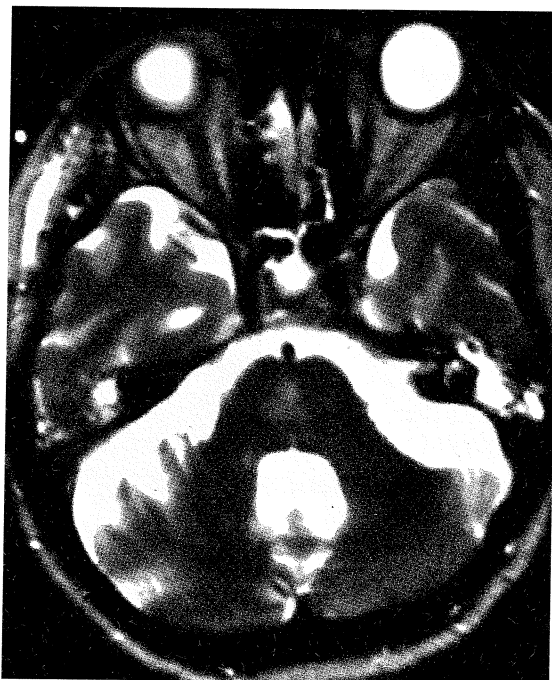


Fig 1a



Fig 1b

Fig 1 – Axial T2-weighted MR scans of the brain (TR/TE 3800/90) taken at the level of the (a) pons and (b) internal capsules.

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CASE PRESENTATION

A 65-year-old woman was admitted for fever and cough. Investigation showed right lower lobe pneumonia. It was complicated by respiratory failure and syndrome of inappropriate antidiuretic hormone secretion (SIADH). She had a serum sodium level of 123 mmol/L, which was corrected to 137 mmol/L the next day. Her condition stabilised and she remained fully conscious, though ventilator-dependent. One week later, she became confused and lethargic, and then developed progressive weakness of all four limbs,

resulting in a flaccid type of paralysis. Computed tomography (CT) of the brain performed at that time and enhanced CT of the brain done one week later were normal. Cerebrospinal fluid analysis and blood biochemistry were unremarkable. Electroencephalography (EEG) showed diffuse theta waves over both hemispheres, compatible with metabolic encephalopathy. Brainstem auditory evoked potential studies showed abnormal slow conduction. What do the magnetic resonance (MR) scans show (Figs 1a – 1b)? What is the diagnosis?

IMAGE INTERPRETATION

MR scans showed a 1 cm area of T2 hyperintensity in the central pontine region (Fig 1a). In a patient with a history of sodium replacement, this finding is in keeping with osmotic myelinolysis (or central pontine myelinolysis). Multiple areas of T2 hyperintensity were seen in the basal ganglia and deep white matter (Fig 1b), representing part of the same process.

DIAGNOSIS

Osmotic myelinolysis (central pontine myelinolysis)

CLINICAL COURSE

The patient did not improve clinically over the following months. She developed spastic tetraparesis, pseudobulbar palsy and horizontal nystagmus. Because of mutism, antidepressants were tried but they were not effective. She remained bed-ridden and ventilator-dependent. During her hospital stay, she developed several episodes of chest and urinary tract infection which were controlled with antibiotics. The patient finally died one year later due to multiple organ failure and sepsis.

DISCUSSION

Osmotic myelinolysis (OM) is a demyelinating disease that can develop following rapid correction of hyponatremia from any cause. It was originally described in chronic alcoholics. Other reported associations include malnourished status, renal failure, diabetes mellitus, and post-orthotopic liver transplantation^(1,2). However, it can also occur in healthy persons with hyponatremia caused by gastroenteritis or diuretic therapy^(3,4). Young children and adults of all ages can be affected⁽⁵⁾.

The pathogenesis of myelinolysis, and the reasons for vulnerability and predilection of particular brain territories to develop myelinolysis are not fully understood. Pathologically, myelin is destroyed but neurons and axons are typically spared. This pattern of damage is opposite to that of infarction. Furthermore, as opposed to other demyelinating diseases such as multiple sclerosis, no accompanying inflammation is found⁽³⁾. Classically, the central pons is involved, hence the original name of central pontine myelinolysis (CPM). This entity is known to affect other extrapontine areas, notably the thalami, basal ganglia, and cerebral or cerebellar gray-white junctions. The latter condition is termed extrapontine myelinolysis (EPM)⁽¹⁾. In both CPM and EPM, bilateral and symmetrical involvement is usually the rule (Figs 2a – b).

Clinical reviews and experimental animal models have shown that the main contributing factor for the development of myelinolysis is correction of hyponatremia^(3,6). OM is especially likely to occur following rapid correction of hyponatremia (eg. more than 12 mmol/L a day), and if the hyponatremia is chronic rather than acute prior to correction.



Fig 2a

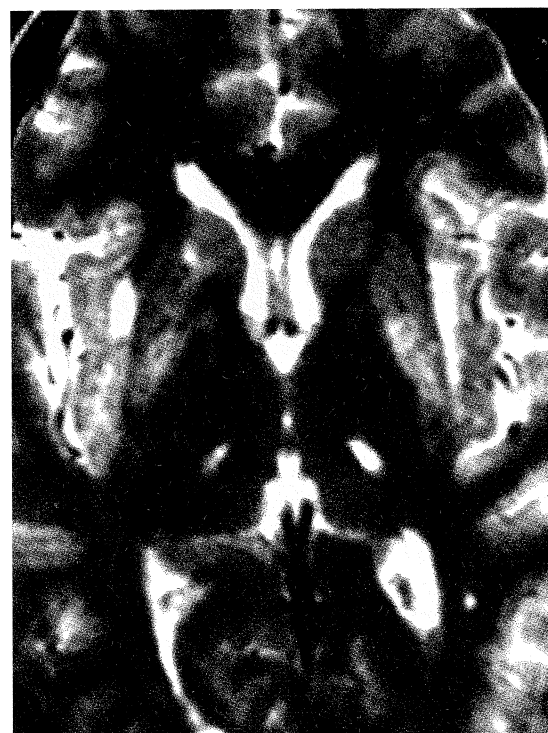


Fig 2b

Fig 2 – Different patient with pontine and extrapontine osmotic myelinolysis due to rapid sodium correction. Axial T2-weighted MR (TR/TE 2940/90) images show typical bilateral and symmetrical hyperintense foci in the (a) central pons, (b) thalami and basal ganglia.

Nevertheless, OM can still occur even after cautious and slow sodium correction, especially in the presence of other recognised risk factors such as hypokalaemia, liver or renal disease, and poor nutritional status. It is impossible to define a level of correction that will be absolutely free of risk⁽³⁾. On the other hand, untreated hyponatremia, regardless of its severity, will not result in myelinolysis. Although human myelinolysis has

been reported in the absence of documented hyponatremia⁽⁷⁾, convincing evidence for a cause of myelinolysis other than serum sodium derangement is lacking⁽³⁾.

The clinical course of affected patients may be biphasic⁽³⁾. Following clinical improvement from hyponatremic encephalopathy, a neurologic syndrome caused by myelinolysis typically ensues 2 to 3 days after the correction of hyponatremia. Initial symptoms include mutism, dysarthria, lethargy and affective changes. These may be mistaken for a psychiatric illness. Later, the classical symptoms of spastic quadriparesis and pseudobulbar palsy develop, reflecting damage to the corticospinal and corticobulbar tracts in the basis pontis. These symptoms may be observed in more than 90% of patients⁽⁶⁾. A large central pontine OM lesion can cause a locked-in syndrome. Extension of injury to the midbrain, medulla and pontine tegmentum can cause various oculomotor and cranial nerve signs. Extrapontine involvement can present with varying movement disorders such as ataxia, dystonia and parkinsonism^(3,6).

Radiologically, OM manifests as regions of increased water content. CT shows areas of hypodensity which are usually bilateral and symmetrical. MR imaging is more sensitive than CT in cases of early or mild OM. Lesions appear hypointense on T1-weighted and hyperintense on T2-weighted acquisitions^(1,4). Enhancement following intravenous gadolinium-DTPA injection is rare though it has been reported⁽⁷⁾. MR scans may even fail to show subtle myelinolytic lesions ultimately found at autopsy, and imaging findings may not be apparent within the first 2 weeks of illness in some cases. For these reasons, a diagnosis of OM should not be ruled out simply on

the basis of negative CT/MR scans^(3,4,6) (Figs 3a – c). There is also no correlation between the size of the lesions on imaging and the clinical severity of the neurological manifestations^(6,7). The regions affected are also characteristic: CPM affects the basal pons with sparing of the descending corticospinal tracts as well as the peripheral pontine tissue. The corticospinal tracts may appear as preserved islands within a zone of hyperintense pontine demyelination on T2-weighted MR images. EPM typically involves the basal ganglia and the lateral thalami nuclei. In a review by Gocht and Colmant of 58 cases of OM⁽⁸⁾, 27 cases had CPM alone, 18 had both CPM and EPM while 13 cases presented as isolated EPM.

The signal intensity changes of CPM on MR imaging are non-specific. Various other disease processes may produce similar findings^(1,5,7). Brainstem neoplasms such as glioma and metastasis may appear somewhat like OM but usually present in a more subacute manner. Infarction, multiple sclerosis, encephalitis and acute disseminated encephalomyelitis (ADEM) often show more diffuse involvement in the supratentorial regions, and therefore clinical differentiation is usually not problematic. In difficult cases, follow-up imaging studies can often reveal the correct answer. Postirradiation and postchemotherapy changes can easily be diagnosed from the clinical history in most cases. Nevertheless, symmetrical involvement of the central pons on CT/MR scans should suggest OM in the acute clinical setting, especially in the presence of recent sodium correction. Furthermore, concomitant involvement of the pons and basal ganglia is fairly specific for OM. Hypoxic encephalopathy, Leigh's disease and Wilson's disease are a few other differential considerations that can

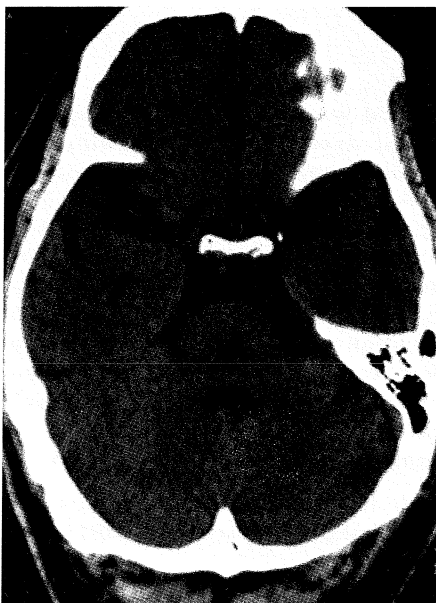


Fig 3a

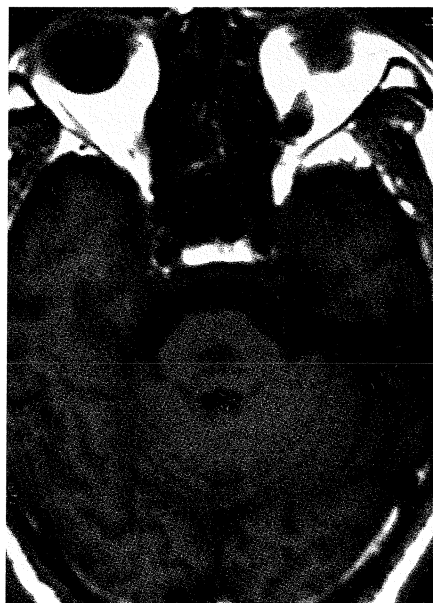


Fig 3b



Fig 3c

Fig 3 – Negative imaging findings early in the course of the disease in another patient with osmotic myelinolysis. A tetraplegic patient (due to previous spinal cord injury) was admitted for general clinical deterioration and poor oral feeding. The sodium level was 124 mmol/L on admission, which was corrected to 139 mmol/L within 24 hours. His clinical condition improved transiently. He deteriorated again and became lethargic and non-responsive a week later. Unenhanced CT scan performed on the day of admission and 2 weeks after sodium correction were negative (not shown). (a) CT scan repeated one month later shows a hypodense area in the central pons. Follow-up MR imaging 1 month later revealed the lesion to be (b) hypointense on T1-weighted (TR/TE 519/9) and (c) hyperintense on T2-weighted (TR/TE 2800/98) sequences. The patient's condition gradually improved, and he was discharged with mild residual neurological signs and symptoms.

usually be excluded on clinical grounds⁽¹⁾.

Other diagnostic tests may be helpful in establishing the diagnosis of OM^(3,6). Brainstem auditory evoked potential studies may identify pontine lesions early in the course of myelinolysis when imaging is normal. As in our patient, the most common abnormality is an increase in the wave I-V interpeak latency, indicating a defect in the auditory pathway within the brainstem. Routine cerebrospinal fluid (CSF) studies are usually normal but CSF protein and myelin basic protein levels may be elevated in OM but not in hyponatremia. Electroencephalograms are non-specific and frequently show generalised slowing. Recently, 18-fluorodeoxyglucose positron emission tomography has been reported to show transient glucose hypermetabolism in pontine lesions in the early stage of the disease, which later evolved into a hypometabolic state⁽⁹⁾. There is no consistent correlation between the persistence of radiographic abnormalities and the persistence of symptoms in surviving patients^(6,7). On the other hand, resolution of the pontine findings on MR imaging usually lags behind clinical improvement for several months⁽²⁾. In the past, it was believed that these pontine signal intensity changes that did not resolve completely represented either residual demyelination or fibrillary gliosis^(1,7). Recent reports have challenged this belief^(2,4). The extrapontine abnormalities, however, have been observed to resolve following clinical improvement.

Treatment of myelinolysis is essentially supportive. Medication can alleviate symptoms of myelinolysis such as depression, psychosis and abnormal somatic movement. The myelinolysis itself cannot be specifically treated once it develops. Corticosteroid administration does not appear to be effective⁽³⁾. Recently, therapeutic plasmapheresis has been reported as a safe and effective method of improving the clinical outcome⁽¹⁰⁾. Larger scale studies are needed to confirm this finding. Although OM was once believed to be fatal with a survival rate of only 5% – 10% beyond 6 months⁽¹⁾, it is now clear that many patients indeed survive much longer⁽⁴⁻⁶⁾. The clinical outcome varies widely, and recovery can be complete or partial.

In conclusion, OM (CPM and EPM) is a distinct condition with a unique clinical presentation. Physicians should be aware of this entity when dealing with hyponatremic patients. Management involves weighing the risk of the illness and possible death from untreated hyponatremia against the risk of developing OM. Obviously, the duration of hyponatremia and the severity of related symptoms should be taken into consideration. Although the radiological findings of OM are not specific, MR imaging is the radiological

modality of choice in investigating suspected OM, and it is usually, but not exclusively, positive within 2 weeks of onset of symptoms. Resolution of the MR imaging findings appears to follow clinical improvement but bears no constant relationship. Ultimately the clinical picture remains the best guide to the patient's prognosis.

REFERENCES

1. Ho VB, Fitz CR, Yoder CC, Geyer CA. Resolving MR features in osmotic myelinolysis (central pontine and extrapontine myelinolysis). *AJNR* 1993; 14:163-7.
2. Martin PJ, Young CA. Central pontine myelinolysis: clinical and MRI correlates. *Postgrad Med J* 1995; 71:430-42.
3. Laaureno R, Karp BI. Myelinolysis after correction of hyponatremia. *Ann Intern Med* 1997; 126:57-62.
4. McGraw P, Edwards-Brown MK. Reversal of MR findings of central pontine myelinolysis. *J Comput Assist Tomogr* 1998; 22:989-91.
5. Gregorio L, Sutton CL, Lee DA. Central pontine myelinolysis in a previously healthy 4-year-old child with acute rotavirus gastroenteritis. *Pediatrics* 1997; 99:738-43.
6. Karp BI, Laureno R. Pontine and extrapontine myelinolysis: a neurologic disorder following rapid correction of hyponatremia. *Medicine (Baltimore)* 1993; 72:359-73.
7. Korogi Y, Takahashi M, Shinzato J, Sakamoto Y, Mitsuzaki K, Hirai T, et al. MR findings in two presumed cases of mild central pontine myelinolysis. *AJNR* 1993; 14:651-4.
8. Gocht A, Colmant HJ. Central pontine and extrapontine myelinolysis: a report of 58 cases. *Clin Neuropathol* 1987; 6:262-70.
9. Roh JK, Nam H, Lee MC. A case of central pontine and extrapontine myelinolysis with early hypermetabolism on 18FDG-PET scan. *J Korean Med Sci* 1998; 13:99-102.
10. Bibi D, Lampl C, Gabriel C, Gerhard J, Brock H, Kostler G. Treatment of central pontine myelinolysis with therapeutic plasmapheresis. *Lancet* 1999; 353:1155.

ABSTRACT

A 65-year-old woman developed progressive neurological deterioration following rapid correction of hyponatremia. Magnetic resonance imaging showed T2 hyperintense areas in the central pons, basal ganglia and deep white matter, typical of osmotic myelinolysis (OM). Previously thought to be uniformly fatal, there are increasing reports of non-fatal cases of OM. The recognition and understanding of this entity is important to prevent or reduce the incidence of its occurrence, as there is no specific treatment once it develops. The clinical and radiological features of OM are reviewed.

Keywords: hyponatremia, pons, osmotic myelinolysis, magnetic resonance (MR) imaging