Case Report

MRI findings in central pontine myelinolysis in a traumatic brain injury patient following rapid correction of severe hyponatremia: A case report
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Abstract:
Central pontine with/without extrapontine myelinolysis, a well-understood entity, is usually manifested by spastic quadripareisis, pseudobulbar palsy, and mental disorders ranging from confusion to coma. Rapid correction of chronic or severe hyponatremia is one of the most important causes. Diagnosis is based on the detection of electrolyte abnormalities and magnetic resonance image findings. We present a case report of central pontine myelinolysis with neurological deterioration in a patient with traumatic brain injury following rapid correction of severe hyponatremia.

Key words: Central pontine myelinolysis, hyponatremia, rapid correction.


Central pontine myelinolysis (CPM), a well-understood entity, is characterized by loss of myelin in the central basis pontis. Symmetrically arranged lesions of similar histology have been identified in other parts of the brain as well, mainly in the basal ganglia, the internal capsules, the lateral geniculate bodies, and the white matter of cerebellum, termed as extrapontine myelinolysis (EPM).¹,² These are usually manifested by spastic quadripareisis, pseudobulbar palsy, with further progression to a 'locked-in' state, mental disorders and impaired level of consciousness ranging from confusion to coma.³

In 1959, Adams and colleagues first described CPM as a unique clinical entity as symmetrical, non-inflammatory demyelination in pons in patients who suffered from alcoholism or malnutrition.⁴ Rapid correction of chronic or severe hyponatremia is frequently implicated as a causative factor, but CPM has also been reported in patients with normonatremia and hypokalemia.⁵,⁶ Almost invariably it occurs in the hospital setting in association with correction of the electrolyte disturbance, and it frequently results in death.⁷

We report a similar case having typical magnetic resonance image (MRI) findings of central pontine myelinolysis with neurological deterioration in a patient with traumatic brain injury following rapid correction of severe hyponatremia who eventually died in spite of therapeutic attempt.

Case Report:
A 49-year-old man was admitted to a local general hospital outside Dhaka (according to the note supplied by the hospital) history of closed head injury followed by diminished consciousness level of Glasgow Coma Scale (GCS) E3V4M6 and no focal neurological deficit. On physical examination, he showed normal sensory and motor functions in all extremities. His pupils were equal and demonstrated a normal light reflex. His vital signs were within normal limits. There were no biochemical abnormalities during his admission and he was managed conservatively. Two days after admission, he suddenly became drowsy, confused and disoriented without evident neurological deficit, but his serum sodium was found to be 106 mmol/L (reference values of 135–145 mmol/L), serum potassium was 3.0 mmol/L (reference values of 3.5-4.5 mmol/L), and chloride was 70.8 mmol/L (reference

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values of 96–112 mmol/L). The serum osmolality was 242 mOsm/kg (normal 185-295 mOsm/kg), and the blood sugar level was 92 mg/dL. A syndrome of inappropriate antidiuretic hormone secretion (SIADH) was suspected on the basis of the following evidence: increased extracellular volume, decreased uric acid levels, urine sodium excretion >20 mEq/L, urine osmolality >100 mOsm/L and blood pressure in the normal range.

He was treated with hypertonic saline solution infusion (3% sodium chloride solution) at the rate of 1-2 ml/kg body weight per hour to elevate his plasma sodium concentrations. Over the next 48 hours the serum sodium was raised to 123 mmol/l, and it was raised further to 141 mmol/l during the ensuing five days. Ten days after admission, he became stupor with a progressive spastic quadriparesis, mixed bulbar and pseudobulbar palsy, anarthria and dysphagia. Computed tomography (CT) of the brain was normal. He was then transferred to our neurological centre and underwent MRI of brain using standard T1- and T2-weighted sequences. Brain MRI showed hypointense, well circumscribed, circular area in the pons sparing the tegmentum and surrounded by a ring of normal appearing pontine tissue with normal size of the fourth ventricle and no mass effect in T1-weighted images (Figure 1), and symmetrical areas of signal hyperintensity in the central portion of the pons on T2-weighted images, consistent with a diagnosis of CPM (Figure 2). There was no evidence of extra-pontine myelinolysis. A cerebrospinal fluid examination was unremarkable, showing no signs of blood–brain barrier damage. Daily levels of serum sodium and potassium were monitored.

He was managed in intensive care unit with ventilator support. Based on sporadic observations in the literature, the patient was initially started on high dose steroid therapy (methylprednisolone 1,000 mg/day intravenously for 2 days). The neurological picture remained stable with the management. But on the following day, the patient eventually died in spite of therapeutic attempt.

Central pontine with/without extrapontine myelinolysis is a well-recognized complication of hyponatremia and rapid correction of hyponatremia. Since the original description in chronic alcoholic patients, this pathology has been encountered in the chronicity of hyponatremia (>48 hours), sodium levels <120 mmol/L, a rapid correction of sodium (>25 mmol/L rise in 48 hours or >12 mmol/L in 24 hours), associated hypokalemia, hypoglycemia or hypoxia, malnutrition, transplant, hepatic, diabetic, HIV, burn and other chronically debilitated patients.1,8,9

Fig.-1: Axial (A) and Sagittal (B) Magnetic resonance (MR) T1 weighted images showing hypointense, well circumscribed, circular area in the pons sparing the tegmentum and surrounded by a ring of normal appearing pontine tissue (Arrow head) with normal size of the fourth ventricle and no mass effect.
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CPM is pathologically defined as a symmetric area of myelin disruption in the center of the basis pontis. Similar symmetric pathologic lesions have also been identified in extrapontine locations, i.e. EPM, including the cerebellar and neocortical white/gray junctional areas, thalamus, subthalamus, amygdala, globus pallidus, putamen, caudate and lateral geniculate bodies. EPM can occur in isolation, but it is found in 10% of patients with CPM.\(^8\)

The clinical presentation of CPM is variable; it can be asymptomatic when the lesion is small. The characteristic clinical manifestations of myelinolysis are spastic tetraparesis and pseudobulbar paralysis leading to dysphagia, dysarthria, weakness of the tongue, and emotional lability. These findings are caused by destructive lesions in the corticospinal and corticobulbar tracts in the pons. In severe cases, patients can be left in a state of mutism and paralysis with relatively intact sensation and comprehension or the patient’s level of consciousness may be impaired, varying from lethargy to coma. A large central pontine lesion can cause a locked-in syndrome. EPM is characterized by tremors and ataxia.\(^3,10\)

Abnormality of the basal ganglia is known to cause various cognitive dysfunctions and abnormal behavior via the involvement of the corticostriatothalamic or cortical–subcortical circuit through the basal ganglia, while the role of pontine pathology for cognitive function and personality remains unclear. One possible hypothesis is that disruption of the corticopontine networks may cause symptoms, and another hypothesis involves the interruption of the neurotransmitter pathways that emerge from the brainstem, possibly the dopaminergic and cholinergic pathways, which impacts on cognitive functioning.\(^11\)

Current guidelines recommend that, in the setting of chronic or severe hyponatremia, the rate of correction should not exceed 12 mEq/L in the first 24 hours and 20 mEq/L in the initial 48 hours.\(^12\) In the present patient, central pontine myelinolysis developed with the rapid correction of severe hyponatremia. Previous reports have also described the occurrence of central pontine myelinolysis despite sodium correction at a rate following the above guidelines, and it has been proposed that greater caution in correction should be used (i.e., <8 mmol/L per 24 hours rise in sodium levels).\(^13\) This may be due to concomitant hypokalemia, which was not treated before sodium correction. Reduced endothelial cell membrane concentration of NaK-ATPase in hypokalemia may predispose the cell to injury by osmotic stress associated with the rapid rise in the serum sodium concentration.\(^14\)

The exact mechanism of demyelination is still unknown. During hyponatremia, cerebral edema is...
limited by the adaptive loss of brain solutes consisting of electrolytes and osmolytes. Following the correction of hyponatremia, the re-accumulation of brain solutes takes place within 24 hours to several days. However, when chronic hyponatremia is corrected rapidly prior to the activation of adaptive mechanisms, blood becomes relatively hypertonic to the brain, with resultant shift water out of the brain. The osmotic injury to the vascular endothelial cells and this causes the release of myelinotoxic factors, the production of vasogenic edema and/or brain dehydration. This then causes separation of the axon from its myelin sheath with resultant injury to the oligodendrocytes, particularly at the interface of the gray and white matter with subsequent myelinolysis and necrosis.\textsuperscript{6,15}

Diagnosis is based on the detection of electrolyte abnormalities and MR findings. Computed tomography of brain may show central pontine and extrapontine lesions as symmetrical areas of hypodensity. Because myelinolytic lesions are not demonstrated within the first 2 weeks using conventional MRI pulse sequences, the diffusion weighted image sequence has been proposed to confirm the diagnostic MRI findings of central pontine myelinolysis, including symmetric signal intensity abnormalities in the central pons on T2-weighted and fluid attenuated inversion recovery imaging. This may progress to classic hyperintense ‘trident-shaped’ central pontine abnormalities, with sparing of the ventrolateral pons and corticospinal tracts. Such lesions are associated with decreased T1 signal intensity without enhancement or mass effect. Myelinolytic lesions do not typically enhance with gadolinium. Diffusion-weighted imaging (DWI) may show the presence of hyperintensity in the same areas with reduction of the apparent diffusion coefficient (ADC) in the abnormal pontine regions.\textsuperscript{3,16}

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.\textsuperscript{17}

There is no specific treatment for CPM. Care is supportive with the goal of preventing complications such as aspiration pneumonia. Central pontine and extrapontine myelinolysis can occur following even gradual correction of hyponatremia, as shown in the present case. More attention should be paid to correcting hyponatremia combined with hypokalemia.\textsuperscript{18,19}

In a study of 44 patients with central pontine and extrapontine myelinolysis,\textsuperscript{19} the outcome did not depend on the severity of neurological deficits during the acute phase of the condition or on concomitant internal diseases, including the degree of hyponatremia. The extent of the initial pontine lesion was not correlated with the severity of clinical findings during the acute phase of disease, nor was persistence of the pontine lesion as usually seen on magnetic resonance imaging correlated with clinical improvement. In that study, of the 34 patients for whom follow-up data were available, 32 survived. Of those, 11 completely recovered, 11 had some deficits but were independent, and 10 were dependent (4 through disorders of memory or cognition, 3 with tetraparesis, 2 with cerebellar ataxia, 1 with polyneuropathy). They concluded that patients with cerebral myelinolysis survive if the nonspecific secondary complications of transient illnesses such as aspiration pneumonia, ascending urinary tract infection with subsequent septicemia, deep venous thrombosis, and pulmonary embolism can be avoided.

In the past, myelinolysis was believed to have a grim prognosis; however, it is now clear that manifestations can vary and patients with severe complications can survive. The outcome varies widely, from almost complete recovery to little or no improvement. Myelinolysis itself cannot be specifically treated once symptoms have developed. Corticosteroids do not appear to be effective.\textsuperscript{3}

Conclusion:

Though typical MRI findings may diagnose central pontine myelinolysis, it is emphasized that prevention is of utmost importance while correcting hyponatremia because once established, central pontine myelinolysis carries a very poor prognosis in terms of mortality and severe disability.

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Patient’s consent: An informed written consent was obtained from the patient’s legal guardian.

Ethical approval: There is no ethics issue in this paper.

Reference: