Osmotic demyelination syndrome due to rapid fluctuations in serum sodium - a case report

RAMYA LAKSHMINARASIMHAN
Department of Neuro Surgery,
CHRISTIAN MEDICAL COLLEGE

Abstract:
Demyelination of the neural structures can occur due to rapid correction of chronic hyponatremia, and the diagnosis can now be made by radiological demonstration of hyperintense signals on T2 weighted MRI sequences. This is a case report of a 13 year old boy with a craniopharyngioma who underwent a transcranial radical excision of the tumour. Post-operatively he developed diabetes insipidus with a wide fluctuation in the serum sodium levels despite management with intravenous fluids and pitressin analogues. He developed spastic paresis of all 4 limbs with preservation of only vertical eye movements, suggestive of a locked in syndrome. MRI brain showed hyperintense signals within the brainstem and the basal ganglia with no mass effect. A diagnosis of osmotic demyelination was made, and the patient gradually recovered with supportive care over a period of 3 months.

Keyword:
craniopharyngioma, diabetes insipidus, osmotic demyelination

Case Report:
A 13 year old boy presented with features of a suprasellar mass with obstructive hydrocephalus (Fig.1). He underwent transcranial radical excision of the mass and the histopathology was reported as a craniopharyngioma. He developed diabetes insipidus from day 1 and was managed with appropriate intravenous fluids and oral / parenteral vasopressin analogues to maintain target sodium levels between 135-145 mEq/ L. In spite of our best efforts his sodium levels fluctuated as shown in Fig 4. He started developing episodes of generalized seizures with hyponatremia on day 7 after surgery. When the seizures occurred the sodium was corrected aggressively, with the result that he developed hypernatremia. He then developed progressive spastic quadriaparesis with dysphagia, dysarthria, ocular paresis...
with only preserved vertical eye movements. He also developed low frequency tremors, distal more than proximal in both the upper limbs. The clinical features were suggestive of a pontine locked in syndrome with possible basal ganglia involvement as well. CT brain done on day 7 after surgery when he developed these symptoms (Fig 2) showed a 10 mm thick right frontal subdural hygroma with no mass effect on the underlying brain. There was no operative site haematoma. T2 weighted sequences of MRI done a month after surgery showed hyperintensities in the pons, midbrain and bilateral basal ganglia with no perilesional oedema (Fig 3). Demyelination due to rapid fluctuations in the serum sodium levels was then considered. He was managed conservatively with supportive therapy including nursing care for the spastic paresis, physiotherapy and speech therapy with which he recovered gradually to independent ambulation over a period of 3 months.

Discussion:
Osmotic demyelination syndrome (central pontine myelinolysis, CPM) has been reported in a variety of instances, commonly in alcoholism, malnutrition and burns. This is a rare instance of osmotic demyelination occurring in a patient with postoperative diabetes insipidus due to rapid correction of correction of hyponatremia. Adams and colleagues first reported CPM in alcoholics in 1959 and a correlation with rapid correction of hyponatremia was established by 1982. The term osmotic demyelination syndrome rather than CPM has been used because of involvement of extrapontine regions. The causative factor could not be identified for a long time and hypokalemia was the first common abnormality identified on the basis of ECG observations. The animal studies done by Laureno in dogs and Kleinschmidt et al in rats established sodium levels as the triggering factor involved in osmotic demyelination syndrome.

Pathogenesis:
The difference in the cellular response to acute and chronic hyponatremia explains the pathogenesis of the osmotic demyelination syndrome. In case of acute hyponatremia, the cell swells due to free transport of water across the cell membrane. To avoid cellular swelling there is active transport of cations as an immediate response, and later a slower process to transport organic solutes from within the cell to outside to adjust cellular tonicity. The percentage contribution of the solutes to maintain the cellular tonicity is as follows - potassium 29%, chloride 19%, amino acids 15% and sodium 13%. When there is rapid correction of hyponatremia, the rate of reversal is faster than the rate of accommodation of the cellular mechanisms. Hence there is cellular dehydration causing cell shrinkage leading to cell death. The oligodendrocytes seem to be more sensitive to this electrolyte disturbance, hence the demyelination changes are more common in the pons because of the increased grey-white matter apposition compared to other regions, followed by the basal ganglia. Hence this pathology is more likely to happen in cases of chronic hyponatremia where all the accommodative shifts have occurred, rather than in acute hyponatremia where the slower shifts have not yet occurred and therefore the accommodation is faster.

Triphasic response in postoperative diabetes insipidus
Diabetes insipidus can present in 3 patterns as transient, permanent or a triphasic response. The pathophysiology behind the triphasic response is initially a hypothalamic dysfunction occurs causing polyuria which lasts for 4-5 days.
This is followed by release of vasopressin from the degenerating pituitary gland which is responsible for the second antidiuretic phase which lasts for another 5-6 days. Finally depletion of vasopressin stores causes permanent diabetes insipidus, the second polyuric phase. In this patient, the initial correction of hypernatremia in the immediate postoperative period with pitressin analogues later lead to worsening of the hyponatremia subsequently when there was release of vasopressin from the degenerated pituitary gland. This period of transition from the first to second and then the third phase might have caused the rapid fluctuations in the serum sodium leading to the osmotic demyelination. He then required a permanent dose of oral vasopressin (Minirin) at discharge due to the depletion of the vasopressin stores.

Management and treatment:
This syndrome commonly develops 2 to 6 days following rapid correction of hyponatremia. It is picked up late due to two reasons, one being myelinolysis is not commonly considered as a differential diagnosis, and the second being that MRI show up the lesions only after a minimum of 2 weeks after the neuronal damage has occurred. The clinical presentation of osmotic demyelination syndrome include flaccid followed by spastic quadriparesis with dysphagia and dysarthria due to corticospinal tract involvement or as a locked in syndrome with ocular paresis when the lesion extends to involve the pontine tegmentum. The midbrain also could be involved, with medullary involvement being less likely. The primary tool for radiological diagnosis of myelinolysis is MR imaging showing hyperintensities on T2 weighted sequences (Fig 3). Diffusion weighted images of MRI are specific, but CT generally does not reveal myelinolysis. There has been no correlation found between the size of the lesion on MRI and the severity of the clinical features, but there has been a strong correlation between the disappearance of the lesions on diffusion weighted sequences and clinical improvement. T2 weighted MRI changes still persisted and hence can not be used to prognosticate the condition.

The management of this clinical syndrome includes supportive care. Good nursing care for a patient with spastic quadriparesis with active physiotherapy remains the mainstay of treatment. Extrapyramidal symptoms have been found responding to dopamine analogues. The prognosis depends on the severity of the clinical features at the onset and the morbidity increases with increased duration of hospitalization. **Correction of hyponatremia:**
Patient has to be allowed to drink water according to the thirst and if he is not able to compensate orally, then we can supplement using hypotonic intravenous fluids as 5% dextrose in water and half-normal saline. The correction of hyponatremia has been recommended to be at the rate advised below.

**Allowed rate of sodium correction**
Change in serum sodium = Infusate (Na+K)-SerumNa
Total body water (L)+1 Max rate of change of sodium=3mmol/3 hrs. This formula does not give an estimate of the ongoing fluid losses, hence the serum sodium should be monitored once in every 6-8 hours for appropriate fluid replacement. The rate of correction of hyponatremia depends on the duration of the hyponatremia and the clinical condition of the patient. The chronicity of hyponatremia is difficult to determine in most cases, and the exact classification of hyponatremia as acute or chronic is also not clear.
Rapid correction of sodium is justified in cases with acute symptomatic hyponatremia and there has been no evidence that this can cause osmotic demyelination. This has been supported by a retrospective study of rapid correction of hyponatremia in 27 instances in 13 patients with psychogenic polydipsia.9

This confusion in treating hyponatremia has been discussed by many3, 10, 11 including Berl et al in his article as “Damned if we do and damned if we don’t”.12 The mortality rate is higher in patients who had a rapid decrease in serum sodium from 134-120mEq/L rather than in patients with a initial low sodium <120mEq/L on admission.13,14 The incidence of mortality increased with slow correction of hyponatremia in such cases.

**Other biochemical parameters:**
Another important factor in osmotic demyelination syndrome is the serum potassium and phosphorus levels. Potassium is a major intracellular cation and its depletion causes osmotic demyelination. Phosphorus depletion limits the function of sodium potassium ATPase, hence restricts adaptation to the osmotic changes.15 Hence potassium and phosphorus need to be corrected before correction of hyponatremia.

**Other treatment strategies:**
The other treatment strategies in osmotic demyelination syndrome is based on the fact that the blood brain barrier permeability is increased in this condition. It was found that corticosteroids can be used as they were found to lower the blood brain barrier permeability. Also another option is re-lowering of the serum sodium after rapid correction of chronic hyponatremia which was found to be beneficial if performed early in the course (12 to 24 h). In a study by Gankam et al16, they compared the mortality, blood-brain barrier permeability, and microglial activation in rats after the rapid correction of chronic hyponatremia. Three groups of rats were studied after correction of chronic hyponatremia, one group treated with sodium chloride with dexamethasone, another with sodium chloride but without dexamethasone and the third group with sodium chloride followed by re-induction of hyponatremia. It was found that treatment with dexamethasone or re-induction of hyponatremia effectively prevented the opening of the blood-brain barrier, reduced neurological manifestations, and decreased microglial activation but only re-induction of hyponatremia resulted in a significant decrease in mortality 5 days after the correction of chronic hyponatremia. Hence re-lowering of sodium after rapid correction of hyponatremia may be more favoured than steroids.

**Conclusion:**
Sodium control should be meticulous in patients with fluid – electrolyte disturbances. The onset of spastic paresis with or without extrapyramidal features in a patient with large fluctuations in serum sodium levels should raise the suspicion of central osmotic myelinolysis.
References:


Fig 1: Preoperative imaging

Fig. 2: Postoperative CT
Fig. 3: T2W MRI sequences showing demyelination in the brainstem and basal ganglia

Fig. 4: Graph showing the fluctuation in the postoperative serum sodium levels