Extra-Pontine Myelinolysis in a Case of Pan-hypopituitarism Due to Empty Sella Syndrome

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Abstract
Rapid correction of hyponatremia is known to cause central pontine myelinolysis (CPM). It may concurrently involve other areas of brain as well, referred as extra-pontine myelinolysis (EPM). Isolated EPM however is a very rare occurrence. We present a case of EPM where the hyponatremia was secondary to hypothyroidism due to empty sella syndrome. Chronic hyponatremia should always be corrected slowly to avoid such osmotic myelinolysis syndromes (OMS).

Introduction
Chronic hyponatremia should always be corrected slowly to avoid osmotic myelinolysis syndromes (OMS). Extra-pontine myelinolysis (EPM) should be suspected in patients who develops ataxia, tremor, decreased speech and oro-bucco-lingual movements after illness requiring intravenous fluids. OMS can be effectively treated with symptomatic support.

Case Report
A 58 year male presented with history of dysphagia, ataxia, and dysarthria. Patient was earlier admitted 15 days back in a nursing home with history of persistent vomiting, generalized weakness and poor oral intake. He was found drowsy on admission and then had an attack of tonic clonic seizure. Routine investigations showed severe hyponatremia (106 meq/L). Other investigations were normal. Hyponatremia was corrected with 3% sodium chloride. Serial electrolytes were monitored (Table 1). CT scan of the brain was normal. Patient was discharged on day 7.

Patient was referred to our centre 5 days later when he presented with dysphagia, ataxia and dysarthria. He was found to be drowsy with a poor gag reflex. He had rigidity in all four limbs and had mask like face. There were no tremors. Rest of neurological finding were normal. Routine blood investigations including blood sugar and electrolytes were normal.

A direct complication of correction of hyponatremia in addition to other differentials was suspected and hence an MRI of brain was requested which showed symmetrical hyperintensities on T2 images in bilateral basal ganglia only in caudate nucleus and putamen with characteristic sparing of globus pallidus (Figure 1). There was no hyperintensity in pons (Figure 2). MRI also showed empty sella (Figure 3). Thyroid function test showed T3 <40.0 ng/dl (81-178 ng/dl), T4- 3.41 mcg/dl (4.5-12.5 mcg/dl), TSH 3.47 IU/ml (0.4-4 IU/ml). Basal cortisol was 3.52 mcg/dl (5-25 mcg/dl).

These reports suggested hypopituitarism. A diagnosis of isolated extrapontine myelinolysis following correction of hyponatremia due to hypopituitarism subsequent to empty sella syndrome was made. Patient was put on Ryles tube feeding. He was started on aspirin, thyroxine

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Table 1: Serial electrolytes (mEq/L)

<table>
<thead>
<tr>
<th>Day</th>
<th>Na</th>
<th>K</th>
<th>Cl</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>106</td>
<td>3.7</td>
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<td>2</td>
<td>110</td>
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<td>73</td>
</tr>
<tr>
<td>3</td>
<td>112</td>
<td>5.0</td>
<td>81</td>
</tr>
<tr>
<td>4</td>
<td>116</td>
<td>3.5</td>
<td>85</td>
</tr>
<tr>
<td>5</td>
<td>129</td>
<td>3.3</td>
<td>88</td>
</tr>
<tr>
<td>6</td>
<td>130</td>
<td>3.1</td>
<td>94</td>
</tr>
</tbody>
</table>

All values in mEq/litre

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Fig. 1: MRI of brain showing symmetrical hyperintensities on T2 images in bilateral basal ganglia (caudate nucleus and putamen with characteristic sparing of globus pallidus)

Fig. 2: MRI: No hyperintensity in Pons

Fig. 3: MRI showing empty sella

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and prednisolone. He was able to swallow full meal after about 10 days of admission. He was discharged on low dose aspirin, statin, thyroxin and maintenance doses of prednisolone.

**Discussion**

Adams et al in 1959 described a new disease named central pontine myelinolysis (CPM), in four alcoholic and malnourished patients. Later it was recognized that identical lesions can occur in other areas of brain as well and this condition is called as extrapontine myelinolysis (EPM).

Our patient had a nursing home admission for symptomatic hyponatremia which was gradually corrected. He presented to us within a week with drowsiness, ataxia, pseudobulbar syndromes and extrapyramidal features.

His differential diagnosis included multi-infarct state, hyponatremia treatment related osmotic demyelination syndrome (OMS), metabolic/nutritional deficiency related disorder and subdural hematoma. MRI brain ruled out multi-infarct state and subdural hematoma. Wernicke’s encephalopathy can be precipitated following a dextrose administration during hospital admission in thiamine depleted patients. However, in addition to drowsiness and ataxia, these patients have ophthalmoplegia which was lacking in our patient. His MRI revealed a unique finding of symmetrical hyperintensities only in caudate nucleus and putamen with sparing of globus pallidus and pons (ruling out classical CPM). Bilateral abnormalities of basal ganglia on MRI have been described in various systemic, metabolic, degenerative and vascular conditions. The differential diagnosis also includes focal flavivirus infections, carbon monoxide poisoning, toxoplasmosis, primary CNS lymphoma and degenerative CNS disorders like Huntington’s disease.2 Our patient denied alcohol addiction and was immunocompetent. The basal ganglia abnormality described above in setting of hyponatremia correction favours diagnosis of EPM.

CPM and EPM usually follow rapid correction of hyponatremia. Together they are described as osmotic demyelination syndrome. The association includes alcoholism, malnutrition, prolonged diuretic use, post liver transplant, lithium toxicity etc. Our patient followed classic dual course described in this condition. Patients presenting with symptoms of hyponatremia responds to the treatment for the same. They then develop signs of osmotic demyelination syndrome (OMS). CPM patients may have dysarthria, dysphagia, quadripareisis and altered sensorium. Coexistent movement disorders would suggest additional diagnosis of EPM.

Isolated EPM is rare. In a necropsy series of 58 cases of OMS, isolated CPM was present in majority of cases followed by combined CPM with EPM. Altered sensorium, ‘locked-in’ syndrome, quadriplegia, pseudobulbar palsy, nystagmus or cranial nerve palsies are usually absent in isolated EPM. Positive findings include ataxia, tremor, decreased speech and oro-bucco-lingual movements.

In our patient, signs of parkinsonism like rigidity, mask like face with ataxia, severe dysphagia and poor gag reflex developed within one week of treatment of symptomatic hyponatremia with hypertonic saline in a private nursing home. Further investigations revealed central hypothyroidism, hypocortisolism with empty sella on MRI scan. The findings of symmetrical hyperintensities on T2 weighted images in basal ganglia with sparing of globus pallidus is classic of EPM. Rapid correction of chronic hyponatremia is more dangerous for development of ODS as compared to acute hyponatremia. Though sodium rise need not be in excess of 10 meq/L/day for condition of OMS to develop, there may be no safe limit for a given patient regarding the rate of sodium rise. The patient poor gag reflex improved and patient had normal meals within 2 weeks of thyroxin and prednisolone replacement, suggesting transient metabolic neurological impairment. Apart from basal ganglia, MRI scan in EPM may show hyperintensities in cerebellum, external capsule, hippocampus, cerebral cortex/sub cortex and thalamus.

Common causes of hyponatremia are therapy with thiazides, syndrome of inappropriate secretion of antidiuretic hormone in postoperative state, polydipsia in psychiatric patients, gastrointestinal fluid loss, ingestion of dilute fluid, and accidental ingestion of excessive water. Hypothyroidism may be a hidden cause behind chronic hyponatremia especially in elderly. Our patient had remarkable finding of empty sella on MRI with hypopituitarism causing central hypothyroidism. The hypocortisolism may also predispose to hyponatremia because of failing inhibition of vasopressin secretion (cortisol is a physiological tonic inhibitor of vasopressin secretion). Recently vasopressin V2 receptor antagonist like tolvaptan have been used in resistant cases of symptomatic hyponatremia.

**References**