# Osmotic Demyelination Syndrome; Treated with Re Lowering of Serum Sodium.

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**Abstract-**

***Purpose:*** This case report demonstrates that if serum sodium is re lowered early in the course of Osmotic demyelination syndrome (ODS), many of its devastating consequences may be avoided. In animal models, initiation of re-lowering within four hours of symptom onset has been associated with better outcomes than initiation within eight to ten hours of symptom onset. As there is no effective therapy for the condition we suggest a trial of re lowering of serum sodium early in its course.

***Case Report:*** A 33 years old woman who was on diuretics presented to us with delirium in the form of hypo responsiveness for two to three days after suffering from an acute gastroenteritis. On evaluation she was found to have hyponatremia that was corrected too rapidly and was followed by an initial improvement and later worsening of neurological signs. T2 weighted MRI of the brain showed hyperintense lesions in pons and in extra pontine areas including thalamus and cerebellum. The patient was diagnosed to be suffering from osmotic demyelinating syndrome. Re-lowering of the patient's serum sodium with dextrose 5% and desmopressin was tried along with aggressive supportive treatment. Patient was reassessed after regular intervals and at 6 months post treatment patient has recovered almost completely and is living an independent life.

***Conclusion:*** Based on the absence of other effective therapies, and the poor prognosis associated with ODS, it is suggested re-lowering the serum sodium to a level that is just below the maximal target value at 48 hours of less than 18 meq/L above the initial serum sodium. Re-lowering therapy should be initiated as quickly as possible after the onset of neurologic symptoms that are attributed to ODS.

**Key Words:** Osmotic demyelination syndrome, re-lowering therapy

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## CASE REPORT

Our patient was a 33 years old woman, married for one year with history of recent childbirth complicated with gestational hypertension.

The patient presented to us with delirium in the

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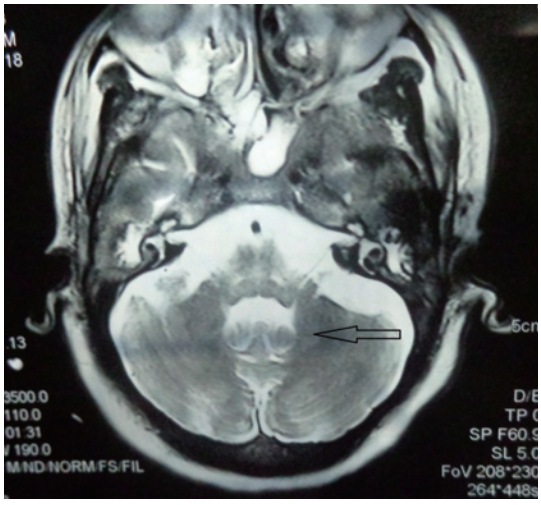

**Figure 1.** T2 weighted MRI of the brain showed hyperintense lesions in pons.

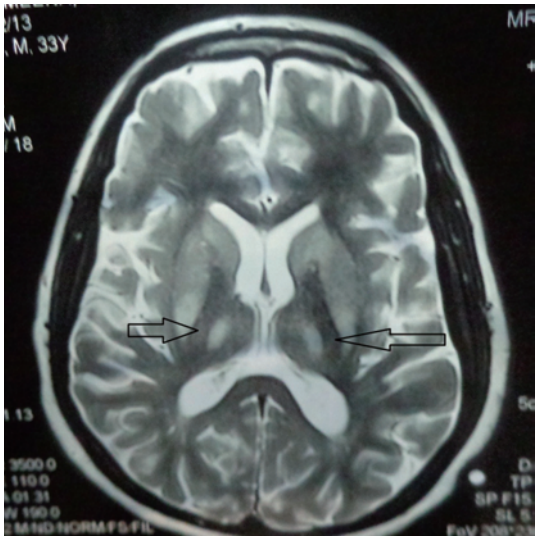

**Figure 2.** T2 weighted MRI of the brain showing hyperin tense lesions in thalami.

form of hypo responsiveness for two to three days after suffering from an episode of acute gastroenteritis. The patient was taking diuretics for hypertension. Serum electrolytes showed hypokalemia and hyponatremia (sodium of 101 meq/l and potassium of 2.6 meq/l). Brain imaging was normal and there were no localizing signs. With this a diagnosis of acute gastroenteritis and diuretic induced hyponatremia and hypokalemia was made. The diuretics were stopped, the patient was given around 1 L of IV hypertonic saline and her mental status started improving and she was soon out of encephalopathy but within 48 hours neurological deterioration started to occur.

The patient again developed a confused mental status, started talking irrelevant, ataxia, and tremor, had horizontal gaze paralysis and soon developed spastic quadriplegia. All limb reflexes were found to be hyperactive and Babinski sign positive. Also signs of pseudo bulbar palsy in the form of head and neck weakness, dysphagia and dysarthria were present. It was noted that the serum sodium was rapidly corrected from 101 to 122 meq/l within a period of 24 hours.

CSF studies demonstrated mildly increased opening pressure and elevated proteins. Electroencephalography showed diffuse bihemispheric slowing. T2 weighted MRI of the brain showed hyperintense lesions in pons and in extra pontine areas including thalamus and cerebellum .The patient was diagnosed to be suffering from osmotic demyelinating syndrome.

Re-lowering of the patient's serum sodium with dextrose 5% and desmopressin at the rate of 1 mmol/hour up to a serum sodium of 116 mmol/L in a span of 48 hours was tried and there was some improvement especially in the mental status and muscle power. Patient was kept in the hospital for 6 weeks during which aggressive supportive treatment and occupational, physical, speech, and language therapies were instituted.

Patient was reassessed after regular intervals and at 6 months post treatment patient has recovered almost completely and is living an independent life.

## DISCUSSION

Central pontine myelinolysis (CPM) was first diagnosed as a unique clinical entity by Adams et al when they published their findings in 1958, observing that patients who suffered from alcoholism or malnutrition developed spastic quadriplegia, pseudo bulbar palsy, and varying degrees of encephalopathy or coma from acute, non inflammatory demyelination that centered within the basis pontis[1]. Osmotic demyelination syndrome was first recognized by Tomlinson in 1976. It is a well recognized complication of treatment of patients with severe and prolonged hyponatraemia, particularly when corrected too

rapidly[2]. It has also been described in patients who are treated for hypernatraemia and in patients with a prolonged period of serum hyperosmolality[3]. Other conditions associated with an increased risk of the syndrome include chronic alcoholism, malnutrition, prolonged diuretic use, liver failure, receiving an organ transplant, and extensive burns[3].

Conditions predisposing patients to central pontine myelinolysis include alcoholism, liver disease, malnutrition, and hyponatremia.

Risk factors for central pontine myelinolysis in the hyponatremic patient include the following:

- Serum sodium of less than 120 mEq/L for more than 48 hours.
- Aggressive IV fluid therapy with hypertonic saline solutions.
- Development of hypernatremia during treatment.

Hyponatremia is common in hospital patients, the incidence being 3-5% for a serum level of 130 mmol/L or less[4] and 0.15% for 120 mmol/L or lower[5]. In most series the mortality from severe hyponatremia (< 120 mmol/L) lies between 40% and 50%, except in settings such as intensive care where it ranges from 10% to 20%.

CPM is defined as concentrated, frequently symmetrical, non-inflammatory demyelination within the central pons. However, in 10% of cases demyelination also occurs in extrapontine regions including the midbrain, thalamus, basal nuclei and cerebellum. The mechanism by which osmotic demyelination syndrome develops involves rapid correction of a chronic osmolar abnormality when there is a deficit of organic osmolytes. This places brain cells, particularly oligodendrocytes, at risk of cell shrinkage and hence demyelination. It is thought that alcoholics and malnourished patients have a general deficiency of organic osmolytes, which puts them at greater risk of cell shrinkage[6] . The pathophysiology is not clear. It has been suggested that, in areas of interdigitation of white and grey matter, cellular edema caused by fluctuations in electrolyte forces results in compression and subsequent demyelination of fiber tracts. The term 'osmotic demyelination syndrome' (ODS) has been coined as it is better suited than CPM for cases, especially those with extra-pontine lesions that result from correction of hyponatremia[4]. In regions of compact interdigitation of white and gray matter, cellular edema, which is caused by fluctuating osmotic forces, results in compression of fiber tracts and induces demyelination. Prolonged hyponatremia followed by rapid sodium correction results in edema. During the period of hyponatremia, the concentration of intracellular charged protein moieties is altered; reversal cannot parallel a rapid correction of electrolyte status. The term osmotic myelinolysis is more appropriate than central pontine myelinolysis for demyelination occurring in extrapontine regions after the correction of hyponatremia [7-10]. Extrapontine myelinolysis, with or without pontine involvement occurs most often in the basal ganglia and thalamus[11]. The difference in location of the lesions results in different clinical presentations. Classically, central pontine myelinosis is associated with dysarthria and dysphagia, due to corticobulbar fibre involvement, as well as an initially flaccid quadraparesis due to lesions in the corticospinal tract. Extrapontine myelinolysis is characterized by tremor and ataxia and may be associated with movement disorders including mutism, Parkinsonism, dystonia, and catatonia[10].

Treatment is supportive, and the outcome is variable. Patients who survive central pontine myelinosis are likely to require extensive and prolonged neurorehabilitation. In a recent study of 34 patients with osmotic demyelination syndrome two died, and, of the remaining 32, a third recovered, a third were debilitated but independent, and a third were dependent[12].

Depending on the severity of the patient's symptoms, aim to raise the serum sodium concentration between 1 mmol and 3 mmol (maximum) every 3 hours. Use the following formula to work out the rate of infusion of the chosen infusate, and then measure the serum sodium concentration every 3 hours. The rate of correction in asymptomatic patients should not exceed 10 mmol/l/day[13].

$$\text{Change in serum sodium} = \frac{[\text{infusate } Na^+ + \text{infusate } K^+] - \text{serum } Na^+}{\text{Total body water (liters)} + 1}$$

A cautious correction of hyponatremia is the best way to prevent the osmotic demyelination syndrome.

The ODS is associated with a poor prognosis and prevention is of primary importance. Among patients who develop ODS, there is support in both animal models and

case reports in humans that re-lowering the serum sodium may be beneficial if initiated soon after the onset of neurologic symptoms of ODS. Supportive therapy is also important.

**Re lowering the serum sodium to treat ODS —** The potential efficacy of relowering the serum sodium after the onset of neurologic symptoms of ODS was demonstrated in a rat model in which severe hyponatremia of three days duration was rapidly corrected with hypertonic saline by 30 meq/L at 24 hours[14].

Data in humans are limited to case reports that suggest benefit from early relowering the serum sodium in patients who have developed symptoms of ODS[15-18].

The optimal approach to the treatment of patients with serum sodium values that have corrected too rapidly and have developed neurologic manifestations consistent with ODS is unclear. Based upon the preceding observations of benefit, the absence of other effective therapies, and the poor prognosis associated with ODS, it is recommended re-lowering the serum sodium to a level that is just below the maximal target value at 48 hours of less than 18 meq/L above the initial serum sodium. The 48 hour goal was chosen because patients with ODS typically present two to six days after overly rapid correction. The efficacy and safety of this approach is unknown.

In the few case reports previously, re-lowering with desmopressin and 5 percent dextrose in water was initiated within hours of the onset of neurologic symptoms and there were substantial reductions in serum sodium (up to 12 meq/L) within the first 12 hours[16-18]. The optimal target serum sodium and rate of re-lowering in patients with ODS have not been defined. A reasonable approach is to lower the serum sodium to a value that is approximately 15 to 17 meq/L above the lowest level when therapy was initiated. As an example, a patient who presented with a serum sodium of 100 meq/L and develops symptoms of ODS with a serum sodium of 130 meq/L should have their sodium level lowered to approximately 115 to 117 meq/L (i.e., an increase just below 18 meq/L, which is the 48 hour goal).

The rate of re-lowering should be approximately 1 meq/L per hour. The patient's neurologic status and serum sodium should be carefully monitored as re lowering is performed.

Re lowering therapy should be initiated as quickly as possible after the onset of neurologic symptoms that are attributed to ODS. In animal models, initiation of re lowering within four hours of symptom onset was associated with better outcomes than initiation within eight to ten hours of symptom onset[14]. In the case reports in humans, re lowering was initiated within a few hours after the onset of neurologic symptoms[15,16]. There is no evidence of benefit in humans when relowering is begun more than 24 hours after the onset of ODS symptoms, but clinicians may choose a trial of re-lowering in this setting.

The re lowering regimen consists of 6 mL/kg lean body weight of 5 percent dextrose in water (D5W) infused over one to two hours plus desmopressin. The usual desmopressin regimen is 1 to 2 micrograms intravenously or subcutaneously at six to eight hour intervals; a 2 microgram dose is preferred in patients with a urine osmolality below the plasma osmolality, since dilute urine can contribute to overly rapid correction. The maximum desmopressin dose is 4 micrograms in patients who do not respond to lower doses.

This regimen should lower the serum sodium by about 2 meq/L; with a goal of lowering the serum sodium at an average rate of approximately 1 meq/L per hour. The serum sodium is measured after each administration of desmopressin and water, and the sequence is repeated until the serum sodium falls to levels that represent a correction of less than 10 meq/L or less than 18 meq/L, depending upon when overcorrection occurred. When this is achieved, the D5W is discontinued and usual therapy for the hyponatremia is reinstituted.

**Supportive therapy —** Some patients with ODS recover function after prolonged periods of severe neurologic impairment. Thus, aggressive supportive therapy should be provided to all patients who were functional prior to the onset of ODS. Since patients with severe ODS frequently develop aspiration pneumonia and respiratory failure, endotracheal intubation and ventilator support are often required. Recovery from seemingly hopeless neurologic deficits can occur and, therefore, supportive therapy should be continued for at least six to eight weeks before concluding that the deficits are irreversible[19,20].

**Plasmapheresis —** Plasmapheresis is an experimental therapy for ODS that may be beneficial[21-23]. A case report of three hyponatremic patients described aggressive

plasmapheresis started immediately after the diagnosis of ODS was confirmed by MRI [8D:\General\manzoor\books\utd\contents\mobipreview.htm]. Although the pontine lesions were unchanged on repeat MRI, two patients markedly improved, with either no or clinically silent residual neurologic deficits, while the third had impaired intermediate-term memory and could walk only with assistance.

Although these results suggest a possible benefit to plasmapheresis, they are difficult to interpret since some patients who undergo rapid correction of hyponatremia experience short-lived, spontaneously reversible episodes of neurologic impairment.

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