

## RAPID OVER CORRECTION OF SODIUM LEADING TO EXTRAPONTINE DEMYELINATION

Abhisek Mukherjee<sup>1</sup>, Arjun Talapatra<sup>2</sup>, Saswati Sinha<sup>3</sup>, S.K. Todi<sup>4</sup>

<sup>1,2</sup>Trainee, Department of Critical Care Medicine, AMRI-Hospitals, Dhakuria, Kolkata, India.

<sup>3</sup>Senior Consultant, Department of Critical Care Medicine, AMRI-Hospitals, Dhakuria, Kolkata, India.

<sup>4</sup>HOD, Department of Critical Care Medicine, AMRI-Hospitals, Dhakuria, Kolkata, India.

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Corresponding Author:

**Dr. Arjun Talapatra,**

Email: arjun.talapatra@rocketmail.com.

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### Abstract

**Background:** Rapid correction of hyponatraemia leads to serious neurological complications, like osmotic demyelination syndrome (ODS). In ODS, magnetic resonance imaging (MRI) often reveals features of pontine myelinolysis, that may occur in isolation or may, sometimes be associated with extrapontine myelinolysis. Isolated extrapontine myelinolysis is rare. We report a case of 47-year-old female who developed dyspepsia & decreased sleep for 6 months. She developed recurrent vomiting after starting some anti-hypertensive and anti-psychotic medications. She was taken to an outside hospital with Na of 95 mEq/L on 31/5/23. Na increased from 95 to 102 to 110 on 31/5/23 and 123 mEq/L on 1/6/23. Her sensorium improved initially but she developed sudden onset unresponsiveness & was shifted back to the ITU on 3/6/23. Her family members shifted her to our hospital on the night of 5/6/23. She developed quadriplegia, depressed level of consciousness and respiratory failure and required ventilatory support.

## INTRODUCTION

Extrapontine myelinolysis, also known as extrapontine demyelination syndrome, is a rare neurological disorder that affects the brain's white matter. It is considered a severe form of osmotic demyelination syndrome (ODS), which is characterized by the destruction of the protective covering of nerve fibers in the central nervous system.<sup>[1]</sup>

Extrapontine myelinolysis primarily affects areas of the brain outside the pons, a region located in the brainstem.<sup>[2]</sup> The condition typically occurs as a result of rapid shifts in the body's sodium levels, often caused by overly rapid correction of low sodium levels (hyponatremia). This can happen during medical treatments or conditions such as chronic alcoholism, liver disease, malnutrition, or hormonal imbalances.

The exact mechanism behind extrapontine myelinolysis is not completely understood. However, it is believed that the rapid correction of sodium levels causes the brain cells to lose or gain water too quickly. This abrupt shift in water content can damage the myelin sheath, which is responsible for insulating and protecting nerve fibers. As a result, the nerve fibers lose their ability to transmit signals efficiently, leading to various neurological symptoms.

The symptoms of extrapontine myelinolysis can vary widely depending on the affected areas of the brain.

Common manifestations include weakness, movement disorders, spasticity, cognitive impairment, behavioral changes, speech difficulties, swallowing difficulties, and vision problems. In severe cases, individuals may experience seizures, coma, or even death.

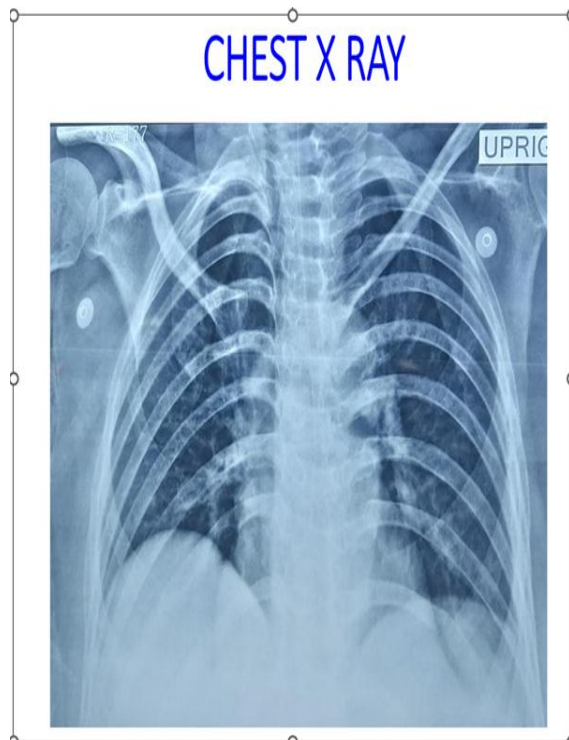
Diagnosis of extrapontine myelinolysis often involves a combination of medical history, physical examination, neurological assessments, and imaging techniques such as magnetic resonance imaging (MRI). MRI scans can help detect characteristic changes in the affected brain regions, such as demyelination or swelling.

Treatment of extrapontine myelinolysis focuses on addressing the underlying cause. In cases where hyponatremia is the cause, a gradual correction of sodium levels is essential to prevent further damage. Rehabilitation therapies may be beneficial to address motor and cognitive impairments and improve overall functional abilities.

### CASE REPORT

A 47-year-old female patient developed dyspepsia and decreased sleep for 6 months. She developed recurrent vomiting after starting some anti-hypertensive (tab Olmesartan 40 mg + Tab Amlodipine 5mg+ Tab Hydrochlorothiazide 12.5 mg) and anti-psychotic medications (Tab Paroxetine 2.5 mg + Tab Clonazepam 0.5 mg). She was taken to an outside hospital with Na of 95 mEq/L

on 31/5/23. Na increased from 95 to 102 to 110 on 31/5/23 and to 123 mEq/L on 1/6/23. Her sensorium improved initially but she developed sudden onset of unresponsiveness and was shifted back to ICU on 3/6/23. The family members transferred her to our hospital on the night of 5/6/23.



	31/5/23	1/6/23	2/6/23	3/6/23	5/6/23	6/6/23	7/6/23	8/6/23	10/6/23	11/6/23
Hb	12.9	11.4	10.8	10.7	11.2					
TC	11,050	6650	14,900	15,000	12,700					
Platelets		2.39 L		2.41 L						
Na	95/110	123	126	124/128	124	128.1	127.6	127.6	126.4	129.5
K	3.2/3.5	3.9	3.1	3.1/3.2	3.5	3.3	4.37	4.7	5.18	4.66
Mg			1.6							
Urea	18	18	19	22						
Creat	0.8	0.7	0.8	0.52						0.53
AST/ALT	33/30		20/29	25/20			19/16			21/15
Alk Phos	108		101							
Albumin/Globulin	3.9/2.8		4/3	3.76/2.8						
Urine Na	23.2									

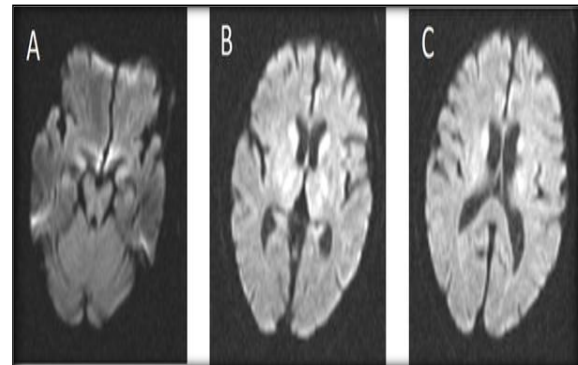
#### ECHOCARDIOGRAPHY (DONE OUTSIDE)

LVEF – 63%, normal sized cardiac chambers, no regional wall motion abnormalities, grade 1 LV diastolic dysfunction.

She was initially managed conservatively, fluid resuscitation started. She was initially given Levitracetam prophylactically. EEG was done which showed diffuse encephalopathy. She was given supportive treatment and shifted to HDU. However, she was shifted back to ITU on 10/6/23 with two

episodes of GTCS. She was given stat dose of midazolam and then started on Levitracetam and Fosphenytoin. Repeat EEG showed frequent epileptiform discharges and background changes. Tab Clobazam was added.

MRI brain done outside showed symmetrical bilateral basal ganglia signal changes. Her sensorium remained poor with no purposeful eye opening. The uncertain prognosis was explained to her family members. They choose to take the patient discharged against medical advice to a lower cost ICU in view of prolonged duration of treatment.



**Axial diffusion weighted MRI images showing normal brainstem (A); hyperintensities in bilateral caudate nucleus and thalami (B); and hyperintensities in bilateral corona radiata and caudate nuclei (C)**

## DISCUSSION

In hospitalized patient's hyponatremia is the most commonly encountered serum electrolyte imbalance. The non-osmotic release of anti-diuretic hormone (ADH) from supraoptic and paraventricular nuclei causes free water retention and dilutional hyponatraemia.<sup>[3]</sup> Severe hyponatraemia (serum sodium < 120 meq/L) is a serious electrolyte disorder associated with life-threatening neurological complications.<sup>[4]</sup> Acute hyponatraemia causes increased intracranial pressure and produces cerebral oedema. At the same time rapid correction of hyponatraemia leads to disastrous consequences like ODS.<sup>[5]</sup> So hyponatraemia should be treated very judiciously, weighing the risks and benefits. ODS causes damage to myelin sheath without affecting axons and neurons. No inflammatory infiltrate is seen.<sup>[6]</sup> In a pathological case series (n=58) isolated pontine lesions were seen in 50% of cases. Pontine and extra-pontine involvement was evident in 30% cases and isolated extra pontine involvement was seen in 20% cases.<sup>[2]</sup> In the present case, there were changes suggestive of extra-pontine myelinolysis only. ODS has a peak incidence in adults aged 30 to 60 years with male predominance.<sup>[7,8]</sup> The clinical presentation of ODS is characterized by changes in the cognitive function, quadreparesis with dysphagia, dysarthria and pseudobulbar symptoms, among others.<sup>[7]</sup> MRI has got a greater sensitivity and specificity than CT in diagnosing changes of myelinolysis. In ODS, MRI

typically reveals trident shaped, symmetrical signal change within the pons on T2-weighted images. Transverse fibres are most affected with relative sparing of peripheral tissue and descending tracts. Contrast enhancement is unusual. Some uncommon manifestations include extrapontine changes, described in the basal ganglia, white matter and cerebellum. Pallidal sparing is usually evident. Diffusion weighted imaging (DWI), which is sensitive to the motion of water is helpful in diagnosing the lesions in ODS during the early clinical phase when conventional MRI imaging may be negative. Restricted diffusion has been described as the first imaging manifestation of ODS in the setting of otherwise normal conventional MRI sequences within 24 hours of onset of tetraplegia.<sup>[9]</sup> Treatment of hyponatraemia should be individualized. Factors taken into consideration when making a treatment decision for a hyposmolar patient are, the severity, duration of the hyponatraemia and the patient's neurologic status. Patients with acute hyponatraemia ( $\leq 48$  hours duration) are usually symptomatic if the hyponatraemia is severe (i.e.,  $< 125$  mEq/L). They are at greatest risk for neurologic complications from the hyponatraemia, but seldom develop demyelination, possibly because sufficient brain volume adaptation has not yet occurred. Patients with chronic hyponatraemia ( $> 48$  hours duration) have minimal neurologic symptoms and are at little risk from complications of hyponatraemia itself but can develop demyelination after rapid correction. In patients who are minimally symptomatic, the lower recommended rate of correction, 0.5 mmol/L or less is preferred. If neurologic symptoms are severe, an initial correction at a rate of 1 to 2 mmol/L per hour may be appropriate. Intensive treatment should be interrupted once the patient becomes asymptomatic or serum sodium levels greater than 125 mmol/L are achieved or a total magnitude of correction of 18 mmol/L is achieved. Hypoosmolal hyponatraemia can be treated with either isotonic or hypertonic saline infusions, depending on the cause of the

hypoosmolality. Patients with hypoosmolality due to volume depletion respond well to isotonic saline infusion. ODS has been reported even after correction of hyponatraemia with normal saline. Our patient developed ODS inspite of very slow rate of hypertonic saline administration. The enthusiastic additional oral salt administration and associated hypokalaemia are probably the causes for ODS in the patient. The predictive factors for poor outcome in ODS include severe hyponatraemia ( $\leq 115$  mEq/L), associated hypokalaemia and low Glasgow Coma Scale (GCS) at presentation.<sup>[10]</sup> The best way to prevent ODS is judicious, regulated administration of normal or hypertonic saline.

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