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Case Report

Osmotic demyelination as locked in syndrome

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ABSTRACT

Osmotic demyelination syndrome (ODS), also known as central pontine myelinolysis, is a disorder that affects the pons and extrapontine regions. This condition clinically presents with a multitude of neurological manifestations. The pathogenesis of ODS is not yet clearly understood. Most common cause of ODS is iatrogenic rapid correction of hyponatremia with a bolus of hypertonic saline. Very rarely it can be directly caused by alcohol intoxication and disrupted neuronal metabolism due to deficiency of essential substrates. A 34-year-old chronic alcoholic male presented with neurological symptoms and signs for 2 days. Clinical examination suggested multifactorial encephalopathy which was attributed to hyponatremia, Wernickes and hepatic encephalopathy substantiated by abnormal lab reports and unremarkable initial magnetic resonance imaging (MRI) findings. Although his sensorium improved over the next 3-4 days following slow correction of hyponatremia, parenteral thiamine and vitamin B12, B6 and B3, he suddenly went into a mute state followed by quadriparesis which aroused the suspicion of locked-in syndrome. Since his quadriparesis was accompanied by mutism and emotional incontinence, a lesion above cervical spine was suspected. So a repeat MRI brain was taken which showed development of demyelination of ventral pons, bilateral lentiform and caudate nucleus, posterior limb of internal capsule and both thalami which were conjunct with pontine and extrapontine ODS. Outcome of an established ODS cannot be predicted. Early diagnosis of ODS is a serious challenge as demyelination can be missed in initial MRI scan. So, a repeat MRI based on meticulous clinical assessment is crucial for early diagnosis and timely intervention.

Keywords: Osmotic demyelination, Locked in syndrome, Hyponatremia, Alcohol intoxication

INTRODUCTION

Osmotic demyelination syndrome (ODS), also known as central pontine myelinolysis, is a disorder that affects the pons and extrapontine regions predominantly cerebellum, lateral geniculate body, thalami, basal ganglia, subcortical white matter and midbrain structures.[1,2]

This condition clinically presents with neurological manifestations like disorientation, mental confusion, memory loss, paresis or spastic quadriplegia, seizure, obtundation, dysarthria, dysphagia, extrapyramidal signs, unresponsiveness, locked-in syndrome, and coma.[1,2]

CASE REPORT

This case report demonstrates the progression of the neurological status of a 34-year-old chronic alcoholic male to quadriparesis accompanied by mutism and emotional incontinence which was conjunct with osmotic demyelination. The patient was brought to Government Medical College, Thiruvananthapuram with complaints of altered behavior, swaying to both sides while walking, slurring of speech, and reduced talk for 2 days. There was no weakness of limbs or fever at the time of presentation. He also did not give a history of loss of consciousness or head trauma. He had a history of heavy binge drinking for the last 1 week. He also gave a history

of reduced food and water intake. He had no previous comorbidities. He was accompanied by his mother who suspected poisoning for her son's present condition.

On examination, vitals were normal. The patient was drowsy and hence higher mental functions could not be assessed. Pupils were equal and reactive to light. The tone was normal. Power could not be assessed due to altered sensorium. Plantar reflex showed flexor response on the left and equivocal response on the right. Deep tendon reflexes were normal except absent ankle jerk. There was no neck stiffness on examination.

On 5th day post admission, the patient's neurological state worsened and he developed quadriparesis with mutism.

Investigations

Toxicology analysis gave negative results. Serum pseudocholinesterase was within normal limits.

Computed tomography (CT) brain was normal. Cerebrospinal fluid (CSF) study was done and the findings were unremarkable. Initial MRI brain at the time of admission revealed no significant changes. A repeat MRI was done after he developed mute state with quadriplegia. Blood routine examination and biochemistry showed results as shown in the Table 1.

Table 1: Blood routine examination and biochemistry.

Parameter	Recorded value	Normal range
Hemoglobin (gm%)	10	13-18 g
TC (cells/mm^3)	9900	4,000-11,000
DLC	N81 L14	
Platelet count (lakh/mm^3)	1.47	1.5-4.5
Calcium (mg%)	8	8.5-10.5
Phosphate (mg%)	1.1	2.5-04.5
Uric acid (mg/dl)	3.5	3.5-7.2
Urea (mg%)	11	15-35
Creatinine (mg/dl)	0.7	0.7-1.4
Sodium (mEq/l)	118	136-145
Potassium (mEq/l)	3.2	3.5-5.3
Cholesterol (mg/dl)	180	150-200
SGOT (IU/l)	1005	12-38
SGPT (IU/l)	175	7-41
Total bilirubin (mg/dl)	1.3	0.2-1.0
Direct bilirubin (mg/dl)	0.4	Less than 0.2
Total protein (g/dl)	6.3	6.2-7.8
Albumin (g/dl)	3.8	3.5-5
Alkaline phosphatase (IU/l)		40-125

Creatine phospho kinase (CPK) was 1191 IU/l (normal range 9-308 IU/l). Peripheral smear showed normochromic normocytic anemia and neutrophilic leukocytosis. Urine osmolality was 742 mosml/l (normal range=50-1500 mOsm/l). Urine Na was 21 mEq/l (normal value >20 mmol/l) and ammonia was 91 mcg/dl (normal range=5-45 µg/dl). Trop T and TSH was within normal limits. USG abdomen was normal.

Treatment and progression

Initially, multifactorial encephalopathy was suspected which was attributed to hyponatremia, Wernicke's, and hepatic encephalopathy. So he was given 1000 ml of NS per day for the next 3 days. His serum sodium improved from 118 to 124,126,127 over the next 3 days. Efforts were taken to avoid rapid sodium correction. He was treated with injection thiamine 500 mg IV q8h suspecting Wernicke's encephalopathy. Injection methylcobalamin (1000 mcg) + vitamin B6 (pyridoxine) (100 mg) + nicotinamide (100 mg) was given in view of absent ankle jerk suspecting nutritional deficiency. MRI brain was unremarkable. Subsequently, his sensorium improved over the next 3-4 days. After this, on 5th day post admission he suddenly went into a mute state followed by weakness of all 4 limbs. His eye movements and gaze were preserved. On examination, he had developed hypotonia and his reflexes had become sluggish. There was no respiratory muscle involvement but emotional incontinence was present. The patient's worsened state rose suspicion of locked-in syndrome. However, the MRI brain taken before the development of quadriparesis was normal. Since his quadriparesis was accompanied by mutism and emotional incontinence, a lesion above the cervical spine was suspected. So a repeat MRI brain was taken.

The repeat MRI brain had T2 FLAIR hyperintense loci in ventral pons, bilateral lentiform and caudate nucleus with involvement of posterior limb of internal capsule and both thalami as shown in Figure 1. These findings are in conjunction with pontine and extrapontine osmotic demyelination syndrome which explains locked in syndrome in this patient.

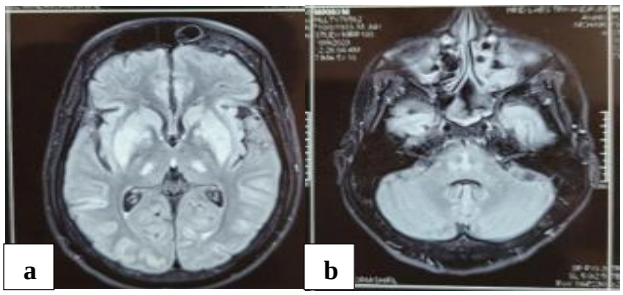

Figure 1 (a and b): MRI brain showing hyperintense loci in pontine and extrapontine regions.

Patient outcome

The patient was followed up after 2 weeks and on examination his muscle tone had improved and power had increased from 0/5 to 3 /5.

DISCUSSION

The pathogenesis of ODS is not yet clearly understood.[1] The osmolality of the brain cell is systematically adapted whenever there is a change in the osmolality of the extracellular compartment. When hyponatremia occurs, the brain interstitium becomes hypotonic while the brain cells become progressively hypertonic. Due to this osmotic gradient fluid shift occurs into the glial cells via the AQP1 and AQP4 water permeable channels resulting in swelling up of these cells. The glial cells adapts to this increase in size by an energy dependent mechanism to lose the inorganic osmolytes (Na^+ , Cl^- and K^+) via Na–K–ATPases, K^+ channels, the K^+–Cl^- co-transporter and the volume-sensitive Cl^- channel. On administration of a bolus of hypertonic saline the osmolyte depleted cells are rapidly exposed to a hypertonic interstitium. This causes the repumping of the osmolytes using ATP but this occurs at a slower rate and with increased metabolic burden. So, even though the size of the cells gets restored, the osmolality of the cells increases. This affects the intracellular protein folding. All these result in cell shrinkage, irreversible cell damage, oligodendroglial apoptosis, disruption of the astrocyte-oligodendrocyte network and myelin degradation. Disrupted blood brain barrier allows circulating lymphocytes, cytokines and complement proteins to enter the brain and mediate astrocyte and oligodendroglial demyelination. Similar pathogenesis is seen in endogenous and exogenous intoxication.[2,3]

Most common cause of ODS is iatrogenic rapid correction of hyponatremia with a bolus of hypertonic saline. Autopsy studies by Norenberg provide evidence to support this aetiology.[4] Adams et al and his colleagues has also proposed intoxication as well as disrupted neuronal metabolism due to deficiency of essential substrates as other causes for ODS.[5]

In this patient the altered sensorium and other neurological symptoms at initial presentation could be due to alcohol intoxication or Wernicke's encephalopathy or alcohol induced hyponatremia-Beer photo mania.[6] Quadriplegia with mute state which developed subsequently after improvement of sensorium aroused the suspicion of brain stem lesion.[7] Quadriplegia due to possible cervical spine injury due to falls common in alcoholics cannot explain the mute state in this patient. This strongly points towards bilateral corticospinal lesions at the level of pons causing UMN palsy of 9 10 cranial nerves–referred to as pseudobulbar palsy. Initial MRI in this patient was normal. Studies show that MRI findings in osmotic demyelination may take more than a week to appear.[8-10] Since this patient's clinical presentation was strongly suggestive of a brain stem lesion a repeat MRI was taken which substantiated our clinical judgment. Locked-in state with preserved consciousness in this patent is explained by the repeat MRI which shows lesion in the ventral pons only sparing dorsal pons with preserved ascending reticular activating system.[11]

Chronic alcoholism causes ADH suppression. This causes interference in sodium-water regulation which results in myelin damage[12]. In addition to this, reduced food and water intake causes further osmotic changes. These mechanisms may have contributed to the development of ODS in this patient. Even though his hyponatremia was not rapidly corrected which could have been a cause, his history of heavy binge drinking might have precipitated the ODS.

The prognosis of the patient can vary from full/partial recovery within several months to those who do not show any recovery or even succumb to death. Satisfactory results have been obtained with re-lowering of serum sodium without delay. Immunomodulating therapies like infliximab, dexamethasone, intravenous immunoglobulin and plasma exchange are being tried to manage ODS.[13] Urea administration has shown improvement in the neurological outcome of these patients.[14] Supportive managements should also be provided.

CONCLUSION

Early diagnosis of ODS is a serious challenge. Although the usual cause of osmotic demyelination is iatrogenic following rapid correction of hyponatremia, very rarely it can be directly caused by alcohol intoxication. Conditions like stroke and demyelination can be missed in initial MRI scan. So, a repeat MRI based on meticulous clinical assessment is crucial for early diagnosis. Since the outcome of an established ODS cannot be predicted we should intervene at the first signs of brain damage which may be determined by sensitive biomarkers instead of waiting for ODS to become fully fledged. Therefore, this case report calls for further research and studies on the various indicators of ODS and treatment modalities which warrants better outcome.

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