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Osmotic Demyelination Syndrome: Why Should Hypernatremia be Corrected Slowly? A Case Report

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Authors' contributions

This work was carried out in collaboration between all authors. Author CR was responsible for admitting, investigating and managing the patient, conception of the writing up the first draft and revision of the manuscript. Authors SWR, DTN, YMN were responsible for investigating of the patient and editing the images, rewrting the discussion. Author RP managed the literature searches and edited the images. All authors read and approved the final manuscript.

Case Study

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ABSTRACT

Aim: Our aim is to present a case of hypernatremia which has led on to a flaccid quadriparesis due to brain stem demyelination. Rapid correction of hypernatremia as a cause for pyramidal tract demyelination is not documented in the literature.
Presentation of Case: A 53 year old male was brought to the emergency services with suspected stroke. He was treated with intravenous mannitol and oral glycerine from the primary health centre. We detected hypoglycemia (blood sugarwas 50mg/dl-Ref range: ≤70mg%) and dextrose was given intravenously. Subsequently the patient went into a hypernatremic state with serum sodium 170milli equivalents /liter which was corrected rapidly. This was corrected over 48 hours to 140milli equalents/litre. The rate of correction exceeded 0.62millimols/liter/hour (Ideal: 0.5 mmol/L/h). On the 6th day the patient developed acute quadriparesis. Magnetic resonance imaging (MRI) of brain revealed bilateral symmetric demyelination of the corticospinal tracts. Over six months the neurological deficit improved with complete resolution of the changes in previous

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MRI.
Discussion: Osmotic Demyelination Syndrome (ODS) has been a recognized complication of rapid correction of hyponatremia. Experiments in animals and clinical experience suggest that correction of chronic hyponatremia should be kept at a slow rate to combat this complication. The characteristic sites include pons and basal ganglia. Such a complication has not been described due to rapid correction of hypernatremia.This is probably the first case report in the literature where acute onset of quadriparesis resulted from demyelination of the pyramidal tract consequent to a rapid correction of hypernatremia. We had to wait about 6 months for the patient to obtain a complete functional recovery and the neuro imaging was repeated after 6 months to confirm the disappearance of the initial findings thus implicating rapid correction of hypernatremia as the cause of his morbidity.
Conclusion: This is the first time extrapontine reversible myelinolysis due to rapid correction of hypernatremia has been documented. To prevent this potentially fatal complication it will be prudent if hypernatremia is corrected slowly.

Keywords: Osmotic demyelination syndrome; central pontine myelinolysis; extrapontine myelinolysis; hyponatremia; demyelinating diseases; hypernatremia pyramidal tracts; reversible myelinolysis.

1. INTRODUCTION

Osmotic demyelination (ODS) syndrome is a neurologic disorder that can occur after rapid correction of hyponatremia [1]. To prevent it, the rate of correction of chronic hyponatremia should be kept to less than 10nmol/L in any 24-hour period as evidenced by clinical experience and experiments in animals [2]. The characteristic sites include pons & basal ganglia [3]. Acute hypernatremia results in sudden shrinkage of brain cells leading to parenchymal or subarachnoid hemorrhages and/or subdural hematomas mainly in pediatric patients [4]. Hypernatremia is a potentially lethal condition that can produce encephalopathy, osmotic demyelination and rhabdomyolysis [5-7]. The cellular response to chronic hypernatremia predisposes these patients to the development of cerebral edema and seizures during overly rapid hydration (overcorrection of plasma sodium concentration by more than 10mM/day [4,8]. In patients with prolonged hyperosmolality, aggressive treatment with hypotonic fluids may cause cerebral edema, which can lead to coma, convulsions, and death [8]. Demyelination of the pyramidal tract due to rapid correction of hypernatremia has not been described in the literature. Although extrapontine myelinolysis due to rapid correction of high serum sodium (more than 0.5mmol/L/h) is described in the literature [9-12], we could not find any reports of cases of demyelination of the pyramidal tract due to rapid correction of hypernatremia. This is probably the first case reported in the literature where acute onset quadriparesis resulted from demyelination of the pyramidal tract consequent to a rapid correction of hypernatremia. Here we pose two questions: 1) why was the pons spared, and 2) whether there is any other disease that could be responsible for his demyelination. We had to wait about 6 months for the patient to obtain a complete functional recovery, and his repeat imaging confirmed the disappearance of the initial findings, thus implicating rapid correction of the hypernatremia as the cause for his morbidity.

2. CASE REPORT

A 53-year-old gentleman, who was neither diabetic nor hypertensive, was brought to our emergency services having been found unconscious by relatives. We detected hypoglycemia (blood sugar was 50mg/dl, Ref range: Hypoglycaemia ≤70mg%), and dextrose was given intravenously. This was continued for the next 24 hours to prevent further hypoglycemia. Due to suspicion of stroke, intravenous mannitol and oral glycerine was given by the referring hospital, but was stopped the following day after Computerised Tomography (CT) scan of the brain was found to be normal. He was fully conscious by the 2nd day, with no focal neurological deficits. Hypernatremia was detected the following day, precipitated by the osmotic diuretic effect of dextrose and mannitol. This was treated with free water feeds and corrected in 48 hours Table 1. After 2 days of correction of hypernatremia, on the 6th day of admission, the patient became drowsy with acute flaccid quadriparesis and bilateral extensor plantar response, with no cranial nerve deficits. His pulse was 80/minute, blood pressure 120/80mm of Hg, respiratory rate 20/minute, temperature 36°C, and other systems were within normal limits. His routine laboratory investigations, including a peripheral smear and urine examinations were within normal limits. Toxicological analysis of the gastric aspirate revealed no benzodiazepines or tricyclic antidepressants. Renal function tests and serum electrolytes were normal. Liver function tests, including PT, INR, arterial ammonia and ultrasound scan of the abdomen revealed no abnormalities. ANA, anti-dsDNA, c-ANCA, p-ANCA HbsAg, VDRL, HIV1&II, Urine Bence Jones protein and serum electrophoresis were normal. Titers of anti-phospholipid antibody IgG and IgM, Protein C and Protein S assays were normal. Echocardiogram and Trans esophageal Echocardiogram (TEE) were normal. Holter monitoring did not reveal any rhythm disturbance. Doppler study of the aortic arch, carotid and vertebral arteries revealed no abnormalities. Cerebrospinal fluid analysis revealed a colorless fluid with normal opening pressure,normal sugar and protein.The microscopy showed no cells. The culture was sterile.Electroencephalogram examination showed normal awake recording. His routine blood counts and daily serum electrolyte values are shown in Table 1. His thyroid function and adrenal functions were normal. The Magnetic Resonance Imaging (MRI) scan of the brain, T2 weighted coronal sections were showing bilateral capsular hyper intensities (Figure.1. Panel.A), diffusion weighted image showed band like hyperintensity at sub cortical level(Figure.1Panel.B),ADC mapping showed hypointensities in the corresponding sections at the sub cortical level Fig. 1. Panel.C, diffusion weighted images showed bilateral hyper intensity of the pyramidal tracts at the midbrain level (Fig. 1 Panel.D) and ADC mapping showed hypointensity of bilateral pyramidal tract at midbrain level Fig. 1. Panel.E. He was given intravenous dexamethasone 4 milligrams 6 hourly, which was tapered off from the 7th day, and he was off steroids by the 21st day.The power of the limbs showed improvement by the 2nd week, and steadily improved with physiotherapy. He was discharged on the 21st day and was asked to continue physiotherapy with weekly monitoring of the electrolytes. He demonstrated complete recovery and was ambulant at 3 months. The repeat MRI of brain was done after clinical recovery. The T2 Weighted image of pyramidal tract at internal capsule level showed resolution of the prior lesion Fig. 2. Panel.A, T2Weighted image of pyramidal tract at midbrain level showed resolution of the prior lesion Fig. 2. Panel.B, MR Flair image at internal capsular level showed resolution of the prior lesionFig.2.Panel.C and MR Flair image at midbrain level showed resolution of the prior lesion in the crus cerebri Fig.2.Panel.D. He was found to be doing well on follow up.

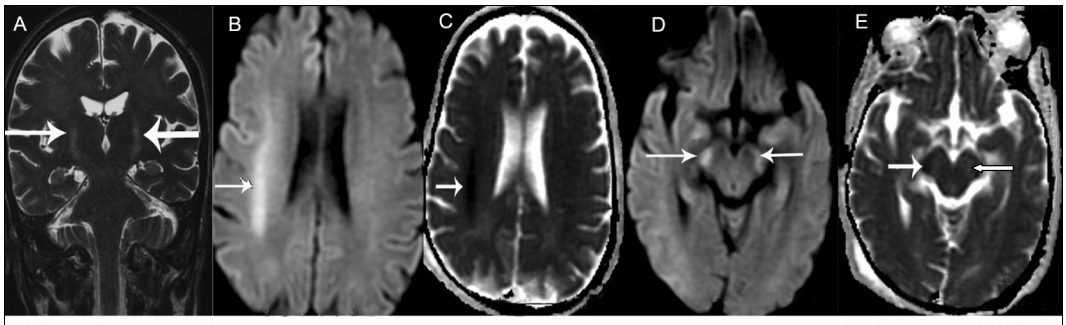

Figure 1 A. MRI brain T2 weighted coronal sections showing bilateral capsular hyperintensities

B.MRI diffusion weighted image showing band like hyperintensity at sub cortical level (white arrow).

C- MRI ADC mapping showing hypointensity in the corresponding sections at the sub cortical level (white arrow).

D.MRI diffusion weighted images showing bilateral hyper intensity of the pyramidal tracts at the midbrain level.

E- MRI ADC mapping showing hypointensity of bilateral pyramidal tract at midbrain level (white arrows)

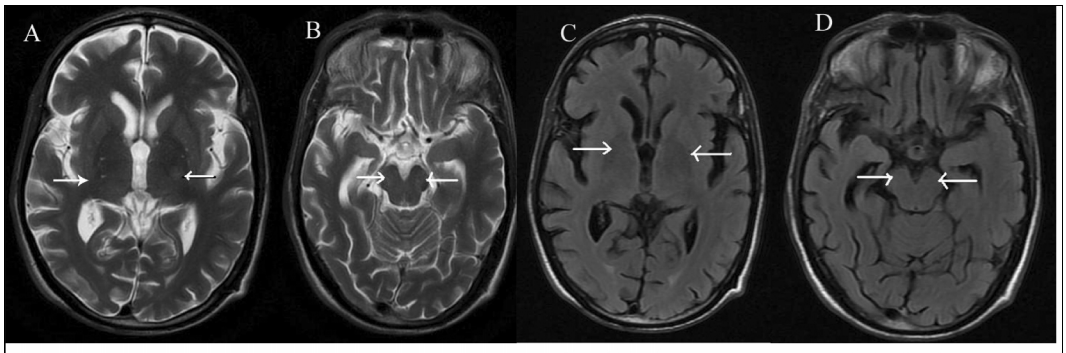

Figure 2 A- MRI T2W image of pyramidal tract at internal capsule level showing resolution of the prior lesion (white arrow)

B- MRI T2W image of pyramidal tract at midbrain level showing resolution of the prior lesion(white arrow)

C- MR Flair image at internal capsular level showing resolution of the prior lesion(white arrow)

D-MR Flair image at midbrain level showing resolution of the prior lesion in the crus cerebri (white arrow)

Table 1. Showing values of serum electrolytes, serum osmolarity, blood urea nitrogen and random blood sugar

Date	S.Sodium (meq/L) Ref.Range:136 -145meq/L	S.potassium (meq/L) Ref.Range:3. 5-5meq/L	S.Osmolarity (mOsm/L) Ref Range:275-295mosm/L	BUN(mg%) Ref.Range: 7-20mg/dL	RBS(mg%) Ref.Range: ≥200mg%
04/03	145	5.0	303.8	12	100
05/03	140	4.6	293.6	10	180
06/03	138	4.1	290.5	14	172
07/03	169.9	3.6	356.1	18	176
08/03	174	4.0	365.9	22	184
09/03	146	5.9	307.7	16	180
10/03	146	3.9	306.2	12	178
11/03	142	4.0	296.9	08	182
12/03	140	3.5	293.7	10	182

3. DISCUSSION

Rapid correction of hyponatremia resulting in Osmotic Demyelination Syndrome (ODS), has been recognized as a complication [1]. Experiments in animals and clinical experience suggest that correction of chronic hyponatremia should be kept at a rate of less than 10mmol/L in any 24-hour period to prevent this complication [1]. The characteristic sites include pons and basal ganglia [2], but such a complication has not been described in the correction of hypernatremia. This is probably the first case reported in the literature where acute onset quadriparesis resulted from demyelination of the pyramidal tract consequent to a rapid correction of hypernatremia. The rapid swelling of the shrunken neurons in the brain on correction of hypernatremia leads to cell injury and transient loss of neuronal function (neuropraxia). The oligodendrocytes that produce myelin are normally maximally functional around the pyramidal tract for rapid impulse conduction [13]. Oligodendrocytes bear the brunt of this neuropraxia. This is attributed to the selective affection of the pyramidal tract in osmotic demyelination. Moreover, the normal homeostasis of myelin is also hampered due to this osmotic effect of rapid correction. Myelin is made up of 45% water, which explains it's vulnerability to osmotic changes.The microglial proliferation in response to this injury is also attributed to the same. Osmotic shifts in the brain lead to complex metabolic events that result in changes in lactate, amino acids, ammonia, and water and alterations in the level of idiogenic osmoles. These changes may be harmful to oligodendrocytes, the myelin forming cells of the central nervous system [14]. The microglia that accumulates in the demyelinative lesions may play a detrimental role in the pathogenesis of ODS by producing proinflammatory cytokines, suggesting that they may be a target for therapeutic intervention [15]. Gankam Kengne et al. demonstrated the use of minocycline in preventing such microglia mediated damage. The effect of rapid correction of hypernatremia has been experimented on in rats, which showed reversible osmotic demyelination in the brain [16]. Animal model experiments have shown that early dexamethasone treatment may protect against osmotic demyelination since glucocorticoids are known to influence BBB permeability and prevent its disruption [17].

4. CONCLUSION

Osmotic Demyelination Syndrome (ODS) can occur with rapid correction of hyponatremia or hypernatremia. The first of its kind our report highlights the importance of rate of correction of Sodium in the brain which may functionally interfere with the rapidly conducting fibers rich in oligodendrocytes resulting in transient or permanent neuronal dysfunction.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

Not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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