Case Report

International Journal of Neurology and Neurosurgery
Volume 8 Number 1, January - June 2016
DOI: http://dx.doi.org/10.21088/ijnns.0975.0223.8116.2

Osmotic Demyelination Syndrome and Rhabdomyolysis Secondary to Postpartum Hypernatremia

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Abstract

Introduction: Extrapontine myelinolysis associated with metabolic abnormalities especially hypernatremia is extremely rare. Osmotic demyelination syndrome resulting from postpartum hypernatremia is recently described entity with hypernatremic encephalopathy, quadriparesis and rhabdomyolysis with myelinolysis on imaging. This communication aims to highlight a case and discuss the pathogensis and management. *Case Report:* A 20 year-old lady presented with fever and disorientation of 5 days and generalized seizures of 1-day. She had undergone a lower segment caesarean section following an uneventful antenatal period, 3 weeks prior to this and was discharged home on 7th postoperative day where she was keeping well for next 1 week. On examination she was febrile, vitals stable, drowsy, flexing limbs and opening eyes to pain, with no verbal response. Limbs were flaccid; deep tendon and bilateral plantar reflexes were unresponsive. Biochemical evaluation revealed a sodium level of 182meq/l, creatinine phosphokinase (CPK) -2207 U/L, urea-135mg/dl, and creatinine-4.3mg/dl. Neuroimaging showed T2/FLAIR hyperintensities in bilateral putamen, isthmus of hippocampus, middle cerebellar peduncles, posterior internal capsule, and subcortical white matter suggestive of extrapontine myelinoysis. Inspite of correction of metabolic abnormalities, she progressively worsened and succumbed to her illness in 7 days. *Conclusion:* Clinicians must be aware of this entity of postpartum hypernatremia secondary to water restriction and diabetes insipidus and treat at the earliest, as mortality remains high (>60%).

Keywords: Hypernatremia; Myelinolysis; Postpartum; Osmotic; Diabetes Insipidus.

Introduction

Hypernatremia is reported in 25% of ICU patients and is acquired in the Intensive care unit (ICU) in most cases [1]. Hypernatremia is a potentially lethal condition, and can cause encephalopathy, rhabdomyolysis, and osmotic demyelination [2]. Even though osmotic demyelinations secondary to hyponatremia or its correction is a fairly recognized entity, similar syndrome following hypernatremia is much rarer in literature.

Osmotic demyelination syndrome resulting from postpartum hypernatremia is a recently described entity wherein young women present with hypernatremic encephalopathy and white matter hyperintensities along with quadriparesis and rhabdomyolysis [2].

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Case Report

A 20 year-old lady presented with fever and disorientation of 5 days and generalized tonic clonic seizures of 1-day duration. She had undergone a lower segment caesarean section 3 weeks prior to this and had an uneventful postoperative period and was discharged on the 7th post operative day and was keeping well for next 1 week at home.

On examination she was febrile, vitals were stable, but she was drowsy, flexing limbs and opening eyes to pain, with no verbal response. Limbs were flaccid, all deep tendon and bilateral plantar reflex were unresponsive. Biochemical evaluation revealed

serum sodium of 182meq/l, serum creatine phosphokinase (CPK) -2207 U/L, B. Urea-135mg/dl, and Creatinine-4.3mg/dl.

MRI brain showed T2/FLAIR hyper intensities in bilateral putamen, isthmus of the hippocampus, posterior internal capsule, subcortical white matter and bilateral middle cerebellar peduncles suggestive of extra-pontine myelinoysis. There was also a wine glass appearance of the pyramidal tract in the coronal section MRI (Figure 1).

Patient underwent correction of metabolic abnormalities however progressively worsened in sensorium and motor weakness and succumbed to her illness over next 7 days.

Table 1: Cause of hypernatremia

Water loss
Insensible loss- Burns respiratory infection exercise
Gasterointestinal loss- Inflammatory & secretory diarrhea, malabsorption syndromes, ileostomy drainage
Renal loss – central DI, (TDIP, Sheehans syndrome, Cardiopulmonary arrest), Nephrogenic DI (sickle cell disease, renal failure , Drugs – lithium, diuresis with mannitol or glucose)
Decrease water intake
Hypothalamic disorders, limited access to water, cultural restriction of water, loss of consciousness
Increase sodium retention
Increase intake of sodium or administration of hypertonic solutions, Saline induced abortion

TDIP- Transient diabetes insipidus of pregnancy,DI- Diabetes insipidus

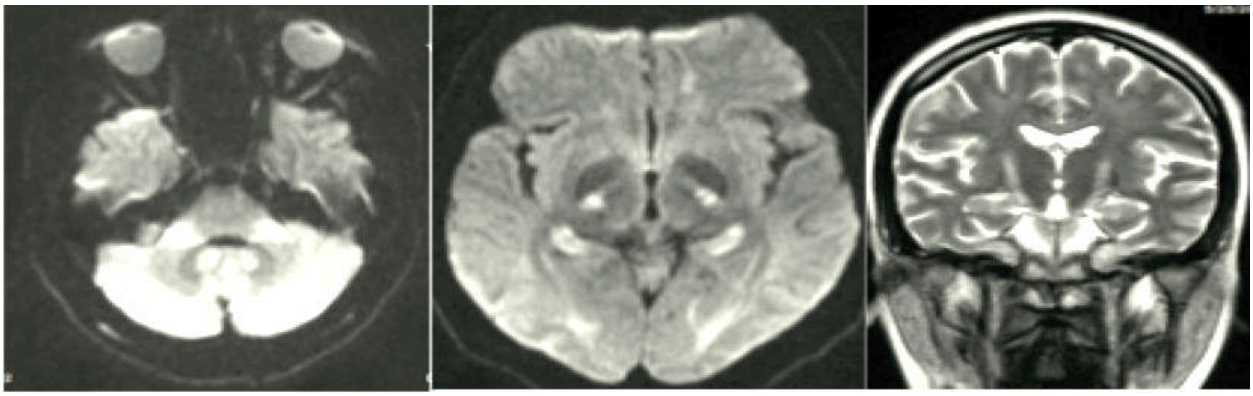

Fig. 1: Flair hyperintensities in middle cerebellar peduncle, isthmus of hippocampus, posterior, limb of internal capsule. Wine glass appearance in the coronal section

Discussion

Review of Literature

Literature search reveals this syndrome to be extremely rare. There has been just two case reports [2,3] and a case series of 11 patients [4] on the hypernatremic osmotic demyelination in the postpartum period. The mortality recorded in the series is nearing 40%. Consciousness was altered in all the patients ranging from confusion to deep coma making it the commonest presenting feature. Quadriparesis, corticospinal, corticobulbar dysfunction, ataxia, and seizures are the other clinical manifestation in decreasing order. The patients were reported to have hypernatremia ranging from 158 to 199mEq/l with hyperchloremia, markedly elevated serum CK levels (2572 - 61,107U) and azotemia. MRI findings included T2 & FLAIR hyperintensities of corpus callosum in all the patients [4]. Symmetrical hyperintensities in internal capsule, corona radiata, cerebellar peduncles and hippocampus in various combinations has also been listed. Another MRI feature reported is wine glass appearance due to extensive white matter changes in a patient with recurrent postpartum hypernatremia [3]. Hypernatremia during antepartum period due to transient diabetes insipidus of pregnancy (TDIP) has also been mentioned earlier [5].

Etio-Pathophysiology

The normal plasma sodium (Na) is 135 -145 mEq/L and hypernatremia is characterized by plasma Na above 145 mEq/L. Hypernatremia can be the result of loss of sodium and water (water loss > Na loss), free water loss, or gain of sodium (more than water). That is loss of hypotonic fluid (resulting in low extracellular volume [ECV]) or free water (normal ECV) or gain of hypertonic fluid (high ECV). The

principal consequence of hypernatremia is increase in the effective osmolality (tonicity) of the extracellular fluid, which draws water out of cells causing shrinkage of cells. This is most evident in central nervous system with clinical manifestations ranging from, agitation, lethargy, seizures, coma and occasionally impaired thirst. The sudden shrinkage of brain cells in acute hypernatremia can also lead to parenchymal or subarachnoid hemorrhage or subdural hematoma especially in pediatric and neonatal patients. The possible mechanisms include neuronal shrinkage and osmotic demyelination [6]. Osmotic damage to the muscle membrane can lead to rhabdomyolysis raising the CPK levels exponentially. The most common cause of community-acquired hypernatremia is loss of hypotonic fluids (all lost fluids are hypotonic to plasma, be it sweat, stools, vomitus, urine or ileostomy drainage). As enumerated in the Table 1 there are numerous disorders responsible for hypernatremia. However two important conditions are specific to pregnancy that can lead to hypernatremia. First is iatrogenic, caused by the hypertonic saline used for second trimester abortion, 20% hypertonic saline infused into the amniotic sac as an abortifacient can gain access to the maternal vascular compartment resulting in hyperosmolar crisis and disseminated intravascular coagulation (DIC). Fortunately this method has mostly been abandoned. The second is transient diabetes insipidus of pregnancy (TDIP), characterized by polyuria, polydipsia. A majority of these patients have preeclampsia and liver abnormalities such as acute fatty liver of pregnancy. Pregnancy is associated with a lower threshold for thirst and a lower osmolarity threshold for release of antidiuretic hormone (ADH). Also placenta produces vasopressinase, which is a cysteine- aminopeptidase that breaks the bond between cysteine and tyrosine of the hormone vasopressin (ADH). The liver is the major site for degradation of vasopressinase [7]. Apart from the above two, specific to India is a ritual in some communities, to restrict the water intake for ladies in post-partum period, which may exacerbate dehydration [2].

Encephalopathy is especially likely with a rapid rise in plasma Na. According to the hypothesis of Norenberg, rapid rise in serum sodium may cause osmotic demyelination [8]. In at least 10% of patients with central pontine myelinolysis, demyelination also occurs in extrapontine regions, including the mid brain, thalamus, basal nuclei, and cerebellum. The exact mechanism that strips the myelin sheath is unknown. One theory proposes that in regions of compact interdigitation of white and gray matter (like the pons and basal ganglia) cellular edema, which is caused by fluctuating osmotic forces, results in compression of fiber tracts and induces demyelination [9].

It is known that sudden lowering of sodium (i.e., more than 10 mEq/day) may affect brain function and myelinolysis is expected, but inspite of correction, such a high level of sodium once achieved is always detrimental to the brain tissue. Even lowering sodium at a slow rate would not help the neurological status to improve [2].

Management Treatment is aimed at 2 consequences of hypotonic fluid loss 1) Loss of sodium that threatens plasma volume and cardiac output as evidenced by low blood pressure, reduced urine output and cold extremities. This is done using *resuscitation with isotonic saline.* 2) Loss of water in excess of sodium which increase plasma osmolality for which free water deficit has to be corrected which is ideally done with half or quarter normal saline. This is done using the following method. Total body water (TBW) in litres in adults is 60% of lean body weight (in kg) in men and 50% in women. An additional 10% reduction in the normal total body water has been suggested for hypernatremic patients who are water depleted. The current TBW after hypernatremia is calculated from the formula

Current TBW = Normal TBW × (140/current plasma sodium)

where 140 equals the normal sodium levels in the plasma.

Eg; For an adult male with a lean body weight of 70 kg and a plasma sodium of 160mEq/L the normal TBW is 0.5×70=35L the current TBW is 35× 140/160=30.5 L. The free water deficit is the normal TBW-current TBW, 35L-30.5L= 4.5 litres. Now the question is how much of which solution needs to be infused and at what rate? Free water deficit is corrected using low sodium concentration fluids such as half normal saline. The volume needed to correct the water deficit depends on the Na levels in the replacement fluid and the desired plasma Na levels. ie if the water deficit is 4.5 litres as calculated above

The replacement volume (in Litres) = water deficit × 140/Na in IV fluid.

The Na concentration in half normal saline is 77mEq/L.

So the replacement volume is 4.5×140/77 = 8.1 litres. To limit the risk of osmotic demyelinations and cerebral oedema the reduction in plasma Na should not exceed 0.5mEq/L/hr during free water replacement. So using the above example the time

needed to reduce the plasma sodium from 160 to 140 at a rate of 0.5mEq/L/hr (160-140/0.5) = 40 hours and the infusion rate of 8.1 litres of half normal saline would be 8.1/40 = 200ml/hr [6]. It is important to monitor the plasma Na frequently considering the dynamic state of plasma.

Conclusion

Apart from the very well recognized cerebral venous thrombosis, ecclampsia and posterior reversible leuko-encephalopathy in pregnant and postpartum women it's very important to know this entity of hypernatremia since the mortality is highest (60%) [6]. Early recognition and appropriate correction is key for a better prognosis.

Conflict of Interest

None of the authors have any financial conflict or interest in the article submitted hereby.

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