A case report of pregnant lady with hyperemesis gravidarum that led to osmotic demyelinolysis

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ABSTRACT

Background: The fall of serum sodium concentration may happen in hyperemesis gravidarum and subsequently can result into hypotonic hyponatremia. This would cause water to move into the brain and develop cerebral edema manifested with neurologic symptoms. However, adaptive mechanism by brain would lower the cerebral volume to a normal range. On the other hand, rapid correction of chronic hyponatremia would damage the brain cells. The symptoms depicted because of rapid over correction of sodium is known as osmotic demyelination syndrome.

Case Presentation: The pregnant lady with hyperemesis gravidarum went to severe hyponatremia. And further, she underwent dilatation and evacuation because of the intrauterine fetal death. The normal saline administered to correct the state of hyponatremia caused the patient to be in depression with catatonia and aphasia. The symptoms were correlated with osmotic demyelinolysis and the event was confirmed with magnetic resonance imaging of brain.

Conclusion: The administration of sodium should be performed with utmost cautions and under the supervision of well-trained healthcare providers. Any sign or symptom of neurological abnormalities observed because of overcorrection should be considered seriously.

Keywords: Dyselectrolytemia, hyperemesis, hyponatremia, intrauterine fetal death, osmotic demyelinolysis.

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Background

Morning sickness is very common in early pregnancy. The severity of illness may vary among individuals, and it may affect them, any time or on all days. Usually, majority of pregnant women get relief from morning sickness after their first trimester. However, for some, the symptoms may prolong until delivery [1].

Hyperemesis gravidarum is a rare disorder of pregnancy with persistent symptoms of nausea and vomiting. Lack of inadequate nourishment or supplementation can lead the patient into dehydration. A balanced and adequate dietary supplement should be provided, in consultation with the dietician. This is essential for fetal development and to preserve the maternal health. Intravenous nutritional administration may be required if they can't tolerate the oral formulations. On the other hand, plasma expanders are vital for replenishing the fluid and electrolytes in the dehydrated body. The crystalloids such as normal saline, dextrose or Ringer's lactate can be administered at suitable rate. However, thiamine supplementation should precede the dextrose infusion to prevent the risk of Wernick's encephalopathy [2].

Hyperemesis can cause hyponatremia which necessitates expert surveillance [3]. The rapid correction of severe hyponatremia (less than 120 mEq/l) can cause central pontine myelinolysis (CPM) [4-6]. The clinical symptoms of CPM are pseudobulbar palsy, depression, movement disorders and coma [7]. Brain magnetic resonance imaging (MRI) is the mainstay for the diagnosis. Lesions are symmetric and hypointense on T2 weighted images, typically sparing the periphery of pons and hyperintense on T2 weighted and fluid attenuation inversion recovery sequence (FLAIR) images [8].

We present a case of a pregnant lady with hyponatremia and hypokalemia. The dyselectrolytemia was managed by rapid over corrections with sodium supplement, which led her to osmotic demylinolysis.

Case Presentation

19-year-old pregnant women with 14 weeks of gestation, presented with complaints of hyperemesis, multiple episodes of diarrhea and weakness and was admitted to a nearby hospital. The patient had severe vomiting

throughout her first trimester. On examination, her blood pressure (BP) was found to be low (90/70 mmHg) and the hypotension was managed with normal saline. ultra-sonography (USG) was performed on the next day, features of abortion was identified and further underwent dilation and evacuation (D & E) on the same day. In spite of the supportive therapy given, she was extensively weak, disoriented and required assistance while walking. On the coming days, the patient had signs of aphasia, an episode of urinary incontinence and involuntary movement of the limbs. The inference from laboratory test depicted hyponatremia with serum sodium of 127.7 mEq/l and hypokalemia with serum potassium of 2.0 mEq/l.

The patient was shifted to a tertiary care referral hospital in search for better treatment. On the 3rd day after the initial illness, tachycardia (Heart rate:110/minute) with normal BP (110/70 mmHg) and mild dehydration was observed. She was conscious, silent and had involuntary movement of the limbs. The Glasgow coma scale values are shown in Table 1. Right foot showed extensor plantar reflex and left foot showed equivocal plantar reflex, abdomen had mild distension with exaggerated bowel sounds. The laboratory investigations from the tertiary care referral hospital are showed in Table 2. As her neurological status did not improve, MRI of brain was performed and there was cortical grey matter and basal ganglia involvement. The patient's right upper lobe of lung collapsed due to aspiration, as result, her consciousness gradually declined over 48 hours. The situation was normalized by fiber optic bronchoscopy and bronchoalveolar lavage. She was also presented with features of ileus with glossy distended abdomen which resolved within 2-3 days by electrolyte administration. In view of gradually decreased sensorium with focal neurological signs, MRI of brain was repeated. There was extensive lesions mostly indicative CPM and extra pontine myelinolysis (EPM) involving cortical grey matter, caudate, putamen and thalamic features. From Figures 1-4, we confirmed the patient had osmotic demyelination syndrome.

The physician-initiated injections, cefotaxime sodium, 0.9% normal saline, potassium chloride 20 mEq/10 ml. Her condition remains more or less the same over night. Serum level of phosphate was low and also patient had hypocalemia and hypomagnesemia, however, they were corrected with their corresponding supplements.

USG showed remnants of conception which was evacuated by dilation and curettage. High dose of

Table 1. *The Glasgow Coma scale of the patient.*

	Glasgow coma scale		
	Eye response	Motor response	Verbal response
Value	4	5	1

Table 2. *The laboratory data of the patient from the tertiary care referral hospital.*

Sl. No	Blood test performed	Value
1.	Hemoglobin	8.7 g/dl
2.	Total leukocyte count	8,100 million/cu
3.	Differential leukocyte count	
a.	Polymorph	74%
b.	Lymphocyte	20%
c.	Eosinophils	3%
d.	Monocytes	3%
4.	Serum electrolytes	
a.	Serum sodium	135 mEq/l
b.	Potassium	2.23 mEq/l

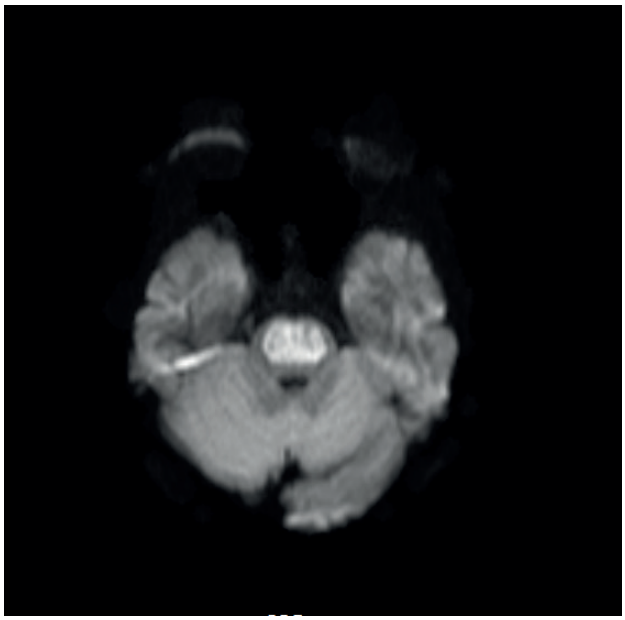

Figure 1. *DWI image showing hyper intense signal.*

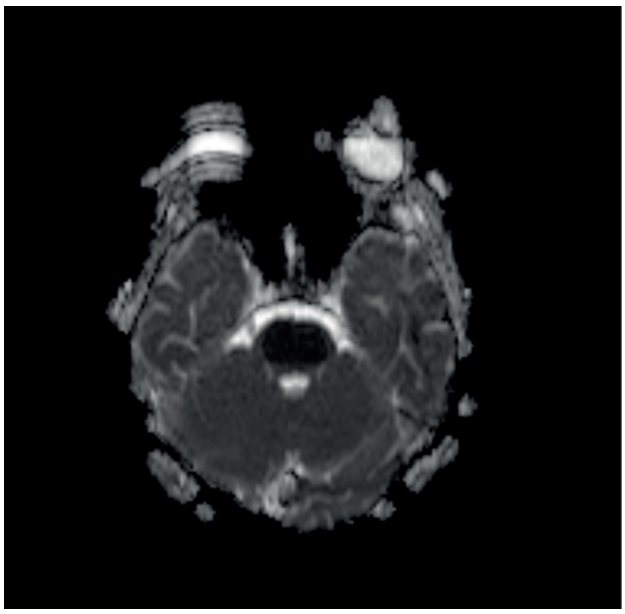

Figure 2. *Corresponding fall in ADC map.*

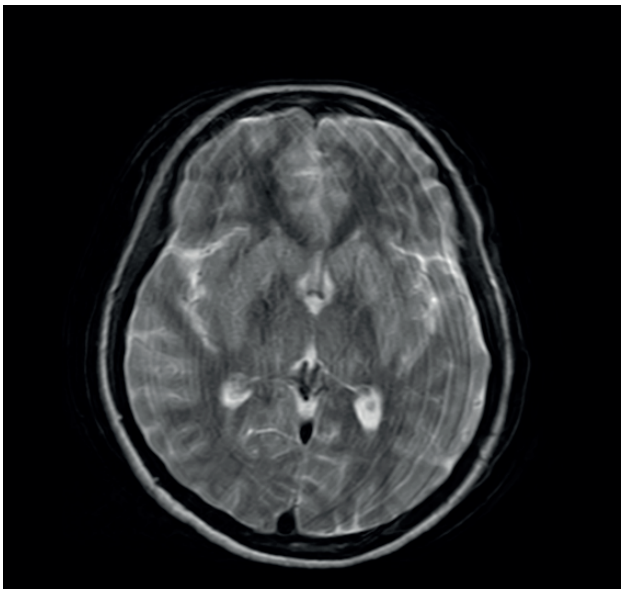

Figure 3. *T2 hyperintensity in caudate nucleus and lentiform nucleus.*

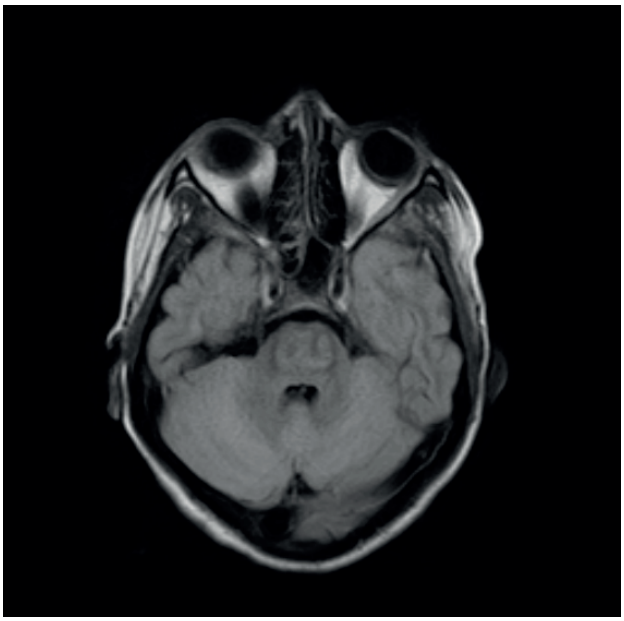

Figure 4. *FLAIR hyper intensity in pons.*

methylprednisolone was stared empirically. After 3 days in the second hospital, her body temperature raised, and the physician ordered for a culture and sensitivity report. *Enterococcus faecalis* was isolated from her urine sample and urospesis was also added to her final diagnosis. The antibiotic was stepped up and methylprednisolone injection was stopped. The injections merpenom and vancomycin initiated, had a better impact on the infection and subsequently the fever subsided on the 8th day after admission, serum sodium and potassium was normalized slowly and their laboratory test values were 132 and 5.19 mEq/l, respectively.

For symptomatic relief, the physician planned for tracheotomy but the patient's relatives was not willing for the same, got voluntary discharge and was transferred to the medical college hospital. Mild to moderate generalized disturbance of electrical function, no epileptiform activity was the inference obtained from electroencephalogram. The patient responded to pain and pulse rate (80 beats/minute) as well as BP (110/70 mmHg) was found to be normal, but involuntary movement of upper limb still persisted. Injection meropenam was continued and citacholine 1 g twice daily, metranidazole 500 mg thrice daily (TID), thiamine 100 mg TID and vitamin B12, B6, B9 TID was added to the patient's treatment regimen, as injectable formulations.

After 4 days of admission in the medical college hospital, the patient was shifted to the previously treated tertiary care referral hospital and tracheotomy was performed. The medicines prescribed from the medical college hospital was continued. Along with the regimen, tablets such as, motelukast 10 mg, levocetirizine 5 mg, N acetylceisteine 600 mg, acebroyhylline 100 mg and injections such as theophylline and hydrocortisone were prescribed.

During the first discharge from the tertiary care hospital, potassium level declined to 2.92 mEq/l and was considerably low on the subsequent days. Hypokalemia worsened even after administration of potassium chloride syrup 1.5g (15 ml) TID. So the physician increased the dose to 2 g (20 ml) four times daily (QID) and the serum potassium became 3.4 mEq/l after 6 days of its initiation. The patient became stable with serum sodium also being normal.

Discussion

The patient had severe vomiting during her pregnancy which did not subside even after her first trimester. The actual mechanism of hyperemesis is not clear, but may be due to the rapid elevation of human chorionic gonadotropin and estrogen in the blood [9]. Hypotension and dehydration are some of the complications of hyperemesis gravidarum. Both of these are more profound among pregnant women [10]. From the first hospital, the physician noticed hypotension in the patient and rectified with normal saline without quantifying the serum sodium. The serum sodium and potassium were measured later from the tertiary care referral hospital and was observed to be low. Women with hyperemesis in the second trimester would have double risk for preterm preeclampsia and three-fold chance for placental rupture [11,12]. This might be the reason behind the intrauterine fetal death at her early gestational period. Severe diarrhea was also accompanied along with vomiting and aggravated her symptoms of hyponatremia, that included - weakness, disorientation, inability to walk, hypotension, reduced speech.

The patient with severe hyponatremia (serum sodium less than 120 mEq/l) would have cerebral edema [13]. However, neurons facilitate the adaptive responses and a quick transport of serum electrolytes with comparatively

slow shift of organic osmolytes would stop the increase in cell volume. This adaptation could be stated as the reason behind the preservation of brain from further damages [14,15]. The cellular reuptake of organic osmolytes can take up to a week and the homeostatic changes happening in the brain cells are susceptible to injury due to rapid rise of plasma sodium [16]. The symptoms of rapid correction will not be evident within 24 hours of hyponatremia, but the situation would worsen after 3 days, and the signs and symptoms of osmotic demyelination syndrome would be visualized [17].

The recommendation from the treatment guideline for correction of hyponatremia states that, the serum sodium increment should not exceed 12 mEq/l per day or 1 to 2 mEq/l per hour [3]. The European expert panel recommends a 10 mEq/l increase limit on the 1st day and 8 mEq/l on the subsequent days until normal [18]. For patients at high risk of demyelinolysis syndrome (serum sodium greater than or equal to 105 mEq/l, malnutrition, hypokalemia), an 8 mEq/l limit and a 4 to 6 mEq/l goal is recommended [13,19,20]. Noncompliance to the guideline could induce neurological symptoms, seizure, coma and death. There are supportive case reports, which had the incidence of the neurological damages in patients with correction done at comparatively slow rate [21]. We assume that the patient was overcorrected with normal saline from the initial hospital and this led to osmotic demyelination syndrome. The MRI of brain showed, pontine lesions was associated with EPM and involves the caudate, putamen and thalamus [7]. The patient also experiences ataxia, catatonia and dystonia of lower limb which are the symptoms of pontine myelinolysis [5,7,22]. The radiological assessment and the signs and symptoms cumulatively confirmed the diagnosis. The physician at the tertiary care referral hospital had followed the treatment protocol and the serum sodium increment was promoted at a slow rate i.e., 11 mEq/l in 5 days.

Severe hyponatremia and its rapid correction were considered as the major etiology for the syndrome. In addition, the degree of damage to the neurons was aggravated by co-existence of low level of serum potassium [6]. From a case series, 89% among 74 osmotic demyelinolysis cases, there was co-existence of hypokalemia. Our patient's hypokalemia was not initially managed at the period when rapid correction of sodium was performed [23]. Reduced endothelial cell membrane concentration of Na/K-ATPase in hypokalemia may predispose the neuronal injury by the osmotic stress, as a factor of rapid rise in serum sodium correction [23]. There was a delay in initiating the potassium supplements for the management of hypokalemia. Later on, potassium chloride syrup of 1.5 g (1.5 g supplying 20 mEq of potassium and 20 mEq of chloride) TID administered, did not normalize the electrolyte. Thus, the physician increased the dose to 2 g QID and it was found to be effective.

Even if the sodium deficit is too high, the physician should always adhere to the treatment guideline. On the other hand, the people have a temptation to increase the rate of intravenous infusion of normal saline by adjusting the IV set roller. This practice is done to get rid of the infusion as fast as possible. Hence, proper counseling regarding the infusion and adverse impact of increase in the rate of administration should be done.

Conclusion

Even though, osmotic demyelinolysis is a rare complication of the sodium correction, hypokalemia also needs to be taken into consideration as a risk factor. The clinicians should understand the irreversible adverse impact on brain. Hence, all pregnant ladies with hyperemesis should be tested for any serum electrolyte imbalance and the patient with dehydration should be supplemented with electrolyte, cautiously.

What is new?

Pregnant women had excessive vomiting and went to severe dyslelectrolytemia, as a result fetal intrauterine death happened. The case became more contagious with sodium correction, which lead her to a condition known as osmotic demyelinolysis. The patient was admitted to three different hospitals, and it was from the tertiary care hospital, the patient's hyponatremia and hypokalemia was normalized. Being a rare case, occurred in a pregnant lady, the report is intended to give an awareness to the healthcare providers on the importance of appropriate sodium correction and adverse effect with incompliance to standard guideline. The uniqueness of the report is the patient, the pregnant lady. This study would also give light to healthcare providers on the need of assessing the possibility of fetal death and neurological issues associated with excessive vomiting and osmotic demyelinolysis with serum electrolyte correction.

Summary

- Hyperemesis gravidarum is a condition that may happen in pregnant ladies which would cause severe electrolyte imbalance or fetal intrauterine death.
- The case is about a pregnant woman who had severe vomiting and had to undergo D & E due to fetal death during the 14-week gestational period.
- The patient was admitted in three different levels of hospitals. The first hospital had over corrected the serum sodium level and caused the damage to pontine and extra pontine region in the brain.
- Furthermore, the patient's serum sodium was normalized slowly and in adherence to standard treatment protocol. However, there was a delay in the management of hypokalemia.
- The osmotic demyelinolysis was diagnosed taking into consideration, the symptoms such as dystonia of limb, catatonic, and depression and MRI of brain.

- The case highlights the need for pregnant lady with hyperemesis to be tested for dyselectrolytemia and proper correction of the electrolytes according to treatment guidelines was followed.

List of Abbreviations

CPM	Central pontine myelinolysis
QID	Four times daily
MRI	Magnetic resonance imaging
TID	Thrice daily
USG	Ultra-sonography

Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this case report.

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Consent for publication

Written informed consent was taken from the patient.

Ethical approval

Ethical approval is not required at our institution for publishing an anonymous case report.

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Summary of the case

1	**Patient (gender, age)**	Female, 19 year old
2	**Final diagnosis**	Osmotic demyelinolysis
3	**Symptoms**	Depression, catatonia, dystonia of limb
4	**Medications**	Normal saline, potassium chloride
5	**Clinical procedure**	Dilatation and evacuation, fiber optic bronchoscopy and brochoalveolar lavage, dilation and curettage, tracheotomy
6	**Specialty**	Gynecology and Obstetrics