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Management of a Parturient with Preeclampsia and HELLP Syndrome Complicated by Gestational Diabetes Insipidus

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Abstract

HELLP syndrome (Hemolysis, Elevated Liver enzymes, Low Platelets) is considered to be a variant or severe form of pre-eclampsia, a life threatening complication of pregnancy. Gestational Diabetes Insipidus (GDI) can coexist with severe preeclampsia and HELLP syndrome. The combination of these two conditions presents a unique challenge to the anesthesiologist and the obstetric team, caring for this parturient. We present the case of a parturient with an unusual presentation of GDI, coexisting with severe preeclampsia and HELLP syndrome. She had two days history of polyuria and polydipsia as well as lethargy and rapidly rising serum sodium in addition to acute renal failure without any neurologic symptoms. Expeditious delivery of the baby and supportive management is essential for optimal outcomes. She underwent a repeat Cesarean section under combined spinal epidural (CSE) anesthesia. This patient was discharged on postoperative day five after clinical resolution of her signs and symptoms.

Keywords

Gestational Diabetes Insipidus, Severe Preeclampsia, HELLP Syndrome

1. Introduction

Preeclampsia is a multisystem, progressive, highly variable disorder unique to pregnancy and a leading cause of maternal and fetal/neonatal morbidity and mortality. Preeclampsia, defined as systolic blood pressure greater than 140 and diastolic blood pressure greater than 90 after twenty weeks of gestation accompanied by proteinuria (>300 mg/d), complicates about 10% of pregnancies. In the United States, preeclampsia

complicates 6% - 10% of all pregnancies; the incidence is believed to be even higher in underdeveloped countries. Hypertension is the most common medical disorder of pregnancy and is a leading cause of maternal and fetal morbidity and mortality. Severe preeclampsia can be associated with blood pressures greater than 160/110 mm of Hg, proteinuria greater than 5 grams/day, oliguria (<500 mL/day), elevated serum creatinine, intrauterine growth restriction, pulmonary edema, neurologic manifestations of headache, visual disturbances, seizures, or stroke as well as hepatic tenderness or HELLP syndrome. Recent evidence suggests that preeclampsia accounts for approximately 15.9% of all maternal deaths in the United States and is a major cause of perinatal morbidity and death. GDI is known to be associated with HELLP and HELLP is known to be associated with GDI; the combination is rare and complicates the management.

In pregnant women, GDI has been described as a rare complication of pregnancy that occurs in about 4 out of 100,000 pregnancies [1]. The mechanism of GDI is that maternal antidiuretic hormone is degraded by the vasopressinase enzyme secreted by placental trophoblasts and it can manifest as early as the seventh week of gestation [2].

The definitive therapy to prevent further progression of the severe preeclampsia and GDI is delivery of the fetus and the placenta. The anesthetic goals of management are geared towards treatment to minimize vasospasm, achieve blood pressure control, improve circulation, optimize intravascular volume and correct electrolyte and acid base disturbances without over correcting the hypernatremia.

2. Case Report

The patient has given consent to publish this case report. A 41-year-old African American female, G3P3, with no significant past medical problems and history of two previous Cesarean sections, presented at 38 weeks of gestational age to the patient presented to obstetrical clinic. Her presenting com-plaints were polyuria, polydipsia, weakness, and headache of two days duration. On examination, she was found to have elevated blood pressures, systolic blood pressure ranging from 160 - 170 mm of Hg, diastolic blood pressures 90 - 100 mm of Hg and heart rate in the range of 100 - 120 beats per minute. She denied any blurring of vision, epigastric pain, neurological abnormalities or breathing difficulties. Examination of the systems did not reveal any significant findings.

On admission, her hematocrit was 42 and platelets were 235,000. Her Liver function tests were abnormal and revealed Serum AST(aspartate aminotransferase) of 270 IU/L, ALT (alanine aminotransferase) of 271 IU/L, LDH (lactate dehydrogenase) of 379 IU/L, Alkaline phosphatase 207 IU/L, Albumin 2.9 IU/L and total bilirubin 0.7 mg/dl. Renal function tests revealed elevated uric acid of 8.9 mg/dl, BUN (blood urea nitrogen) of 15 mg/dl and elevated creatinine of 1.2 mg/dl. Serum electrolytes showed elevated sodium of 148 mmols/L and chloride 121 mmols/L, and potassium 4.6 mmols/L. Her PT and PTT were within normal limits (10.7 and 26.4 seconds). Pelvic examination revealed cephalic fetal presentation, cervical dilatation of 0 cms and intact membranes. Bedside Ultrasound examination showed vertex presentation, anterior placenta, BPP 6/8 and

AFI 2.7 cms.

A diagnosis of HELLP syndrome with severe oligohydramnios was made. In the presence of HELLP syndrome, severe oligohydramnios and elevated sodium and chloride in the setting of polyuria and polydipsia, the decision was to proceed with repeat C-Section for expeditious delivery of the fetus and the placenta. Patient received a bolus of 4 grams of magnesium sulfate for eclampsia prophylaxis. Two units of PRBCs were typed and cross-matched.

Patient was placed on standard ASA monitors in the operating room. Additionally, a 20 gauge arterial line was inserted for continuous blood pressure monitoring and repetitive blood sampling for electrolytes. Combined Spinal Epidural(CSE) was per-formed at 3 - 4 lumbar interspace with preservative free morphine 0.3 mg, fentanyl 15 ug, and 1.5 ml of hyperbaric bupivacaine 0.75% with dextrose 8.5 mg/ml. Left uterine displacement was done. Cesarean section course was uncomplicated. A healthy baby boy with APGAR scores of 7 and 9 was delivered. Intraoperative fluid management consisted of the administration of 2200 ml of lactated Ringers over a period of 100 minutes.

Immediate postoperative course was complicated by the rapidly rising serum sodium with high calculated Serum Osmolality of 331 in the context of renal failure and urine output > 2000 ml over a period of 5 hours. She was transferred to the medical intensive care unit for hydration, blood pressure monitoring and correction of hypernatremia. 0.9% normal saline infusion at 300 ml/hr was initiated, which was titrated to achieve a goal of sodium correction rate of less than 10 mEq in twenty four hours or 0.5 mEq/hr. Serum sodium levels were checked every two hours. On postoperative day one, the hypernatremia peaked at 163 meqs and decreased with hydration to 153 meqs. The hepatic enzyme levels peaked at aspartate transaminase and alanine transaminase levels of 1359 and 848 and had decreased significantly by day 3. Her serum creatinine peaked at 1.8 and gradually decreased (Table 1). Her pan cultures were negative.

Both Endocrinology and Neurology consults were obtained. The antidiuretic hormone, follicle stimulating hormone, luteinizing hormone, and adrenocorticotropic hormone levels were assayed. Serum ADH level was <1.0 pg/ml (normal range 1 - 13.3 pg/ml). Magnetic resonance imaging/magnetic resonance angiogram of the brain was

Table 1. Patients daily laboratory results.

Peak Serum levels	Postoperative Day (POD)[a]					
	POD 0	POD 1	POD 2	POD 3	POD4	POD 5
Sodium (mmols/L)	147	163	152	143	142	141
Creatinine (mg/dl)	1.2	1.8	1.6	1.3	0.9	1.0
ALT (IU/L)	271	848	473	249	___	105
AST (IU/L)	270	1359	449	141	___	38
LDH (IU/L)	379	1480	___	___	___	142
Uric acid (mg/dl)	8.9	11.5	___	___	___	6.8

a. Patients daily laboratory results. ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; IU: international Units.

negative for pituitary pathology and there was no evidence for posterior reversible encephalopathy syndrome. She was diagnosed, by exclusion, with gestational diabetes insipidus (GDI). Desmopressin was not administered due to rapid, clinical improvement, decreasing serum sodium levels, decreasing urine output and no neurologic deficits. Optimization of blood pressure with labetalol was continued, and she was maintained on magnesium sulfate infusion for seizure prophylaxis.

On postoperative day two, the sodium and creatinine normalized, her urine output decreased, and the Foley catheter was removed. On postoperative day three, the patient's liver function tests profile normalized. On postoperative day four, she was transferred to the regular maternity floor. On postoperative day five (POD), the patient was discharged with normal labs on labetalol 100 mg PO every 12 hours with an electronic blood pressure monitoring device. Patient was discharge home POD 6, and post-partum follow after 2 weeks was uneventful.

3. Discussion

Diabetes insipidus during pregnancy is a rare phenomenon and its incidence varies from two to six cases per 100,000 pregnancies. It can occur at any stage of the gestation, but commonly presents at the end of the second or during the third trimester of a first pregnancy. Occasionally, it can manifest in the postpartum period.

DI can be the manifestation of several factors, the most frequent being a deficit in the secretion of ADH (Antidiuretic Hormone) from the hypothalamus, which results in neurogenic or central diabetes insipidus (DI). The second cause is renal tubular insensitivity to ADH (antidiuretic hormone), nephrogenic or peripheral DI. The third variety is the result of a deficit in ADH production, secondary to excessive fluid intake because of psychogenic polydipsia. During pregnancy, an abnormal clearance of the hormone can cause ADH deficiency and result in gestational DI.

Symptoms of DI usually develop over a few days and include polyuria, polydipsia, fatigue, nausea, weight loss, and decreased skin turgor. The symptoms of polyuria and polydipsia may be difficult to distinguish from normal pregnancy as the normal thirst threshold in pregnancy is reduced. In fact, the clinical examination is often normal in patrturients who are drinking fluids without any restriction. Disturbances in hydration become evident in obtunded or comatose patients because of their inability to compensate for increased urinary losses. To differentiate between the various causes of GDI, history of neurosurgical interventions for pituitary tumors and psychological disturbances should be sought.

In a normal pregnant patient, plasma osmolality decreases by almost 10 mmols/L and sodium concentration by almost 5 meq/L. Urinary osmolality is also decreased. GDI can be suspected when serum osmolality is equivalent to that of a non-pregnant woman (285 mosmol/L) with urinary osmolality under 300 mosmols/L. Measurement of the vasopressinase serum concentrations is not available commercially, and the diagnosis is usually established based on the clinical presentation and the appropriate laboratory studies. Blood glucose levels are usually normal in GDI. Serum glucose, sodium, ADH concentration, hepatic transaminases, creatinine and uric acid, all need to

be measured. Plasma levels of ADH should be assayed in the presence of a vasopressinase inhibitor since parturients have high concentrations of cysteine aminopeptidase which degrades vasopressin in vitro. Urine volume, urinary electrolytes including sodium and glucose and osmolality need to be measured.

Goals of Anesthetic management in a parturient with HELLP syndrome and GDI (both have similar perioperative management goals, each has its own particular management that does not interfere with the management of the other condition):

The focus of perioperative management is on:

- Blood pressure control with appropriate antihypertensive medications;
- Seizure prophylaxis with Magnesium therapy;
- Strict intake-output monitoring;
- Cautious administration of fluids, avoiding a rapid fall in serum sodium concentration of no more than 0.5 meq/hour to prevent cerebral edema (In HELLP syndrome, over hydration can lead to pulmonary edema, whereas, in DI it can lead to a rapid fall in sodium concentration);
- Treatment with desmopressin;
- Frequent monitoring of serum electrolytes;
- Expeditious delivery of the fetus and placenta (delivery of the placenta alleviates the GDIas well as the HELLP syndrome and preecamplcia.);
- Utilizing spinal/epidural blocks- preferable since monitoring of the mental status and avoidance of the airway is facilitated;
- Invasive hemodynamic monitoring- An arterial line insertion is highly desirable, as it allows for close monitoring of the blood pressure in a severe preeclamptic parturient, but also allows serial estimation of electrolytes. CVP monitoring, though not routinely necessary, will aid in volume resuscitation as needed;
- Continued postoperative care in a monitored setting is highly desirable.

Initially, our parturient was treated with repeated doses of labetalol for blood pressure control and magnesium sulfate for eclampsia prophylaxis, but the definitive treatment for her preeclampsia, HELLP syndrome, and gestational diabetes insipidus was the delivery of fetus and placenta [3]. Treatment with desmopressin was not initiated in this patient due to her rapid improvement. The use of an arterial line not only allows for expeditious monitoring and treatment of elevated blood pressures but also allows for close monitoring of electrolytes and creatinine postoperatively. While not routinely necessary, central venous pressure monitoring in addition to arterial line monitoring has been described in GDI to assist with careful volume resuscitation in the setting of suspected dehydration in a parturient with extreme thirst and severe preeclampsia [4]. It is postulated that hypernatremia leads to increased local anesthetic potency due to the increased intra-extra neural sodium gradient and careful titration and administration of the local anesthetics is essential. If time permitted, fluid resuscitation with an arterial line and central venous pressure monitoring based on her calculated water deficit as well as desmopressin supplementation would have been desirable to at least partially correct the patient's fluid deficit and serum sodium, allowing careful titration of

epidural anesthesia for Cesarean section [5].

Administration of intranasal desmopressin is the treatment of choice in GDI [6]. Caution should be exercised to avoid desmopressin overdose which can lead to hyponatremia. Patients with gestational diabetes insipidus may require intranasal desmopressin spray 5 mcg twice a day after an initial dose of 10 mcg. Breastfeeding can stimulate secretion of ADH and the dose of desmopressin can be decreased. Desmopressin is secreted in the mother's milk in very small quantities and minimally absorbed by the GI tract; hence, poses little risk for fluid and electrolyte disorders in the neonate.

Alternative treatment is hydrochlorothiazide. Potential complications include fetal hypoglycemia and neonatal DI. Remission of DI occurs two to three weeks after delivery and hydrochlorothiazide must be discontinued.

4. Conclusion

During pregnancy, the diagnosis of DI is not easy to consider since polyuria in pregnancy is generally considered normal. In general, GDI per se does not seem to result in serious complications. However, certain varieties, especially in association with HELLP syndrome, can have serious consequences and need to be kept in mind. A multidisciplinary, collaborative approach between obstetric anesthesiologists, maternal-fetal medicine specialists, intensivists and neonatologists is essential to weigh the maternal and fetal risks of prolonging the pregnancy versus the potential benefits of expectant management to further fetal maturation.

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