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Postpartum gestational diabetes insipidus related to preeclampsia: A case report

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ABSTRACT

Gestational diabetes insipidus (GDI) is a rare complication of pregnancy thought to be due to increased vasopressinase produced by the placenta. It typically occurs at the end of the second or in the third trimester. This report describes a case of GDI diagnosed postpartum in the setting of newly diagnosed superimposed preeclampsia. A 39-year-old Hispanic woman (gravida 2 para 2) presented ten days postpartum with a persistent headache and elevated blood pressures in the setting of a history of chronic hypertension, meeting criteria for superimposed preeclampsia. Repeat lab work was notable for mild elevation of liver function enzymes. Despite normalization of blood pressures, her headache persisted and further workup revealed polyuria, suspected to be vasopressinase-induced diabetes insipidus. The patient was started on oral desmopressin with improvement of polyuria and symptoms.

1. Introduction

Gestational diabetes insipidus (GDI) is a rare complication of pregnancy thought to be due to increased vasopressinase, an enzyme produced by the placenta that degrades arginine vasopressin (AVP). As increased urinary frequency and polyuria may be dismissed as normal symptoms in pregnancy, GDI is likely underdiagnosed. Early recognition of this condition is important because if untreated, diabetes insipidus can lead to dangerous and life-threatening consequences for the mother and fetus. GDI typically occurs at the end of the second or in the third trimester, and rarely presents postpartum [1]. This report describes a case of GDI diagnosed postpartum in the setting of newly diagnosed superimposed preeclampsia.

2. Case Presentation

A 39-year-old Hispanic woman (gravida 2 para 2) presented to Labor & Delivery ten days postpartum following a vacuum-assisted vaginal delivery with a persistent headache. Her medical history was notable for chronic hypertension not requiring medications. She was previously admitted for induction of labor for premature rupture of membranes at 39 weeks and 1 day of gestation. Her admission labs included a baseline preeclampsia workup which was notable for a urine protein to creatinine ratio of 0.57 mg/dL; however, the sample was not via catheterization so likely invalid in the setting of ruptured membranes; one week earlier the ratio had been 0.17 (normal <0.3 mg/dL). Her renal and hepatic function labs were normal, and she had no evidence of hemolysis or thrombocytopenia. There was no evidence of superimposed preeclampsia during her admission.

Her labor course was unremarkable except for fetal heart rate decelerations with pushing as well as maternal exhaustion, for which she underwent an uncomplicated vacuum-assisted vaginal delivery of a female infant weighing 3675 g (78%ile) with Apgars of 6 and 9, at 1 and 5 min of life respectively. Her inpatient postpartum course was unremarkable, and she was discharged on her second postpartum day. Following her delivery, her blood pressures remained stable and within a normal range (<140 systolic and 90 diastolic), and never reached the threshold criteria for severe (160 systolic and 110 diastolic). Again, there was no evidence for the development of preeclampsia prior to her discharge.

She then presented on postpartum day ten with new-onset headaches. She had tried acetaminophen at home without improvement. Her vital signs were notable for blood pressures that were elevated beyond her previous baseline, with values reaching the severe range on multiple occasions. Given the patient's new persistent headache and elevation in blood pressures, a diagnosis of superimposed severe preeclampsia was

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made, and she was admitted for intravenous magnesium sulfate therapy for seizure prophylaxis. She received a 4-g loading dose and then was maintained on a continuous rate at 2-g/h for 24 h. A repeat preeclampsia lab workup was performed. Hepatic function labs were slightly elevated from prior, not yet twice the upper limit of normal (ALT 37 U/L increased from prior admission level of 13 U/L). There was no evidence of worsening renal function, hemolysis or thrombocytopenia. Her urine protein creatinine ratio also was within the normal range at 0.1. Given her elevated blood pressures, she was started on a daily oral dose of extended-release nifedipine 30 mg daily.

After cessation of her magnesium therapy and initiation of a new antihypertensive, her blood pressures returned to her baseline; however, her headache persisted. She denied any photophobia, phonophobia, nausea or vomiting. Her headache was in band distribution and positional. She was afebrile. No focal neurological deficits or nuchal rigidity were detected on physical examination. The headache did not seem to be related to her new antihypertensive as it had begun prior to the initiation of nifedipine. A review of her urine output showed polyuria, with 8.95 L of urine output over 24 h. Given her polyuria, orthostatic vital signs were performed and were positive, suggesting hypovolemia. It was therefore suspected that dehydration could be the underlying etiology of her headache.

Upon further questioning, the patient endorsed a history of both polyuria and polydipsia for a week prior to this presentation. Neurology, endocrinology and nephrology consultations were placed for further evaluation of her symptoms. The neurology team recommended an MRI brain scan; it proved unremarkable, and therefore they did not suspect a central cause or Sheehan syndrome. Endocrinology recommended further evaluation of anterior pituitary function with ACTH, morning cortisol levels, GH, IGF-1, thyroid panel, all of which resulted normal. Prolactin was high in the setting of breastfeeding with appropriately suppressed FSH and LH. Nephrology recommended a serum osmolality as well as a 24-h urine collection for urine osmolality and electrolytes. Serum and urine osmolalities were performed and were 295 mOsm/kg and 187 mOsm/kg respectively (reference ranges: 278–305 mOsm/kg, and 500–800 mOsm/kg respectively). Her serum sodium was 138 mmol/L.

After evaluation by Nephrology and Endocrinology, the working diagnosis was vasopressinase-induced diabetes insipidus, secondary to preeclampsia versus peripartum state. The patient was started on oral desmopressin 0.05 mg BID on hospital day 4 and continued through day 6. Her urine osmolality increased to 534 mOsm/kg following the first dose. Her headache and dizziness also resolved. She was discharged on hospital day 7. On the day of her discharge, her urine output improved to 3.1 L over 24 h.

3. Discussion

Diabetes insipidus (DI) is characterized by polyuria (defined as >3 L/day urine output) and polydipsia due to loss of ability to concentrate urine [2]. Gestational DI is a transient and rare condition of pregnancy, occurring in about 1 per 30,000 pregnancies [3]. The pathophysiology of GDI is thought to be related to excessive vasopressinase activity. Vasopressinase is an enzyme expressed by placental trophoblasts that degrades AVP, or antidiuretic hormone (ADH). The enzyme activity increases as trophoblast mass increases; therefore, the condition most commonly occurs in the third trimester and there is higher risk in multiple gestation. It rarely occurs postpartum associated with hepatic insufficiency or pituitary dysfunction. GDI typically resolves spontaneously 4–6 weeks postpartum, and usually does not recur in future pregnancies [1,4].

Vasopressinase is metabolized by the liver, so patients with impaired hepatic function are at risk of decreased enzyme degradation, and therefore increased AVP clearance leading to GDI. Hepatic dysfunction in pregnancy can be seen in acute fatty liver of pregnancy, preeclampsia, hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome or chronic disease such as hepatitis and cirrhosis. DI in pregnancy can also be a result of worsening of preexisting central or nephrogenic DI. Postpartum DI could be related to postpartum hemorrhage causing hypoperfusion of the pituitary gland or placental abruption releasing vasopressinase into the maternal bloodstream [5].

Recognizing and initiating treatment early in the disease course is important as water restriction can result in hypernatremia and uteroplacental insufficiency, leading to devastating outcomes for both patient and fetus. Case reports have associated the condition with fetal demise as well as oligohydramnios [6,7].

The mainstay treatment for GDI is desmopressin, a synthetic form of AVP not degraded by vasopressinase. Desmopressin is considered safe in pregnancy as well in breastfeeding as a minimal amount is excreted into breast milk and it is poorly absorbed by the neonate [4]. Desmopressin has minimal effect on vascular tone, and therefore does not contribute to risk of hypertension, which is important when used in preeclampsia [1].

GDI in the postpartum setting is rare, mostly occurring in the setting of marked hepatic dysfunction, pituitary infarction or placental abruption. Our case demonstrates GDI presenting postpartum in the setting of mild hepatic dysfunction. Even though her liver enzymes were not remarkably elevated (AST 23, which is within normal limits, and ALT 37, which is slightly elevated), both demonstrated an increase from her baseline, signifying some degree of impairment. This could lead to a decrease in vasopressinase clearance and thus an increase in ADH degradation.

In our patient's case, symptoms of DI seemed to resolve approximately 2.5 weeks postpartum. Per her nephrology outpatient follow-up 2 days after her hospital discharge, her 24-h urine volume normalized to 1950 mL, with urine osmolality 572 mOsm/kg. Given the transient nature of her symptoms, our patient's DI was most likely vasopressinase induced in the setting of preeclampsia.

4. Conclusion

Polyuria is often dismissed as a normal symptom in pregnancy; however, it is important to recognize that it may indicate pregnancy-related DI, as this condition may lead to serious consequences for both the patient and fetus. Our patient's presentation highlights the importance of being aware of the risk of DI in pregnant women with even mild impairment of liver function.

Contributors

Alisa Goldrich contributed to patient care, conception of the case report, acquiring the data, drafting the manuscript, undertaking the literature review.

Jessica Yuan was involved in the care of this patient and revising the article critically for important intellectual content.

Hindi Stohl was involved in the care of patient, conception of the case report, and revising the article critically for important intellectual content.

All authors approved the final submitted manuscript.

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Conflict of interest statement

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the work reported.

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