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The Approach to the Diagnosis of Diabetes Insipidus in Pregnancy

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Abstract

Background: *Diabetes insipidus is rare in pregnancy. Management differs by etiology.*

Methods: *This is a case report and discussion for the diagnosis and management of diabetes insipidus diagnosed in pregnancy.*

Results: *Evaluating the etiology of polydipsia and polyuria in pregnancy is difficult. A basic metabolic panel, glucose screen and 24-hour urine should be performed at minimum. Appropriate work up of diabetes insipidus is important as it can cause electrolyte disturbances, especially if water is restricted, which may be the case on labor and delivery.*

Keywords: Antidiuretic Hormone, Central, Diabetes Insipidus, Nephrogenic, Polydipsia, Polyuria, Pregnancy, Vasopressin's

Introduction

Diabetes insipidus (DI) is a rare complication of pregnancy. The estimated incidence is 4 in 100,000, though this may be an underestimate as not all cases are reported and mild cases may be missed if symptoms are interpreted as normal symptoms of pregnancy [1,2].

DI can be acquired during pregnancy as it is outside of pregnancy, pregnancy may un-mask pre-existing DI, or pregnancy can directly cause DI through placental production of vasopressinase. If caused by pregnancy, DI usually develops in the latter half of pregnancy when the levels of vasopressinase produced by the placenta are highest, and will resolve after delivery. Multiple gestations may be at increased risk due to larger placental volume and production of vasopressinase [1,2]. Most pregnancies can compensate for the increased levels of vasopressinase by increasing synthesis and release of antidiuretic hormone (ADH) [3]. Patients with pre-existing undiagnosed or subclinical DI may be unable to compensate resulting in an exacerbation or unmasking of DI [2]. Diseases that cause hepatic dysfunction, including pregnancy specific diseases such as preeclampsia, can decrease the degradation of vasopressinase resulting in decreased levels of ADH and causing DI [4,5].

Case

26yo G4P0030 with a history of chronic hypertension, unexplained elevated MSAFP, and fibroid uterus was admitted at 21 weeks and 4 days for uncontrolled blood pressure and evaluation for suspected superimposed preeclampsia. As part of the evaluation for pre-eclampsia she underwent a 24-hour urine collection, which resulted in a 7.3-liter collection with 508mg of protein and 1.7g of creatinine. Correct collection was confirmed with the patient. A repeat 24-hour urine was performed to confirm the results, which resulted in a 5.7-liter collection with 342mg of protein, 1.8g of creatinine. At this time urine osmolality was measured at 215 mosmol/kg. Nephrology was consulted and a third collection was performed at their request, which resulted in 4.2 liters with 378mg of protein, 1.6g of creatinine. Her glucose tolerance test and HgA1c were normal.

The patient reported consciously trying to drink less water after being told about her excessive urine output. She stated that the amount of water she drank and urinated felt normal to her and that even when not pregnant she estimated that she drank five liters of water per day and urinated four to five times an hour, getting up several times to urinate in the night. Early in prenatal care she performed a 24-hour urine collection to assess baseline proteinuria, which resulted in 2.8 liters, 193 mg of protein and 1.0 g of creatinine, but stated that she did not collect all of her urine of the 24-hour period as she urinated much more than would fit in the one container, she was given to take home. She also reported prior to pregnancy collecting a 24-hour urine with her primary care attending in which she also urinated more than could fit in the three-liter container, so was an incomplete collection. During her hospital stay, her serum sodium ranged from 133 to 137 mEq/l.

A water deprivation test was considered but deferred due to concern for water deprivation causing uteroplacental insufficiency. Nephrology then conducted a DDAVP test which resulted in an increase of urine osmolality from 144 mosmol/kg to 825 mos-

mol/kg over two hours. The working diagnosis was gestational DI, however, due to her reported history, central DI was also a possibility. As a water deprivation test was not performed, primary polydipsia also remained a possibility.

An endocrinology consult was placed to discuss possible need for DDAVP treatment, however, the patient left against medical advice. Endocrinology recommended treatment if there was hypernatremia or if nocturia was bothersome to her. The plan was for additional evaluation postpartum as long as her laboratory tests remained normal, and she developed no concerning symptoms.

Subsequently, the patient returned at 23 weeks and 5 days with prelabor preterm rupture of membranes. Antibiotics and magnesium sulfate were administered, and she was managed expectantly in the hospital. She was then delivered at 24 weeks and 3 days by classical cesarean delivery for preterm labor with malpresentation. During this hospitalization her electrolytes were monitored, and her sodium was between 130 and 137 mEq/l. Postpartum day 7, her sodium was 139 mEq/l.

Discussion

Pregnant patients should be evaluated for DI if they have polyuria (>3L of urine per day) and polydipsia [7]. The patient should be evaluated for solute diuresis, such as glucosuria. Water diuresis can be the result of primary polydipsia, central DI, and nephrogenic DI. In water diuresis, the urine osmolality is low and serum osmolality may be high or normal if water loss is balanced by increased water intake [6].

In a non-pregnant patient, the standard confirmatory test is a water deprivation test followed by a desmopressin stimulation test [6]. However, if the patient is already hypernatremia the desmopressin stimulation test can be performed without the water deprivation test as it will worsen hypernatremia. Water restriction may be used in pregnancy, but need to be performed cautiously and in a hospital setting with close monitoring as it can cause dehydration with resultant uteroplacental insufficiency, and hypernatremia [9, 11] .

It is important to take into consideration that serum sodium in pregnancy is normally lower in pregnancy: 133-148 mEq/L in the first trimester, 129-148 mEq/L in the second trimester, and 130-148 mEq/L in the third trimester [12]. Values that may appear in the normal range for non-pregnant adults, may be relatively elevated in pregnancy.

In the water deprivation test the urine osmolality is measured after the patient avoids fluid intake for approximately 12 hours [13]. If there is adequate production of normally functioning ADH and normally functioning kidneys, the plasma osmolality should trigger release of ADH and the kidneys should resorb urine. Therefore, if the urine osmolality is high after the water deprivation test, this proves the patient can concentrate urine if water intake is restricted and her polyuria is not from DI. Primary polydipsia is a separate disease process that presents similarly with polyuria and polydipsia, however, there is ADH production and action is normal, but rather, the patient is drinking too much water [9]. Causes of primary polydipsia should be investigated and brain MRI may be appropriate [6].

If the urine osmolality is low, diabetes insipidus is confirmed. A DDAVP stimulation test is then performed by giving DDAVP and then checking urine osmolality for several hours. Central diabetes insipidus will respond to DDAVP and the urine should concentrate. In nephrogenic DI, the kidneys are still unable to appropriately respond to DDAVP and the urine remains dilute [9].

Once a diagnosis of central diabetes insipidus is established, an MRI should be performed to assess for structural lesions and other investigations for etiology directed by clinical circumstances [2]. However, an MRI does not have to be completed in pregnancy unless there is concern for trauma, hemorrhage or mass [8]. If nephrogenic DI is diagnosed, the cause should be investigated based on other clinical findings [6].

Management

DI caused by an increase in vasopressinase should resolve within a few days to weeks of delivery. If treatment of gestational DI is needed, DDAVP is the treatment of choice as it is not degraded by vasopressinase [6]. Treatment for gestational DI would be warranted if the symptoms (polyuria, nocturia, etc.) are significant enough to interfere with normal daily functioning or if hypernatremia is present. Intranasal or oral DDVAP can be administered at bedtime or twice daily and titrated to relieve symptoms and maintain appropriate serum sodium [8,9].

Treatment requires close monitoring of urine output, serum sodium, serum osmolality, and urine osmolality, in addition to fluid restriction [8]. Parenteral fluid administration, as may be received on labor and delivery, must be closely monitored as these patients can develop water intoxication and hyponatremia from an inability excrete adequate amounts of urine [8,9]. Treatment can be stopped days to weeks after delivery and is safe to use during lactation. If DI continues after six weeks of delivery or recurs, central DI should be reconsidered [6,8].

Central DI is similarly treated with DDAVP. Nephrogenic DI is harder to treat. Partial nephrogenic DI may be treated with higher doses of DDAVP. Outside of pregnancy, thiazides and NSAIDs may be employed [8,9]. Primary polydipsia is treated with education and psychotherapy to help decreased the volume of water intake [6,8]. Ice chips and hard candy can be used to stimulate salivary flow and reduce the sensation of dry mouth and reduce thirst [2]. DDAVP is not used for treatment because though it will eliminate the polyuria, the polydipsia will continue and water intoxication can occur [6].

Conclusion

Complaints of excessive thirst or polyuria pregnancy should be evaluated and may warrant further diagnostic testing with a basic metabolic panel, glucose screen and 24-hour urine. Appropriately diagnosing DI is important as it can cause electrolyte disturbances, namely hypernatremia if water is restricted, which may be the case on labor and delivery.

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