

Diabetes Insipidus in Pregnancy

Arun Kumar, MD

Vallur S. Thirumavalavan, MD

Vinita Kumari, MBBS

Diabetes insipidus (DI) is a rare endocrinopathy, and its association with pregnancy is even rarer. Although pregnancy involves physical changes that predispose patients to diabetes insipidus, the disorder occurs only in approximately 4 of every 100,000 pregnancies.^{1,2} This article presents the case of a woman who had recurrent DI during pregnancy in association with abnormal results on liver function tests. Her clinical course was complicated by oligohydramnios and culminated in eventual fetal loss.

CASE PRESENTATION

Initial Patient Evaluation and Treatment

A multiparous 28-year-old woman at 18 weeks' gestation was admitted to our hospital because of a 3-day history of vaginal spotting, fever, and chills. On examination, the patient was euvolemic and vital signs were stable, although her temperature was 38.3°C (101°F). There also was mild right subcostal tenderness. She was treated for a presumed urinary tract infection with intravenously administered antibiotics. Posttreatment, she was afebrile and without pain.

Subsequent pelvic ultrasonography showed severe oligohydramnios but no abnormalities in the fetal bladder and kidneys. Fetal size was consistent with known dates. The patient's cervix was dilated 1 to 2 cm with a small area of ferning, consistent with premature rupture of the fetal membrane. Phenolphthalein paper testing was not performed to avoid false-positive results in the presence of a bloody discharge. Renal ultrasonography showed mild bilateral hydronephrosis. Initial laboratory tests were performed (**Table 1**).

Hospital Course

The patient was kept on strict bed rest because of the oligohydramnios and threatened spontaneous abortion. On hospital day 2, she reported excessive thirst and urination. Urine output on days 2 through 4 was 3000, 6000, and 5400 mL per day, respectively. On hospital day 5, urine output increased to 500 to 800 mL/h, and she developed postural hypotension. Further labo-

ratory testing showed a urine osmolality of 129 mOsm/kg H₂O, a serum osmolality of 301 mOsm/kg H₂O, and an antidiuretic hormone level of 2.5 pg/mL. Magnetic resonance imaging of the posterior pituitary gland revealed no abnormalities. A water deprivation test was not performed because of her postural hypotension.

On further questioning, the patient recalled a 2-week history of excessive urination 5 years earlier during her previous pregnancy, which had ended in spontaneous abortion and complete resolution of her polyuria. She reported no history of diabetes mellitus, head trauma, pneumonia, or use of medications.

After a tentative diagnosis of diabetes insipidus was made, the patient was started on subcutaneously administered 1-deamino-8-D-arginine vasopressin (DDAVP) 1 mg twice daily and intravenously administered hydration. There was a dramatic response to DDAVP therapy: over the next 3 days, urine output decreased to daily levels of 2200, 1250, 1900 mL and urine osmolality increased to daily levels of 747, 855, 526 mOsm/kg H₂O; during this time, the patient also reported decreased thirst. Subsequent ultrasonography, however, showed persistent, severe oligohydramnios. The pregnancy was terminated because of the oligohydramnios and inevitability of spontaneous abortion. Subsequently, DDAVP was administered via a nasal route and was eventually discontinued after 6 weeks when the patient became asymptomatic.

DISCUSSION

Definition and Etiology

DI is the primary clinical manifestation of posterior pituitary insufficiency. The disorder is characterized by the excretion of a high volume of unconcentrated urine. Triggered by a defect in the action of the antidiuretic

Dr. Kumar is a former resident and Dr. Thirumavalavan is the Associate Program Director, Department of Medicine, Jersey City Medical Center, Jersey City, NJ. Dr. Kumari is currently not in practice but also contributed to this report.

Table 1. Results of Initial Laboratory Testing in the Case Patient

Serum chemistries	Hematologic findings
Alanine aminotransferase (ALT, SGPT), 73 U/L	Leukocyte count, $6.1 \times 10^3/\text{mm}^3$
Albumin, 2.5 g/dL	Hemoglobin, 10.3 g/dL
Alkaline phosphatase, 82 U/L	Urologic findings
Aspartate aminotransferase (AST, SGOT), 48 U/L	Blood, moderate
Bilirubin (total), 0.2 mg/dL	Erythrocytes, numerous
Creatinine, 0.4 mg/dL	Leukocytes, > 10/high-power field
Glucose, 83 mg/dL	Leukocyte esterase (large), positive
Potassium, 3.5 mEq/L	Protein, 30 mg/dL
Sodium, 130 mEq/L	Specific gravity, 1.01
Urea nitrogen (blood), 6 mg/dL	

Table 2. Typical Diagnostic Measurements in Various Types of Polyuria

Diagnostic Measurement	Neurogenic DI	Nephrogenic DI	Psychogenic Polydipsia
Random serum osmolality	Increased	Increased	Decreased
Random urine osmolality	Decreased	Decreased	Decreased
Urine osmolality during mild water deprivation	No change	No change	Increased
Urine osmolality during administration of nicotine or hypertonic saline	No change	No change	Increased
Urine osmolality, following intravenous administration of vasopressin	Increased	No change	Increased
Plasma vasopressin	Decreased	Normal or increased	Decreased

DI = diabetes insipidus.

Adapted with permission from Greenspan FS, Gardner DG, editors. Basic and clinical endocrinology, 6th ed. New York: Lange Medical Books/McGraw-Hill; 2001:156.

hormone arginine vasopressin, DI can result from any 1 of 4 fundamentally different causes: (1) impaired secretion of arginine vasopressin (causing neurohypophyseal DI, the most common form), (2) impaired renal response (causing nephrogenic DI), (3) excessive fluid intake (leading to primary polydipsia), or (4) increased metabolism of arginine vasopressin (resulting in gestational diabetes insipidus).

Diagnosis

Diagnosis of DI usually is made on the basis of a high serum osmolality (ie, > 290 mOsm/kg H₂O) associated with a decreased urine osmolality (ie, < 275 mOsm/kg H₂O) and (occasionally) copious excretion of urine. An increase in urine osmolality of at least 50% following administration of DDAVP is diagnostic of the disorder.³ It is crucial to differentiate DI from other types of hypotonic polyuria (**Table 2**).

Gestational Diabetes Insipidus

As mentioned previously, pregnancy is associated with a number of physiologic changes predisposing pregnant women to DI, such as a decreased thirst threshold, an increased secretion of vasopressinase (with a reduced vasopressin secretory capacity), an increased degradation of vasopressin (4- to 6-fold) by placenta-derived vasopressinase, and a decreased renal responsiveness to vasopressin.¹⁻⁶ In pregnant women who develop the disorder, the signs and symptoms of DI usually resolve soon after the placenta is delivered.^{3,4}

The latter characteristic is well illustrated by this case; the patient remained symptom free when she was not pregnant but developed polyuria during two different pregnancies. Hence, there may be a subclinical form of DI that remains undiagnosed until it is unmasked by the physiologic changes occurring during pregnancy.⁴

Administration of DDAVP is the only effective and

safe treatment for gestational DI. DDAVP is effective because, unlike naturally occurring vasopressin, it is not degraded by endogenous vasopressinase.^{3,7-9} **HP**

REFERENCES

1. Iwasaki Y, Oiso Y, Kondo K, et al. Aggravation of subclinical diabetes insipidus during pregnancy. *N Engl J Med* 1991;324:522-6.
2. Hanson RS, Powrie RO, Larson L. Diabetes insipidus in pregnancy: a treatable cause of oligohydramnios. *Obstet Gynecol* 1997;89:816-7.
3. Robertson GL. Diabetes insipidus. *Endocrinol Metab Clin North Am* 1995;24:549-72.
4. Hamai Y, Fujii T, Nashina H, et al. Differential clinical courses of pregnancies complicated by diabetes insipidus which does, or does not, pre-date the pregnancy. *Hum Reprod* 1997;12:1816-8.
5. Soule SG, Monson JP, Jacobs HS. Transient diabetes insipidus in pregnancy—a consequence of enhanced placental clearance of arginine vasopressin. *Hum Reprod* 1995;10:3322-4.
6. Lindheimer MD, Davison JM. Osmoregulation, the secretion of arginine vasopressin and its metabolism during pregnancy. *Eur J Endocrinol* 1995;132:133-43.
7. Ray JG. DDAVP use during pregnancy: an analysis of its safety for mother and child. *Obstet Gynecol Surv* 1998; 53:450-5.
8. Kallen BA, Carlsson SS, Bengtsson BK. Diabetes insipidus and use of desmopressin (Minirin) during pregnancy. *Eur J Endocrinol* 1995;132:144-6.
9. Davison JM, Sheills EA, Philips PR, et al. Metabolic clearance of vasopressin and an analogue resistant to vasopressinase in human pregnancy. *Am J Physiol* 1993;264:F348-53.

Copyright 2001 by Turner White Communications Inc., Wayne, PA. All rights reserved.