Note

Pregnant Woman with Transient Diabetes Insipidus Resistant to 1-Desamino-8-D-Arginine Vasopressin

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Abstract. We encountered a pregnant woman with transient diabetes insipidus which developed during the third trimester. A hypertonic saline infusion study did not concentrate the osmolality of urine. Her laboratory data showed hypokalemia, hyperreninemia, an increased concentration of plasma aldosterone and an increased urinary excretion rate of prostaglandin E2, which resembled hyperprostaglandin E-syndrome. T1-weighted magnetic resonance imaging of the posterior pituitary gland revealed decreased intensity. Polyuria reached 4–6 L daily, and urine osmolality remained dilute despite a lapse of four days since treatment with intranasal 1-desamino-8-D-arginine vasopressin (dDAVP: 10–25 μg every 12 h). The patient was conservatively managed without medical treatment, then delivered in the 38th week of pregnancy without complication. The osmolality of the patient’s urine was higher than that of the plasma when tested 3 days postpartum. The abnormality of magnetic resonance imaging of the posterior pituitary gland disappeared at 6 months after delivery. We consider that subclinical nephrogenic diabetes insipidus in our patient was exacerbated during pregnancy.

Key words: Diabetes insipidus, Pregnancy, Prostaglandin, Hydronephrosis, Magnetic resonance imaging

Received: February 2, 1998
Accepted: June 19, 1998
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Transient polyuria and polydipsia during pregnancy are rare conditions [1-4], and their cause is not entirely clear. Possible explanations include the exacerbation of preexisting altered osmotic thresholds for the secretion of arginine vasopressin (AVP) and abnormally large increases in circulating cystine-aminopeptidase (vasopressinase) [5-8]. Several cases of preeclampsia were reported to manifest transient nephrogenic diabetes insipidus (DI) [9-12]. The AVP resistance during the pregnant condition may be related to the increased production of prostaglandin E2 (PGE2) [13-17], so that the mechanism(s) of transient DI during pregnancy is complex.

Case Report

We encountered a pregnant woman with transient DI which developed during her 7th gestational month.

A 33-year-old pregnant Japanese woman was transferred to our hospital in her 33rd week of pregnancy (August 10, 1996) because of progressive polyuria and polydipsia. She was thirsty and kept requesting a cold drink.

The patient had a past history of spontaneous abortion 75 months before admission and intrauterine fetal death 55 and 28 months, respectively, before admission. Physical examination on admission revealed that her blood pressure was 120/76 mmHg, her pulse regular at 70 bpm, and body temperature 36.5 °C.
She was alert and oriented. Her skin turgor, head and neck were normal. No heart murmur or abnormal respiratory sounds were audible. The abdomen was distended due to her enlarged uterus.

Her RBC count was $307 \times 10^4/\mu l$, WBC was $6100/\mu l$ and platelet was $16.8 \times 10^4/\mu l$. The fasting plasma glucose level was 71 mg/dl, her serum level of total protein 5.8 g/dl, sodium 143 mEq/l, potassium 3.3 mEq/l, chloride 109 mEq/l, AST 19 U/l, ALT 15 U/l and osmolality was 287 mOsm/kg. Blood gas analysis showed that pH was 7.49, PaO$_2$ was 85.5 torr, PaCO$_2$ 38.7 torr, base excess 4.3, and HCO$_3$ was 24.6 mEq/l. Osmolality of urine was 128 mOsm/kg. The plasma level of AVP was 0.8 pg/ml, plasma renin activity 16.0 ng/ml/h, urinary excretion of PGE$_2$ was 980 pg/day and the other endocrinological data on admission are shown in Table 1. The blood was obtained at the spine position in the early morning.

Echography of the abdomen revealed a remarkable bilateral hydronephrosis.

A hypertonic saline infusion test at the 36th week of pregnancy failed to concentrate the urine and increase the plasma level of AVP (Fig. 1). T1-weighted magnetic resonance imaging (MRI) of the posterior pituitary gland revealed a decreased intensity at the 37th week of pregnancy (Fig. 2A). Based on a diagnosis of DI, we treated the patient with intranasal 1-desamino-8-D-arginine vasopressin (dDAVP). But treatment with dDAVP up to 50 µg per day did not concentrate her urine. Since there was no exacerbation of polyuria, polydipsia, dehydration or abnormality of electrolytes, we discontinued her medication.

At the 38th week of pregnancy she delivered a 3328-g healthy male infant without complication. Her symptoms subsided in the puerperium, and the osmolality of her urine increased to 688 mOsm/kg when tested 3 days postpartum under 12-h water deprivation. Six months after delivery, the findings of T1-weighted MRI of the posterior pituitary gland were normalized (Fig. 2B).

**Discussion**

A pregnant patient with transient DI who was diagnosed in the third trimester is described. A hypertonic saline infusion study did not concentrate the osmolality of urine. These findings excluded primary polydipsia. In central DI, T1-weighted MRI usually reveals an absence of a high intensity signal of the posterior pituitary. The abnormal findings of MRI probably reflect a decreased reserve of AVP in the posterior pituitary gland, so MRI findings are observed also in the pathological condition with AVP hypersecretion such as nephrogenic DI or diabetes mellitus [18, 19].

The administration of dDAVP did not serve to concentrate her urine, which strongly suggested
that resistance to AVP (nephrogenic DI) was the main cause of her polyuria. The abnormality in pituitary MRI was due to marked consumption of AVP for hypersecretion to resistance to AVP.

The intensity of the posterior pituitary gland is known to be stable throughout pregnancy on MRI [20]. To our knowledge, ours is the first case revealing the absence of a high intensity signal of posterior pituitary MRI among transient pregnant patients with DI.

Ford et al. reported a pregnant patient with transient DI refractory to treatment with a large dose of dDAVP [21]. The other similarities between our case and theirs were: 1) both patients could concentrate their urine after delivery, 2) the severity and the clinical course of polyuria were similar and 3) the urinary excretion level of PGE2 was high. The pathogenesis of DI in both patients seemed to be due to nephrogenic factors which might cause resistance to dDAVP. We speculate that the two cases should be classified under the same entity of DI. Plasma AVP of the case reported by Ford et al. was higher than that of our case. The explanation of the differences may be two fold: First, the degree of cystine-aminopeptidase activity in our case was greater than in the case reported by Ford et al., second, no cystine-aminopeptidase inhibitor, such as phenanthroline monohydrate was added to the tube for the assay for AVP in our case.

It is well known that some patients who develop transient nephrogenic DI are associated with pregnancy complicated by preeclampsia. These patients with DI subside spontaneously within several days after delivery [9-12]. Since our case was not complicated by preeclampsia, the contribution of preeclampsia to AVP resistance is unlikely.

Hyperprostaglandin E-syndrome (HPS), a variant of Bartter’s syndrome (BS), resembles BS in a number of symptoms. Similar to BS, HPS is characterized by congenital hypokalemic alkalosis, hypertrophy of the juxtaglomerular apparatus, hyperreninemia, secondary aldosteronism, normal blood pressure and nephrogenic DI [13]. The hypokalemic alkalosis, hyperreninemia, secondary aldosteronism, normal blood pressure and DI observed in our case suggested that she presented a transient HPS-like condition during pregnancy.

High renal PGE2 levels have been found in patients with lithium-induced nephrogenic DI and have been implicated in the pathogenesis. Indomethacin had an antidiuretic effect and normalized the high PGE2 levels [14]. The increased level of PGE2 in our patients may therefore be related to her resistance to dDAVP.

It was also reported that PGE2 production was significantly increased in hydronephrotic kidneys [22, 23]. Our patient’s severe bilateral hydronephrosis may be related to the increased excretion of PGE2 or AVP resistance.

Other investigators supported the relationship between PGE2 overproduction and AVP resistance [13-17]. We considered that in our case, subclinical nephrogenic DI may have been unmasked in late pregnancy, in connection with the change in osmotic thresholds for AVP release, excessive cystine-aminopeptidase activity and/or increased AVP resistance resulting from PGE2 overproduction.
References