Int J Endocrinol Metab. 2010;8(2):94-96
International Journal of
Endocrinology & Metabolism
Journal home page: www.IJEM.org

Transient diabetes insipidus in a woman with a twin pregnancy: A case report

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ARTICLE INFO

Article Type:
Case Report

Article history:
Received: 28 Feb 2010
Revised: 5 Apr 2010
Accepted: 5 Sep 2010

Keywords:
Diabetes insipidus
Women
Twin pregnancy

ABSTRACT

Transient diabetes insipidus (DI), a rare complication of pregnancy, results from excessive activity of placental vasopressinase. If unrecognized, it may threaten the life of both mother and fetus. Here we report a case of 33 year-old women with a twin pregnancy and transient diabetes insipidus, believed to be due to increased vasopressin degradation rate. The purpose of this case report is to reassess gestational DI and to discuss its appropriate management.

Please cite this paper as:
Abbasi Ranjbar Z, Bahrami A , Najafipoor F, Mobassery M. Transient diabetes insipidus in a woman with a twin pregnancy: A case report. *Int J Endocrinol Metab*.2010;**8**(2):94-96.

Introduction

Diabetes insipidus (DI), a rare occurrence in pregnancy, has an incidence, varying from 1-6 per 300,000 pregnancies (1-8). There are three different types of pregnancy associated DI, central, nephrogenic and a transient condition called, gestational DI (GDI), which is believed to be associated with increased activity of vasopressinase (5). Occurring usually in the third trimester of pregnancy, the etiology of transient GDI is probably excessive activity of placental vasopressinase, an enzyme synthesized by the placenta and degraded by the maternal liver. Vasopr-essinase can degrade arginine vasopresine (AVP), but not the synthetic analogue, 1-deamino-8D-arginine vasopre-ssin (dDAVP); AVP level remains in the normal range during pregnancy, but its production rate increases to compensate for the escalating degradation rate and to maintain sufficient antidiuretic activity.

Here we report a case of 33 year old woman, pregnant with twins and diagnosed with transient GDI. Because this syndrome is rare, especially in a twin pregnancy, there is often confusion about its cause and the appropriate management.

Case report

A 33-year-old woman in her 36th week of a monochorionic diamniothic twin pregnancy was admitted in November 2009 to the endocrine ward of the Emamreza Teaching General Hospital of Tabriz University (Medi-cal Sciences), Tabriz, Iran; she had a 2 month history of polyuria and excessive thirst. She had had regular monthly obstetric visits and the course of her pregnancy had been unev-entful until 2 month ago, when she noted excessive urination. She was a nulliparous gravid 1 woman, with no remarkable past medical or family history, other than a 7 year history of infertility, despite which she had conceived without any intervention. She was on prenatal supplements of iron, folic acid and calcium carbonate

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plus vitamin D. On the day of admission she was alert and oriented. Examination revealed blood pressure of 110/60 mmHg, pulse rate of 78 bea-ts/min, respiratory rate of 15/min, temperature of 36.4 C and body mass index of 33.3 kg/m2. Her skin turgor was normal and no heart murmur or abnormal respiratory sounds were audible. The abdomen was distended due to her enlarged uterus. Laboratory evaluation revealed urine volume was 7000 cc and creatinine 950 mg /24h. Urine specific gravity was 1005 and 1004 on 2 occasions and urine and plasma osmolalities were 175 and 293 mosmol/L respectively *(Table 1)*.

Due to fasting blood glucose of 110 mg/dL, a 100 gram oral glucose challenge test was performed and the results were normal. There was no significant hemoconcentration in our patient. She had no significant abnormality on liver ultrasound. Pelvic ultrasound showed two live fetuses with adequate amminiotic fluid, male sex, monochorionic and diammniotic, without any major congenital anomaly. Pituitary MRI could not be obtained due to the patient being concerned regarding the exposure of the fetuses to the contrast material.Because of the worsening clinical condition of the patient, and considering the results of urine relative hyposmolality and serum hypertonicity, the water deprivation test was not performed and intranasal dDAVP was administered with close monitoring of fluid balance, weight, pulse rate, blood pressure and frequent measuring of the serum sodium, and serum and urine osmolalities. Recovery was uneventful and she responded appropriately to desmopressin therapy. Her polyuria and polydipsia reduced and urine output dropped to 2500 mL/day, serum sodium to139 mml/L and patient was discharged and scheduled for weekly follow ups. Two weeks later she admitted to another hospital for cesarean section and delivered two healthy male infants with 1 minute Apgar scores of 9 and 8 and birth weights of 2590 and 2560 grams. On the second postnatal day, progressive jaundice developed in both infants, which was treated by phototherapy.

Within the first few postnatal days, the patient's dDAVP requirement decreased to 5 microgram only at night. One month after delivery dDAVP was withheld and she remained free of symptoms. Pituitary MRI after delivery showed no hypothalamic lesion, and normal appearance of posterior pituitary bright spot was visible in the Sagittal T1 weighted unenhanced images of the pituitary fossa.

Discussion

In a normal pregnancy during the first trimester there are many hemodynamic, renal, and electrolyte changes, which reach their peak during the second trimester, remain relatively stable during the third trimester, and rapidly reverse after delivery. Usually, the plasma osmolality in pregnancy falls to a new set point of about 270 mOsm/kg, the plasma sodium concentration falls by approximately 5 to 10 mEq/L and serum sodium is almost always less than 140 mEq/L in normal pregnancy (1, 2). Arginine vasopressin (AVP) is a nonapeptide that is secreted by the axonal terminals of neurosecretory neurons located in the supraoptic and paraventricular nuclei of the hypothalamus. A rare disease in pregnancy (9, 10). DI presents with neurologic symptoms in a patient near term with a high output of dilute urine, intense thirst, and hypernatremia (11). Hanson and *et al.* reported a patient with severe oligohydroamnios that resolved after treatment of DI (12). If suspected, the diagnosis of DI should be confirmed by performing a water deprivation test, in which after an overnight fast, the patient is asked to withhold water intake until 3% of her body weight is lost or urine osmolarity shows no increase in three successive hourly specimens; In women who have DI, urine osmolarity remains unchanged, whereas plasma osmolarity increases significantly. Because of the risks that are associated with dehydration, in severe cases with high urine output this test is best performed by an endocrinologist (9).

During pregnancy, and in the absence of glycosuria, hypokalemia or hypercalcemia, DI can be established if a patient with a syndrome of polyuria-polydipsia has a serum osmolality > 285 mOsm kg. There is a direct relationship between serum vasopressinase activity and the weight of the placenta, explaining why in multiple gestations an increase in vasopressinase activity is encountered, as well as the appearance of DI in the 3rd trimester (8). Gestational DI is a transient syndrome and may be associated with acute fatty liver of pregnancy and preec-

Table 1. Laboratory findings

	Admission day	Day 1 After treatment	Day 7 After treatment	Day 10 Post partum	Day 40 Post partum	Day 14 After drug cessation
Blood						
FBS (mg/dL)	110	86	-	88	-	-
Hemoglobin (gm/dL)	11.8	-	-	12	-	-
Hematocrit (%)	34.8	-	-	35	-	-
Na (mEq/L)	143	140	139	140	138	139
K (mEq/L)	4.2	4	-	4.2	-	-
Creatinine (mg/dL)	0.8	-	0.8	0.9	-	-
Osmolality (mosmol/kg)	293	284	-	284	280	284
Urine						
Volume (CC)	7000	2500	-	-	-	-
Osmolality (mosmol/kg)	175	635	700	730	700	850

lampsia (2-6, 8, 9, 12, 13). On the other hand it may be the first manifestation of a latent central DI. This condition is often idiopathic, but rarely is the first symptom of a hypothalamic or pituitary lesion (7, 12). Some cases are discovered for the first time during pregnancy, and can be divided into two major groups:

1) Subclinical forms that are due to changes in the osmoregulation found during pregnancy or pathological situations in the osmoregulation of the mechanisms operating during pregnancy (reduction in the arginine-vasopressin production, abnormal function of vasopressin, placentary increase in vasopressin clearing, and subclinical form of nephrogenic diabetes insipidus stemming from pregnancy, etc.)

2) Forms associated with hepatic pathologies during pregnancy, where there is a slow degradation of vasopressinase (5).

An investigation by Davison *et al.* showed that the hormonal metabolic clearance rates (MCR) of AVP, similar to nonpregnant values during gestational weeks 7-8, increases fourfold by weeks 22-24 and remains at these elevated levels throughout term; these rises seem to parallel the periods of rapid increase in both the trophoblastic mass and circulating vasopressinase levels. The increase in hormonal disposal rates may explain the appearance of certain polyuric syndromes in late gestation (14).Yamanaka *et al.* reported DI in a twin pregnancy associated with the HELLP syndrome (15). Our patient had a twin pregnancy, and normal liver function tests. GDI occurs in the third trimester and usually lasts from days to weeks. This transient polyuria resolves spontaneously within days or weeks of delivery. The condition generally does not occur in subsequent pregnancies (2).

In healthy individuals, the posterior lobe of the pituitary gland normally demonstrates a characteristically hyperintense signal on Tl-weighted MR images (bright spot). This hyperintense signal is absent when the vasopressin content in the posterior lobe becomes markedly decreased (16). In our patient, MRI of the pituitary gland after delivery showed no hypothalamic lesion, and there was a normal appearance of the bright spot. The use of desmopressin (dDAVP) in symptomatic cases has been proven to be a safe management method for both the mother and the fetus during pregnancy (4). In contrast to vasopressin that has a rapid plasma disappearance rate, the action of desmopressin acetate persists for about 12 hours. The period of time around labor and delivery is particularly precarious for these patients because oral water intake is frequently restricted (11). GDI should be con-sidered in pregnant woman with unexplained polyuria and polydipsia. In determining whether DI is present, a urine osmolality below that of the plasma suggests its presence(1, 2). GDI can present with the rapid onset of life-threatening hypernatremia, especially around the time of labor when the oral water intake is frequently restricted (2, 11). Clinicians need to be aware of this serious disorder, and its management.

In summary, although GDI is a rare complication of pregnancy that can readily be treated with desmopressin, special attention should definitely be paid to appropriate electrolyte and hemodynamic management.

Financial support

None declared.

Conflict of interest

None declared.

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