Transient diabetes insipidus with severe maternal and fetal hypernatremia

Abstract: Diabetes insipidus is a condition characterised by polyuria and polydipsia with excretion of diluted urine. Transient diabetes insipidus has been reported in pregnancy and is often associated with acute fatty liver of pregnancy, pre-eclampsia, HELLP syndrome and multiple pregnancy. Presenting symptoms can be vague. In our case, a primigravida with spontaneous monochorionic diamniotic twin pregnancy presented at 36+3 weeks in early labour. Severe hypernatremia was found in the patient and in both twins after a caesarean section was performed. Transient diabetes insipidus was diagnosed based on paired serum and urine osmolality. The hypernatremia was corrected gradually and 1-deamino-8D-arginine vasopressin was given. A high index of suspicion and early involvement of physicians and paediatricians are needed to avoid catastrophic consequences.

Keywords: Gestational diabetes insipidus; hypernatremia.

Case

A 32-year-old gravida 1, para 0 woman with spontaneous monochorionic diamniotic twin pregnancy was seen at our antenatal clinic since 11 weeks of gestation. She had good past health and her antenatal course was uneventful. Results of the morphology scan and oral glucose tolerance test were normal. Subsequent ultrasound scans also showed satisfactory foetal growth for both twins with no evidence of twin-twin transfusion syndrome. Her blood pressure was normal throughout and there was no proteinuria. She presented to the admission ward at 36+3 weeks in early labour. The blood pressure on admission was 140/98 mm Hg, which was 130/70 mm Hg upon recheck. She had no symptoms of pre-eclampsia. The urine dipstick was negative for protein. Both twins were in cephalic presentation and the cardiotocogram result was normal. She opted for caesarean section for twin pregnancy.

Lower segment caesarean section was performed under spinal analgesia 2 h after admission in view of increasing uterine contractions. The caesarean section was uneventful and she delivered twin boys. Twin 1 weighed 1955 g, had an Apgar score of 7 at the first minute, 10 at the fifth minute, and had thick meconium-stained liquor. Twin 2 weighed 2210 g, with an Apgar score of 6 at the first minute and 8 at the fifth minute. Both babies were admitted to the special care baby unit and were noted to have hypernatremia [twin 1: 162 mEq/L (mmol/L); twin 2: 167 mEq/L (mmol/L)]. They were given intravenous fluid consisting of 2.5% dextrose and 0.45% sodium chloride solution together with 50% dextrose aimed at a gradual lowering of serum sodium of no faster than 12 mEq/L per day (mmol/L per day). Serum sodium levels normalized on days 3–4.

The admission laboratory results were available after the caesarean section: haemoglobin 15.7 g/dL (157 g/L) (normal 11.7–14.8 g/dL), haematocrit 47.6% (0.476) (normal 0.34–0.44), platelet 237×10^3/μL (237×10^9/L) (normal 170–380×10^9/L), sodium 169 mEq/L (mmol/L) (normal 136–148 mmol/L), potassium 4.4 mEq/L (mmol/L) (normal 3.6–5.0 mmol/L), urea 40.6 mg/dL (14.5 mmol/L) (normal 2.5–6.4 mmol/L), creatinine 2.4 mg/dL (213 μmol/L) (normal 49–82 μmol/L), urate 15.7 mg/dL (934 μmol/L) (normal 177–400 μmol/L), alkaline phosphatase 457 U/L (normal 32–93 U/L), aspartate aminotransferase 1212 U/L (normal 14–30 U/L), alanine aminotransferase 1047 U/L (normal 7–36 U/L), prothrombin time 13.7 s (normal 11.3–13.5 s), activated partial thromboplastin time 29.7 s (normal 25.9–33.7 s). Blood pressure was normal after delivery, in the range of 120–140/70–90 mm Hg.

The mother was suspected to have acute fatty liver of pregnancy and diabetes insipidus. Her urine output after the operation was 50 mL/h, but she was very dehydrated. The medical team was consulted. She was administered intravenous infusion of 5% dextrose for correction of severe hypernatremia at a rate of <12 mEq/L per day (mmol/L). Her urine output increased to 3 L/day with gradual fluid replacement. She retrospectively reported
polyuria and polydipsia for a few days prior to admission. Further investigations, which were performed about 24 h after admission, showed the following results: serum/urine osmolality 343/274 mOsm/kg (mmol/kg), serum cortisol 42.77 μg/dL (1180 nmol/L) (normal 130–600 nmol/L), prolactin 2914 μIU/mL, thyroid-stimulating hormone 0.32 mIU/L (normal 0.35–5.50 mIU/L) and free T4 0.78 ng/dL (10 pmol/L) (normal 12–23 pmol/L). Autoimmune markers and hepatitis serology result were negative. Random glucose was 73.87 mg/dL (4.1 mmol/L), which was within normal range. Ultrasound result of the hepatobiliary and renal systems was normal. Magnetic resonance imaging (MRI) 2 months later showed a normal pituitary gland with preserved posterior bright spot. The placenta was that of monochorionic diamniotic twins and did not show significant pathology.

She was given a 1-μg trial of 1-deamino-8D-arginine vasopressin (dDAVP) intravenously, which increased the urine osmolality to greater than the serum osmolality of the paired samples 2 and 4 h post test. She was then started on oral dDAVP 50 μg twice daily and had significant reduction in urine output overnight.

She was discharged 9 days after delivery with a normal renal function and an improving liver function (aspartate aminotransferase 70 U/L, alanine aminotransferase 110 U/L). Liver function was only checked again 8 weeks after delivery, which was normal. The dosage of dDAVP was then decreased to 50 μg daily and was stopped 3 months later by the endocrine team as she was asymptomatic despite poor compliance to dDAVP. She remained well at 8 months after delivery.

**Discussion**

Diabetes insipidus is a rare complication in pregnancy postulated to be due to an increased level of vasopressinase produced by the human placenta, with an incidence of between two and six cases per 100,000 pregnancies [1]. Vasopressinase breaks down anti-diuretic hormone (ADH) and results in a decrease in ADH level, which, in turn, leads to polyuria [1, 5] (Figure 1). The activity of vasopressinase was found to correlate with the size of the placenta [1, 3, 4, 5, 7]; therefore diabetes insipidus tends to occur in the late second or third trimester and has been reported in cases of multiple pregnancy. As vasopressinase is degraded by the liver, it is also associated with conditions causing deranged liver function, as in the case of fatty liver, HELLP syndrome or pre-eclampsia [1, 3, 4, 5, 7]. Ellidokuz et al. [4] demonstrated that the degree of liver dysfunction correlates with diuresis. Transient gestational diabetes insipidus should resolve in the puerperium when the source of vasopressinase is removed and pregnancy complications causing the deranged liver function are resolved [1–3]. However, there have been reports of intrauterine death as a result of maternal diabetes insipidus [7]; therefore early diagnosis is essential.

A high vigilance is required to diagnose transient diabetes insipidus owing to vague presenting symptoms. Our patient reported polyuria and polydipsia retrospectively, which she willfully attributed to symptoms of pregnancy. A successful diagnosis was made possible by the measurement of urine and plasma osmolality, with the urine osmolality being below that of the plasma. The response to dDAVP further confirmed the diagnosis. The MRI of the pituitary gland of this patient 2 months after delivery gave a normal result but, unfortunately, was not performed in the acute phase and therefore cannot exclude transient abnormality [5].

Of interest was the duration of dDAVP given in this case, which was only stopped 3 months after delivery. With the main source of transient diabetes insipidus being placental vasopressinase, resolution of transient gestational diabetes insipidus is expected when the source of vasopressinase is removed and the deranged liver function resolves, which usually occurs within 2–3 weeks after delivery [1]. Most cases of transient diabetes insipidus of pregnancy resolve within days after delivery, and only rarely would it take weeks to resolve [2]. In retrospect, it was perhaps possible to stop dDAVP sooner in view of the rapid recovery of the patient’s liver function. Despite a rapid improvement of liver function, it was only rechecked again 8 weeks after delivery, and the patient had in fact remained asymptomatic after discharge from the hospital. A joint endocrine-obstetric clinic would have improved the coordination between endocrinologists and obstetricians in the management of such patient.
A significant underlying condition is less likely as our patient was completely asymptomatic when she was last seen 8 months after delivery. However, a subclinical diabetes insipidus can still be present and be manifested as a recurrence if the patient becomes pregnant again [1, 5], which should be kept in mind and symptoms be taken note of in a subsequent pregnancy.

Maternal hypernatremia is a well-known complication of diabetes insipidus due to dehydration and contraction of the intravascular volume. In contrast, the effect of transient maternal diabetes insipidus to the fetus is largely unknown. Although there have been case reports of intrauterine death associated with diabetes insipidus in pregnancy, the exact mechanism leading to intrauterine death is unclear. Wiser et al. [7] reported the presence of multifocal perivillous thrombosis and infarcts in the histological examination of a patient with transient gestational diabetes insipidus and intrauterine death of monochorionic twins. They further postulated the cause of intrauterine death to be related to a reduction in uterine blood flow due to the maternal hypovolemic-hemoconcentrated state [7].

In our case, both twins developed hypernatremia, which is likely secondary to maternal hypernatremia. In neonates, severe hypernatremia is mostly associated with dehydration owing to inadequate feeding, with reported complications including acute renal failure, elevated liver enzymes, disseminated intravascular coagulopathy, cerebral edema, intracranial haemorrhage, venous sinus thrombosis, bilateral iliac artery thrombosis, seizures and deaths [6]. With this knowledge, although hypernatremia was caused by a different mechanism in this case, it is important to coordinate with the neonatal team after delivery to maintain hydration and monitor the electrolytes of the neonates to prevent aggravation of metabolic disturbance. Currently, there are no guidelines as to whether hypernatremia should be corrected prior to delivery to minimise the effect to the baby, or delivery should be expedited and correction of hypernatremia done ex utero.

Our patient was only diagnosed to have transient diabetes insipidus incidentally when she developed preterm labour, but blood tests already showed severe hypernatremia for herself and for both twins. It is hoped that awareness of the condition in pregnancy can be raised with this report. Presenting symptoms of transient diabetes insipidus can be vague, but can cause life-threatening hypernatremia to the mother and the baby. We also would like to highlight the importance of multidisciplinary involvement of the physicians and paediatricians for timely diagnosis and management in this case. If managed appropriately, the obstetric outcome can be favourable.

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References


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Article note: We report our experience on the diagnosis and management of a patient with transient diabetes insipidus.