DOI: 10.4274/tpa.933

Successful intranasal desmopressin acetate treatment in a very low birth weight premature infant who developed central diabetes insipidus secondary to pituitary hemorrhage

Hasan Kahveci[1], Müge Payaslı[2], Fuat Laloğlu, Halil Keskin[1], Başak Adaklı Aksoy[1], Zeynep Türkyılmaz[1]

[1]Nenehatun Gynecology and Obstetrics Hospital, Neonatal Intensive Care Unit, Erzurum , Turkey

[2]Kanuni Sultan Süleyman Education and Research Hospital, Neonatal Intensive Care Unit, İstanbul, Turkey

Summary

Central diabetes insipidus is characterized by polydipsia, polyuria, dehydration, irritability, poor feeding, failure to thrive and hypernatremia. This disease is caused by lack of antidiuretic hormone. Here, a very low birth weight premature infant who developed central diabetes insipidus secondary to pituitary hemorrhage in the newborn period and was treated successfully with intranasal desmopressin acetate was presented. It was emphasized that desmopressin acetate might be an effective method also in the treatment of very low birth weight premature infants. *(Turk Arch Ped 2013; 48: 241-243)*

Key words: Central diabetes insipidus, desmopressin acetate, premature infant

Introduction

Central diabetes insipidus (DI) is a clinical picture arising from antidiuretic hormone (ADH) deficiency which leads to polyuria, polydipsia, dehydratation, restlessness, inadequate nutrition, inadequate growth and hypernatremia (1,2). Central DI is a rarely reported disorder in newborn infants (3,4). In the literature, no case of central DI secondary to pituitary hemorrhage has been reported in any newborn infant. It was aimed to emphasize that desmopressin acetate could be used as an efficient method in treatment of these patients and to increase the awareness of clinicians on this issue.

Case

A male patient who was born as the second child of a 18-year old mother who had remote consanguinity with her husband at the 27th gestational week following premature rupture of membranes was admitted to our Neonatal Intensive Care Unit because of premature delivery and respiratory distress. APGAR scores at the first, fifth and 10th minutes were learned to be 3, 6 and 8, respectively. Physical examination revealed prematurity findings, pes equinovarus deformity in the left leg and marked respiratory distress. The weight was found to be 980 g (50-75th percentile), the height was found to be 38 cm (25-50th percentile) and the head circumference was found to be 28 cm (50-75th percentile). The infant was followed up regularly in the prenatal period and there was no pathology in the familial history. The patient was connected to mechanical ventilator for respiratory support because of severe respiratory distress. Afterwards, intratracheal surfactant was administered at a dose of 100 mg/kg by endotracheal tube (Survanta®, Abbott Laboratories, North Chicago, IL, USA). Since the clinical picture could not be differentiated from pneumonia, ampicillin and cefotaxim

Address for Correspondence: Hasan Kahveci MD, Nenehatun Gynecology and Obstetrics Hospital, Neonatal Intensive Care Unit, Erzurum , Turkey
E-mail: drhasankahveci@hotmail.com **Received:** 10.05.2011 **Accepted:** 08.08.2012
Turkish Archives of Pediatrics, published by Galenos Publishing

treatment was started. The first laboratory examination revealed the following: hemoglobin: 16 mg/dL, WBC: 12 000/mm^3, platalets: 315 000/mm^3, prothrombin time: 12.5 s, activated partial thromboplastin time: 38.5 s. The patient was seperated from ventilator on the 10th day of hospitalization. Blood and cerebrospinal fluid cultures were found to be negative. Intravenous aminophylline was administered for 7 days for intermittent prematurity apneas to stimulate respiration. Cranial ultrasonography examinations performed on the 24th and 72nd hours and fifth day were reported to be normal.

On the 18th day of life, the patient developed polyuria and severe hypernatremia acutely while being fed orally (180 mL/kg/day). Serum sodium increased from 138 mEq/dL to 155-168 mEq/d L and urinary excretion increased from 2,5-3 mL/kg/hour to 4-10 mL/kg/hour. The sodium level of the breastmilk he consumed was 4 mEq/dL (normal values: 2-6 mEq/dL). Serum blood urea nitrogen, creatinine, potassium, glucose, adrenocorticotropic hormone, cortisol, growth hormone, thyroid hormones and blood gases were found to be normal. When hypernatremia was found, the following laboratory tests were performed: serum sodium: 155 mEq/kg, serum osmolarity: 335 mOsm/l, urinary sodium: 8 mEql/dL, urinary density: 1008, urinary osmolarity: 177 mOsm/l and plasma ADH level: < 0.5 pmol/l (normal values in premature infants: 2.5-13 pmol/l). Urinary ultrasonographic examination was reported to be normal. Since the patient was a newborn and serum osmolarity was found to be 335 mOsm/l, "water deprivation" test was not performed. With these findings a diagnosis of central DI was made. There was no similar history in the family. Serological tests for congenital TORCH infections were found to be negative. Coagulation tests performed for disseminated intravascular coagülation were found to be normal. Brain magnetic resonance imaging (MRI) was assessed to be normal. On non-contrast MRI of the pitiutary gland, increased density which was considered to be compatible with subacute hemorrhage was observed in T1A series in the posterior part of the pituitary gland which was thought to belong to the neurohypophysis (Figure 1).

Intranasal desmopressin acetate solution with an intensity of 100 µg/10 mL at a dose of 0.25 µg two times a day was started to be administered with the recommendation of pediatric endocrinology. The dose of desmopressine acetate was increased to 5 µg two times a day by controlling until the serum and urinary osmolarity reached the normal limits. With this treatment serum sodium level was 138-145 mEq/dL, serum osmolarity was 290-297 mOsm/l, urinary excretion was below 3 mL/kg/h and urinary osmolarity was 120 mOsm/l. It was observed that there was a daily increase of 20-30 g in body weight during treatment, weight gain increased after the 56th day of his life and oliguria developed. On the 60th day of his life, hyponatremia improved, urinary density increased (serum sodium: 130 mEq/l and urinary density: 1003, respectively) and serum osmolarity decreased (285 mOsm/l). The dose of desmopressin acetate administered was decreased by 25%. Urinary excretion increased, weight loss occured and hyponatremia improved. The dose of desmopressin acetate was adjusted according to serum and urinary osmolarity and the drug was discontinued on the 70th day of his life. In the follow-up, it was observed that the serum and urinary osmolarity were within normal limits. On MRI performed in this period, it was observed that hemorrhage findings disappeared completely.

The patient was discharged on the 85th day of his life without any problem or sequela. He was called back for regular follow-up visits and his growth was monitored. At the follow-up visit performed at the age of one year, his development was normal and there was no sequela.

Discussion

Congenital infections including cytomegalovirus and toxoplasmosis, sepsis, asphyxia, disseminated intravascular coagulation, meningitis, hemorrhage, edema, injury and abscess in the brain parenchyma, congenital middle line anomalies of the central nervous system including holoprosencephaly and genetic causes are involved in the etiology of central DI in term infants (3,4,5,6,7,8,9). Central DI is reported very rarely especially in very low birth weight (VLBW) premature newborns (3,10,11,12). In central DI observed in premature newborns, interventricular hemorrhages and/or hemorrhages in the brain parenchyma and idiopathic causes predominate (13).

We could find no information related with any case presentation of central DI developing secondary to pituitary hemorrhage in term and/or premature newborns in the literature. The fact that central DI occured two weeks later in this patient who probably developed pituitary hemorrhage

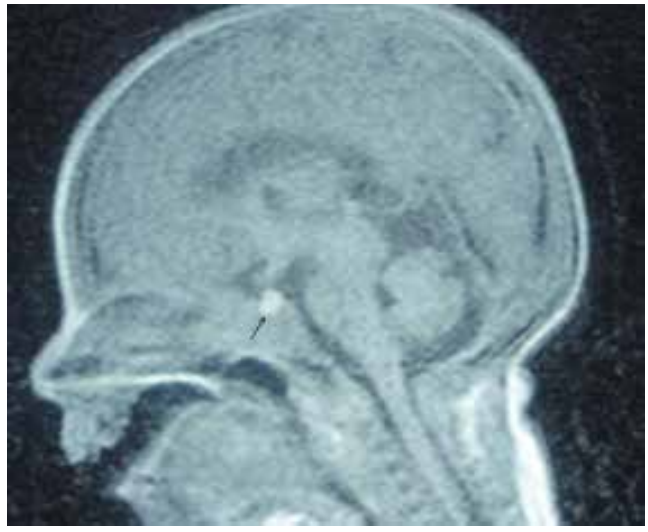

Figure 1. Pituitary MRI of the patient: the arrow shows hemorrhage in the posterior hypophysis

during the first five days of life and whose hemorrhage could be found only by MRI suggests that findings related with posterior pituitary failure can be observed also in the late period.

ADH which has the most significant role in retention of water which is required by the body to regulate extracellular tonicity (osmolarity) is synthesized in the supraoptic and periventricular nuclei in the pituitary gland and is transferred to the posterior hypophysis by axonal transportation. Any lesion in the neurohypophysial unit which is responsible of synthesis, release and transportation of ADH may result in central DI. In brain lesions which lead to central DI, the serum ADH level is inadequate (4).

Atasay et al. (10) reported a case of central DI which developed secondary to hemorrhage in the brain parenchyma in a premature newborn. Çaksen et al. (1) presented a case of central DI which developed secondary to hemorrhage in the brain parenchyma at the age of 30 days resulting from vitamin K deficiency. Praskahas et al. (11) presented a case of fallopian tube torsion secondary to meconium peritonitis and transient central DI in a premature infant.

The difference of central DI in our patient from the cases reported in the literature was the fact that it developed only secondary to pituitary hemorrhage and this had not been reported before.

It is thought that central DI in cases of hemorrhage in the brain parenchyma occurs as a result of damage to the ADH pathways by the compression of hemorrhage (1). We think that central DI in our patient developed as a result of anatomical compression of the posterior pituitary hemorrhage or inflammation of hemorrhage.

Pitressin tannate in oil which had been used in treatment of central DI and is a synthetic peptide is not appropriate for long-term use, since it is administered intramuscularly. Lysine vasopressin which is another synthetic peptide can be administered both intravenously and intramuscularly. However, this drug has to be administered for 3-8 times a day. Both pitressin and vasopressin act by way of V1 and V2 receptors. Both have severe vasopressor action and may lead to severe gastrointestinal side effects. Vasopressin-like desmopressin was developed in 1960s and has become preferrable in patients with central DI because it can be administered intravenously, intramuscularly and orally. This drug acts by way of V1 receptor and its vasopressor action is low. In addition, desmopressin does not alter endogeneous ADH production and tolerance develops rarely in long-term use (3). Although its use in children has been demostrated well, it has been debated whether desmopressin acetate is an appropriate drug in long-term treatment of central DI in newborns in previous publications (14,15). In recent years, desmopressin acetate has been used successfully in long-term treatment of transient or persistent central DI in older children, term infants, premature infants with normal body weight and VLBW premature infants (1,3,6,10,12).

Desmopressin acetate which can be used intranasally for two times a day because of its long action appears to be a good candidate for long-term treatment of central DI in newborns (2,11).

Conclusively, the possibility of central DI should be considered in VLBW premature newborns who develop polyuria and hypernatremia and it should be kept in mind that this may be secondary to hemorrhage in the posterior hypophysis and transient and intranasal desmopressin acetate is efficient in treatment. After the diagnosis of central DI is confirmed, serum electrolytes and serum and urinary osmolarity should be monitored carefully during treatment to prevent severe morbidity.

References

1. Caksen H, Odabaş D, Kaya A, Cesur Y, Kiymaz N, Etlik O, Turhan S. Central diabetes insipidus following intracranial hemorrhage due to vitamin K deficiency in a neonate. Acta Paediatr Taiwan 2005;46: 42-45.
2. Dell KMC, Davis ID. Fluid, electrollyte, and acide - base homeostasis. In: Martin RJ, Fanafor AV, Walsh MC, (eds). Fanfoff and Martin's neonatal - perinatal medicine disease of the fetus and ınfant. 8th ed. Philadelphia: Mosbby-Elsevier, 2006: 695-711.
3. Stapleton G, DiGeronimo RJ. Persistent central diabetes insipidus presenting in a very low birth weight infant successfully managed with intranasal DDAVP. J Perinatol 2000; 2: 132-134.
4. Breault DT, Majzoub JA. Diabetes insipidus. In: Kliegman RM, Berhman RE, Enson HB, Stanton BF, (eds). Nelson testbook pediatrics. 18 th ed. Philadelphia: Saunders-Elsevier, 2007: 2299-301.
5. Ghirardello S, Malattia C, Scagnelli P, Maghnie M. Current perspective on the pathogenesis of central diabetes insipidus. J Pediatr Endocrinol Metab 2005; 18: 631-635.
6. Lee YJ, Huang FY, Shen EY, Kao HA, Ho MY, Shyur SD, Chiu NC. Neurogenic diabetes insipidus in children with hypoxic encephalopathy: six new cases and a review of the literature. Eur J Pediatr 1996; 155: 245-248.
7. Karadag A, Erdeve O, Atasay B, Arsan S, Deda G, Ince E, Ocal G, Berberoglu M. Isolated central diabetes insipidus in a newborn with congenital toxoplasmosis. J Pediatr Endocrinol Metab 2006; 2: 173-175.
8. Wang LC, Cohen ME, Duffner PK. Etiologies of central diabetes insipidus in children. Pediatr Neurol 1994; 11: 273-277.
9. Malhotra A, Bajpai A, Hunt WR. Central diabetes ınsipidus in association with neonatal brain abscess. J Pediatr Endocrinol Metab 2010; 23: 235-236.
10. Atasay B, Berberoğlu M, Günlemez A, Evliyaoğlu O, Adiyaman P, Unal S, Arsan S, Ocal G. Management of central diabetes insipidus with oral desmopressin in a premature neonate. J Pediatr Endocrinol Metab 2004; 17: 227-230.
11. Manikoth P, Vaishnav A, Zachariah N, Sajwani MJ, Nair AK, Pai MG. Meconium peritonitis secondary to torsion of fallopian tube cyst and transient central diabetes insipidus in a preterm infant. J Perinat Med 2005; 33: 76-78.
12. Quetin F, Garnier H, Brauner R, Vodovar M, Magny JF. Persistent central diabetes insipidus in a very low birth weight infant (abstract). Arch Pediatr 2007; 14: 1321-1323.
13. Madan A, Hamrick SEC, Ferriero DM. Central nevrus system injury and neuroprotection: In: Taeusch HW, Ballard RA, Gleason CA, (eds). Avery's diseases of the newborn. 8 th ed. Philadelphia: Elsevier- Saunders, 2005: 965-972.
14. Fjellestad-Paulsen A, Paulsen O, d'Agay-Abensour L, Lundin S, Czernichow P. Central diabetes insipidus: oral treatment with dDAVP. Regul Pept 1993; 4: 303-7.
15. Stick SM, Betts PR. Oral desmopressin in neonatal diabetes insipidus. Arch Dis Child 1987; 62: 1177-1178