Gazi Tıp Dergisi / Gazi Medical Journal

OLGU SUNUMU - CASE REPORT

2008: Cilt 19: Sayı 4: 197-199

A RARE ASSOCIATION: RECURRENT HYPERNATREMIA, CLEFT LIP/PALATE, AND HOLOPROSENCEPHALY

Eboru ARHAN, Derya SOY, Özlem ARMAN, Zehra AYCAN, Gülsen KÖSE

ABSTRACT

We report a female infant with facial dysmorphism, ectrodactyly, holoprosencephaly, and associated hypernatremia. A 7-month-old female infant with cleft lip and palate, and ectrodactyly was admitted to our hospital with recurrent hypernatremic dehydration. Magnetic resonance imaging revealed holoprosencephaly. Plasma osmolality was increased whereas urinary osmolality was decreased. Serum ADH level was low. A water deprivation test revealed diabetes insipidus. By presenting this case,we would like to point out that midline facial defects may be associated with cerebral malformations and diabetes insipidus must always be kept in mind as a co-presenting condition.

Key Words: Cleft Lip/palate, Holoprosencephaly, Hypernatremia.

NADİR BİR BİRLİKTELİK: TEKRARLAYAN HİPERNATREMĐ, YARIK DAMAK-DUDAK VE HOLOPROSENSEFALĐ

ÖZ

Fasiyal dismorfizm, holoprosensefali ve hipernatremi birlikteliğinin olduğu bir olgu sunulmustur. Yarık damak dudak, ektrodaktilisi olan yedi aylık kız hasta hastanemize tekrarlayan hipernatremik dehidratasyon ile basvurdu. Manyetik rezonans görüntülemede holoprosensefali görüldü. Plasma osmolalitesi artmıs, idrar osmolaritesi ise düsüktü. Serum ADH düzeyi düsük idi. Sıvı kısıtlama testi diabet insipitus ile uyumlu idi. Bu olgu sunumu ile, orta hat yüz defektlerinin serebral malformasyonlar ile birliktelik gösterebileceği ve diabet insipitusun akla getirilmesi gerektiği vurgulanmak istenmistir.

Anahtar Kelimeler: Yarık Damak-Dudak, Holoprosensefali, Hipernatremi.

Geliş Tarihi: 31/10/2008 *Kabul Tarihi: 26/11/2008*

Received: October 31, 2008 *Accepted: November 26, 2008*

Dıskapı Children's Hospital, Dıskapı Children's Hospital, ANKARA, TURKEY

INTRODUCTION

The combination of holoprosencephaly, cleft lip/palate, and ectrodactyly has rarely been reported in the literature.[1,2] Hypernatremia and diabetes insipitus are seldom complication of holoprosencephaly in these patients.[3-5] We report a female patient with a constellation of malformations, including cleft lip/palate, holoprosencephaly, ectrodactyly, and recurrent hypernatremia.

CASE REPORT

A 7-month-old female infant was hospitalized because of hypernatremic dehydration and pneumonia. She was born at 40 weeks of gestation with a birth weight of 3300 g following an uneventful pregnancy. No significant data were mentioned in the family history. On physical examination her weight, length, and head circumference were all below the third percentile for age. Her physical features included microcephaly, cleft lip and palate, flat nose, ectrodactyly, and psychomotor delay (Figure 1). She showed signs of severe dehydration with an excessively dry tongue and buccal mucosa. She had dyspnea and tachypnea. The laboratory examination revealed the following: hemoglobin 9.6 g/dl (12-14 g/dl), white blood cell 16.900/mm3 (4000-10,000/mm3) , and platelet count 436.000/mm3 (150- 400 x 103).

Erythrocyte sedimentation rate and C-reactive protein were elevated. Biochemistry studies yielded blood urea nitrogen (BUN) 57 mg/dl (10-40 mg/dl), Na 164 mEq/L (135-145 mEq/L), and creatinine 0.12 (0.4-1). Other biochemical parameters were normal. Her chest X-ray revealed bilateral pneumonic infiltration. Her urine sediment was normal. She was administered 20 cc/kg 0.9% saline in the first hour and then 0.2% saline with dextrose was applied within 48 hours as the replacement fluid to reduce brain injury. After the fluid replacement, BUN returned to the normal level. Ceftazidim and aminoglicoside were started for a lower respiratory tract infection. Although we applied appropriate fluid treatment, hypernatremia persisted. We evaluated for persistent hypernatremia. Serum osmolality (332 mosm/l) was elevated while urine osmolality (162 mosm/l) was decreased. Her clinical state deteriorated. Klebsiella pneumoniae was isolated in the hemoculture. The antibiotherapy was changed to imipenem (40 mg/kg) according to the sensitivity pattern of the hemoculture.

Cerebral magnetic resonance imaging showed the Dandy-Walker variant and lobar holoprocencephaly (Figure 2). No conspicuous changes were detected in anterior pituitary function tests. The antidiuretic hormone level (ADH) was low. The water deprivation test was consistent with diabetes insipitus.

Karyotype analysis revealed 46 XX. We scheduled her for treatment with ADH. Despite appropriate antibiotherapy and fluid replacement, she died due to sepsis.

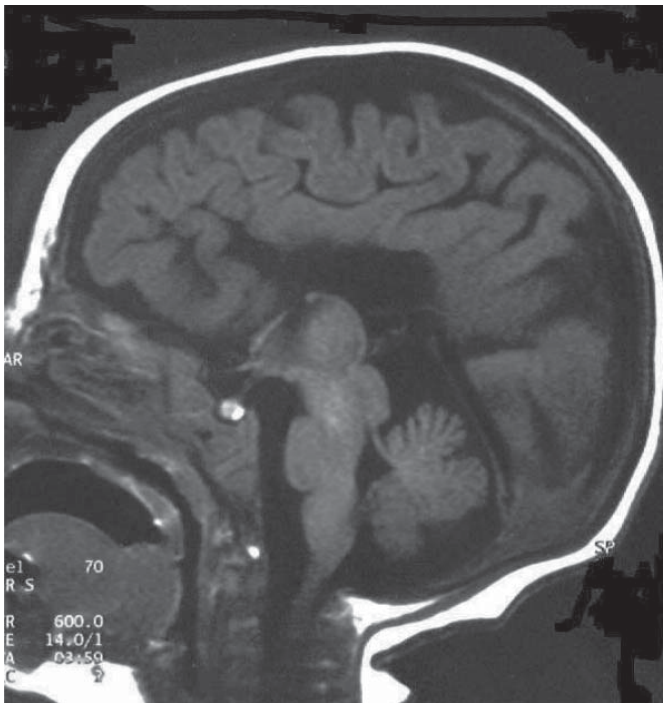

Figure 1: T2 weighted Magnetic resonance imaging.

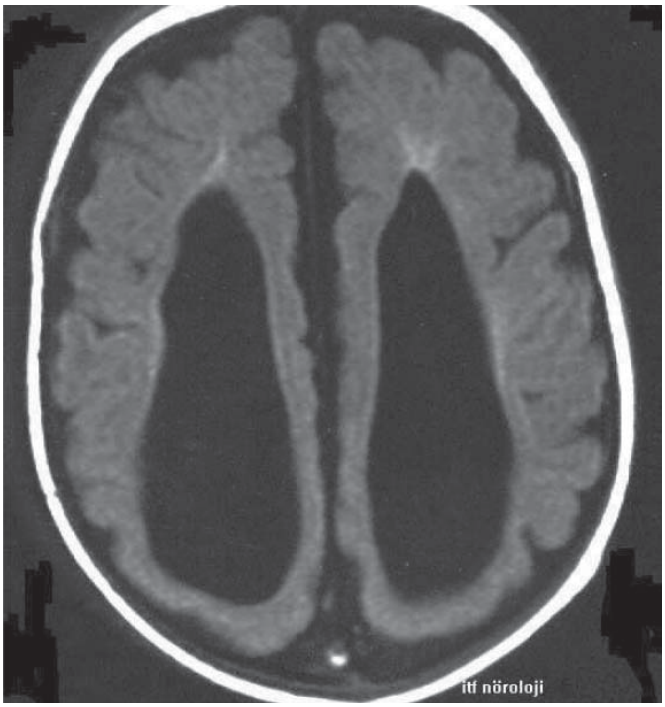

Figure 2: Demonstrating lobar holoprosencephaly and Dandy Walker variant.

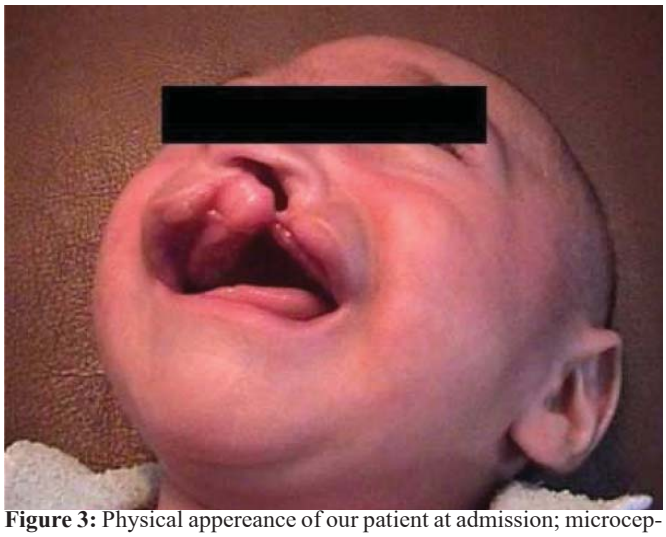

Figure 3: Physical appereance of our patient at admission; microcephaly, cleft lip and palate.

DISCUSSION

The main signs in our patient were holoprosencephaly, cleft lip and palate, ectrodactyly, hypernatremia, and psychomotor retardation. In the differential diagnosis, we suspected HHES (holoprosencephaly, hypertelorism, ectrodactyly) syndrome. This diagnosis was disregarded since she did not have hyper- or hypotelorism.

Holoprosencephaly is described as a defective cleavage of the porencephalon to symetric cerebral hemispheres. It is classified into three groups depending on the severity of the pathology: alobar, lobar, and semilobar.[6] It includes a spectrum of conditions that have in common the associated anomalies of median cleft lip or palate, nasal malformation, and brain malformations.[7] Complications of holoprosencephaly are diverse and may involve diabetes insipitus, neurogenic hypernatremia, and hypopituitarism. Hypernatremia or diabetes insipitus occurring in holoprosencephaly may be explained by functional or structural pathologies of the hypothalamohypophyseal axis.[6]

Case notes of patients with holoprosencephaly have shown that in clinical trials of adipsia or hypodipsia associated with hypernatremia ADH secretion is decreased.[8] Plasma osmolarity and hypernatremia can be corrected by the administration of ADH. When we reviewed the literature, we found just a few patients with holoprosencephaly, cleft lip and palate, and hypernatremia.[3,4,9,10] In our patient, the serum ADH level was decreased, serum osmolality was increased, and urine osmolality was decreased. These results were consistent with diabetes insipitus. The water deprivation test indicated diabetes insipidus. As shown by its low serum level in our patient, defective synthesis or release of ADH will disrupt renal concentrating capacity and lead to hypernatremia. Holoprosencephaly contributes to this clinical aspect by causing a defect in the thirst mechanism. Therefore, she could not maintain her needs and recurrent hypernatremic episodes occurred.

In hypernatremic dehydration, intracellular water loss is prominent. Therefore, clinical findings that are not compatible with the level of dehydration may occur. Hypernatremia must be corrected slowly to reduce the effect on the central nervous system. In our patient, hypernatremia was corrected in 48 hours as recommended in the literature.

Forty-five percent of live births with holoprosencephaly have been shown to be associated with chromosomal abnormalities but this report does not include milder cases.[11,12] It may be associated with trisomy 13, trisomy 18, and several multiple malformation syndromes like Pallister-Hall syndrome, Rubinstein Taybi syndrome, and Smith Lemli Opitz

syndrome. The exact inheritance pattern is not still clear. Eight genes have been found to be associated with holoprosencephaly so far: SHH (7q36), ZIC 2 (13q32), SIX3 (2p21), and TGIF (18P11.3). Although we were unable to perform mutation analysis in our patient, we suggest to perform it in patients with holoprosencephaly to inform the families for the sake of their subsequent children.

We conclude from this case that magnetic resonance imaging of the brain should be performed in patients with midline facial defects and recurrent hypernatremia attacks because of the large possibility of underlying central nervous system malformation. Diabetes insipitus should also be searched for as a complication.

Treating clinicians must always be aware of the complex nature of these patients and their potential for early demise and should inform parents about it.

Correspondence Address
Ebru ARHAN
Dışkapı Children's Hospital, Dışkapı Children's Hospital,
ANKARA, TURKEY
Tel: 3122026025
petekarhan@yahoo.com.tr

REFERENCES

1. Hartsfield JK, Bixler D, DeMyer WE. Syndrome identification case report 119. Hypertelorism associated with holoprosencephaly and ectrodactyly. Clin Dysmorphol 1984; 2: 27-31.
2. König R, Beeg T, Tariverdian G, Scheffer H, Bitter K. Holoprocencephaly, bilateral cleft lip and palate ectrodactyly:another case and follow up. Clin Dysmorphol 2003; 12:221-225
3. Ohtake M, Suziki H, Igarashi Y, Kobayashi Y, Saito T. Chronic hypernatremia associated with holoprosencephaly . Tohoku J Exp Med 1979;128: 333–344.
3. Kappy MS, Sondere E. Sublingual administration of desmopressin. Effectiveness in an infant with holoprosencephaly central diabetes insipidus. Am J Dis Child 1987;141: 84-85.
5. Arranz Gomez J, Vidal Sampedro J, Herranz Fernandez JL, Arteaga Manjon-Cabeza R, Lozano de la Torre MJ. Semilobar holoprosencephaly associated with central diabetes insipidus. An Esp Pediatr 1987; 27: 385–389.
6. Takato T, Nakatsuka T, Ohara Y. False median cleft. J Oral Maxillofac Surg 1985;43: 884–888.
7. Braitwaite F, Watson JA. Report on three unusual clefts of the lip. Br J Plast Surg 1949;2: 38–49.
8. Jacobson RI, Abrams GM. Disorders of the hypothalamus and pituitary gland in adolescence and childhood. In: Swaiman KI, Ashwal S (eds). Oediatric Neurology: Principles & Practice. St. Louis, Missouri: Mosby; 1999:1311-1339.
9. Karabay-Beyazıt A, Hergüner Ö, Altunbasak S, Noyan A, Yüksel B, Anarat A. Hypodipsia hypernatremia syndrome associated with holoprosencephaly in a child: a case report. Turk J Pediatr 2002;44:263-266.
10. Akil Đ, Yüksel H, Gözmen S, Tarhan S. Hypernatremic dehydration and renal vein thrombosis in a case with Cornelia de lange syndrome associated with holoprosencephaly. Erciyes Medical Journal 2004; 26: 201-205.
11. Croen LA, Shaw GM, Lammer EJ. Holoprosencephaly: Epidemiologic and Clinical Characteristics of a California Population. Am J Med Genet 64:465-472.
12. Croen LA, Shaw GM, Lammer EJ. Risk Factors For Cytogenetically Normal Holoprosencephaly in California: A Population- Based Case- Control Study. Am J Med Genet 90:320-325.