Hypodipsia-hypernatremia syndrome associated with holoprosencephaly in a child: a case report

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SUMMARY: Karabay-Bayazıt A, Hergüner Ö, Altunbaşak Ş, Noyan A, Yüksel B, Anarat A. Hypodipsia-hypernatremia syndrome associated with holoprosencephaly in a child. Turk J Pediatr 2002; 44: 263-266.

We report a child with diabetes insipidus and hypodipsia associated with holoprosencephaly. A two-year-old girl with the history of several admittances to hospital during and after the newborn period with hypernatremic dehydration, acute renal failure and convulsions is presented. The patient had hypodipsia, hypernatremia, microcephaly, failure to thrive, and unilateral cleft lip and palate. Magnetic resonance imaging revealed lobar type holoprosencephaly. Increased plasma osmolality and decreased urinary osmolality were detected. Her urine ADH level was 10 ng/day. Plasma osmolality levels returned to normal after hydration and administration of a vasopressin analogue. These findings suggest that in children with hypernatremia-hypodipsia syndrome, the possibility of cerebral malformations should always be kept in mind.

Key words: hypodipsia, hypernatremia, holoprosencephaly.

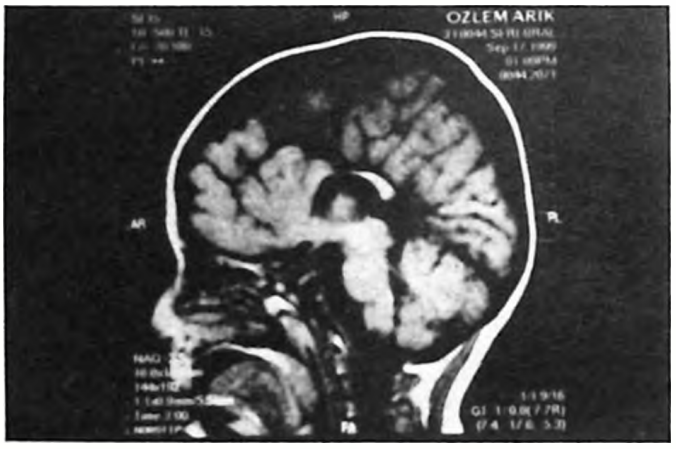
Adipsia or hypodipsia as an isolated defect of the thirst center is extremely rare and most often occurs in patients with hypothalamic disorders, congenital malformations and microcephaly[1]. One of the causes of hypernatremia is hypodipsia-hypernatremia syndrome, and its association with median structures of the brain and face is known[2]. We present here a child with facial abnormalities, which included unilateral cleft lip and plate, flat nose, and orbital hypertelorism associated with lobar holoprosencephaly, and diabetes insipidus.

Case Report

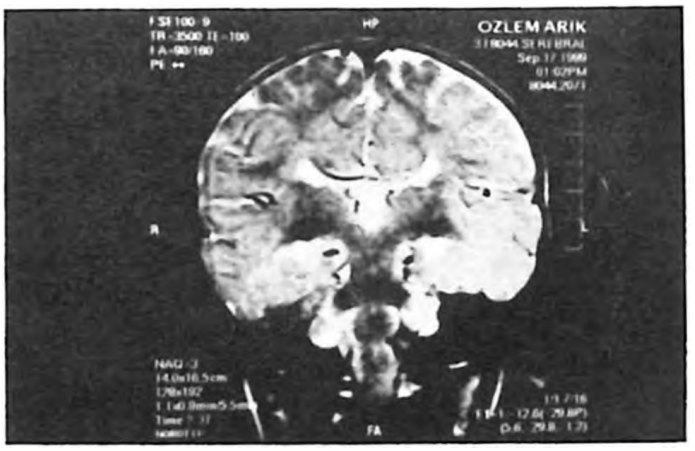
A 2 ½-year-old female was hospitalized because of hypodipsia, convulsions, unconsciousness, hypernatremic dehydration and acute renal failure. She was born after eight months of pregnancy by cesarean operation because of her mother's diabetes. Due to unilateral cleft lip and palate and prematurity, she had been hospitalized for one month in neonatal period. She had been re-admitted several times there after because of hypernatremic dehydration. She had history of convulsions when she was six- and twenty-months-old, and also had an operation to repair cleft lip at 1 ½ years. She had two cousins with cleft lip and palate in her family history. The parents also mentioned a significant adipsia and retardation of development in the patient. On physical examination, she was lethargic. Her tongue and buccal mucosa were excessively dry. She had anuria for eight hours preceding admission. Her height, weight and head circumference were under the third percentile for age. She had abnormal facial appearance with cleft palate, operated cleft lip, flat nose and hypertelorism. The following laboratory data were obtained: BUN, 80 mg/dl; creatinine 3.4 mg/dl; Na, 186 mEq/L; uric acid, 18 mg/dl; anion gap, 15; serum osmolality, 449 mOsm/kg; and urine osmolality 78 mOsm/kg. Blood counts- Hct, 41.4%; white blood cell count, 8,100/mm^3; platelet count, 176,000/mm^3; urinalysis –pH, 5; specific gravity, 1010; and 3-4 erythrocytes in the sediment.

She was severely dehydrated. The deficit was replaced uniformly within 48 hours with a solution of 0.2% saline with dextrose, so as to minimize the risk of central nervous system

dysfunction. Renal function tests returned to normal after hydration. Her cerebral magnetic resonance imaging revealed dysgenesis of corpus callosum, agenesis of septum pellucidum, hypoplasia of falx and sella turcica. Lobar holoprosencephaly was diagnosed (Fig. 1). Her chromosome analysis was found as 46, XX. Water deprivation test was performed over a two-hour period. The patient was closely observed to avoid severe rapid development of dehydration. At the beginning of the test, blood and timed urine were obtained from the child for serum and urinary antidiuretic hormone (ADH) levels, then 10 mg desmopressin was given intranasally. ADH administration led to a decrease in urine flow and increase in urinary concentration and urinary osmolality. The results of the test supported our diagnosis of central diabetes insipidus (Table I). A nasogastric feeding tube was placed in and her family warned about the importance of giving water to the child.



(a)



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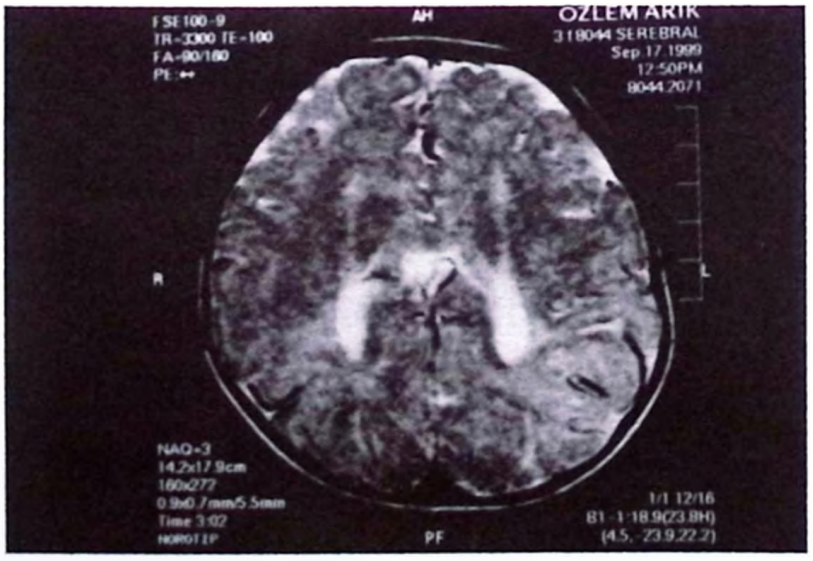

(c)

Fig. 1. Dysgeensis of corpus callosum, hypoplasia of falx, sella turcica and agenesis of septum pellucidum are seen.
a) sagittal T1-weighted section;
b) coronal T2-weighted section;
c) axial T2-weighted section.

Table I. Results of Water Deprivation Test

	Before AVP	After AVP
Maximum U_{OSM}/S_{OSM}	61/335 mosm/L	591/336 mosm/L
Serum ADH	3.5 pg/ml	—
Urinary ADH	<10 ng/day	not performed

ADH: antidiuretic hormone.

Discussion

Two important mechanisms are responsible to prevent hyperosmolality in normal individuals: water intake is increased and the release and action of ADH is also increased to produce a concentrated urine[1]. Central diabetes insipidus may evolve from various problems that lead to a deficiency of ADH secretion from the posterior pituitary gland[3]. There is close communication among neural centers regulating thirst and water conservation, and intrinsic central nervous system (CNS) disease may occasionally manifest with symptoms of disordered thirst in association with impaired ADH secretion. This finding has been observed in a group of disorders loosely termed adipsia/hypernatremia[3]. These patients usually have a central lesion that impairs the thirst and ADH release centers, causing their destruction[4]. Adipsia-hypodipsia and recurrent hypernatremia are usually manifestations of structural abnormalities of the hypothalamic-pituitary area[5]. Also, dysfunction of the anterior pituitary lobe, obesity, abnormal regulation of body temperature, psychomotor dysregulation and episodic muscular weakness could be encountered in these patients[6]. A decreased release of thyroid stimulating hormone (TSH), prolactin and growth hormone may be detected[7]. In our patient, thyroxine, triiodothyronine and TSH levels were normal, and a rate of growth of 0.5 cm/month documented in the last four months. Her body percentiles were below the third percentile.

These patients have recurrent or persistent hypernatremia without thirst. History of convulsions, polyuria, hypodipsia, and recurrent hypernatremia attacks and midfacial defects led us to suspect a central pathology associated with diabetes insipidus in our patient. Holoprosencephaly results from failure of separation of the embryonic forebrain, or prosencephalon, into symmetric cerebral hemispheres[8]. It was detected on the patient's cerebral magnetic resonance imaging. Holoprosencephaly involves forebrain and facial malformations that can range from mild to severe and it occurs more commonly in infants born to diabetic mothers[8,9], as was the case in our patient. It has been demonstrated that chromosomal abnormalities detected in some patients with holoprosencephaly include trisomies 13 and 18, deletions 18p- and 13q-, ring 18, the "pseudo-trisomy 13 syndrome", and triploidy[8,9]. Our patient's chromosomal analysis was found as 46, XX.

Holoprosencephaly and its association with hypernatremia and diabetes insipidus has been reported rarely in the literature[10-12]. Ohtake et al.[10] reported two young children with chronic hypernatremia, midline facial defects and holoprosencephaly. Kappy et al.[11] had restored serum electrolytes to normal with desmopressin acetate in a three-month-old child with holoprosencephaly and central diabetes insipidus. Arranz Gomez et al[12]. reported the clinical and neuroradiological findings in a case of semilobar holoprosencephaly associated with hypernatremia behaving like diabetes insipidus. In our patient, defective ADH release was shown with water deprivation test. It is known that defective synthesis or release of ADH will impair renal concentrating capacity and these patients will have a risk of hypernatremia. Because of the defective thirst mechanism caused by holoprosencephaly, our patient could not maintain the necessary high water intake, and hypernatremic episodes occurred.

In conclusion, if recurrent hypernatremic dehydration attacks with hypodipsia and convulsion are seen in a young child, CNS abnormalities associated with diabetes insipidus should always be searched.

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