Neonatal central diabetes insipidus in a case of hydranencephaly

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Received - 29 January 2019 Initial Review - 20 February 2019 Accepted - 28 February 2019

ABSTRACT

Neonatal diabetes insipidus (DI) poses both diagnostic and therapeutic challenge to the neonatologists. Neonatal central DI (CDI) is an uncommon disorder which is characterized by polyuria, hypernatremia, high plasma osmolality, and low urine osmolality. Our full-term neonate with an antenatal magnetic resonance imaging showing hydranencephaly presented to us on day 4, with persistent hypernatremic dehydration along with the polyuria which was not getting corrected by the routine management of hypernatremic dehydration. Further investigations revealed urine hypo-osmolality and high serum osmolality and a good response to oral desmopressin (DDAVP). This helped to diagnose CDI secondary to hydranencephaly. The baby was discharged on oral DDAVP, but unfortunately, the baby succumbed at 3 months of age.

Key words: *Desmopressin, Hydranencephaly, Hypernatremia, Neonatal diabetes insipidus, Polyuria*

Central or nephrogenic diabetes insipidus (DI) is an extremely rare entity encountered in neonates. Neonatal central DI (CDI) has an incidence of approximately 2/100,000 live births [1]. The common underlying etiologies of neonatal DI include infections such as meningitis, congenital viral infections, intraventricular hemorrhage, hypoxic-ischemic encephalopathy, and cerebral malformations such as septo-optic-dysplasia, holoprosencephaly, hydranencephaly, corpus callosum agenesis, and familial pituitary hypoplasia. Persistent polyuria with hypernatremic dehydration with low weight gain, despite adequate treatment, should arouse the suspicion of neonatal DI [2].

Hydranencephaly is an uncommon congenital anomaly characterized by necrosis of the cerebral hemispheres and its replacement by a membranous sac containing cerebrospinal fluid. The pathogenesis is thought to be intrauterine bilateral internal carotid artery occlusion at the gestational age of 8–12 weeks. The various etiologies include maternal infections, drugs, and multiple gestations. The spectrum of symptoms includes lethargy, feeding difficulties, feeble crying, irritability, hypertonia, and seizures [3]. Here, we present a case with antenatally diagnosed hydranencephaly with neonatal CDI. This is the first such reported case to the best of our knowledge in our country.

CASE REPORT

Our case, a male baby full-term vaginal delivery weighing 3 kg (50th centile) was born to a primigravida mother without any antenatal risk factors. The antenatal ultrasound at the 7th month was suggestive of massive hydrocephalus. A fetal magnetic resonance imaging (MRI) was performed in the 8th month of gestation which was reported as hydranencephaly (Figs. 1 and 2).

At birth, examination did not reveal any dysmorphic features. Head circumference was 35 cm (10th to 50th centile), and total length was 48 cm (50th centile). There was generalized hypotonia, and rest of the systemic examination was normal. The baby was admitted to neonatal intensive care unit for his poor activity on day of life one.

From the 4th day of life, he started having dehydration and was found to be polyuric, urine output being around 6 ml/kg/h. On further evaluation, the baby had hypernatremia along with persistent polyuria (Table 1). He was treated according to the protocol for the management of hypernatremic dehydration. Simultaneously, investigations were sent for the evaluation of polyuria which included serum and urine osmolality with urinary electrolytes. The reports were suggestive of high serum osmolality (343.2 mOsmol/L) with low urine osmolality (281.6 mOsmol/L). Hence, a diagnosis of DI was made, and the baby was started on oral desmopressin (DDAVP) at a dose of 2 µg/kg/day. There was a gradual correction of the hypernatremia and polyuria after starting oral DDAVP which confirmed the diagnosis of CDI. The dose of oral DDAVP was adjusted according to the serum electrolytes and urine output, and finally, a dose of 0.75 µg/kg/day was continued.

He was also evaluated for other hormone deficiencies in the hypothalamic axis which were in the normal ranges (thyroid-stimulating hormone – 2.4 uIU/ml and serum cortisol – 1.2 µg/dl).

An MRI brain was planned to look for structural anomalies of pituitary gland but could not be done because of non-availability in our institute, and a computed tomography scan of the brain revealed hydranencephaly. The neonate was discharged on the 26th day of life. The baby had an erratic follow-up and unfortunately succumbed at 3 months of age.

DISCUSSION

DI is a rare disease in the newborn period. It is a disorder of water homeostasis due to absence (central DI) or resistance of the kidney to the hormone arginine vasopressin (nephrogenic DI) [2]. The diagnosis is difficult because excessive water loss through the skin is often attributed as the cause of high serum sodium in the neonatal age group thus delaying its medical treatment. This condition is characterized by the passage of large amounts of dilute urine leading to dehydration and hypernatremia [4]. The clinical manifestations of CDI usually occur later, as a result of gradual degeneration of the vasopressin-producing neurons [5]. The possible etiologies in neonates include birth asphyxia; congenital infections such as toxoplasmosis, varicella, and Coxsackie B1 virus; meningitis; tumors; periventricular hemorrhage; and various central nervous system malformations such as holoprosencephaly, hydranencephaly, and corpus callosum agenesis [2,6].

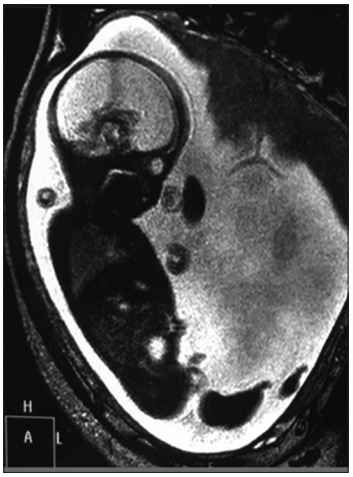

Figure 1: Fetal magnetic resonance imaging showing cerebrospinal fluid-filled cerebral hemispheres

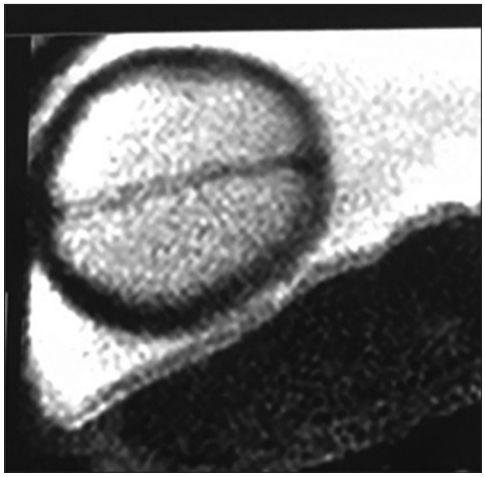

Figure 2: Fetal Magnetic resonance imaging showing cerebrospinal fluid-filled cerebral hemispheres

Hydranencephaly is one of the malformations attributed to the process of vascular disruptions and is caused by occlusion of the internal carotid artery in between the 8th and 12th week of gestation. The cerebral hemispheres are replaced by a membranous sac with the diencephalon and posterior brain structures being relatively preserved [3,7,8]. A single gene mutation in FLVCR2 was identified recently in one infant with hydranencephaly [7]. The pre-disposing conditions include maternal infections, exposure to teratogenic agents, twin pregnancies, and fetal genetic disorders [8]. Symptomatic management is possible which includes measures to reduce intracranial pressure like drugs or drainage surgeries. The treatment in hydranencephaly is surgical either in the form of shunt placement or a ventriculostomy. However, many question the need for surgery in these cases when most newborns with this disorder succumb within the 1st few weeks or months of life although rare cases of children with hydranencephaly growing up to adolescence have been reported [3].

The key to recognition of DI in neonatal group is to investigate the cause for hypernatremia without any other electrolyte abnormalities with a proper history and examination for dehydration. The diagnostic clincher is a low urine osmolality (< 300 mOsmol/L) and high serum osmolality (>300 mOsmol/L) [9]. Our neonate had a serum osmolality of 343 mOsmol/L and urine osmolality of 281.6 mOsmol/L. Recent studies have used plasma copeptin, which is the "C" terminal of arginine vasopressin precursor, as a marker for the diagnosis of CDI [2,4]. Further investigations are to look for other hypothalamic-pituitary axis hormone involvement, sepsis screen, and cranial MRI with high-resolution images of the pituitary gland. The normal posterior pituitary lobe contains secretory granules which are responsible for hyperintense signal on T1-weighted MRI imaging. This finding is absent in idiopathic CDI [6]. In our case, other pituitary hormones were within the normal limits for age; however, MRI brain could not be done.

The treatment of CDI depends on the type of the condition which may include hormone replacement in CDI or drugs such as thiazides in the nephrogenic type of DI. Neonatal DI is traditionally treated with DDAVP, which is a synthetic analog of vasopressin [10,11]. The different routes of administration of vasopressin are intranasal,

Table 1: Serum electrolytes before and after starting DDAVP

Serum electrolytes and urine output	Day 1	Day 4	Day 9	Day 14		Day 15	Day 18	Day 19	Day 22
Serum Na (mEq/L)	141	169	186	179		168	161	152	142
Serum K (mEq/L)	4.7	4.0	4.5	4.1	Desmopressin started	4.0	5.1	4.5	3.9
Urine output (mL/kg/h)	5.1	5.1	9.6	9.6		9.2	4.2	3.1	3.6

DDAVP: Desmopressin

subcutaneous, intravenous, and oral, with the oral route being the most commonly used in the treatment of neonatal DI [1]. In our case, we used oral DDAVP dissolved in sterile water along with breast milk. The oral administration was preferred as it was easy to titrate the dose as compared to the intranasal route. The baby responded to the therapy and was discharged after adjustment of the dose. In a study done by Mavinkurve *et al*., it was found that oral administration of diluted nasal DDAVP was safe and enabled proper dose titration [1]. In another case report by Biset and Claris *et al*., in an extremely low birth weight neonate with CDI, oral DDAVP was used initially, and the route of administration was changed to intranasal before discharge [4]. Titration of the dose has to be done while administrating this drug to neonates to prevent fluid overload and life-threatening hyponatremia. New literature has shown usefulness of thiazide in CDI; however, it is not being widely used [10,11].

CONCLUSION

Prompt evaluation of a persistent hypernatremic neonate (not responding to routine treatment) for DI is a lifesaving measure. Starting DDAVP along with the treatment of the underlying etiology in these neonates is mandatory. Dose of DDAVP should be adjusted as per the clinical condition and laboratory investigations. MRI brain is an important tool in the assessment of DI.

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Funding: None; Conflict of Interest: None Stated.

How to cite this article: Malik S, Gandhi PS, Mukherjee A, Shah NJ, Lichade VM, Wade PA. Neonatal Central Diabetes Insipidus in a Case of Hydranencephaly. Indian J Child Health. 2019; 6(3):136-138.

Doi: 10.32677/IJCH.2019.v06.i03.010