

CENTRAL DIABETES INSIPIDUS IN A 4-YEAR-OLD CHILD – A CASE REPORT

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Abstract: *Central diabetes insipidus (CDI) is a rare paediatric endocrine disorder. The authors report the case of a 4-year-old child admitted with polyuria and polydipsia with sudden onset and no recent history of head trauma. Laboratory investigations confirmed the polyuria and showed an urinary concentration defect and low urinary osmolality. A water deprivation test was performed to confirm the diagnosis and 1-deamino-8D-arginine-vasopressin (dDAVP) test was done to distinguish between central (CDI) and nephrogenic(NDI) diabetes insipidus. Water deprivation test is an useful diagnosing tool despite the risks it entails (severe dehydration). CDI can be successfully managed with desmopressin administered orally.*

Key words: *central diabetes insipidus, water deprivation test, desmopressin*

1. Introduction

Central diabetes insipidus (CDI) is a heterogeneous syndrome characterized by the inability to concentrate urine secondary to a deficient synthesis of the antidiuretic hormone, arginine vasopressin (AVP). The main clinical manifestations are polyuria and subsequent polydipsia [9].

AVP is a hormone with a central role in the maintenance of water balance. It is produced within the magnocellular neurons of the paraventricular and supraoptic nuclei of the hypothalamus

which send their axons to the posterior pituitary gland. The pituitary gland releases the hormone into the bloodstream [11].

AVP and its carrier protein, neurophysin II (NPII), are encoded by a gene on the chromosome 20p13 [4], [12].

CDI can present at any age, depending on its underlying etiology. [4] It is most frequently an acquired condition, usually secondary to traumatic injuries [5]. In rare situations, congenital cases with structural malformations of the hypothalamus-hypophysis axis can be identified.[16] Genetic forms of CDI present with

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autosomal or recessive mutations of genes encoding the AVP-NP11 complex.[10] Less common causes are infiltrative lesions - tuberculosis, sarcoidosis, langerhan cell histiocytosis [18], [10].

Water deprivation test is the gold standard in differentiating between NDI, CDI and compulsive water drinking. Dilute urine with an osmolality of less than 300 mOsm/kg and serum osmolality greater than 300 mOsm/kg is diagnostic for central diabetes insipidus. [18], [4] Additionally, 1-deamino-8D-arginine vasopressin (dDAVP) test is performed in order to distinguish between CDI and NDI. [9]

Currently CDI can be successfully managed through therapy with desmopressin – a syntetic analogue of AVP which can be prescribed in oral, intravenous or intranasal form. [16]

2. Case Report

We present a case report of a 4-year-old male child admitted at the Clinical Children's Hospital of Brasov with polyuria and polydipsia with a recent onset. The mother reported that in the last 4 months she has noticed a change in the boy's behaviour as he was constantly thirsty, requesting more liquids than usual and becoming irritable in the absence of water and had frequent micturition. He also began waking up through the night asking for water, but no nocturia or enuresis was reported.

The child had no significant family history of similar symptoms and both parents were healthy. He was born at 38 weeks gestation by caesarean section due to a breech presentation, after a healthy pregnancy. He had a birth weight of 3850gr., an APGAR score of 9, was vaccinated accordingly and had received

rickets prophylaxis with vitamin D3 until the age of 2. The mother denied any recent history of head trauma.

Prior to the admission the child has received paediatric outpatient care and completed the following laboratory investigations: blood glucose levels and 25-OH-vitamin D which showed values within the normal range, therefore excluding diabetes mellitus and hypervitaminosis D, conditions that could have presented with a polyuria-polydipsia syndrome.

At the time of the admission he had a satisfactory medical state, without fever, with normal vital signs. Clinical examination revealed relatively dry skin. He had a weight of 17 kg (Z score of 0.34) and a height of 112cm. For these values, calculated BMI was 13.6, falling into the underweight category.

Routine blood tests were drawn and have showed normal blood cell counts and normal haemoglobin (12.6 g/dl). Blood chemistry tests showed, once again, a normal serum glucose level (81.5 mg/dl), normal kidney function and normal electrolyte balance with sodium levels at the upper limit (143mmol/L).

During the first day of hospitalization we confirmed polyuria (diuresis >2L/24h) and performed urine analysis which showed a discoloured urine with low specific gravity of 1000, with no other pathological findings.

An endocrine consult was requested and investigations were completed with the evaluation of the anterior hypophysis function which showed normal TSH (1.525µUI/mL) and FT4 (17.57 pmol/L) levels, normal prolactine (7.48 ng/ml), serum cortisol (425.2 mmol/L) and normal IGF-1 (56.2 ng/mL).

Clinical and laboratory findings were

suggestive of a polyuria-polydipsia syndrome with a high suspicion of diabetes insipidus. Consequently, a water deprivation test was performed in order to confirm the diagnosis.

We began test preparation by placing a reliable intravenous cannula and by assessing baseline weight (17 kilos) and serum (308.mOs/L) and urine osmolality (<300 mOs/L). All liquid intake has been stopped and the test began at 6 AM.

The child was weighted hourly, monitoring the vital signs (heart rate and blood pressure) and the quantity and colour of each micturition was assessed. (Table 1)

Table 1

The dynamic of weight, blood pressure and urine volume during the water deprivation test

Time	Weight (kg)	Blood pressure (mmHg)	Urine volume (mL)
7 AM	16.9	104/79	200
8 AM	16.8	90/50	100
9 AM	16.6	80/40	80
11 AM	16.5	90/40	60
12 PM	16.5	-	30

Urine analysis performed on each of the samples showed a constant, unchanged value of the specific gravity despite the level of dehydration. As far as colour was concerned, the changes were minimal from discoloured to light yellow before the administration of desmopressin, changing to a normal yellow after the test.

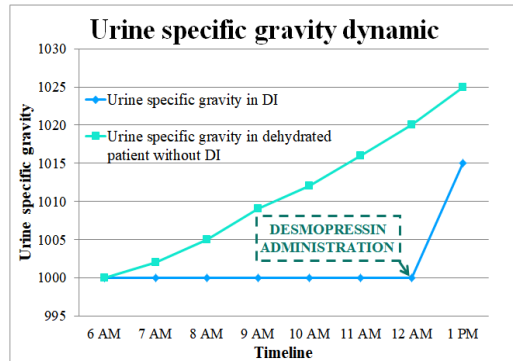


Fig.1. Comparison of urine specific gravity during water deprivation test in a healthy patient and a patient with DI – in the first situation there would be a gradual reduction of diuresis and a gravity increase whereas in the DI patient the urine remains hyposthenuric.

The test lasted 6 hours as the child became gradually more irritable, agitated, crying for water. Physical examination showed a slightly prolonged capillary refill time (3”) and a delay in skin turgor. By the end of the test he had lost 500 gr.

We administrated 60 mcg of desmopressin sublingually and repeated the urine analysis. The tests showed an increase in urine specific gravity and osmolality (549mOsm/kg), therefore confirming the diagnosis of central diabetes insipidus.

In addition to the water deprivation test we also measured the copeptin (C-proAVP) which served as a further confirmation of the diagnosis.

In order to determine the etiology of the CDI we have performed a head CT scan which came back normal. However, a MRI scan has been scheduled in 6 month time to further investigate possible causes.

As under treatment his general condition improved, the patient has been discharged with the recommendation of free water access and pharmacological

treatment with 120mcg of desmopressin/day, divided in two administrations.

On the 3 months follow up visit, he was asymptomatic, with an ascendant weight curb and good tolerance for the treatment, with no side effects.

3. Discussions

We have reported a case of central diabetes insipidus in a previously healthy 4 year-old-child. The main characteristics of this case were the sudden onset of symptoms and the lack of recent history of head trauma and of family history of DI.

In children, diabetes insipidus is a rare endocrine disease with an overall prevalence of 1:25.000 cases [14], which makes its diagnosis a challenge for most clinicians. However, DI should be suspected in a young child with polyuria and polydipsia.

The diagnosis of CDI in children requires a high index of suspicion because the presenting symptoms and clinical aspects are nonspecific [16]. Polyuria – polydipsia syndrome can be encountered in a number of conditions that make the differential diagnosis with CDI. These conditions are: diabetes mellitus, primary polydipsia (compulsive water drinking), chronic renal failure [13].

Our patient had normal levels of blood glucose and normal renal function based on BUN and creatinine values, therefore we could easily exclude such conditions. In addition to what the literature suggests, we have taken in consideration the possibility of a hypervitaminosis D but blood tests also excluded this hypothesis.

Other frequent symptoms in CDI are new onset nocturia, determining the child to wake up at night [16], and enuresis in a

child that was previously able to control his micturition.[11] Nevertheless, enuresis was not reported by the mother in our case.

Children with CDI have a typical craving for cold water [18] which was also not found in our patient. On the other hand, the inability to promptly satisfy his thirst provoked excessive agitation and irritability to the point of even becoming physically aggressive towards the mother during the water deprivation test.

Focal neurologic signs and neurologic deficits in the presence of polyuria should raise suspicion for central DI secondary to an intracranial mass. [1] In particular, visual defects at a young age are often associated with an intracranial mass. [16] No such signs and symptoms were reported in our case.

Early morning measurements of serum osmolality, urine osmolality and serum electrolytes are very important in the paediatric age group when a case of DI is suspected. [3] As the literature reports [17], hypernatremia is most common in infants, but it can present in children as well. In our case, serum electrolytes showed a borderline sodium level. The value was further elevated by the dehydration during the test we performed.

A cardinal finding in all cases of diabetes insipidus is the urine concentration defect. [16] In our patient, we have also performed urine analysis that have showed a hyposthenuric gravity of 1000.

If the requirement of a serum osmolality higher than 300 mOsm/kg is met, a water deprivation test has to be done in order to confirm the diagnosis. The test needs to be performed under strict supervision because of the life threatening potential of dehydration. [2] Our team has followed the guidelines and has carefully monitored vital signs, weight loss and

clinical signs of dehydration. However, we were not able to perform the test until a urine osmolality higher than 600mOsm/kg [4] was reached due to the change in our patient's general state. The signs of dehydration and excessive irritability determined us to end the test after 6 hours. Based on the increase of osmolality (from <300mOsm/kg up to >500mOsm/kg) we evaluated the response to vasopressin and made the positive diagnosis.

Direct AVP measurement is a viable, safer alternative to the test, but requires specialized personnel and a specific clinical setting and longer time to be processed. [9]

Because direct AVP measurement was not available, we have opted to perform a water deprivation test in order to confirm the diagnosis and distinguish between the two possible forms of DI.

Fenske et al. brought to attention the promising diagnostic potential of copeptin – the C-terminal part of the AVP precursor which is much easier to measure. [8] In our case the low value of copeptin further confirmed the diagnosis.

As far as etiology is concerned, children require neuroimaging to point out evidence of evolving central nervous system pathology such as tumors, infiltrative or post-traumatic lesions. [16], [5]. MRI is the gold standard investigation for these patients. The most frequent finding is the absence of posterior pituitary bright signal and an enlarged pituitary stalk [6], [1]. As recent studies have shown, symptoms can precede structural changes in the brain by 6 months or more. [7] As a result, we have decided to postpone the investigation and monitor his evolution under oral treatment with desmopressin and perform the MRI in a 6 month time.

The treatment of choice in CDI is is

intranasal desmopressin. [16] In our patient we have opted for the oral administration of 60mcg twice a day, which proved to be well tolerated.

Moreover, free access to water should be allowed in children with DI in order to preserve the function of their thirst mechanism. [4] Therefore, we made the same type of recommendation to our patient, advising the mother to continue to monitor the quantity of ingested liquids and diuresis.

4. Conclusions

The authors report a case of central diabetes insipidus in a pediatric patient. The particularity of this case consisted in the small prevalence of this disease which required close collaboration between pediatric and endocrine departments in order to reach the diagnosis. Water deprivation test has proved to be an efficient diagnosis tool even in the absence of an AVP determination.

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