


Case Report

A good night's sleep after two decades: a case report of idiopathic central diabetes insipidus

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Introduction

Polyuria is a condition characterised by excess urine output, defined as more than 3 litres per day in an adult and 2L/m² in children. The cause of polyuria can be solute (osmotic) diuresis or water diuresis. The most common cause of polyuria due to osmotic diuresis is uncontrolled diabetes mellitus where glucose induced diuresis occurs. The other three major causes of polyuria are due to water diuresis including primary polydipsia, central diabetes insipidus (CDI) and nephrogenic diabetes insipidus (NDI). All present with large volumes of dilute urine where urine osmolality is usually lower than 300 mOsm/kg [1]. If the urine osmolality is less than 300 mOsm/kg it is likely that the aetiology of the polyuria is either DI or primary polydipsia. Therefore, these patients should undergo water deprivation, or, if necessary, desmopressin administration to distinguish primary polydipsia from DI and also to determine the type of DI [2].

DI is a rare disease with a reported prevalence of 1:25 000 [3]. Out of the two forms, CDI is more common than NDI. Any condition, either inherited or acquired, causing impairment of the synthesis, transport and release of ADH cause CDI. This condition is equally distributed among both sexes and the most frequent age of onset is between 10 to 20 years of age [4]. Acquired causes of CDI are more common than congenital forms. Considering acquired causes of CDI, there are instances where no clinical evidence is found for any injury or disease that could be linked to DI. These cases account for 25% of CDI cases and are considered as idiopathic CDI [5].

Patients with DI primarily present with persistent polyuria (8-16 L diluted urine per day) and polydipsia (up to 20 L intake per day). Other symptoms include weakness, dizziness, fatigue, nocturia and features of dehydration such as fever, dry skin and mucous membranes, loss of weight and poor skin turgor. Rarely they can present with hypotension, tachycardia and altered level of consciousness [2,6]. Until the thirst centre

remains intact, the patient can drink water and keep the plasma osmolality at a value slightly exceeding 290 mOsm/kg [7].

The water deprivation test (Hare-Hickey test) and desmopressin challenge test are used to distinguish between the ability of the central nervous system to synthesize ADH and the kidneys to respond to it. In CDI, urine osmolality remains lower than plasma osmolality after dehydration and, following desmopressin injection, urine osmolality increases by more than 50% or more than 750 mOsm/Kg. In NDI, urine osmolality remains lower than plasma osmolality following dehydration and with desmopressin the rise of urine osmolality is lower than 50% [2,4]. Other method is the direct or indirect measurement of plasma AVP [2].

Case report

The case we present is a 39-year-old woman who was admitted to National Hospital, Kandy, Sri Lanka with a twenty-year history of polyuria, nocturia and polydipsia with sleep deprivation due to nocturia. She denied any long-standing headache or visual disturbance. Her family history was unremarkable and she was not on any long standing medications. She was being evaluated for diabetes mellitus but her sugar levels and HbA1c levels were normal. Her general and systemic examinations including neurological assessment and mental state assessment were normal. Following admission, she was kept under observation regarding her intake and urine output which revealed an average urine output of 6 litres per day.

During the hospital stay she was investigated for her current presentation. Since her basic screening for polyuria and polydipsia (Table 1) was unremarkable, we proceeded with the water deprivation test (WDT). The test had to be abandoned and intranasal desmopressin spray of 20 mcg started as there was a more than 3% reduction in body weight as well as a serum osmolality rise to 307 mOsm/kg within four hours of commencing the WDT (Table 2).

Table 1: Basic investigations

Test	Value	Reference range
Fasting blood sugar	93mg/dl	65-110mg/dl
HbA1c	5.4%	4-5.6%
Serum ionized Calcium	1.22mmol/l	1.15-1.33 mmol/l
Serum Potassium	4.4 mmol/l	3.6-5.2 mmol/l
Serum creatinine	58.8 µmol/l	44-80 µmol/l
TSH 3 rd generation	0.809 mIU/l	0.465-4.680 mIU/l
Baseline serum osmolality	289 mOsm/kg	275-295 mOsm/kg
Baseline urine osmolality	78 mOsm/kg	300-900 mOsm/kg

Table 2: Water deprivation and desmopressin test

Time	Weight (kg)	Urine volume (ml)	Serum osmolality (mOsm/kg)	Urine osmolality (mOsm/kg)
08.00	52.2	350	298	72
09.00	51.7	400		62
10.00	51.1	420	300	80
11.00	50.7	380		92
12.00	50.4	300	307	130
Water deprivation test abandoned. 20mcg intranasal desmopressin given				
01.30		50		235
02.30		25		464
03.30				469

A diagnosis of cranial diabetes insipidus was made based on the results of the WDT. For further aetiological evaluation, the patient had undergone cranial imaging with magnetic resonance imaging (MRI) of the brain. Her brain MRI was reported to be normal and all other investigations for secondary causes were negative. Ultimately, we arrived at a diagnosis of "idiopathic cranial diabetes insipidus".

She was started on desmopressin nasal spray 10mcg only before sleep and reviewed in the medical clinic on the following week. There was a remarkable improvement in her symptoms during this one week, where she had undisturbed sleep at night.

Discussion

Diabetes insipidus is a disease characterised by the passage of copious amounts of dilute urine which can interfere with the patient's day to day activities and can even be fatal if not properly diagnosed and treated. Primarily, these patients present with polyuria and polydipsia. Polyuria is the passage of more than 3 litres of urine per day (4). So, it is important to measure actual intake and output in a patient who is coming with a history of polyuria prior to proceeding with further evaluation. It is important to differentiate other causes of polyuria from DI.

DI is considered as a spectrum of disorders associated with either reduction in synthesis of ADH or an inadequate renal response [5]. ADH/AVP or vasopressin is an oligopeptide hormone synthesized predominantly in the supraoptic nuclei of the hypothalamus and transferred along an axonal pathway to the posterior pituitary from where it is secreted. This hormone has multiple functions including regulation of body's osmotic balance, blood pressure regulation, renal functions and sodium homeostasis [8]. In the kidneys ADH acts on specialised medullary transporters known as aquaporin water channels. The collecting duct water permeability is targeted by ADH in the short term via aquaporin-2 and targeted for long term regulation via both aquaporin 2 and 3 [8,9].

Considering all aetiologies, CDI is the most common disorder causing polyuria and polydipsia. This is usually due to a lesion in the neurohypophysis or the hypothalamic median eminence causing defective synthesis or release of ADH. There are a number of

causes of CDI which may be classified as congenital, acquired or idiopathic (2,4,5,10). Although 20%- 50% of CDI was considered as idiopathic CDI recent advancements in brain imaging and the finding of antibodies against AVP (AVPc-Abs) secreting cells has reduced this proportion [2,5].

Current clinical evidence suggests that autoimmunity plays a role in the pathogenesis of idiopathic CDI. A thickened pituitary stalk on brain imaging is seen in patients with autoimmune polyendocrinopathy and CDI. In addition, 25% of idiopathic CDI has a relationship with a prior viral infection as a [11]. There is an association between the presence of AVPc-Abs and idiopathic CDI but these antibodies are also associated with germinomas and Langerhan cell histiocytosis [2]. Autopsy series on patients with idiopathic CDI revealed atropic neurohypophyses as well as hypothalamic nuclei [4].

In our patient, urine osmolality was 78 mOsm/Kg which is an indication for a water deprivation test. During water deprivation urine output, body weight and urine osmolality are measured hourly and serum osmolality is measured two hourly. Primary polydipsia was excluded as there was no rise of urine osmolality more than 600 mOsm/kg with water deprivation [4,11]. Neither CDI nor NDI respond to water deprivation and the test should be abandoned if serum osmolality rises more than 300 mOsm/kg, there is a weight loss of more than 3% from baseline, rise of serum sodium more than 146-150 mmol/L or when patient develops orthostatic hypotension or intractable thirst. The procedure is repeated with administration of desmopressin 2mcg intramuscularly or 20mcg intranasally. Complete CDI is diagnosed if the initial urine osmolality was less than 300 mOsm/kg and a rise of more than 50% is seen. NDI is diagnosed if urine osmolality remains less than 300mOsm/kg or there is only a partial rise of less than 50% [4,10]. Based on the findings our patient was diagnosed to have complete CDI.

Other useful diagnostic tests include direct measurement of plasma ADH or measurement of copeptin, which is the C- terminal part of the AVP precursor during water deprivation. Copeptin has a higher stability ex vivo and is much easier to measure than ADH [12]. Both copeptin and direct ADH measurement were not available to us.

Along with sufficient replacement of water, the current recommended drug for long term therapy of CDI is desmopressin (1-deamino-8-D-arginine vasopressin, DDAVP). This can be given as an intranasal spray, orally or parenterally at night, with a starting dose of 10mcg. A morning dose may be added if there are severe daytime symptoms. Dosage can be adjusted on an individual basis [4]. Other potential treatments include chlorpropamide (only if neurohypophysis has some residual capacity), carbamazepine, clofibrate and thiazide diuretics [4]. Our patient was started on 10mcg of desmopressin nasal spray at night with a remarkable improvement in her symptoms, including an undisturbed sleep after two decades.

Conclusion

It is important to exclude the possibility of diabetes insipidus in an adult patient presenting with polyuria polydipsia syndrome while evaluating for other aetiologies.

Patients can compensate for a very long duration in non-progressive conditions like idiopathic CDI due to an intact thirst mechanism but correct diagnosis and treatment can lead to near complete symptom resolution.

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