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Dipsogenic Form of Primary Polydipsia in a Young Man and an Emerging Treatment Modality

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Authors' contributions

This work was carried out in collaboration between all the authors. Author AOI designed the study, managed the literature search, wrote part of the initial manuscript and performed critical review of the manuscript. Author TOA participated in the study design, wrote part of the initial manuscript and reviewed the manuscript. Author OOO reviewed the manuscript. All authors approved the final manuscript.

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Case Study

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ABSTRACT

Dipsogenic primary polydipsia is a subset of primary polydipsia characterised by disordered thirst in which the osmotic threshold for thirst is below the threshold for Arginine Vasopressin (AVP) release in patients without underlying psychiatric illness.

We report a case of a 19-year-old male undergraduate referred on account of 16 years history of polydipsia and polyuria, with no history suggestive of psychiatric illness. General physical and systemic examinations revealed no abnormality. He was otherwise healthy. He has been normonatremic and polyuric, with low urine osmolality.

The result of his water deprivation test showed intact urinary concentrating ability, low-normal serum osmolality and effective diluting capacity, which was consistent with the diagnosis of dipsogenic primary polydipsia.

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For symptomatic control, a low dose of intermittent desmopressin was given, the frequency of which was tapered down to usage as at when needed and strict water restriction was followed during drug dosing.
Making a clear distinction between dipsogenic primary polydipsia and partial central diabetes insipidus, it is required to guide effective therapeutic approach because of the fear of hyponatremia that could arise as a result of ingestion of excessive amount of fluid which can become more pronounced if the patient is on treatment with desmopressin.

Keywords: Dipsogenic primary polydipsia; partial central diabetes insipidus; arginine vasopressin (AVP); polyuria; polydipsia; Nigeria.

1. INTRODUCTION

Primary polydipsia is defined by excessive ingestion of copious amount of fluids and accompanying the production of large quantities of dilute urine (≥3 litres per day), for a considerable period of time, having excluded the secondary causes of polydipsia.

A dipsogenic form of primary polydipsia is characterised by disordered thirst in which the osmotic threshold for thirst is below the threshold for arginine vasopressin release (AVP). It typically occurs in patients without psychiatric illness.

However, different authors have reported primary polydipsia as a behavioural abnormality in patients with underlying psychiatric disorders that includes; schizophrenia, anxiety disorders, bipolar affective disorders and depression [1,2], where it is termed psychogenic polydipsia.

Nevertheless, defect with the thirst mechanism as a result of hypothalamic lesions, habitual consumption of several litres of water per day due to presumed health benefits has increased the prevalence of primary polydipsia outside the setting of those with background mental health disorders.

Hyponatremia is a feared possible complication that could arise as a result of ingestion of excessive amount of fluid [3], which can become more pronounced if the patient is on treatment with desmopressin, and this contributes to an increase in morbidity and mortality.

The present study reports a case of a young man diagnosed with primary polydipsia of dipsogenic origin. The paucity of reports on non-psychogenic causes of primary polydipsia especially in Africans, can lead possible misdiagnosis that can arise if the painstaking effort is not made to properly correlate the clinical presentation with investigation findings and a successful plan of treatment that has not been widely recognised in the medical field necessitated this case write-up.

2. CASE PRESENTATION

A 19-year-old male undergraduate was referred from another medical facility to our centre on account of a 16-year history of copious amount of water intake, the passage of large quantities of dilute urine (approximately 14-16 times each day) and nocturia. The symptoms were said to have worsened as he advanced in age. There was no history of blurring of vision, hearing deficit, anorexia, easy fatiguability, weight loss or linear growth defect. No history suggestive of renal impairment or mental illness. There was no history of head injury, neurosurgical intervention or any prior history suggestive of CNS infection or granulomatous disease and he is not a known diabetic. No history of use of lithium, demeclocycline, antidepressants or other drugs of interest. His haemoglobin genotype is AA. No family history of diabetes mellitus or psychiatric illness was found.

His past medical history is unremarkable except for occasional common cold which is relieved with cold therapies and he does not self-medicate.

On physical examination, he was a healthy-appearing young man. Blood pressure was 112/62 mmHg, pulse rate, 72 beats per minute and weight was 76 kg. The physical examination was generally unremarkable.

He was managed at the referring centre as a case of cranial diabetes insipidus (DI), with subcutaneous desmopressin 1 mcg twice daily, but there was no significant clinical improvement.

The result of the following tests ordered for were all within normal limit: electrolyte, urea and

creatinine with serum calcium and albumin, fasting plasma glucose, urinalysis and urine microscopy/culture and sensitivity, serum AVP, and calculated serum osmolality.

Estimated urine volume in 24 hrs was 10 litres. The water deprivation test result shown below was in keeping with primary polydipsia and the urine specific gravity was 1.004. The basal plasma copeptin value was 1.5 pmol/l (1.0-28.2 pmol/l) at serum osmolality of 279 mosm/kg and serum sodium level of 135 mmol/l. The Brain MRI was a normal study with preservation of pituitary bright spot on the T_1-weighted image.

A diagnosis of dipsogenic primary polydipsia was made.

On a follow-up visit to the clinic, his subcutaneous desmopressin was increased to 2 mcg twice daily. The patient was also advised to restrict fluid intake at least in the 6 hours following desmopressin administration. One week after commencing desmopressin, he developed a headache, restlessness and nausea within three hours of taking the evening dosage of the medication, but he did not seek for help at any hospital. During the next clinic visit, he was frankly counselled on the need to comply strictly with instructions on fluid restriction to avoid repeat symptoms suggestive of water intoxication.

Patient has since made a remarkable improvement as evidenced by a reduction in polyuria and better compliance with fluid restriction. After 6 weeks, the frequency of use of subcutaneous desmopressin was gradually tapered down to usage as at when needed during subsequent follow-up visits.

Table 1. Water deprivation test result of the index patient

Time (h: min)	Weight (kg)	Urine volume (ml)	Serum osmolality (mOsm/Kg)	Urine osmolality (mOsm/Kg)
0:00	80.2	400	295	130
1:00	79.4	380		109
2:00	79.3	100	293	297
3:00	79.3	50		724
4:00	78	38	297	744
5:00	79.3	55		601

Table 2. Typical laboratory values

	Primary polydipsia	Cranial DI	Nephrogenic DI
Serum osmolality	<295	>300	>300
Urine osmolality	>600	<300	<300

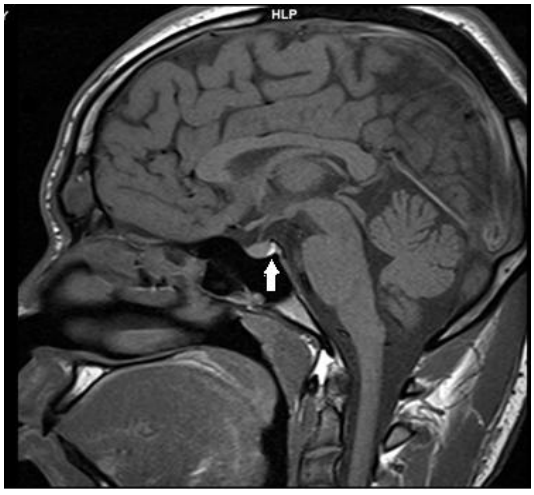

Fig. 1. The Brain MRI of the patient, with an arrow pointing at the preserved bright spot of the posterior pituitary gland on a T1 weighted image

3. DISCUSSION

The study describes a case of a young man with a polyuric-polydipsic disorder which was noticed when he was 3 years old characterised by near-constant thirst for water, the passage of a copious amount of urine, with no underlying psychiatric disorder and reduced urine osmolality which increased after water deprivation test.

The water deprivation test was able to demonstrate intact urine concentrating ability of the kidneys and normal Arginine vasopressin (AVP) release in response to the rise in serum osmolality. This effectively narrows down the possible diagnoses to partial central Diabetes Insipidus (DI), partial nephrogenic DI and primary polydipsia.

Persistent thirst with frequent ingestion of water in cases of primary polydipsia could be as a result of hypothalamic lesions of the thirst centre, psychiatric illness or iatrogenic cause. The patient does not have a history of psychiatric disorder, and circumstances along with the symptoms that were noticed ruled out the possibility of iatrogenic cause.

Partial central DI is a very close differential of primary polydipsia. A valuable diagnostic clue to differentiate these two entities is the serum sodium value which is elevated in the former and normal in the latter [4] was found consistent with the finding in this patient.

Striking features noticed in this patient include; long duration of polyuria, fear of being dehydrated and serum sodium value of 135 mmol/l (135-145 mmol/l) which is the lower limit of normal threshold, strongly favours the diagnosis of primary polydipsia as shown by this report [5]. The diagnoses of complete central and nephrogenic DI were ruled out based on the history of presenting complaints, the result of the water deprivation test, baseline plasma copeptin value and other ancillary investigations result. In addition, the presence of the normal hyper-intense signal on T1 – weighted MR imaging of the posterior pituitary, which was exhibited by the patient rules out a complete central diabetes insipidus. However, some authors have reported this finding in only about 80 percent of normal subjects [6].

The diagnosis of an inherited form of central DI known as autosomal dominant Familial Neurogenic DI (adNFDI) characterised by: onset at the first decade of life, characteristics of partial central DI at the initial stage and good response to desmopressin was considered. But the absence of family history and lack of features suggestive of anterior pituitary hypofunction, with apparently normal brain MRI findings 15 years after the onset of symptoms makes this diagnosis unlikely [7].

The challenge was in differentiating partial central DI from primary polydipsia. The subsequent development of features of hyponatremia in this patient after the use of desmopressin rather supports primary polydipsia as compared to partial central DI in which the serum sodium level is within the reference range with no manifestation of symptoms of water intoxication.

Central to the management of patients with primary polydipsia is voluntary water restriction to avoid precipitating hyponatremia, but in patients with an underlying psychiatric illness who may be uncooperative, behavioural management to limit daily water intake is very important [3].

Ferrer et al. [8] described a case of water intoxication presenting with multiple fits in a patient with dipsogenic primary polydipsia that was managed with intranasal desmopressin, this further put a huge clinical importance on differentiating dipsogenic primary polydipsia from partial central insipidus.

The ability of the patient to raise the urine osmolality to 744 mOsm/kg during the water deprivation test supported our diagnosis of primary polydipsia which is similar to the finding of a previous study [9]. In recent times, copeptin has been proposed as a surrogate measure for AVP. Copeptin is co-secreted with AVP from the neurohypophysis, it has a high in vitro stability and relatively easy to measure [10,11]. The basal and stimulated copeptin value has a similar result to the assay of the plasma AVP and has been proved to be more valuable in differentiating between partial central DI from primary polyuria with 94% specificity and sensitivity [12].

The challenges of measuring plasma arginine vasopressin include; pre-analytical instability, inter-assay variability, short half-life and a wide range of inconsistent results [13,14]. A diagnosis of primary polydipsia was supported by the plasma level of copeptin that is low-normal with episodes of hyponatremia in the patient [15].

The patient was given subcutaneous desmopressin to control his symptoms and was advised to restrict his water intake six hours after the use of the medication, a treatment approach that was adopted to prevent reduction of his serum sodium and keeping in mind the half-life of the drug. The treatment approach has been used in a previous report with a good result [16].

Dipsogenic primary polydipsia is attributed to a defect in hypothalamic thirst centre characterised by a severe unquenchable thirst for water. Therefore, there is a need to carry out further research to determine the impairment in the osmotic and non-osmotic drive for thirst in affected patients.

Our limitations majorly based on patient's financial constraints includes; inability to carry out hypertonic saline test which has been accepted and considered a safe option to the water deprivation test especially in a patient with low-risk for hypervolemic complications. Also, measurement of thirst via the visual analogue scale would have helped us to determine the osmotic threshold for the development of thirst in this patient and the comparison to the threshold for AVP release [17,18].

Another limitation of our report was that we were not able to sequence for AVP-NPII gene or get osmotically stimulated copeptin value in this patient which would have helped to exclude the diagnosis of adNFDI and to rule out partial central DI from primary polydipsia respectively.

4. CONCLUSION

The report concludes that there is a place for the use of targeted low-dose desmopressin with strict adherence to time-limited water restriction in the management of dipsogenic primary polydipsia. We have been able to further buttress the importance of comprehensive evaluation involving thorough clinical findings, the use of Brain MRI, water deprivation test and basal Copeptin values to overcome the diagnostic dilemma of evaluating primary polydipsia.

The use of a water deprivation test combined with basal and osmotically stimulated copeptin value helps to diagnose various forms of Diabetes insipidus with high accuracy. However, a sound clinical judgement based on comprehensive evaluation of the history and examination findings properly correlated with results of the investigations still remains the "gold standard" of making a diagnosis.

CONSENT

Informed consent was obtained from the patient for the publication of this case report and the accompanying images.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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