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Central Diabetes insipidus in a Nigerian child : A case report

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Abstract *Background:* Central diabetes insipidus (CDI) is rare in children. About 30 - 50% of cases are idiopathic. Early and accurate diagnosis are crucial for safe and effective treatment. This is the first report of Central diabetes insipidus in a child in Nigeria.
Case report: We report a case of central diabetes insipidus in a female toddler who presented at the University of Port Harcourt Teaching Hospital with polydipsia and polyuria with a urine specific gravity of 1.000 and normal blood sugar. The diagnosis of CDI was confirmed by her inability to concentrate urine after a water deprivation test followed by an increase in urine osmolality from 59mOsm/kg to 158mOsm/kg and serum osmolality from 286mOsm/kg to 321Osm/kg following intravenous administration of desmopressin. The patient responded well to oral desmopressin.
Conclusion: Central diabetes insipidus occurs in Nigerian children and responds to oral desmopressin. We recommended high index of suspicion in children with polyuria and polydipsia.

Key words: Central diabetes insipidus, polyuria, polydipsia, desmopressin, Nigerian child

Introduction

Central diabetes insipidus (CDI)is a heteregenous condition characterized by polyuria and polydipsia due to deficiency of arginine vasopressin (AVP).[1-3] It is a rareendocrine disorder in children and results from the destruction or degeneration of AVPsecreting neurons in the supraoptic and paraventricular nuclei of the hypothalamus or from impairment to the release or transport of AVP. CDI may be idopathic, inherited or acquired. Approximately 30 to 50% of cases of CDI are considered idiopathic. Congenital or inherited forms which are very rare and may be due to genetic defects in the synthesis of AVP that are inherited as autosomal dominant or X-linked recessive traits. Acquired or secondary causes include head trauma resulting from surgery or accident; central nervous tumors such as germinoma and craniopharyngioma; Langerhans'cell histiocytosis; central nervous infections such as tuberculosis, meningitis; autoimmune disorders andvascular lesions such as aneurysms and arteriovenous malformations.[1-3]

Deficiency of AVP causes excessive and uncontrolled loss of water from the kidneys with resultant hyposthenuria, inordinate thirst and an increase in serum osmolality. The complications which include dehydration, hypernatraemia and seizures are usually fatal.[4] Therefore, early recognition and accurate diagnosis arecrucial to limit morbidity and mortality.

In Nigeria, Diabetes insipidus has been reported in adults following burns andsurgery.[5]To the best of the knowledge of the authors, no of case CDI has been reported in children in Nigeria. We therefore report the first case of CDI in a toddler in our centre in order to share our experience and also to review available literature.

Case report

C.N was a two year eight month old female referred from Federal Medical Centre, Yenegoa, Bayelsa State to the Children's Emergency Room of the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt, Rivers State with complaints of excessive ingestion of water and urination of two months duration. Onset of symptoms was gradual with excessive ingestion of water increasing from about 500mililitre (ml) per day to 9- 10Litres (L) per day. She wakes up about 6-7 times at night to drink water and this usually disturbs sleep. There was also increase in both frequency of urination and volume of urine voided; from1- 2 times to 10 -15 times during the day and from nil to 5-7 times at night. There was no history of body swelling, polyphagia, fever, head trauma, chronic cough, weight loss, seizures, use of nephrotoxic drugs or surgery prior to onset of symptoms. She was initially treated in a private clinic for malaria but with persistence of symptoms, she was taken to the referral hospital. Random blood sugar (RBS) done was 6.4mmol/L; urinalysis showed a low specific gravity (S.G) of 1.005. She was subsequently referred to UPTH with a presumed diagnosis of Diabetes insipidus (DI). Pregnancy, birth, neonatal and developmental histories were essentially uneventful. She is the

second of three children (all females) in a monogamous family. Mother is a 26 year old nurse and father is a 38 year old business man with tertiary education. There was no history of similar symptoms in the parents, siblings or close relatives.

On examination, she was conscious, calm, a febrile, well hydrated with moist buccal mucosa with no loss of skin tugor. Her weight was 15kg (115% of expected); height was 96cm (108% of expected). Her radial pulse was regular, full volume with a rate of 110beats per minute; blood pressure was 80/50mmHg (which was normal). Examination of the systems were essentially normal. A bedside dipstick urinalysis showed a colourless urine with a pH 6 and a very low S.G of 1.000 without glycosuria or proteinuria. Random blood sugar was 5.4mmol/L (which was within normal range). An initial diagnosis of Diabetes insipidus was made.

Serum electrolytes, urea and creatinine done on admission showed Sodium of 139mmol/L (normal range: 128 - 142mmo/L); Potassium of 3.7mmol/L(normal range: 3.4 - 4.8mmol/L); Bicarbonate of 22mmol/L (normal range: 24 - 30mmol/L); Urea of 2.2mmol/L (normal range: 2.4 - 6mmol/L) and Creatinine of 40µmol/L (normal range: 60 - 120µmol/L). Serum Osmolality [calculated from the formula[6]: serum osmolality in mOsm/Kg = 2 × serum Sodium (mmo/L) + serum Glucose (mmol/L) + serum Urea (mmol/L)] was 286mOsm/kg. Serum calcium was 2.2mmol/L (normal range: 2.1 - 2.6mmol/L). Full blood count which was within normal limits showed a packed cell volume of 31%; white blood cell of 6.2×10^9; neutrophils of 44%; lymphocyte 56%; normal electrolyte sedimentation rate of 8mm/hour. Blood film was essentially normal. Urine microscopy and culture showed heavy growth of E.coli sensitive to nitrofurantoin and ceftazidine.

Abdominal ultrasonography was normal showed that both kidneys were normal in size, position and echogenicity with good corticomedulary differentiation. There were no renal cysts or calculi. Radiograph of the skull showed normal bones and sella turcica; there was no abnormal lucency or calcification. Assay for serum levels of AVP, Magnetic Resonance Imaging (MRI) and genetic studies were not done due to unavailability of such studies in our centre and environs.

A water deprivation test was done over six hours. She was weighed two hourly throughout the duration of the test. There was no change in the weight pre and post water deprivation at 15Kg. Total volume of urine voided was 2,030mls (11ml/kg/hour) and the urine S.G remained 1.000.Serum and urine samples for osmolality analysed at Pathcare laboratory showed that urine osmolality was 59 mOsm/Kg and serum osmolality was 286mOsm/Kg. Intravenous desmopressin 2µg was given after the water deprivation test. Total volume of urine voided 2hours later was 125ml (2.6mls/kg/hour); urine SG increased to 1.010. There was increase in the urine osmolality and serum osmolality to 158mOsm/kg and 321Osm/kg respectively. The diagnosis of CDI in the index patient

was made based on the symptoms of excessive water intake and urination, craving for water; persistent hyposthenuria, passage of large volume (11ml/Kg/hour) of urine despite lack of oral input during the water deprivation test, absence of urine concentration on water deprivation followed by an increase in urine and serum osmolalilty following the administration of desmopressin. The urinary tract infection was treated with oral nitrofurantoin 25mg three times a day for 10 days.

She was allowed free access to water and received desmopressin tablets (25mg twice a day initially then increased to 50mg twice a day due to poor response. There was reduction of urine volume to 2.5L during the day and nil at night noticed on the second day of commencement of desmopressin. Urine specific gravity also increased ranging from 1.010 - 1.016 throughout the duration of hospitalisation. She was discharged after three weeks of admission on oral desmopressin. She came for follow up once one week after discharge. On follow up visit, polyuria and polydipsia had reduced; urine frequency had reduced to 1 -2 times during the day and nil to once at night. Telephone conversations with the mother revealed that child is alive, still on desmopressin; polyuria and polydipsia had greatly subsided.

Table 1: Biochemical parameters before and after water deprivation test and desmopressin administration in the patient with Central diabetes insipidus

Parameter	Urine specific gravity	Urine osmolality (mOsmol/kg)	Plasma osmolality (mOsmol/kg)	Total volume of urine voided
Before water deprivation	1.000	-	286	10 - 20ml/kg/hr
After water deprivation	1.000	59	289	2030ml (17ml/kg/hr)
After IV desmopressin	1.010	158	321	125ml (4.2ml/kg/hr)

Discussion

CDI is a form of polyuric polydipsic disorder which occurs mainly due to lesions of the neurohypophysis or the hypothalamuc median eminence resulting in deficient synthesis and or release of AVP.[7]The clinical manifestation of CDI is variable, depending on the extent of neuronal destruction. Usually 80 to 90% of the magno- cellular neurones in the hypothalamus need to be damaged before symptoms of DI arise.[7]Polyuria and polydipsia which are the essential features[4] were present in the index patient. The onset of symptoms is usually abrupt or sudden in CDI due to head trauma or neurosurgical interventions and gradual in other forms of non-trauma conditions.[8]However, in some cases, CDI may be a chronic complication of head injury or subarachnoid haemorrhage.[9]In the index patient, the onset of symptoms was gradual and there was no history of

trauma or surgery. The age at presentation also varies depending on the underlying aetiology.[4,8] Severe neonatal forms are rarely described in children. In contrast, hereditary Nephrogenic DI manifests in early infancy, often before the age of 1 week.[4,8]The familial autosomal recessive formmay manifest at infancy while that due to developmental defects of midline brain structure may present early.[8,10]Symptoms in the index patient developed at the age of 2 years and 6 months. Maghnie at al[1]in Italy in a study of children with CDI reported that the mean age at presentation were 6.4 years, 7.5 years and 1.4 years for the idiopathic, secondary form due to intracranial tumor and the familial forms respectively.

The clinical manifestations of CDI are due to deficiency of AVP and disturbance in water metabolism. Excessive loss of water from the kidney (polyuria) will result in dehydration, hypernatraemia and a corresponding increase in serum osmolality.[4]However, in ambulatory patients with intact thirst mechanism and free access to water, hypernatraemia and dehydration do not occur.[11]This may explain the absence of dehydration, normal serum sodium levels and serum osmolality in the index patient.

The water deprivation test (Miller-Moses test) together with the intravenous administration of desmopressin are useful in the confirmation of the diagnosis of CDI and also to distinguish between Nephrogenic DI and Primary polydipsia.[4]In CDI, urine osmolality is usually less than 300 mOsm/kg after dehydrationand greater than 750 mOsm/kg following desmopressin administration.[12]In the index patient, the diagnosis of CDI was confirmed based on the absence of urine concentration on water deprivation followed by an increase urine and serum osmolalilty following the administration of desmopressin. Although, the urine osmolality was less than 750 mOsm/kg after desmopressin administration, there was more than a double-fold increase in urine osmolalilty from 59mOsm/kg to 158mOsm/kg. Similar finding has been reported in children by Wong et al[13] in Hong Kong where the urine osmolality was less than 750 mOsm/kg post desmopressin administrationin all ten children with CDI. A possible explanation to this is that in long standing polyuria there is partial washout of the medullary interstitial gradient and downward regulation of AVP release leading to defect in urinary concentration.[12]

The urinary concentration test is an indirect measure of AVP activity. The combination of the water deprivation test and direct AVP determination would allow the diagnosis of more than 95% of all cases of CDI correctly.[14] However, AVP assay has failed to be a diagnostic reference standard to date due to its methodological limitations of a very short half life of 10 -30 minutes, high pre analytical instability and high turnaround time in most laboratories.[15] More recently plasma copeptin levels have been studied as a surrogate marker of AVP in the differential diagnosis of DI.[16]Copeptin, the C-terminal part of the AVP precursor, co-secreted with AVP is much easier to measure. It was demonstrated that plasma copeptin is a valuable surrogate of AVP release in patients with the DI, exhibiting a promising diagnostic potential.[16]

MRI of the pituitary gland has emerged as another useful addition to the biochemical tests in the diagnosis of CDI. The physiological bright spot in the posterior pituitary o the sella turcica is persistent in patients with Primary polydipsia and is absent inCDI.[17]However, individual cases of CDI with persistent pituitary bright spot have been reported most likely due to an early stage of the disease.[18] Also, anage-related absence of the signal has been described in up to 20% of normal subjects.[19] Conversely in NDI, the bright spot is present in some patients and absent in others.[20] Consequently, the role of MRI as a diagnostic test in patients with DI remains to be clarified. It has been suggested that MRI is a more useful tool for ruling out than for ruling in a diagnosis of CDI.[21] A very similar conclusion also seems to apply to measurements of thepituitary stalk, whose enlargement beyond 2–3 mm has been considered to be pathological, but not necessarily specific for idiopathic CDI.[22]MRI was not done in the index patient due unavailability of the services in the hospital.

The therapeutic goals of treatment of CDI are primarily to reduce polyuria and decrease thirst so that the child is able to grow adequately and maintain a normal life style. Free access to water will facilitate maintenance of tonicity if the thirst mechanism is intact.[8] The index patient was allowed free access to water. Excess fluid intake in the long term may lead to hydronephrosis and hydroureters.[23] The index patient did not have clinical or radiologic evidence of hydronephrosis or hydroureters. Desmopressin (1-deamino-8-*D*-arginine vasopressin, dDAVP), an analogue of vasopressin, is the current drug of choice for long-term therapy of CDI.[4] It increases the cellular permeability of the collecting ducts resulting in an increase in water reabsorption and therefore minimises water excretion. The index patient responded well to oral desmopressin.

Conclusion

CDI would occur in Nigerian children and responds well to oral desmopressin. We recommend a high index of suspicion in children with polyuria and polydipsia as early recognition and accurate diagnosis is crucial to both safe and effective disease treatment.

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