Central Diabetes Insipidus Secondary to Posterior Pituitary Aplasia in a 7month Old Nigerian Infant

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Abstract

Central diabetes Insipidus (CDI) represents a rare disease entity in childhood. About 20 – 50% of all cases in children are idiopathic. Early recognition and diagnosis is crucial to successful management. This is the first report of CDI in an infant in Nigeria.

Case report: We report a case of central diabetes insipidus in a 7 month old female infant who presented at the University College Hospital, Ibadan with polydipsia, polyuria and weight loss with a urine specific gravity of 1.005 and normal blood sugar. There was a history of treatment of hypovolemic shock at the referral hospital but patient was moderately dehydrated at presentation at our hospital. The diagnosis was confirmed by a plasma osmolality of 307mOsmol/L, urine osmolality of 395mOsmol/L in the presence of dehydration and hypernatremia of 150mmol/l. A significant correction of polyuria was also demonstrated with intravenous administration of desmopressin. The radiographic evidence of an absent posterior pituitary bright spot on MRI was demonstrated in the patient.

Conclusion: Central diabetes Insipidus occurs in Nigerian children and responds well to desmopressin. We therefore recommend that this diagnosis must be considered in all patients presenting with a triad of polyuria, polydipsia and euglycemia.

Keywords: Central diabetes; Insipidus; Infant in Nigeria; Posterior pituitary Aplasia

Abbreviations: CDI: Central Diabetes Insipidus; NDI: Nephrogenic Diabetes Insipidus; AVP: Arginine Vasopressin Deficiency; UCH: University College Hospital, TSH: Thyroid Stimulating Hormone

Introduction

Diabetes insipidus is either caused by inadequate posterior pituitary arginine vasopressin production (central diabetes insipidus), renal vasopressin signaling defects (nephrogenic diabetes insipidus, NDI), increased AVP degradation during pregnancy or excessive water intake with AVP suppression seen in primary polydipsia [1]. Central diabetes Insipidus (CDI) is a rare, heterogeneous disorder of serum osmolality and water balance. Prevalence is as low as 1: 25,000 with no gender predisposition except in the X-linked genetic forms of the disease [2]. It is characterized by polyuria, polydipsia,
high plasma and low urine osmolality [3]. Large volumes of dilute urine are excreted due to arginine vasopressin deficiency (AVP), AVP resistance or excessive water intake which leads to secondary suppression of AVP production (primary polydipsia). CDI arises from agenesis, degeneration or damage to the vasopressin-secreting neurons in the supra-optic and paraventricular nuclei of the hypothalamus [2]. It may also be as a result of defective release or transport of this hormone.

CDI may be inherited or acquired. It has been found to be idiopathic in about 20 – 50% of cases. CDI due to inherited genetic defects are very rare and are responsible for less than 10% of cases [3]. They are mostly inherited as autosomal dominant and as X-linked recessive traits. Over 55 different mutations resulting in a defective prohormone and a deficiency of AVP have been identified [2]. Acquired causes may be due to CNS infections like meningitis and encephalitis; granulomatous lesions such as histiocytosis and sarcoidosis; traumatic brain injury or injury during neurosurgical procedures; brain tumors like germinoma or craniopharyngioma; and inflammatory/ autoimmune disorders like lymphocytic infundibuloneurohypophysitis [3,4]. Vasopressin is a nanopeptide hormone produced in the hypothalamus and it plays a vital role in the maintenance of plasma osmolality [3]. This is achieved by its action on the collecting tubules and ascending loop of Henle promoting reabsorption of water molecules via water channels. This results in the excretion of concentrated urine [5].

Deficiency of this hormone leads to loss of this vital function and passage of large volume of highly dilute urine, extreme thirst, hypernatremia and high serum osmolality [6]. Therefore, early recognition and prompt intervention are critical to preventing morbidity and mortality. In Nigeria, a case of CDI was reported by Okpere et al. [6], in which a 2 year and eight months old girl was managed as a case of CDI based on the clinical presentation of polyuria, polydipsia and abnormal osmolalities, following a water deprivation test. We report the first case report in an infant in Nigeria. This case report is intended to corroborate the earlier report and bring to our awareness that even though the disease is rare, it exist in our environment.

**Case Report**

JAW was a seven month old female infant referred from an out patient hospital to the children’s emergency room of the University College Hospital (UCH), Ibadan, Oyo state, Nigeria, with complaints of excessive water intake and weight loss of three months duration. Onset of symptoms was insidious, with excessive intake of water: an average of 10 times per day. She was also said to wake up to drink water about 6 times at night. There was associated irritability relieved by water intake. Child also started passing large volume of urine evidenced by frequent diaper change and each diaper is usually fully soaked and dripping urine. Weight loss was also noticed at this time with loose fitting of previously normal fitting clothings. There was associated dryness of buccal mucosa and skin with prominence of facial bones and ribs. No history of fever, vomiting, passage of loose stool, no body swelling, polyphagia, head trauma, chronic cough, seizure, use of nephrotoxic drug nor of herbal preparation. There was no similar illness in siblings, nor was there a family history of diabetes. She was initially taken to the source of referral where she was managed for hypovolemic shock, admitted for 11 days and given intravenous fluids. She was referred to UCH due to persistence of symptoms.

She was exclusively breastfed, currently on complementary feeds. Developmental milestones have been age appropriate and she is up to date with vaccination according to National programme for immunization schedule. No adverse pregnancy or perinatal event. Mother is 34 years old, sells non-alcoholic beverages. Father is a 37 year old architect. The child is the 3rd of 3 children in a monogamous setting. On arrival in UCH she was febrile with a temperature of 38°C not in respiratory distress but had features of moderate dehydration. Weight was 5.9kg (72% of expected weight for age) Length was 80centimetres (100% of expected length for age and sex). Child had hepatomegaly while packed cell volume was 40%. Urinary output was 10mls – 17 mls/kg/hr over the next few days. Full blood count done showed leukocytes (25,800) with predominant polymorphonuclear cells and thrombocytosis. Urine specific gravity ranged between 1.005 – 1.010, while urine osmolality was 395mosm. Electrolyte and urea showed Sodium of 150mmol/l, Potassium was 3.6mmol/l Chloride was 106, Bicarbonate was 12 and Urea was 6 while creatinine was 0.3. Blood culture was sterile. Plasma osmolality was 307.

She was managed with antibiotics and intravenous fluids. She continued to pass large volumes of urine and had several episodes of dehydration which were corrected. Water deprivation test was not carried out because child was unstable for that. She was therefore commenced on a trial of desmopressin at 10microgram / day then increased to 30 micrograms with dramatic resolution of the polyuria. She was discharged and readmitted via 2weeks after on account of polyuria and refusal of feeds and was managed for dehydration and infection.

Evaluation of her anterior pituitary hormone function revealed normal adrenal function with early morning
cortisol of 512nmol/l and evening cortisol of 540nmol/l. Thyroid function test however, revealed a slightly elevated thyroid stimulating hormone (TSH) of 3.98mI.u/l (reference range 0.27 - 3.75) and a free T₄ of 15.9pmol/l (reference range 7.2 - 16.4). She was commenced on levothyroxine 50micrograms  per day with normalization of values. Her growth hormone and IGF-1 assays could not be carried out because of exorbitant cost and the patient could not afford to pay. The child had series of MRI of the brain done, which consistently showed absence of the T1W hyper intense signal intensity (bright spot) of the posterior pituitary gland. Diagnosis of diabetes insipidus was made in this child and she was subsequently continued on oral desmopressin 50microgram daily and also 50microgram noxte of Levothyroxine. Patient has not been back to clinic in a year.

Discussion

CDI is a vasopressin deficiency disorder with polyuria and polydipsia being invariable presenting features. It occurs due to lesions of the hypothalamus or posterior pituitary manifesting as deficiency of synthesis or release of vasopressin hormone. The diagnosis of CDI in our patient was based on a history of polyuria and polydipsia, findings on physical examination, results of blood and urine investigations as well as imaging studies of the brain. About 90% of the AVP-producing neurons are damaged before clinical manifestations become apparent [3]. Clinical manifestations of CDI will vary with etiology but most especially with age of patient. The loss of excess of free water, excessive thirst, dehydration and hypernatremia manifests differently depending on their ability to replenish water [7]. The index patient presented with polyuria and polydipsia. In addition, our patient presented with severe dehydration and came in in shock. This is an uncommon feature in older children who can request for water in response to the sensation of thirst [3,7].

Infant's generally rely on caregivers to provide all their needs including water at the time of thirst. The only means of expressing thirst in this age group is with extreme irritability which is nonspecific for thirst [7]. They can also manifest with vomiting, recurrent episodes of fever without a cause, weight loss and seizures. These may not be recognized by the caregivers as being as a result of water loss. If recognized however, response of caregiver may not be accurate enough to maintain optimal hydration status. Therefore, it is not surprising that our patient was dehydrated at presentation.

The onset of CDI is abrupt in traumatic causes; accidental or iatrogenic during neurosurgical procedure. It is slowly evolving in non-traumatic causes. Onset of symptoms was insidious in our patient which is consistent with non-traumatic etiology [7,8]. A plasma osmolality of >300mosm/L, a urine osmolality of <300mosm/L, polyuria of > 4 – 5mLs kg/hr in the presence of hypernatremia is diagnostic of DI [2,8]. Adrenal insufficiency can mask the signs of partial CDI and may be more manifest only after glucocorticoid replacement [8]. Water deprivation test was unnecessary in our patient as the test is used when biochemical features are equivocal, it is not a routine test required to establish the diagnosis. A water deprivation test is not indicated for patients with polyuria and hypernatremia, but it is indicated in situations where patient presents with polyuria but has normal serum sodium levels. The presence of hypernatremia with dilute urine is confirmatory of DI. Hypernatremia is a maximum stimulus for vasopressin production making a water deprivation unnecessary [9].

Urine osmolality was markedly reduced- 395m0sm/L (normal range is 600-800m0sm/L) and serum osmolality was high- 307m0sm/L (normal range is 285-295m0sm/L). There was also hypernatremia. Therefore, biochemical features combined with the clinical presentation were adequate to establish diagnosis in our patient. More so, our patient was dehydrated at presentation which precludes water deprivation test. Copeptin, a surrogate biomarker for AVP release, is a promising tool for differential diagnosis of polyuria polydipsia syndrome in Pediatrics. Its assessment has been reported to be safer, easier and faster than performing a water deprivation test [10].

AVP assay was not done in our patient. AVP assay has failed to be a diagnostic reference standard due to its short half-life (10-30 mins) and high pre analytical instability, and the radioummunoassay analysis is complex, lasting more than 24hours, making it an unreliable marker for diagnosis [11-13]. In our patient, brain MRI shows absence of the bright spot of the posterior pituitary which is consistent with the diagnosis of CDI. CDI is usually characterized by the absence of the post pituitary bright spot in T1- weighted imaging, whereas the bright spot is thought to be preserved in NDI. However, this could be relatively unspecific because an absent bright spot is uncommonly also noted in some cases of NDI possibly due to depletion of intracellular AVP stores in the vasopresseronergic neurons. A bright spot should however always be visible in primary polydipsia [14].

Our patient had CDI and also had evidence of anterior pituitary hormone problems because she was also hypothyroid and was commenced on Levo-thyroxine. Her cortisol levels were however within normal range.
Anterior pituitary dysfunction in patients presenting with CDI has also been reported [4,15]. The most frequent manifestation being growth hormone deficiency, followed by hypothyroidism, hypogonadism and then less commonly adrenal insufficiency [2]. The ultimate goal of treatment of CDI is to reduce polyuria and thirst inorder to allow for adequate growth and ensure normal lifestyle [8]. Since the child is still very young, the need for caregiver to maintain unrestricted access to water was reiterated. Desmopressin, a synthetic analogue of vasopressin remains the drug of choice for long term management of CDI. The dosage for oral and intranasal desmopressin is 5-20microgram once or twice daily while that of parenteral is 0.1-1microgram. Our patient had parenteral desmopressin initially then later commenced oral form when she got better and has been on this ever since. Our patient’s response to this drug was dramatic with rapid resolution of symptoms.In the paediatric population, the younger the child, the more difficult to determine appropriate dose of desmopressin. Complications of over dosing include hyponatremia, which can manifest as headaches, nausea, vomiting, seizures, coma and ultimately death [16-18]. Thankfully we have not recorded any side effects so far since the commencement of the drug.

**Conclusion**

This case report is the second case of CDI in Nigerian children. Both demonstrated good response to oral desmopressin. A high index of suspicion in children who present with polyuria and polydipsia is essential as early recognition is critical to prevent mortality and for effective management.

**References**


