CASE REPORT

Profound Hypernatremia Due to Central Diabetes Insipidus

Abeer Vaqar, Asim Rafiq, Khalid Hussain Javaid, Rashida Parveen and Rabia Sadaf

ABSTRACT

Diabetes insipidus is a rare endocrine disorder in paediatric patients. Polyuria is a cardinal manifestation that is extremely difficult to recognize in diapered infants. Careful urine quantification is the key to diagnosis in appropriate clinical setting. We report a case of a 4 months old infant presenting with an acute life threatening event following an episode of vomiting and decreased oral intake. She had profound hypernatremia which persisted after stabilization. Polyuria unrecognized by the mother was revealed by 24-hour urine output measurement. A diagnosis of diabetes insipidus was made after appropriate laboratory investigations including serum and urine osmolality. The central nature of the disease was confirmed by neuroimaging which showed holoprosencephaly.

Key words: *Polyuria. Diabetes insipidus. Holoprosencephaly. Desmopressin. Hypernatremia.*

INTRODUCTION

Diabetes insipidus (DI) is characterized by polyuria due to decreased water reabsorption by the collecting tubule. It is caused by either decreased secretion of antidiuretic hormone (central DI) or resistance to its action at the renal level (nephrogenic DI). The degree of polyuria is primarily determined by the degree of ADH lack or resistance.[1] Age of onset varies from the first week of life to adulthood depending on the underlying etiology. Serum osmolality of > 300 mosm/L and urine osmolality of < 300 mosm/L in the presence of polyuria, polydipsia and hypernatremia sets the stage for diagnosis. Treatment includes liberal intake of nutritive fluids. Desmopressin for central DI and thiazides diuretics in nephrogenic DI are the primary pharmacologic options.

Polyuria being the earliest clinical clue to diagnosis requires precise quantification. We present a case of central DI in whom polyuria was not recognized by the mother and was only confirmed after careful urine collection.

CASE REPORT

A 4 months old girl was evaluated for profound hypernatremia. Her birth weight was 3.2 kg. Early feeding problems occurred due to a deviated nasal septum interfering with nasal breathing. She was slow to grow despite a daily intake of about 850 ml of properly diluted formula milk. The mother thought her baby's urine output was normal. At 3 months the infant suffered from an acute life threatening event. She collapsed during a febrile respiratory infection, following a period of reduced oral intake. She was severely dehydrated requiring fluid resuscitation. Investigations revealed a hypernatremic state (serum sodium 181 mmol/ L) with normal K^+, Cl^- and glucose levels. Complete blood picture, cerebrospinal fluid and blood/urine cultures were normal. Serum ammonia, serum organic acids and urine for metabolic screen were also normal. Arterial blood gas showed minimal alkalosis.

After stabilization her serum Na^+ was still high (170 mmol/L). She had microcephaly, a deviated nasal septum and hypotelorism (Figure 1). She was hypotonic and unable to hold her neck. Her visual acuity and hearing were normal. Her growth parameters including occiptofrontal circumference fell below the 5th percentiles. Her BP and systemic examination was normal.

Total urine output in 24 hours was 990 ml indicating significant polyuria (defined as urine volume ≥ 2 L/ m^2/ 24 hours) which her mother had failed to notice. Further investigations revealed a serum osmolality of 310 mosm/L and urinary osmolality of 174 mosm/L. The very low urinary osmolality in the presence of high serum osmolality accompanied by polyuria confirmed the diagnosis of diabetes insipidus. A vasopressin/ desmopressin stimulation test was not performed in this infant due to her small size. Instead, a trial of treatment with oral desmopressin 25 μg/day was started to help differentiate between nephrogenic and central DI.

After 7 days of therapy, her polyuria and serum sodium improved considerably, confirming the diagnosis of central diabetes insipidus.

Pre-treatment and post-treatment values are presented in Table I.

Magnetic resonance imaging (MRI) of the brain revealed an absent corpus callosum, holoprosencephaly and mild ventricular dilatation (Figure 2). Other tests of anterior pituitary function were normal with a 46 XX karyotype.

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Received August 28, 2010; accepted March 22, 2012.

With continued treatment her serum Na^+ normalized, weight gain improved and she achieved partial neck control. She continued to have developmental delay owing to her structural brain defects although the contribution of high serum osmolality to the brain damage was effectively removed following treatment with desmopressin.

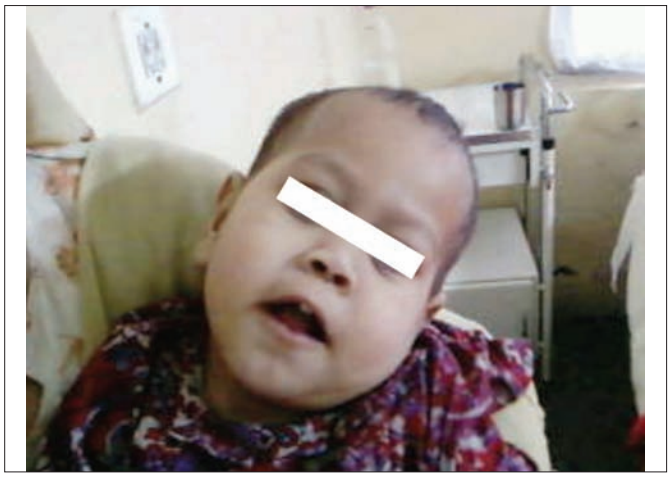

Figure 1: Photograph of the infant showing hypotelorism and microcephaly.

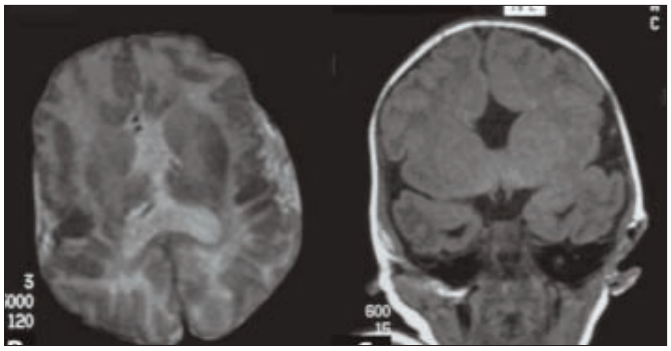

Figure 2: MRI scan showing partial holoprosencephaly. Axial T2-weighted image shows absence of septum pellucidum and hypoplastic frontal horns. Coronal T1-weighted image shows absence of septum pellucidum and corpus callosum.

Table I: Clinical and laboratory parameters (pre-treatment and post-treatment).

Clinical and laboratory parameters	Pre-treatment	Posttreatment (after seven days)
Urine output (24 hours)	990 ml	285 ml
Serum sodium	181 mmol/L	151 mmol/L
Serum potassium	4.2 mmol/L	3.4 mmol/L
Urine osmolality	174 mosm/L	330 mosm/ L
Serum osmolality	310 mosm/L	275 mosm/L

DISCUSSION

Central DI may either be congenital or acquired. While a rare vasopressin gene mutation may cause congenital central DI,[2] congenital malformations of the hypothalamus or pituitary such as septo-optic dysplasia and holoprosencephaly are more common causes. Acquired causes of central DI include neoplastic, inflammatory, infiltrative, traumatic, or autoimmune processes affecting the vasopressin neurons or fiber tracts. Primary brain tumours like craniopharyngiomas, germinomas and pinealomas are commonly associated with DI while Langerhans cell histiocytosis and lymphocytic hypophysitis are infiltrative disorders usually implicated.[3] CDI can be induced by trauma or neurosurgery (usually trans-sphenoidal) to the hypothalamus and posterior pituitary.[4] Autoimmune destruction of vasopressin producing cells account for 30-50% cases of idiopathic central DI.

Nephrogenic diabetes insipidus (NDI) results from resistance to the action of antidiuretic hormone (ADH) at its site of action in the collecting tubules. Genetically determined NDI involves mutations in the AVPR 2 gene or the Aquaporin gene.[5] Electrolyte disturbances, drugs (lithium, rifampin, amphotericin etc.) and chronic kidney disease are among the common causes of acquired NDI.[6]

Diabetes insipidus, a rare endocrine disorder, often presents insidiously in children especially infants. Polyuria may go unnoticed by caregivers particularly in diapered children as happened in this case. Infants may present with irritability, failure to thrive, and intermittent fever.[7] In severe and untreated cases altered sensorium ranging from sleepiness to coma may occur.[8] Visual field defects, dysmorphic features and signs of chronic kidney disease may point towards an acquired etiology.

The diagnosis of diabetes insipidus requires a high index of suspicion especially in infants. Urine volume measurement is mandatory to confirm or exclude pathological polyuria which in children is defined as > 2 $L/m^2/24$ hour. Once pathologic polyuria is established, urine specific gravity, serum and urine osmolality, serum electrolytes, BUN, creatinine, glucose, and Ca are determined. Based on serum and urine osmolality the diagnosis of DI is established if the serum osmolality is greater than 300 mosm/kg and the urine osmolality is less than 300 mosm/kg. DI is unlikely if the serum osmolality is less than 270 mosm/kg and the urine osmolality is greater than 600 mosm/kg indicating normal urinary concentrating ability. If the serum osmolality is less than 300 mosm/kg but greater than 270 mosm/kg a water deprivation test is required to establish the diagnosis of DI. The water deprivation test is also needed to differentiate central from nephrogenic diabetes insipidus.

Water restriction is not performed in very young infants. The preferred diagnostic test in this setting is the administration of desmopressin. Patients with the central DI usually achieve a urine osmolality of 300 mosmol/kg or higher after desmopressin administration, while patients with NDI continue to pass hyposmolar urine. In older children, the water deprivation test should be performed under close supervision. Monitoring includes vital signs, hydration status and body weight. Care

should be taken not to cause more than 5% dehydration. Urine osmolality is measured on each sample of urine voided during the test period. The plasma sodium and osmolality are measured at 4 hours and then every 2 hours. Desmopressin is given at the end of the test in children who continue to have impaired urinary concentration despite reaching a plasma osmolality of 295 mosmol/kg or plasma sodium of 150 mEq/L. Urine volume and osmolality are then measured to detect response.

Treatment of DI depends on the underlying pathology. The mainstay of therapy in central DI is desmopressin. The appropriate dose is determined empirically and ranges from 0.05 mg to 1.2 mg/day. Response is determined by the length of antidiuresis and serum sodium and serum osmolality. Children on vasopressin analogs, require a certain degree of water restriction to prevent water intoxication and hyponatremia. Nephrogenic DI is more difficult to treat. Intake of adequate calories for growth and prevention of severe dehydration are the principal goals of treatment. Foods with low sodium and high caloric content are required to optimize growth.[9] Thiazide diuretics are the most commonly employed agent for NDI. Indomethacin and amiloride may be used in combination with Thiazides to further reduce polyuria.[10] Some patients with NDI especially those with V2 receptor defects may benefit from high dose desmopressin.

This case report presenting a rare endocrine disorder highlights the significance of serum electrolyte measurement in children suffering from an apparent life threatening episode. It also emphasizes the importance of careful urine volume estimation in diapered infants suspected to have polyuria.

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ERRATUM

Due to an inadvertent mistake in the submitted Author's Certification Proforma, the affiliation/workplace of second author Mueenullah Khan of the article titled **"Rotational vs. Standard Smooth Laryngeal Mask Airway Insertion in Adults"** published in JCPSP 2012, Vol. 22 (5): 275-279 has been erroneously printed as Department of Anaesthesia, The Aga Khan University Hospital, Karachi.

Mueenullah Khan's affiliation/workplace may be corrected as Department of Anaesthesia, College of Medicine, King Saud University, Riyadh, KSA.

Editor