Case Report

Nephrogenic Diabetes Insipidus (NDI): a Rare Presentation in Early Infancy- A Case Report

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Abstract:
A 30 months old boy presented with polyuria and polydipsia since 6 months of age. There was no family history of similar illness. Investigations revealed serum hyperosmolarity and normal renal function. Diagnostic findings correlated with nephrogenic diabetis insipidus (NDI) as the patient was non-responsive to vasopressin in water deprivation test. MRI of brain was normal and ultrasonogram of kidney, ureter, and urinary bladder was normal and other investigations showed no abnormality.

Keywords: Nephrogenic diabetes insipidus; Infancy.

Introduction:
Diabetes insipidus (DI) is a rare disorder in infant and children. Incidence of DI is approximately 3 in 100,000 with higher incidence among male (60%)[1]. DI is two types: central and nephrogenic. Nephrogenic diabetes insipidus (NDI) is less common than central. NDI can be either congenital or acquired.[2,3] The majority of patients (87%) were diagnosed within the first 2.5 year of life.[4] NDI a disorder of resistance to action of antidiuretic hormone (ADH) is characterized by polyuria, polydipisa, low urine osmolality and high serum osmolality.[5] Majority of congenital NDI follow the X-linked recessive mode of inheritance. It is caused by an X-linked mutation affecting only male. Autosomal dominant and autosomal recessive forms of NDI equally affect both sex and only 10% of the families with congenital NDI.[6] Diagnosis of DI may be difficult in infants and children because of non-specific presenting features like; failure to thrive, irritability, vigorous sucks with vomiting, fever without apparent cause and difficulty in micturition. Sometimes family history of DI or mental retardation can be clue for diagnosis.[7,8] The defect in NDI has been suspected to be located at any of the steps from the binding of antidiuretic hormone to the renal tract.[9]

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Case report:
A 30 months old boy of non-consanguineous parents presented with excessive intake of water since 6 months of age. He used to pass excess volume of urine for the same duration. On enquiry, the boy had no fever or vomiting but constipation present. He was on usual family diet. His development of mile stone was age appropriate. No other family member had similar illness.

On examination, patient was alert and active with a pulse rate 98/min, respiratory rate 24 /min, temperature 98.4 F and blood pressure 80/60 mm of Hg (normal), with no dehydration. His weight was 10 kg (weight /height -2.6 SD), length 86 (height/age -1.7SD), fundoscopy normal. Renal systemic examination was normal.

Investigations revealed normal sodium (142 mEq/L) and potassium levels (4mEq/L). Renal functions were normal with serum creatinine 0.27 mg/dl and serum calcium 10.5 mg/dl, plasma osmolality 303 mOsm/L urine osmolality 1005 (low) and normal arterial blood gas analysis. Ultrasound for kidney, urinary bladder and MRI of brain were normal.

The striking finding was persistent polyuria; urine output in 24 hour was documented in hospital more than 3 litre/m2/day. Based on the findings of polyuria and high plasma osmolality with low urine osmolality, a diagnosis of DI was done and water deprivation test was performed which failed to increase urinary specific gravity above 1005. Nasal spray of vasopressin increased urine osmolality from 104 mOm/l to 105 mOsm/L with no change of plasma osmolality which was diagnostic of NDI.

The child was treated with free fluid in the form of water every day and hydrochlorthiazide (2.5mg/kg/day). After three months evaluation, weight gain was age appropriate, daily water intake reduced to 2-2.5 litre /24 hours and had serum osmolality of 305mOm/kg, urinary osmolality 90mOsm/kg and urinary specific gravity 1005. The child was followed up monthly for 3 months, then 3 monthly for one year.

Discussion:
NDI is caused by the insensibility of the collecting tubules of kidney to normally secreting antidiuretic hormone (ADH). In infancy, the common presentations of NDI are vomiting, failure to thrive, constipation, fever, dehydration and developmental delay5 but polyuria and polydipsia is very uncommon presentation. This patient presented with only polyuria and polydipsia.

The congenital X-linked form of NDI results from mutations in the vasopessin receptor, AVPR2. Rarely, the transmission may be inherited as autosomal recessive in which case mutations in the gene encoding for aquaporin 2(on chromosome 12q) have been identified.[10]
NDI occurs in people of wide age range.[5] This infant presented at the age of 6 month. In a study by Angenita F V

L 4, 87% cases were diagnosed within the first 2.5 years of age.

DI may occur at any sex. This patient was a male child. In a study by Angenita F V L2, 60% cases were found male. The child height was slightly below 50th percentile but not failure to thrive. Failure to thrive is one of the presentations in NDI.

Clinical diagnosis of NDI relies on demonstration of subnormal ability to concentrate the urine despite the presence of the antidiuretic hormone argenine vasopressin (AVP).[10]

The diagnosis is usually delayed till hypernatremia develops. This highlights the importance of high index of suspicion and early diagnosis of DI in infancy.[11] This child did not develop hypernatremia.

Management is usually the provision of free access to drinking water and it must be offered between regular feedings. Lowering of solute load to kidneys helps by decreasing free water loss. As long as an individual's thirst mechanism remains intact and the person is otherwise well, these measures prevent hypernatremic dehydration. Education of parents, teachers and a willingness to find creative solutions are helpful.[11,12]

Lowering of solute load to the kidneys helps by decreasing free water loss. This can be achieved by using hypocaloric formula or diluting the milk. Congenital NDI is often difficult to treat.[5]

Administration of hydrochlorthiazide 2 to 4 mg/kg/day when combined with sodium restriction can lead to a very significant reduction of urine volume. Amiloride (0.3mg/kg/day) has an additive effect. Combination of hydrochlorthiazide and amiloride has been shown to decrease urine output in this patient as much as 30-40%.[13] Indomethacin(3mg/kg/day),a prostaglandin synthesis inhibitor, increases proximal tubular sodium absorption and has been shown to have synergestic effect to thiazide diuretics in children with NDI.[5,14,15] its prolonged use is not recommended since it may reduce glomerular filtration rate and cause gastrointestinal side effect.[16]

Conclusion:

NDI is one of the rare disorders with wide age range. High index of suspicion may be help in diagnosis. Prenatal testing is available for risk for X-linked NDI. Prevention of recurrent dehydration and hypernatemia is to prevent mental retardation.

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