

Case Report

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Nephrogenic Diabetes Insipidus Secondary to Obstructive Uropathy – An Unusual Presentation- A Case Report

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Introduction

Diabetes insipidus is a clinical condition characterized by polyuria and polydipsia that results from either insufficient production or end organ resistance to antidiuretic hormone (ADH). Diabetes insipidus is of two types: central diabetes insipidus (CDI) and nephrogenic diabetes insipidus (NDI) [1]. Central diabetes insipidus results from destruction of the posterior pituitary

Diabetes insipidus is a clinical condition, characterized by polyuria and polydipsia, that results from either insufficient production or end organ resistance to antidiuretic hormone (ADH). Diabetes insipidus is of two types: central diabetes insipidus (CDI) and nephrogenic diabetes insipidus (NDI). Children with diabetes insipidus may present with polyuria, polydipsia, frequent dehydration, constipation, and failure to thrive. Acquired NDI may result from various drugs and conditions but NDI due to obstructive uropathy is very rare. There are very few case reports of NDI due to obstructive uropathy. We report a 2-year-old child who presented with diabetes insipidus as a consequence of obstructive uropathy.

Keywords: Nephrogenic diabetes insipidus; Obstructive Uropathy; Child.

Running Title: Nephrogenic DI Secondary to Obstructive Uropathy

gland by tumors or trauma resulting deficiency of vasopressin, and nephrogenic diabetes insipidus results from end-organ resistance to vasopressin [2].

ADH is a hormone that helps the kidney and body to preserve the correct amount of water. It is secreted from the posterior pituitary gland which is regulated by paraventricular and supraoptic

nuclei of the hypothalamus [2]. In healthy individuals, when the body fluids are depleted, ADH is released from the pituitary gland which prevents the excretion of fluids from the body in the form of urine. ADH acts on the kidneys to increase water permeability in the collecting duct and distal convoluted tubule. Specifically, ADH acts on transmembrane protein channels called aquaporins that open to allow water into the collecting duct. Once the permeability increases, the water is reabsorbed into the blood, reducing urine volume and increasing its concentration [3]. Diabetes insipidus is a rare disease. The incidence in the general population is estimated to be 3 cases per 100,000 (0.003%). The male-to-female ratio is 3:2 [4]. Its prevalence is 1: 25,000. Less than 10% of the cases of diabetes insipidus can be attributed to hereditary forms. In particular, X-linked NDI represents 90% of the cases of congenital NDI and occurs with a frequency of 4–8 per 1 million male live births; autosomal (both dominant and recessive) NDI accounts for approximately 10% of the remaining cases [5]. The frequency of CDI is currently unknown [5]. Both in central and nephrogenic diabetes insipidus, the children have polyuria, polydipsia, frequent dehydration, constipation, and failure to thrive [4].

Nephrogenic DI (NDI) may be genetically transmitted as an X-linked, autosomal recessive, or autosomal dominant disease, or may be acquired. Congenital X-linked NDI results from inactivating mutations of the vasopressin V2 receptor. Congenital autosomal recessive NDI results from defects in the aquaporin-2 gene. An autosomal dominant form of NDI is associated with processing mutations of the aquaporin-2 gene [6].

Acquired NDI can result from hypercalcemia or hypokalemia and is associated with some drugs such as lithium, demeclocycline, foscarnet, clozapine, amphotericin, methicillin, and rifampin. It can also be seen with obstructive uropathy, chronic kidney disease, polycystic kidney disease, medullary cystic disease, Sjögren syndrome, and sickle cell disease [6]. NDI due to obstructive uropathy, unilateral renal artery stenosis, or acute tubular necrosis is associated with poor water reabsorption in the renal collecting ducts, resulting in both increased production and poor concentration of urine [6]. It may be due to either a lack of adequate vasopressin production, or failure of collecting duct epithelium to recognize vasopressine [7,8].

In our country, obstructive uropathy patients with rare complications of NDI are yet to be reported to create awareness among the pediatricians. So, we are reporting here a child who presented with NDI as a complication of obstructive uropathy.

Case Report

A 2-year-old immunized boy, the only child of his non consanguineous parents, was admitted to the Pediatric Nephrology Department of Bangabandhu Sheikh Mujib Medical University (BSMMU) with the complaints of polyuria and polydipsia along with excessive water drinking at day and night since six months of age (Fig 1). He had a history of recurrent episodes of low grade intermittent fever. His growth was not age appropriate. On query, his mother gave a history of straining during micturition occasionally associated with crying and vomiting.

He had no history of perinatal asphyxia, respiratory distress, convulsion or taking any offending drugs. None of his family members suffered from such an illness. For this illness, they had consulted several specialist physicians. The child was finally referred to BSMMU for further evaluation and management.

On examination, he was ill looking, fretful, mildly pale, and febrile (temp: 101 °F). There was no sign of dehydration. Bed side urine albumin (BSUA) was nil. He was normotensive with a pulse rate of 110/min and a respiratory rate of 36 br/min. He was severely underweight and severely stunted (Weight = 8.3 kg (Z score -3.8), Height = 78cm (Z score -3.2), OFC = 46.5 cm on 5th centile). His 24 hour fluid intake and output was 2200 ml and 2500 ml (12ml/kg/hour), respectively. Systemic examination revealed no abnormality.

Laboratory investigations revealed a low specific gravity (1.000). There was no proteinuria on urine microscopic examination. Culture and sensitivity of urine revealed the growth of *E. coli* which was sensitive to amikacin, imipenem, and nitrofurantoin. Twenty four hour urine for protein was normal for his age range. Urine PH was 6.0. The hemoglobin level was 9.6 gm/dl. Serum iron and serum ferritin levels were normal. Serum Creatinine was 0.44 mg/dl. Estimated GFR was 79.77 ml/min/1.73m². Inorganic phosphate was 3.6 mg/dl. Serum Calcium (9.1 mg/dl) was normal. Serum Electrolytes were normal, too (Na-140 mmol/L, K-3.7 mmol/L, Cl-106 mmol/L, TCO2-30 mmol/L).

As there was evidence of low specific gravity of the urine, we performed some further

investigations such as serum and urine osmolality. Reports showed normal plasma osmolality (285 mosm/kg) but inappropriately low urine osmolality (29 mosm/kg). After giving intranasal desmopressin spray (DDAVP), no significant changes occurred. Serum and urine osmolality was then 295 mosm/kg and 35 mosm/kg respectively, suggestive of tubular defect causing NDI.

Ultrasonography (USG) of the kidney, ureter, and bladder (KUB) showed that the bipolar length of both kidneys was normal for his age range (Rt Kidney -6.4×3.6 cm, Lt Kidney -6.8×3.2 cm, corticomedullary differentiation was well maintained, pelvicalyceal system was mildly dilated in both kidneys, bladder was normal, post voidal residual (PVR) volume was 27 ml). Micturating cystourethrogram (MCUG) revealed grade five vesicoureteral reflux (VUR) on the left side with a large PVR and distended bladder. So, the patient was diagnosed with NDI with left sided grade four VUR (Fig. 2).

Treatment was started, including the restriction of salt along with liberal fluid intake. For correction of anemia, haematinics (iron, zinc, folic acid, vitamin B- Complex) were administered. For NDI, a combination of hydrochlorothiazide and amiloride was given at a dose of 3 mg/kg/day and 20mg/1.73m²/day in two divided doses, respectively. After seven days, a significant decrease was noted in polyuria and polydipsia. His urine output declined from 2.5 litre to 1.7 litre. Serum and urine osmolality also tended towards normal values. Then, the patient was discharged and advised to return for regular follow-ups.



Figure 1. Showing the patient of nephrogenic diabetes insipidus due to obstructive uropathy.



Figure 2. MCUG showing grade five reflux in left side with distended bladder.

Discussion

NDI secondary to chronic urinary tract obstruction is a rare event [7]. The exact cause is unknown but it is likely that increased collecting duct pressure damages the tubular epithelium, resulting in insensitivity to the action of arginine-vasopressin (AVP) [7]. It usually presents at early age with polyuria and polydipsia, or with signs of severe dehydration, fever, vomiting, and convulsion [7].

This reported patient had polyuria, polydipsia, and voiding dysfunction. A diagnosis of NDI was made via the DDAVP challenge test. The patient had obstructive uropathy due to posterior urethral valve and was operated two weeks earlier. The diagnosis of obstructive uropathy was confirmed by MCUG showing grade five vesicoureteral reflux (VUR) on the left side with a large PVR and distended bladder. We excluded other causes of NDI. This patient had normal calcium and potassium levels so NDI due to chronic hypercalcemia or hypokalemia was excluded. He had no history of taking any medications which could be responsible for NDI like lithium, demeclocycline, foscarnet, clozapine, amphotericin, methicillin, and rifampin [6].

There are very few case reports of NDI due to obstructive uropathy in children. In adult patients,

there are limited reports of such an acquired type of NDI. One report revealed a 77-year-old man developed polyuria and polydipsia, and was diagnosed with NDI due to bilateral hydronephrosis resulting from prostate cancer [7]. Another report revealed a 32-year-old man who developed NDI due to bilateral ureteral obstruction as a result of leiomyosarcoma [9]. Both cases were treated with hydrochlorothiazide and NSAIDs and improved.

Our patient was treated with a combination of hydrochlorothiazide and amiloride at a dose of 3 mg/kg/day and 20mg/1.73m²/day in two divided doses respectively. Hydrochlorothiazide increases sodium excretion, resulting in contraction of extracellular sodium content that leads to an increase in the proximal tubular reabsorption of sodium and water [10]. These two agents have different sites of action in the tubule. A combination of the two agents also reduces the risk of hypokalemia.

After seven days of treatment, we observed a significant decrease in polyuria and polydipsia, and serum and urine osmolality also tended towards normal levels. Then, the patient was discharged and advised to return for regular follow-ups.

Conclusion

Although NDI is a rare disease, its association with VUR is very rare. However, if a child with unilateral primary VUR presents with polyuria, polydipsia, and failure to thrive, diabetes insipidus needs to be excluded.

Conflict of Interest

None declared

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