Nephrogenic Diabetes Insipidus Associated with Bilateral Ureteral Obstruction

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Nephrogenic diabetes insipidus associated with ureteral obstruction is rare. We report a case of nephrogenic diabetes insipidus associated with ureteral obstruction caused by ileal leiomyosarcoma in a 32-year-old man. The treatment with trichlorothiazide and diclofenac sodium reduced urine output from 8 L/day to 4 L/day. Six months after nephrostomy, urine output decreased to 2.5 L/day without any drug administration. This case suggests that ureteral obstruction may cause an increase in urine output to 8 L/day and that surgical treatment for ureteral obstruction is effective in reducing urine output in nephrogenic diabetes insipidus patients with ureteral obstruction.

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Key words: polyuria, arginine-vasopressin, leiomyosarcoma, nephrostomy

Introduction

Nephrogenic diabetes insipidus results from a variety of causes including polyuria after a relief of urinary tract obstruction (1). Nephrogenic diabetes insipidus complicated with ureteral obstruction, however, is rare, and only 12 cases have been reported in the literature (2-11). We herein report a case of nephrogenic diabetes insipidus which occurred in bilateral ureteral obstruction due to ileal leiomyosarcoma, and subsided following the removal of obstruction.

Case Report

A 32-year-old man was admitted to our hospital with complaints of polyuria, nocturia and thirst on October 22, 1992. He had no family history of diabetes insipidus and had been healthy until he underwent radical surgery for ileal leiomyosarcoma in September 1991. At the time of the operation his renal function was within normal range. Recurrence of tumor in liver and intrapelvic lymph nodes was found 2 months after the operation. The tumor in the pelvic space gradually became enlarged. Polyuria, nocturia and thirst occurred in August 1992, when he received no drug treatment. Physical examination revealed the following: body height, 175 cm; body weight, 54 kg; temperature, 36.7°C; blood pressure, 156/110 mmHg; and heart rate 78 beats/min. A hard mass of 20 cm was palpable in the lower abdomen. Neurological examination showed bilateral paresthesia below the ankle joint. Laboratory findings disclosed the following values: serum sodium, 141 mEq/L; serum potassium, 4.0 mEq/L; serum chloride, 100 mEq/L; serum calcium, 4.5 mEq/L; serum phosphate, 4.0 mg/dl; serum creatinine, 26.2 mg/dl; creatinine clearance, 62 L/day; blood white cell count, 8,200/mm³; hemoglobin, 14.0 g/dl; and plasma osmolarity, 289 mOsm/kg H₂O. Daily urine output was 8 L/day. The urine was hyposthenuric (136 mOsm/kg H₂O) and negative for protein. Urinalysis revealed 1-3 white cells and 5-10 erythrocytes per high power field. Urinary excretion of beta 2-microglobulin and N-acetyl-beta-glucosaminidase were 206 µg/L and 2.0 U/L, respectively. Urine culture was negative.

Skull roentgenogram and computerized tomography of the pituitary region showed no abnormality. An intravenous pyelography and abdominal echography revealed bilateral hydronephrosis and hydroureter. Plasma arginine-vasopressin (AVP) level was elevated at 22 pg/ml. The urine osmolarity after the subcutaneous administration of 5 units of aqueous desmopressin was 126 mOsm/kg H₂O. Plasma level and urinary excretion of cyclic-adenosine monophosphate (cAMP) were 72.0 pmol/ml and 4.4 µmol/day, respectively. Nephrogenic cAMP was 1.25 nmol/dl glomerular filtration rate. Urinary excretions of 17-OHCS and 17-KS were within normal range. Thyroid and parathyroid function were within normal range.

He was diagnosed as having nephrogenic diabetes insipidus and was treated with trichlorothiazide. Urine output decreased...
to 5 L/day 1 week after the start of treatment. The addition of diclofenac sodium further reduced urine output to 4 L/day. An increase in the serum creatinine level to 3.2 mg/dl was found on November 10, 1992, and echographic examination revealed aggravation of bilateral hydronephrosis, especially in the left kidney. Radiological examination revealed complete obstruction of the left ureter. Following left nephrostomy on November 11, urine output increased transiently to 6 L/day, and decreased to 4 L/day 5 days after relief of the obstruction. With nephrostomy, the serum creatinine level gradually decreased and reached 1.2 mg/dl in January 1993. In December 1992, the administration of tri-chlorothiazide and diclofenac sodium was discontinued but urine output remained 3-4 L/day. Urine output eventually decreased to 2.5 L/day in April 1993, when the serum creatinine level was 1.1 mg/dl. Plasma AVP level was decreased to 3.8 pg/ml.

**Discussion**

In the present case, polyuria with hyposthenuria was associated with bilateral ureteral obstruction. No metastasis of leiomyosarcoma in the pituitary region was observed. The diagnosis of nephrogenic diabetes insipidus was made because the plasma AVP level was high and the administration of vasopressin failed to increase urine osmolarity. He received no medication and had no metabolic disorders when he noted polyuria.

Polyuria after the relief of urinary tract obstruction is well known (12). In this case, nephrogenic diabetes insipidus occurred in bilateral ureteral obstruction and subsided following the relief of obstruction. Six months following continuous nephrostomy, urine output decreased from 8 L/day to 2.5 L/day. Nephrogenic diabetes insipidus observed in the presence of ureteral obstruction has been reported in 12 cases in the literature (Table 1) (2–11). The causes of urinary tract obstruction in these reports are bladder neck obstruction (N=4), prostate hypertrophy (N=2), posterior urethral valve obstruction (N=2), vesicoureteral reflex (N=1), neurogenic bladder (N=1), prostate cancer (N=1) and invasion of recurrent rectal cancer (N=1). In all 9 cases, surgical relief of urinary tract obstruction was performed and it was followed by a decline in urine volume in 1 week to 3 years after the procedure. In contrast, in two cases without treatment of occlusion, no improvement in polyuria was observed. In one case, urine output was decreased by treatment with phenoxybenzamine hydrochloride and hydrochlorothiazide. In the present case, the combined treatment with hydrochlorothiazide and diclofenac sodium reduced urine output by about 50%. However, a more marked decrease in urine output was observed after the relief of urinary tract obstruction.

In this case, renal function was impaired. Renal failure is known to result in a defect in urine concentrating capacity, and thereby to cause polyuria. However, it is known that polyuria in chronic renal failure is less than 3–4 L/day (1). It is unlikely, therefore, that the polyuria of up to 8 L/day in the present case was caused by the impaired renal function.

Experimental studies demonstrate that ureteral obstruction induces an increase in intrarenal prostaglandin E2 (PGE2) production (13). PGE2 is well known to inhibit the antidiuretic action of ADH. The efficacy of prostaglandin synthesis inhibitor for the reduction of polyuria was reported in congenital and lithium-induced nephrogenic diabetes insipidus patients (14, 15). In the present case, diclofenac sodium reduced the urine output, suggesting that enhanced production of PGE2 in the post-obstructed kidney might result in the attenuation of the antidiuretic effect of AVP. Unfortunately, urinary PGE2 excretion in our case was not measured.

Interestingly, Feibusch et al (16) reported a 47-year-man with nephrogenic diabetes insipidus associated with recurrent leiomyosarcoma without obstructive uropathy. The onset of

<table>
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N.D.: not demonstrated, D: day, M: month, Y: year.

Reference

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polyuria was coincident with the appearance of liver metastasis of ileal leiomyosarcoma, and polyuria persisted with advancing liver metastasis. These findings suggest that mechanisms other than ureteral obstruction might cause polyuria in leiomyosarcoma. Urine output in our case, however, was reduced by surgical relief of obstructive uropathy without reduction in tumor mass, suggesting an important role of urinary tract obstruction.

In summary, we report a case of nephrogenic diabetes insipidus associated with bilateral ureteral obstruction caused by an invasion of leiomyosarcoma. Following continuous nephrostomy, urine volume decreased from 8 L/day to 2.5 L/day. This case suggests that ureteral obstruction may cause an increase in urine output to 8 L/day, and that relief of ureteral obstruction is important to reduce polyuria.

References