Dent’s disease in a child with nephrolithiasis

To the Editor

Nephrolithiasis one of the most common diseases of the childhood. Its prevalence in the normal population is 3-5% (1). In Turkey, the prevalence of nephrolithiasis has been reported to be 0.8% in school-age children and 17% below the age of 14 years (2,3).

In childhood, nephrolithiasis is associated with metabolic disorders including hypercalciuria, hyperoxaluria, hypocitraturia and cystinuria (4,5,6). More rare causes include diseases characterized with hereditary renal tubular dysfunction (7).

Dent’s disease is a proximal tubulus disease which is transmitted by x-linked recessive inheritance and which is characterized with low molecular weight (LMW) proteinuria, hypercalciuria, nephrocalcinosis and/or nephrolithiasis (8). It is manifested by polyuria, microscopic hematuria, asymptomatic proteinuria or renal stone in childhood. Patients may be diagnosed with Fanconi syndrome. Chronic renal failure (CRF) develops in male patients affected at the ages of 30-50 years. CRF may be prevented or delayed by early diagnosis (8,9,10).

In this article, a male patient who was found have nephrolithiasis on ultrasonography (USG) performed because of urinary tract infection and was diagnosed with Dent's disease was presented to emphasize the importance of considering Dent’s disease which is a rare disease in the differential diagnosis of nephrolithiasis.

A 1-year old male patient presented because stones were found on USG which was performed following urinary tract infection at the age of six months. In his history, it was learned that the mother and two daughters of the mother from the previous marriage had renal stones and the uncle was lost because of chronic renal failure 14 years ago. System findings were found to be normal on physical
Multiple calcifications with the largest one being 2 cm were found in both kidneys on repeated urinary tract USG (Picture 1).

Laboratory tests performed because of nephrolithiasis were as follows: BUN: 12 m/dL, creatinine (Cr): 0.54 mg/dL, Na: 138 meq/L, K: 4.2 meq/L, Ca: 10.2 mg/dL, P: 4.2 mg/dL, iPTH: 24.3 pg/mL, 24-hour urine Ca: 7.3 mg/kg/day. Thiazide treatment was started in the patient who was found to have hypercalciuria and he was started to be followed up. Blood gases and 25(OH)D3 levels were found to be normal. In the follow-up of the patient, microscopic hematuria was observed from time to time and this was related with hypercalciuria. In the sixth month, proteinuria (+++) was found in complete urinalysis. In detailed evaluation, protein/Cr was found to be 7.9 mg/mg, β2 mikroglobulin/Cr was found to be 5744 mg/g and it was evaluated to be LMW proteinuria. Urinary density was found to be 1015, TRP was found to be 41% and FENa was found to be 0.7%. Extensive aminoaciduria was found in urinary amino acid analysis. Hypercalciuria was reduced with thiazide treatment, but higher than normal levels were found in the follow-up from time to time. Serum Cr level was found to be 0.5-0.6 mg/dL. Glomerular filtration rate was found to be 105 ml/min/1.73 m² and serum cystatin C levels were found to be high.

Dent's disease was considered in the patient with the present findings. In genetic analysis, a pathological change described as p.Y342C (c.1025A>G) in CLCN5 gene was found and this was compatible with Dent's disease (Picture 2).

Nephrolithiasis is mostly associated with metabolic disorders in childhood (4,5). In Turkish children, metabolic disorders accompany nephrolithiasis in 87% of the patients (5). Hypercalciuria is observed in 34% of the children with nephrolithiasis (11). Hypercalciuria was also found in our patient and thiazide treatment was started.

In the follow-up, urinary β2 mikroglobulin levels were found to be high and a diagnosis of Dent's disease was made clinically because of hypercalciuria, nephrolithiasis, LMW proteinuria, amino aciduria and a positive familial history. Presence of at least one of the findings including nephrolithiasis, nephrocalcinosis, hypophosphatemia, renal failure, amino aciduria, rickets or positive family history associated with hypercalciuria and LMW proteinuria constitute the clinical diagnostic criteria of Dent's disease (12).

The diagnosis of Dent's disease usually cannot be made in the early period during which the clinical and laboratory findings are absent in patients with nephrolithiasis/nephrocalcinosis. Keeping the findings of Dent's disease in mind in the follow-up facilitates early diagnosis. Finding of LMW proteinuria in the follow-up of our patient facilitated making the diagnosis together with the present clinical findings.

Mutation is found in the chloride channel 5 (CLC-5) gene on Xp11.22 chromosome in 60% of the patients and in the OCRL1 gene in 15% of the patients (8,9,10). Different phenotypes are also found in which mutation cannot be detected in both genes (12). Carrier women can display some clinical findings because of inactivity of the X chromosome (13).

The clinical diagnosis is supported by detection of positive mutation in related genes. However, patients usually can not be diagnosed because of limitation of genetic diagnostic opportunities. In our patient, a pathological change which was defined as p.Y342C(c.1025A>G) in the
CLCN5 gene was found. This was reported to be one of the changes observed in Dent’s disease (12).

Although the glomerular filtration rate in our patient who was diagnosed with Dent’s disease was found to be normal, the fact that cystatin C levels were found to be high showed that renal dysfunction started.

Conclusively, Dent’s disease which is a rare disease should be considered in patients with a diagnosis of nephrolithiasis especially if proximal tubulus dysfunction accompanies nephrolithiasis. Early diagnosis is important in terms of delaying the progress to CRF with appropriate supportive treatment.

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References