

A case report: Paracellin-1 gene mutation and nephrocalcinosis

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Abstract

Nephrocalcinosis is quite common in society. Bilateral kidney stones, family history of stones should be examined with genetic testing. Here we present our patient who was previously diagnosed with a genetic mutation and had a bilateral kidney stones. Renal function tests and electrolytes should be evaluated carefully. It is very important to follow up closely.

Keywords: Paracellin-1 gene; Claudin-16 protein; Nephrocalcinosis; Consanguineous marriage; Hypomagnesemia.

Introduction

Nephrolithiasis are highly prevalent and affecting approximately 10% of adults worldwide, incidence of stone disease is increasing and nephrolithiasis is a major health problem worldwide. About 80% of urinary stones are composed of calcium and hypercalciuria is found in up to 40% of stone-formers [1]. A genetic control of hypercalciuria has been suspected for a long time. Approximately half of the patients with idiopathic hypercalciuria have a family history of nephrolithiasis, and stone disease is more common seen a family member [1]. Claudin-16 is a renal tight junction protein encoded by the Claudin-16 gene [2]. As we know, it is a rare autosomal recessive disease. Claudin-16 gene plays a role in the absorption of magnesium and calcium in the thick ascending limb of the loop of Henle [2]. It is characterized by hypercalciuria and hypomagnesemia. We report an extremely rare case of Claudin-16 gen mutation patient kidney stones.

Case Report

A 38-year-old female patient presented with intermittent bilateral flank pain. She was a first child as a result of consanguineous marriage. She has a hyperparathyroidism and ventricular septum defect. She

is followed by nephrology department and cardiology department due to ventral septal defect. She has a previously undergone operation four time left-side percutaneous nephrolithotomy operations, bilateral ureterorenoscopy also bilateral retrograde intrarenal surgery operations. In the Dimercapto Succinic Acid (DMSA) taken on the patient, it was seen that the left kidney was functioning at 39% and the right kidney was functioning at 61%. The patient's magnesium values were below the normal limit value, and the creatine value was 1.2 mg/dL on average (Figure 2). Other laboratory investigations serum creatinine 1,23 mg/dL, serum urea 31 mg/dL, serum uric acid 6,1 mg/dL, sodium 143 mmol/L, potassium 4,5 mmol/L, calcium 9,2 mg/dL, phosphorus 1,3 mg/dL (below normal range). The results of 24-h urine tests were as follows: magnesium 121,31 mg/day, calcium 263,57 mg/day, oxalate 115,06 mg/day (normal range 4-31), citrate 162,68 mg/day (normal range 320-1260), uric acid 365,8 mg/day. The patient had previously used Potassium Citrate and Thiazide group drugs. Computer tomography taken at her last admission showed multiple stones filling the bilateral kidneys (Figure 1).

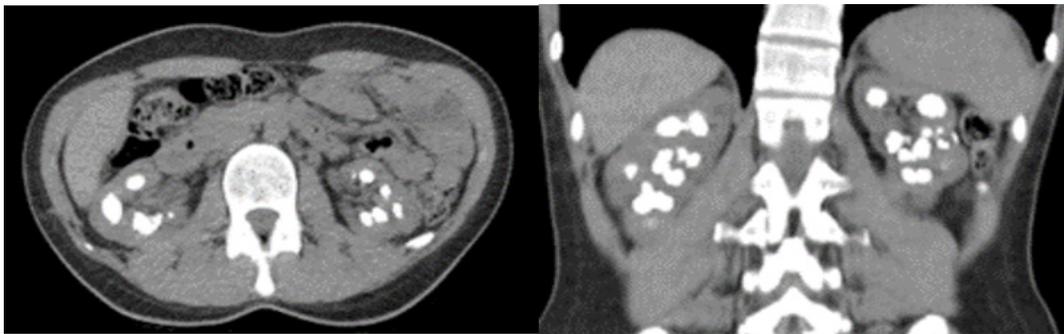
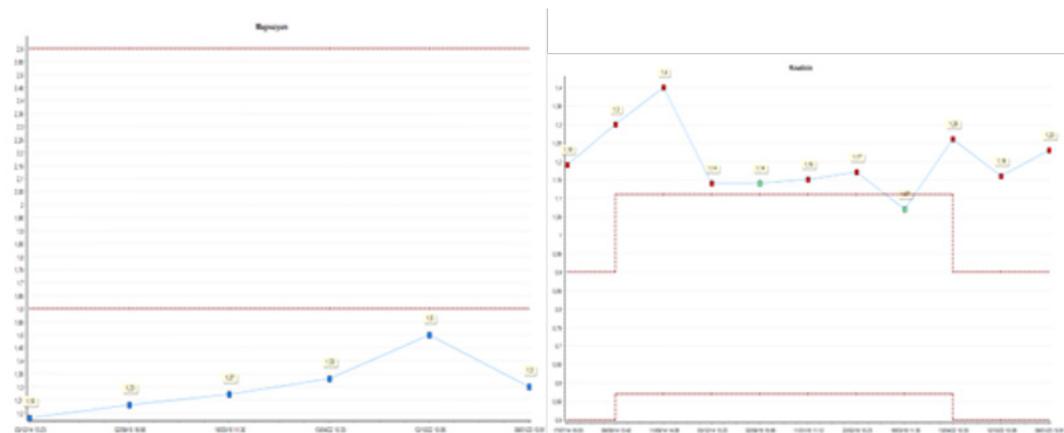


Figure 1: CT show a bilateral kidney stones.



Therefore, discuss about relationship between estrogen level and nephrocalcinosis [5]. The most common finding nephrocalcinosis due to calcium deposit and kidney cysts [6]. Also we can see ocular defects especially Claudin-19 gene mutation [6]. A rare related to Familial Primary Hypomagnesemia with Hypercalciuria and Nephrocalcinosis (FHHNC) mutation between chondrocalcinosis [6]. Here we report a female patient with bilateral nephrocalcinosis, hypomagnesemia, hypophosphatemia and hypocitraturia. The patient was diagnosed with paracellin gene mutation 30 years ago. Nephrocalcinosis and recurrent infection play an important role in a chronic kidney disease due to paracellin-1 gene mutation. Also, paracellin-1 gene mutation affects renal function is unclear. Konrad et al. had a related phenotype-genotype correlation between renal impairment progression in FHHNC patients [3]. This study suggested that the presence of at least one partial-function Claudin-16 gene allele is sufficient to predict the clinical phenotype. It is also seen in distal renal tubular acidosis in FHHNC patients. Weber S et al. found that 17 of 20 patients with Claudin-16 gene mutation had distal renal tubular acidosis [3]. The reason for this is due to distal acidification defect. Although it is controversial in the literature but most of patients especially in the 2nd or 3rd decade of life Familial Primary Hypomagnesemia with Hypercalciuria and Nephrocalcinosis (FHHNC) progresses to end-stage renal failure [7]. Blanchard et al. has been shown that consanguineous marriage is quite common in this mutation group. This causes family members tend to be hypercalciuria and hypomagnesemia, as in our patient [8]. There is no specific method for the treatment of this disease. Paracellin-1 gene mutation patients who have a nephrocalcinosis can be treated by thiazide diuretics (reduce urinary calcium excretion), potassium citrate, Magnesium supplement. In addition salt restriction and high fluid intake may be helpful. The only treatment of end-stage renal disease is renal replacement therapy [9].

Conclusion

Finally, metabolic evaluation should be performed in high-risk patients with a family history of stones, bilateral kidney stones, and frequently recurring stones. Supportive therapy including magnesium salts, thiazides, and citrate, as well as abundant fluid intake and dietary restrictions, are widely used to delay the progression of renal failure. Kidney transplantation remains the only curative option for kidney failure in these patients. In this group of patients who have a Paracellin - 1 gene mutation, calcium/creatinine, magnesium/creatinine ratios should be followed and they should be followed frequently and approached more carefully in order to prevent rapid development of renal failure. We recommend a genetic evaluation in young patients who have a nephrocalcinosis and a consanguineous marriage.

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