

Nephrocalcinosis in adolescent girl with medullary sponge kidney and mild hemihypertrophy

A case report

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Abstract

Rationale: Medullary sponge kidney (MSK) is a rare congenital abnormality characterized by cystic dilatation of the medullary collecting tubules. The disorder is likely to be complicated by nephrocalcinosis, urolithiasis, tubular dysfunctions, and urinary tract infections. In addition, it may be rarely associated with extrarenal anomalies.

Patient concern: We present a case of 17-year old girl who was referred for metabolic evaluation of bilateral nephrocalcinosis. Physical examination showed signs of mild, left-sided hemihypertrophy involving the lower limb, buttock, trunk, face, and tongue. The imaging studies of kidneys including intravenous urography and contrast computed tomography showed numerous medullary calcification and a typical picture of MSK—“paint brush”/“bouquet of flowers” appearance of the dilated tubules within the renal medulla. Laboratory evaluation revealed sterile pyuria, hypercalciuria, and hypocitraturia.

Intervention: The patient was subsequently treated with potassium citrate, hydrochlorothiazide, low sodium and low oxalate diet accompanied by high fluid intake. Outcomes: After a 1-year therapy the normalization of calciuria and citraturia occurred and no progression of nephrocalcinosis was observed.

Lessons: We conclude that MSK should always be considered as a cause of nephrocalcinosis. Since the final diagnosis requires specific imaging techniques, the concomitant extrarenal abnormalities such as hemihypertrophy may facilitate diagnostic decisions.

Abbreviations: CT = computed tomography, eGFR = estimated glomerular filtration rate, GDNF = glial cell-derived neurotrophic factor, HC = hypercalciuria, IVP = intravenous pyelography, MRI = magnetic resonance imaging, MSK = medullary sponge kidney, NC = nephrocalcinosis, P-CS = pyelocalyceal system, UL = urolithiasis, uroCT = computed tomography with contrast, US = renal ultrasound, UTI = urinary tract infections.

Keywords: hemihypertrophy, medullary sponge kidney, nephrocalcinosis

1. Introduction

Nephrocalcinosis (NC) is a rare condition characterized by the accumulation of calcium oxalate or calcium phosphate crystals within renal interstitium. Although NC and urolithiasis (UL) may have a similar etiology and both may coexist, the incidence of NC is much lower than that of UL. In addition, NC may be a sign of some rare metabolic disorders.^[1] Clinically NC is diagnosed by

renal ultrasound (US) and classified into medullary, cortically, or diffuse one.^[2] In a minority of patients the pathomechanism of NC, similarly to UL, may be influenced by anatomical alternations. In this study, we present a 17-year old girl with NC caused by medullary sponge kidney (MSK) associated with hemihypertrophy (HHT).

2. Case report

A 17-year old girl was referred to our department for metabolic evaluation of NC which was incidentally detected during outpatient US performed due to nonspecific abdominal pain. Medical history revealed one episode of acute pyelonephritis at the age of 6 years and probably renal colic at the age of 14 years when stone 3 mm in diameter within the left pyelocalyceal system was found. Since infancy, a length leg discrepancy was observed. Family history was uneventful and healthy Caucasian parents were nonconsanguineous.

On admission, thorough physical examination revealed signs of mild, left-sided HHT involving the lower limb, buttock, trunk, face, and tongue. (Figs. 1–4, Table 1)

The US examination showed normal sized kidneys with bilateral, irregularly hyperechoic pyramids with numerous calcifications 3 to 6 mm in diameter (Fig. 5). In addition, nonspecific lesion within the right-adrenal gland was found. Due to the coexistence of HHT, MSK was suspected. It was subsequently confirmed by intravenous urography (IVU) and

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Informed consent was obtained from the patients for the publication of this study (Supplemental Digital Content 1).

The authors have no conflicts of interest to disclose.

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Figure 1. Mild, left-sided facial HHT in presented patient. HHT = hemihypertrophy.



Figure 2. Mild, left-sided tongue HHT in presented patient. HHT = hemihypertrophy.



Figure 3. Mild HHT of the left leg and buttock in presented patient. HHT = hemihypertrophy.



Figure 4. Mild HHT of the left foot in presented patient. HHT = hemihypertrophy.

Table 1

Selected physical parameters in presented patient.

| | Right side, cm | Left side, cm |
|---------------------|----------------|---------------|
| Thigh circumference | 56.8 | 59,2 |
| Crus circumference | 36 | 38 |
| Foot length | 22.5 | 24,5 |

contrast computed tomography (uroCT) which was additionally performed due to unclear adrenal lesion. They revealed accumulation of contrast medium in dilated tubules within the renal medulla (“paint brush”/“bouquet of flowers” appearance) and NC which are pathognomonic for MSK. NC was more pronounced in the right kidney (Figs. 6–8). uroCT scan showed benign calcifications within otherwise normal right adrenal gland.

Metabolic evaluation disclosed normal renal function (eGFR 147 mL/min/1.73 m²; normal >90 mL/min/1.73 m²), sterile pyuria, hypercalciuria (HC) (4.3 mg/kg/24 h; normal <4.0 mg/kg/24 h), slightly decreased urinary citrate excretion (1.29 mmol/L, 73 m²/24 h normal >1,3 mmol/L, 73 m²/24 h) and low serum 25-OH D₃ level (10.8 ng/mL; normal 30.0–80.0 ng/mL). Other laboratory parameters, including urinary excretions of oxalate, uric acid and phosphate, as well as serum levels of

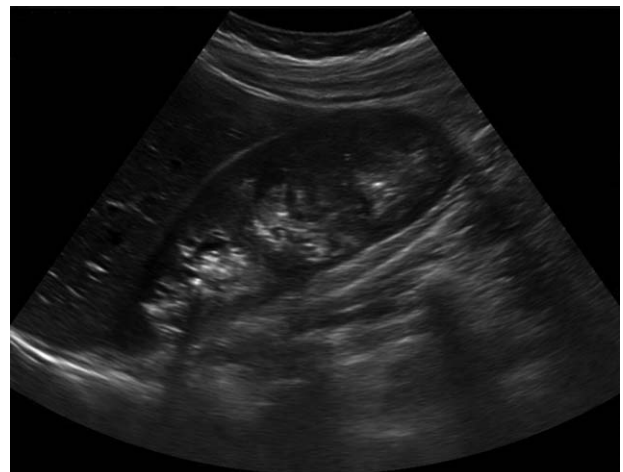


Figure 5. Ultrasound of the right kidney with irregularly hyperechoic pyramids (NC) and stones in presented patient. NC = nephrocalcinosis.



Figure 6. Intravenous pyelogram showing “paint brush”/“bouquet of flowers” appearance of the dilated tubules within the renal medulla (red arrows) in presented patient.

sodium, potassium, calcium, phosphate, PTH, and bicarbonate were within normal ranges.

Over the succeeding year, the patient was treated with potassium citrate and hydrochlorothiazide accompanied by high fluid intake and dietary restriction of sodium and oxalate. The therapy resulted in the normalization of calciuria and citraturia but sterile pyuria did not resolve. The follow-up US examinations showed no detectable progression of NC. One episode of acute

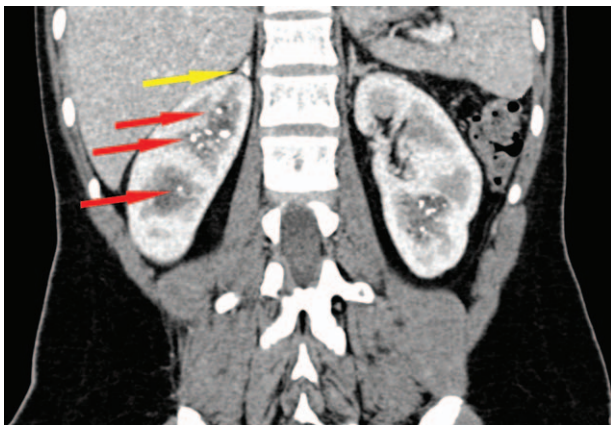


Figure 7. Contrast CT scan with bilateral calcifications within the renal pyramids (red arrows) and in the right adrenal gland (yellow arrow) in presented patient.

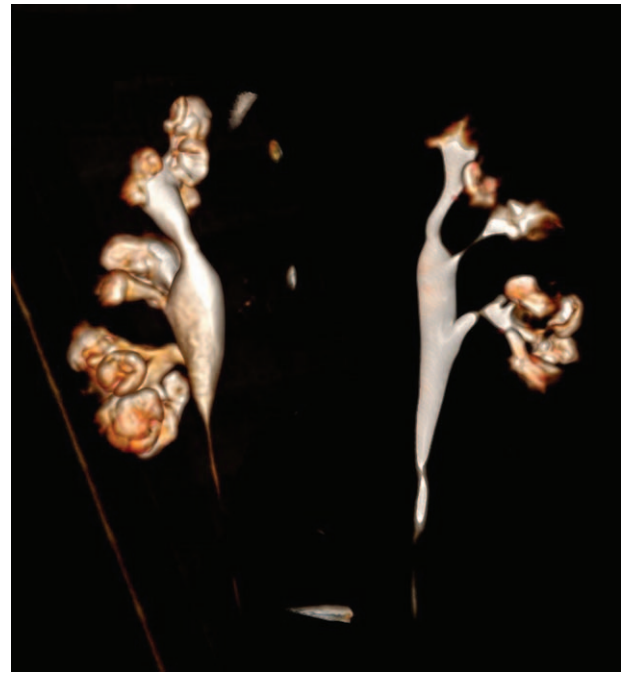


Figure 8. 3D reconstruction of the pyelocalyceal systems in contrast CT imaging showing cystic bilateral dilated tubules of renal medulla in presented patient.

urinary tract infection (UTI) was noted. At the age of 18 years, she was transferred to the adult care.

3. Discussion

The medullary sponge kidney also known as Lenarduzzi–Cacchi-Ricci disease is a rare congenital malformation characterized by cystic dilatation of the medullary collecting tubules. They are usually from 1 to 7.5 mm in diameter.^[3] The nephropathy may be associated with NC, UL, renal tubular dysfunctions, UTI, and reduced bone mineral content.^[4] MSK was reported to coexist with uncommon disorders such as HHT, Beckwith–Wiedemann syndrome, Ehlers–Danlos syndrome, Marfan syndrome or may occur as an isolated form.^[4,5] The pathogenesis of MSK is still not fully understood, but in some patients autosomal dominant inheritance is suggested and alternations in glial cell-derived neurotrophic factor (GDNF) are probably involved.^[6] It was found that 12% of patients with MSK had a rare variation in *GDNF* gene.^[4,7] The exact prevalence of MSK is unknown but it is estimated to be approximately five cases per 10,000–100,000.^[3,8] In 7% of patients, both kidneys are affected. The majority of individuals with MSK are asymptomatic but 12% to 20% of them are presented with renal colic due to UL.^[4] MSK is also a risk factor for upper UTI.^[4] Therefore, diagnosis of MSK is usually made during evaluation of these conditions but it may be also discovered incidentally. Most commonly, MSK is recognized in early adulthood.^[9,10]

The vast majority of MSK patients develop medullary NC which may be noticeable on US as renal pyramid hyper-echogenicity of different intensity. Due to the small size of calcium salt deposits, they are usually not accompanied by acoustic shadows.^[9] In patients with suspected MSK, further imaging techniques are required hence the US signs are not specific of the condition. The gold standard for diagnosis of MSK remains IVU showing accumulation of contrast medium within

dilated collecting ducts. They are noticeable as linear papillary densities or even as forms called “paint brush”/“bouquets of flowers” which are the hallmark of MSK.^[4,11] If IVU is unavailable it may be replaced by uroCT. Magnetic resonance imaging is not helpful in diagnosis of MSK.^[11]

The pathomechanism of NC and UL in MSK comprises urinary retention within dilated collecting ducts, HC and hypocitraturia.^[4,12] In some patients, increased urinary calcium excretion may lead to reduction in bone mineral content as a consequence of the negative calcium balance.^[7] This may be aggravated by secondary hyperparathyroidism.^[13]

The main goal of treatment of MSK is prevention of recurrent UL and inhibition of progression of NC. In all patients, oral potassium citrate supplementation and high fluid intake are indicated.^[11,14] It is believed that alkali citrates reduce the risk for stone formation and increase bone mineral content in patients with MSK.^[14] In some affected individuals, therapy with thiazides may decrease urinary calcium excretion.^[4] In addition, low sodium and low protein diet may be beneficial. A high intake of fruits and vegetables is also advisable.^[2] In patients with MSK, most kidney stones are small and may be passed spontaneously but in acute ureteral obstruction minimal invasive urological procedures may be necessary.

The coexistence of MSK and HHT was first described by Steyn and Logie in 1964.^[15] Only a few such cases were reported so far.^[16] It is estimated that MSK may occur in approximately 5% to 10% of patients with HHT.^[17] To date, the exact pathomechanism of this association remains unknown.^[17,18]

4. Conclusions

MSK should always be considered as a cause of NC. Since the final diagnosis requires specific imaging techniques, the concomitant extrarenal abnormalities such as HHT may facilitate diagnostic decisions.

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