Progressive Bilateral Childhood Urolithiasis of Rare Etiology: Ultrasound Images and Evidence-Based Therapeutic Recommendations

Al-Mosawi AJ1,2*

1Department of Pediatrics and Pediatric Psychiatry, Children Teaching Hospital of Baghdad Medical City, Iraq
2Head, Iraq Headquarter of Copernicus Scientists International Panel, Iraq

1. Abstract

Background: Multiple, recurrent and bilateral renal stones causing progressive bilateral urolithiasis is rare during childhood and metabolic disorder such as cystinuria and oxalosis are commonly. The aim of this paper is to report the very rare presentation of hypercalciuria and hypercalciuria with progressive bilateral renal stone disease, with stones predominantly composed of ammonium and phosphate suggesting infective etiology.

Patients and methods: A boy with progressive bilateral renal stone disease since early infancy and had been treated by several urologist during the previous three years was studied. He was first referred at the age of five years requesting the opinion about the use of medical therapies and therefore an evidence-based recommendation was made.

Results: The boy was initially diagnosed as having bilateral urolithiasis at about the age of two years and during the previous three years with three surgical operations and two lithotripsy sessions. Stone were predominantly composed of ammonium (+++++) and phosphate (++++) but they also contained calcium (+++) and uric acid (+). There was evidence of urinary infections with Klebsiella and Enterobacter species suggesting an infective etiology of the stone disease. On referral, Sodium nitroprusside test for cystine was also negative. 24-hour urine examination (volume 1600 ml): Calcium 264 mg/24 hr (more than 12 mg/kg/24hr) and oxalate 0.17 g/24 hr (Normal: 0.01-0.04 g/24).

Conclusion: Urologists should make an early consultation with a pediatrician expert in renal disorders to provide the necessary medical therapies. Bilateral progressive renal stone disease is rarely caused by infective etiologies alone and the presence of recurrent urinary infections should not lead to ignoring the possibility of metabolic abnormalities.

2. Keywords: Progressive bilateral renal stone disease; Ammonium-phosphate stones; Hypercalciuria; Hyperoxaluria

3. Introduction

Multiple, recurrent and bilateral renal stones causing progressive bilateral urolithiasis is rare during childhood and metabolic disorder such as cystinuria and oxalosis are commonly. Treatments for childhood urolithiasis are ideally preventive and dissolution with medical therapies can be helpful when used early during the course of the disease. Therefore, treatment with open surgery is reported in childhood lithiasis. Treatment with lithotripsy may require several

*Corresponding author: Al-Mosawi AJ, Department of Pediatrics and Pediatric Psychiatry, Children Teaching Hospital of Baghdad Medical City, Iraq, E-mail: almosawiAJ@yahoo.com
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sessions and urethral stent may be required and the shock waves used during lithotripsy have the potential renal damage. Treatments of the underlying associated etiologies such as metabolic disorders and urinary tract infections are crucial [1-7]. The aim of this paper is to report the very rare presentation of hypercalciuria and hypercalciuria with progressive bilateral renal stone disease, with stones predominantly composed of ammonium and phosphate suggesting infective etiology.

4. Patients and Methods
A boy with bilateral renal stone disease since early infancy and had been treated by several urologist during the previous three years was studied. He was first referred at the age of five years requesting the opinion about the use of medical therapies and therefore an evidence-based recommendation was made.

5. Results
The boy was initially presented with passage of turbid and dusty urine and was diagnosed as having bilateral urolithiasis at about the age of two years. At the age of two and half years, a stone in his right kidney was removed surgically and stone chemical analysis showed that the main compositions was phosphate without carbonate, uric acid and oxalate. At the age of four, ultrasound study (Figure 1) showed multiple stones at the left kidney and a 6 mm stone in the upper pole of the right kidney with hydronephrosis of the lower pole calyx. Urinalysis showed turbid yellow urine having acidic reaction, microscopic hematuria (10 RBCs/HPF) and pyuria (20 pus cells/HPF). Urinalysis suggested a urinary tract infection, but the results of a urine culture was not recorded.

Three months later, Urinalysis showed smoky turbid urine, hematuria (30 RBCs/HPF) and pyuria (8-10 pus cells/HPF). Urine culture showed growth of klebsiella sensitive only to ceftazidime Laboratory tests was also performed and showed normal renal function tests, normal serum calcium, uric acid and serum potassium. A large number of irregular stones were removed from the left kidney.

Figure 1: At the age of four, ultrasound study showed multiple stones at the left kidney and a 6 mm stone in the upper pole of the right kidney with hydronephrosis of the lower pole calyx. Their diameters ranged from 3 to 10 mm and had chalky color. Stone chemical analysis showed that the stones were mainly composed of ammonium (++++) and phosphate (++++), but they also contained calcium (+++) and uric acid (+). Two weeks after the second operation, ultrasound study (Figure 2) showed three large stones in the left kidney, 7,15,17 mm in diameter respectively and two stones in the right kidney with bilateral moderate hydronephrosis. The left kidney was 9 cm x 3 cm in diameter, while the right kidney was 8 cm x 3.5 cm in diameter.

Treatment with two lithotripsy sessions moved two stones to the bladder and a third surgery was performed about three months before referral to remove the two bladder stones. Urine culture before the third operation showed Enterobacter species sensitive only to ceftazidime and ceftriazone.

On referral, Sodium nitroprusside test for cystine was negative and paper chromatography for cystine was
also negative. 24-hour urine examination (volume 1600 ml): Calcium 264 mg/24 hr (more than 12 mg/kg/24 hr) and oxalate 0.17 g/24 hr (Normal: 0.01-0.04 g /24).

Figure 2: Two weeks after the second operation, ultrasound study showed three large stones in the left kidney, 7, 15, 17 mm in diameter respectively and two stones in the right kidney with bilateral moderate hydronephrosis.

The evidence based therapeutic recommendations for the treatment of this child included:
1. Prevention of urinary infections by monthly urine culture with early appropriate treatment based on the antibiotic sensitivity tests.
2. Aggressive triple therapy with aim of preventing renal damaged which was considered to be the logic ultimate outcome as suggested by the serious nature of the condition. Treatment consists of oral hypocalciuric diuretic (hydrochlothiazide and amiloride HCl) as half tablet of Moduretic (Merck & Co.; hydrochlotiazide 25 mg and amiloride 2.5 mg) daily, oral pyridoxine 100 mg daily to reduce hyperoxaluria and an essential oil terpene capsule (two capsule twice daily) [7].

6. Discussion
The occurrence of progressive bilateral renal stone disease, with stones predominantly composed of ammonium and phosphate suggesting infective etiology, has not been previously reported during childhood [2,5-7]

Zafar et al. (2018) from Karachi, Pakistan studied 976 young children up to the age of two years with 1038 urinary stones (1992 and 2016). 70% of the children were malnourished, 13% had a history of chronic diarrhea and 5%, had urinary tract infections. 487 (46.9%) children had bladder stone, 246 (23.6%) children had renal stone, 142 (13.6%) children had ureteral stone and two (0.2%) children had urethral stone. 772 (74.37%) children had ammonium acid urate stone, 410 (39.5%) children had calcium oxalate, 119 (11.46%) children had uric acid, 96 (9.25%) children had calcium phosphate apatite, 45 (4.34%) children had magnesium ammonium phosphate (Struvite), 12 (1.16%) had cystine stone, 40 (3.85%) children had xanthine in. Frequency of compounds was similar in genders [8].

Meiouet, El Kabbaj and Daudon (2019) from Rabat, Morocco studied the composition of 432 stones from children (302 boys, 130 girls). Calcium oxalate was the main component in 51.6% of the stones, followed by struvite (18.1%), ammonium urate (9.5%) and carbapatite (9%) [9].

Schwaderer and Wolfe (2017) emphasized that although the contribution of urinary tract infections to stone formation has long been recognized, the mechanisms remains largely unclear [10].
Ma et al. (2010) studied 146 patients with urinary stone treated with percutaneous nephrolithotomy. Urinary infection was present in 72 (49.3%) patients including 70 (86.4%) patients with gram-negative bacteria, Escherichia coli accounted for 30.9% (25 strains), Pseudomonas aeruginosa accounted for 23.5% (19 strains) and Enterobacter cloacae bacteria 12.3% (10 strains). Resistance to ampicillin/sulbactam was observed in 88.7%, resistance to ceftriaxone was observed in 81.3% and resistance to ciprofloxacin was observed in 67.5%. However, the rate of resistance to amikacin, imipenem and piperacillin/tazobactam were 8.6%, 10.0%, 10.0%, respectively.

Ma et al. emphasized that multiple bacteria can be associated with urinary stones and the majority are Gram-negative bacteria and antibiotic resistance pattern variable [11].

Chen et al. (2018) studied 3892 patients with urinary stones and found that 48.7% patients had infection with Escherichia coli, 10.4% patients had infection with Klebsiella pneumoniae, 8.7% patients had infection with Enterococcus faecalis and 5.2% patients had infection with Proteus mirabilis. The majority of infections in patients with stones were highly resistance to fluoroquinolones, ceftriaxone, ceftazidime, cefepime, penicillins, sulfonamides and monobactams [12].

Progressive childhood urolithiasis is generally caused by metabolic disorders that are associated with recurrence and/or the progression to nephrocalcinosis. Repeated surgical operations and lithotripsy have no effect on these underlying metabolic abnormalities and not helpful in preventing the recurrence of stone or the progression to renal damage [1-4].

Al-Mosawi (2005) reported a beneficial effect of essential oil preparations of terpenic in the treatment of six children (5 boys and 1 girl) with ultrasonographically proven renal or urethral stones. Four of the treated patients had hypercalciuria and two each had hyperoxaluria and distal renal tubular acidosis. The ages of the patients were from 10 months to 5 years. The patients also received treatments for the underlying metabolic abnormalities, such as hypocalciuric diuretics for hypercalciuria. They were treated for a period ranging from 10 days to 12 weeks. All the patients achieved a stone-free state without the occurrence of any adverse effects [1].

Al-Mosawi (2006) reported the treatment of infantile idiopathic hyperuricosuria and idiopathic hypercalciuria causing infantile renal stone disease with the use of essential oil preparations of terpenic. The 8.5-month-old boy with bilateral multiple stone disease was treated with triple therapy consisting of hypocalciuric diuretics, allopurinol and essential oil terpenes with the aim of achieving a stone-free state and preventing renal damage. Treatment was associated with early symptomatic relief during the first week of therapy and stone-free state was achieved after 3 months of treatment without the occurrence of any side effects [2].

Al-Mosawi (2020) described the treatment of a three-year and 4 months old girl with urolithiasis resulting from idiopathic hypercalciuria plus idiopathic hyperuricosuria. The girl presented with recurrent abdominal pain without hematuria and was treated for about four months with triple therapy consisting of oral hypocalciuric diuretic, oral allopurinol and an essential oil terpene capsule. The effect of treatment on urolithiasis was studied by monthly ultrasound examination which showed significant improvement. The study showed that essential oil terpenes can have important therapeutic benefits in the treatment of childhood urolithiasis associated with hypercalciuria plus hyperuricosuria.

7. Conclusion

Urologists should make an early consultation with a pediatrician expert in renal disorders to provide the necessary medical therapies. Bilateral progressive renal stone disease is rarely caused by infective etiologies alone and the presence of recurrent urinary
infections should not lead to ignoring the possibility of metabolic abnormalities.

References

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