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ORIGINAL PAPER

Acute renal failure due to bilateral uric acid lithiasis in infants

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Abstract Acute renal failure (ARF) is one of the complications of urolithiasis, but the role of medical treatment to relieve urinary obstruction in children with ARF is uncertain. We report on infants with acute obstructive uric acid lithiasis. We describe presentation features as well as diagnosis methods and medical treatment in five infants who were admitted to our institution with ARF due to uric acid lithiasis. The medical treatments for all patients were fluid liberalization, urine alkalinization, and oral allopurinol. Two children underwent urinary diversion. Within 8 h, urine output improved in all patients, and the stones passed spontaneously. All obstructed kidneys were relieved with medical treatment, and no renal sequel remained. So this series has showed a role of medical therapy in acute obstructive uric acid lithiasis.

Keywords Acute renal failure · Obstructive anuria · Uric acid lithiasis · Infant

Introduction

Urolithiasis remains a considerable health problem in adults, with the incidence estimated to be as high as 12% [1]. The real incidence in children is not known, but it is an uncommon problem in childhood [2]. The acute presentation of urolithiasis in children occurs at a low but steady rate and can have a markedly variable presentation, and one of them is acute obstructive uropathy [3]. Although up to 80% of children will pass small calculi spontaneously, unremoved stones can lead to renal damage. Fast diagnosis and treatment of acute obstructive urolithiasis may prevent the development of acute renal failure (ARF), which is associated with high morbidity and mortality rates [4].

Uric acid stones can be dissolved by medical agents. This chemolytic treatment is successful in 90% of patients [5–7]. Although, previously we have reported on preliminary results in infants with bilateral uric acid stones and ARF [8], to our knowledge, the role of medical treatment in this condition has not been clarified. We aimed to analyze the clinical and laboratory characteristics of infants with acute obstructive uric acid lithiasis and to discuss the pathogenesis, treatment methods, and outcomes.

Patients and methods

Patients

Between January 2002 and May 2006, infants with ARF due to obstructive uric acid lithiasis were retrospectively reviewed. Those suffering from ARF were included for further investigation on the basis of the following properties: (1) acute anuria since at least 6 h; (2) documented serial rise in blood urea nitrogen (BUN) and uric acid levels; (3) bilateral urolithiasis choking the ureteropelvic junction with minimal or no pelvicaliceal dilatation on USG; (4) absence of any other disease cause to ARF except predisposing conditions; and (5) urate on stone analysis.

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Table 1 Demographic characteristics and presentations of the patients are summarized

Patients	Sex	Age (months)	Weight (g)	Presentation	Duration of symptoms (h)	Predisposing factor
1	Girl	10	7,000	Anuria, vomiting, irritability	12	AGE
2	Boy	11	7,300	Anuria, fever	6	AGE
3	Boy	6	5,200	Anuria, irritability	24	ARD
4	Boy	10	7,900	Anuria, vomiting, fever	12	AGE
5	Boy	9	8,500	Anuria, vomiting, fever	18	AGE

AGE acute gastroenteritis, *ARD* acute respiratory disease

Table 2 Laboratory features in infants with acute obstructive urolithiasis on admission

Patients	Htc (%)	WBC (per mm^3)	Urea (mg/dl)	Cre (mg/dl)	Na (mEq/l)	K (mEq/l)	Urate (mEq/l)
1	29	5,330	92	3.5	123	3.8	14
2	27	8,660	126	2.9	135	3.1	13
3	28	35,700	154	1.0	147	4.2	12
4	29	8,650	103	2.9	130	3.2	14
5	30	19,500	147	3.1	131	4.9	17

Management

The evaluation of each patient included anamnesis, clinical examination, laboratory tests (serum creatinine, BUN, uric acid level, serum electrolytes, and blood gases), plain X-rays of the abdomen, and gray-scale USG. The empiric diagnosis of urate stones was based upon biochemical parameters associated with finding stones by ultrasound and absence of radiopaque calculi on plain film radiography. Initial resuscitation consisted of respiratory control, vascular access, fluid, monitoring vital signs, and urinary catheter insertion. After initial resuscitation, medical treatment was carried out for stones to eliminate spontaneously, as soon as a percutaneous nephrostomy was performed, if possible. The medical treatment consisted of fluid loading with loop diuretic to force diuresis (0.9% saline solution 20 cm^3/kg/h and furosemide 1 mg/kg mg IV). Allopurinol treatment (10 mg/kg/day) was started to inhibit uric acid production in all patients. 8.4% Sodium bicarbonate (1 mEq/kg) was administered IV to alkalinize urine (desired urine pH > 7). Ampicillin (100 mg/kg/day) was added to medical treatment routinely for prophylaxis. Following the relief of obstruction, to diagnose and evaluate accurately stone disease, urine cultures, stone analysis, and additional tests were performed using 24 h urine collections and IVU.

Results

Five consecutive infants (four boys and one girl, mean age 9 months, range 6–11 months) presenting with acute anuria and postrenal azotemia were referred to our institute during the 4-year period. The mean duration of symptoms prior to admission was 16 h (range, 6–24 h). The demographics and clinical spectrum of patients are presented in Table 1. Acute gastroenteritis was detected in all but one infant. The main symptoms were anuria, fever, and irritability. All patients had normal blood pressure and electrolytes, but increased BUN, serum creatinine, and serum uric acid levels (Table 2). Blood arterial gases revealed metabolic asidosis with normal bicarbonate levels.

At least one stone was lodged in each renal unit in the ureteropelvic junction, and it had a mean diameter of 5.5 mm (range 5–8 mm) on USG. Other stones of same sizes were located in the renal pelvis or calices. USG also showed no or minimal pelvicaliceal dilatation in each kidney. A left percutaneous nephrostomy drainage and a left JJ catheter application via lower ureterotomy could be performed in two patients (Table 3). Laboratory and radiologic data indicated an ARF due to bilateral uric acid stones in patients. After three unsuccessful efforts to force diuresis, medical treatment with fluid restriction was started. Any renal replacement therapy in the form of peritoneal or hemo-dialysis was not performed in patients, even if clinically indicated. Diuresis started in the next 8 h (mean, 6 h) after the beginning of therapy. No serious side effect was observed in patients who underwent medical treatment. Patients improved gradually, and about 2 days later, stones 2–3 mm in diameter started to pass spontaneously (Table 4). All stone analyses revealed pure uric acid. Subsequent USG and IVU studies indicated no anatomical abnormalities or residual stones. The timing of follow-up imaging was based on renal function. The time interval for dissolution or spontaneous passing of all uric acid calculi in patients was 6 days (range 3–15 days). The urine cultures were sterile. First urine analysis displayed low-pH level, but subsequent 24 h urine collections showed normal urine

Table 3 Number of stones and pelvicaliceal (Pc) dilatation on ultrasonography

Patients	Right/left stones	Pc dilatation on USG	Intervention
1	4/3	No	Left nephrostomy
2	1/1	No	No
3	2/1	No	No
4	2/2	No	No
5	1/2	Minimally on left	Left JJ catheter insertion

Table 4 The outcomes are displayed

Patients	Diuresis time (h)	Stone passing time	Complication	Follow-up period
1	8th	24 h later	No	5 years
2	6th	3 days later	No	4 years
3	8th	2 days later	No	4 years
4	7th	2 days later	No	1 year
5	8th	24 h later	Thrombocytopenia	8 months

pH (mean 7.1, average 6.5–7.5), urate (mean 3.65 mmol/dl, average 3.34–4.28), oxalate (mean 267 μmol/dl, average 214–390), and citrate (mean 2.81 mmol/dl, average 1.98–3.93) levels. The catheters were removed 3 weeks later. After treatment, the patients entered into a surveillance program with regular USG and MAG-3 scintigrams of their kidneys. During the follow-up period, no recurrence or renal sequel was seen in the patients.

Discussion

Urolithiasis in the pediatric population is an endemic problem especially in developing countries [9]. Many of these patients are presented in an emergency condition with acute obstruction [3, 4]. Although bilateral acute obstructive urolithiasis may therefore require immediate renal replacement therapy and/or urinary diversion, these interventions may not be suitable for infants. To our knowledge, this is the first series about medical treatment in infants with acute obstructive uric acid lithiasis.

The pathogenesis of hyperuricemia and uric acid lithiasis in young children is unknown. Clinically, uric acid is rather uncommon as a constituent of childhood urolithiasis: uric acid stones occasionally develop in conditions associated with excessive production of uric acid, such as tumor lysis syndrome, lymphoproliferative/myeloproliferative disorders, or inborn errors of uric acid metabolism [10, 11]. The important factors for precipitation of uric acid crystals are a high excretion of urate, a small urine volume, and a low-urinary pH [12]. Any metabolic abnormality or previously undiagnosed disease was absent in the presenting cases. Nevertheless, gastroenteritis was diagnosed in the most of cases as a predisposing condition. The exact mechanism of uric acid overproduction in gastroenteritis is not clear. Fujinaga et al. [10] have focused on uric acid formation in gastroenteritis. They have speculated that dehydration resulted in decreased renal blood flow; this in combination with increased tissue breakdown of the gastrointestinal tract from rotavirus infection might play an important role. Finally, we have put forward the idea that increased gastrointestinal tissue destruction is an important cause of uric acid stone formation in our patients. Dehydration may also have contributed to ARF in these children. Actually, dehydration caused by vomiting, diarrhea, and to lack of fluid intake is the commonest cause of prerenal ARF in children who suffer from gastroenteritis. As a result, diarrheal losses or perspiration all predispose to dehydration and decrease urine volume, decrease urine pH level, and finally precipitate uric acid crystals.

Emergency treatment of obstructive stone disease is based on urinary diversion, ideally by percutaneous nephrostomy under ultrasonographic control [13]. Because the majority of our cases had minimal or no pelvicaliceal dilatation, a urinary diversion was not preferred for initial management. According to the literature, ~4–5% of adult patients with obstructive renal failure have minimal or no dilatation of the renal pelvis [14, 15]. Cause of nondilatation of the pelvicaliceal system remains uncertain. Kulkarni et al. [16] have explained that there could be either decompression of the pelvicaliceal system by extravasation of the urine from the fornices or modification in the physical properties of the urinary tract wall. In spite of minimal or no pelvicaliceal dilatation, urinary diversion could be performed in two kidneys. Our main indication to place percutaneous nephrostomy in one patient was urinary diversion to relief obstruction. Because the USG revealed a stone persist in the left lower ureter of the patient 5, ureterotomy was performed, but no stone was found in the ureter, and a JJ catheter was inserted. Actually, renal drainage was initially indicated for emergency diversion of an obstructed upper urinary tract. Recently, this procedure has been used also in the treatment of sepsis aggravated by ureteral obstruction, to assess potential recovery of renal function of an obstructed kidney, and as a first step toward interventional techniques such as dissolving on basketing of renal calculi, dilatation of ureteral strictures, and placement of antegrade stents in patients with umeteral fistulas [17].

Currently, almost all stones can be fragmented with ESWL or removed by minimal invasive methods [14, 18]. However, there have been concerns about the suitability and safety of these instrumentations required to undertake

minimally invasive procedures in young children [19]. Alternatively, a selective medical therapy provides almost complete dissolution of some nonobstructive renal stones. Dissolving uric acid stones with medical therapy is established clearly [5–7]. This series has also showed that medical treatment can be successful in acute obstructive uric acid lithiasis. The mean diameter of the stones that were passed decreased to 2–3 mm, and this supports the fact that chemical dissolving in infants is successful. In the follow-up period, 24 h urine analyses were normal, and no sequel has remained in the patients. In addition, because acute illness causes dehydration, the subsequent finding that those patients had a normal urine pH and urate excretion was consistent with their condition. We consider the earlier finding of a low-urine pH and high-urate levels incompatible with the patients' health status in the absence of an acute illness that might have caused transient acidosis. None of the patients underwent genetic testing, and we would not recommend such testing if the disease does not recur.

In conclusion, for smaller stones, unilateral and incidental stones, allowing time for the stone to pass is appropriate with using medical treatment, ESWL, and/or minimal invasive techniques. Patients with uric acid lithiasis and normal renal function are typical candidates for medical treatment. This series also demonstrated that the bilateral obstructed kidneys with uric acid stones can be relieved with medical treatment. There are also reasons to think that the passage of other stones may be aided by such specific therapies, but they are less compelling.

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