Pediatric Nephrolithiasis: A Review

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ABSTRACT

The incidence of pediatric nephrolithiasis is on the rise. The composition of kidney stones in children is different than in adults, as most stones in children have a composition of calcium oxalate and calcium phosphate mixed with a small amount of uric acid. The symptoms of pediatric nephrolithiasis are nonspecific. Computed tomography (CT) is the gold standard for diagnosis; however, because of radiation exposure associated with a CT scan, ultrasonography is also an accepted modality for the diagnosis. Extensive metabolic evaluation is important to rule out an underlying metabolic disorder. Urinary decompression, medical expulsion therapy, and surgical interventions such as ureteroscopy and extracorporeal shockwave lithotripsy are some of the options available for treating pediatric nephrolithiasis.

Because children with nephrolithiasis constitute a patient population who are at increased risk of stone recurrence during their lifetimes, prompt evaluation and management is important. However, because pediatric nephrolithiasis is an uncommon condition, not much is known about it. This review article summarizes the current clinical knowledge of pediatric nephrolithiasis.

EPIDEMIOLOGY

According to a study by van Batvia and Tasian, the incidence of pediatric nephrolithiasis has risen 6% to 10% annually over the course of the past 20 years in the United States, with estimates of contemporary mean annual incidence ranging from 36 to 57 per 100,000 children in US population-based observational studies. Another study concluded that the greatest increase was noted among youth age 15 to 19 years, with an increase in incidence of 26% every 5 years from 1997 to 2012. This study also noted that adolescent girls and African-American children were most drastically affected by the increase in annual incidence of kidney stones. Other studies have shown that the risk of kidney stones appears to be higher among boys in the first decade of life, and higher among girls in the second decade of life. This age discrepancy tapers off toward a male predominance at approximately age 26 years and then is sustained throughout adulthood.

Furthermore, in some studies, the authors suspect that obesity may play a role in the increased incidence and risk of nephrolithiasis in the pediatric population. A study by Kovesdy et al. suggests that obesity is associated with a number of risk factors contributing to nephrolithiasis, including lower urine pH, as well as increased urinary oxalate, uric acid, and sodium and phosphate excretion. This study also indicates that the association of insulin resistance with obesity can contribute through its impact on the tubular sodium-hydrogen Na-H exchanger and ammoniagenesis, along with the promotion of an acidic milieu. However, this hypothesis of increased incidence of nephrolithiasis among obese children has not been accepted by all. According to van Batvia and Tasian, most studies show no association between body mass index and pediatric nephrolithiasis. The incidence of nephrolithiasis has doubled while prevalence of obesity in children and adolescents has remained constant from 1999 to 2010, suggesting that other factors are responsible for the rise in incidence. Some of these hypothesized factors include elevated blood pressure and asthma. A study by Nikolis et al. showed that children with urolithiasis had significantly greater absolute systolic and diastolic blood pressures than children without stones. This study adjusted for differences in age and height among the two groups.
PATHOPHYSIOLOGY

The pathophysiology of nephrolithiasis can be divided into three broad conceptual categories. The formation of stones requires (1) solutes exceeding in concentration relative to their solubility in the urine; (2) crystallization due to an imbalanced presence of promoters and inhibitors; and (3) the attachment and growth of crystals into nephroliths due to epithelial abnormalities. Examples of common stone-forming solutes include calcium, oxalate, phosphate, citrate, uric acid, and cysteine. In addition, common stone inhibitors include citrate, magnesium, macromolecules, and pyrophosphate.

CHEMICAL COMPOSITION OF KIDNEY STONES

The composition of nephroliths in the pediatric population differs from that in the adult population. These differences can be attributed to the greater association of nephrolithiasis in children with metabolic abnormalities. A retrospective study carried out by Kirejczyk used data from 135 patients (71 boys and 64 girls age 12-18 years) with upper urinary tract lithiasis. The study revealed that most stones had a mixed composition. A combination of calcium oxalate and calcium phosphate admixed with a small amount of uric acid was the most common chemical composition. The second most common was a combination of just calcium oxalate and calcium phosphate. However, all struvite stones were primarily composed of magnesium ammonium phosphate, along with small amounts of other solutes. Furthermore, urine abnormalities were seen in most of the patients studied. These abnormalities included hypercalciuria, hypocitraturia, hyperoxaluria, and cystinuria.

According to Kirejczyk, calcium oxalate stones were the predominant nephroliths of the upper urinary tract. In this study, the occurrence of these stones rose with increasing calciuria, oxaluria, and acidification of the urine. The role of magnesium in calcium oxalate stone formation needs further evaluation. Calcium phosphate stones were the second most common stones in children. These stones occurred with alkaline urine, uricosuria, and phosphaturia. Struvite stones are formed when there is an infection with urease-producing bacteria. The patients with struvite stones were often younger than other subgroups. A moderately inverse correlation existed between calciuria and oxaluria in relation to the content of struvite stones. There was also low citrate excretion in children with struvite stones. Pure uric acid stones, uncommon in childhood, were not identified, but small fractions of uric acid were noted in almost half of the stones identified in the study.

CLINICAL PRESENTATION

The clinical presentation of nephrolithiasis varies with age. According to Chu et al., common presentations of abdomen or flank pain may be seen in older children or adolescents, whereas, younger children often present with vague symptoms such as nausea, vomiting, and irritability. Gross hematuria is an uncommon presentation and the diagnosis of stones often occurs as an incidental finding on imaging studies for other conditions. Furthermore, infants tend to present with even more nonspecific symptoms. A retrospective study conducted by Naseri evaluated 75 term and 2 preterm infants, age 4 to 60 days. The most common clinical presentations found were restlessness and vomiting, with most patients presenting with irritability.

DIAGNOSIS

Nephrolithiasis shares a similar presentation with numerous other genito-urinary pathologies within the pediatric population. These pathologies can be of both renal and bladder etiology. Some common differential diagnoses include polycystic kidney disease, hemolytic-uremic syndrome, pediatric immunoglobulin A nephropathy, pediatric nephritis, and urinary tract infection. Many conditions can be ruled out with urinalysis alone, but imaging modalities such as ultrasound and CT studies are necessary to establish the diagnosis of nephrolithiasis.

EVALUATION

Both laboratory studies and imaging studies are used to evaluate a child with nephrolithiasis. Urinalysis should be performed whenever nephrolithiasis is suspected. The most common abnormal laboratory finding is microhematuria, which is found in 60% to 95% of patients, followed by pyuria in approximately 20% of patients. According to Hernandez, the presence of cystine crystals can be demonstrated on microscopic analysis in cystinuria. The study also emphasizes the importance of retrieving kidney stone material when possible to narrow the differential diagnosis by analyzing the stone composition. This can be immensely helpful to guide further evaluation and management. Metabolic evaluation, such as measuring calcium, magnesium, and phosphorous levels, is also an essential component of the evaluation. It can help in not only determining the cause, but also in correcting the underlying pathology, such as hypercalciuria caused by vitamin D deficiency. Due to the high risk of recurrence of kidney stones in children associated with metabolic abnormalities, the laboratory evaluation for pediatric nephrolithiasis should also include a 24-hour urine collection. Spot urine samples for patients who are unable to provide the 24-hour urine sample, such as children not yet toilet trained, may be sufficient.
The best imaging modality for diagnosing nephrolithiasis in terms of sensitivity and specificity is CT without contrast. However, one should take into consideration the detrimental effects of radiation exposure and try to adjust the radiation dose based on the patient’s size and weight. If dose adjustment is not possible, ultrasound is the next imaging study of choice. The sensitivity of ultrasound remains high (up to 90%) for nephroliths.12

MANAGEMENT

A number of options are available for the management of pediatric nephrolithiasis. These include urinary decompression, medical expulsive therapy, and surgical interventions such as ureteroscopy (URS) and extracorporeal shockwave lithotripsy.7 As with adult nephrolithiasis, the initial step in the acute management in children is to assess the need for urinary decompression. Some indications include obstruction along the urinary tract and infection or evidence of pyelonephritis.14 Decompression can be achieved by cystoscopy and retrograde ureteral stent placement. Medical expulsive therapy consists of the use of receptor blockers, such as alpha-1 adrenergic receptor blockers (alpha-blockers) and calcium channel blockers, inducing the dilation of the ureter and facilitating the easier passage of stones. This method is most effective for stones less than 5 mm in size and those located in the distal ureter.14,15 A meta-analysis performed by Velazquez et al.16 found that medical expulsive therapy performed with an alpha-blocker significantly increased the odds of stone passage compared to placebo, and that alpha-blocker use was safe in children.

Alternatively, URS has also been shown to be safe and effective in the pediatric population. Studies demonstrate primary ureteroscopic access to be successful in 50% to 60% of children with low complication rates, which favor initial URS attempts with stent placement for passive dilation.2 Furthermore, although extracorporeal shockwave lithotripsy (ESWL) treatment has been rising in popularity due to its noninvasive approach and high success rates, many complications are associated with this treatment. These complications range from short-term effects, such as hematuria (in up to 44%), to long-term effects, such as the stunting of renal growth and renal scarring.17 Thus, more studies are needed before ESWL can be considered as first-line therapy. During the past few decades, open and laparoscopic pyelolithotomy have fallen out of favor, making way for procedures such as URS and percutaneous nephrolithotomy due to many technological advances and the development of equipment specifically tailored to pediatric anatomy.18,19 Ultimately, the decision for a particular intervention relies on many factors, including physician preference, location and size of stones, and equipment availability.

REFERENCES