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Case Report

Nephrogenic adenoma of the ureter in a teenager with history of leukemia

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ABSTRACT

Nephrogenic adenomas represent a suspected metaplastic response of the uroepithelium to chronic inflammation and are typically associated with recurrent urinary tract infections, stones, prior radiation therapy and other irritative factors, more commonly seen in adults. Nephrogenic adenoma (also known as nephrogenic metaplasia) usually involves the bladder in adults and represents a rare lesion that can easily be misdiagnosed as a malignancy. We present the case of a 14-year-old male with prior history of acute lymphoblastic leukemia (ALL) who presented with a several month history of vague flank pain which increased in intensity, leading to an emergency department presentation with the only significant finding on exam being microhematuria. Subsequent imaging showed a tumor like replacement of the right ureter with proximal hydronephrosis, initially felt to represent recurrent leukemia. Pathology revealed the tumor like ureteral replacement to represent a nephrogenic adenoma, a benign entity which often responds to conservative management, though not previously reported in the ureter in pediatrics.

Introduction

Nephrogenic adenoma (also known as nephrogenic metaplasia) was initially described in 1949 as a hamartoma of the bladder [1] and has since then been referred to as mesonephric adenoma/metaplasia, adenomatoid tumor, and adenomatoid metaplasia [2]. Nephrogenic adenomas represent a suspected metaplastic response of the uroepithelium to chronic inflammation and are typically associated with recurrent urinary tract infections, stones, prior radiation therapy, chemical agents and other irritative factors. In a series of 80 adult cases, Dropkin et al found 55% of nephrogenic adenomas arising in the bladder, 41% arising in the urethra, and 4% arising in the ureter [3]. Nephrogenic adenomas primarily occur in adults, with males 3 times more likely to have NA than women [4]. Ten percent of nephrogenic adenomas occur in children [5]. Reported cases of nephrogenic adenomas in children exclusively involve the bladder with the most frequent predisposing factor being reimplantation of the ureters for vesicoureteral reflux [6].

These tumors are often treated with local resection, stent placement and even nephrostomy tubes to preserve renal function. Tumors can recur after resection but typically do not undergo malignant transformation [4].

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Case report

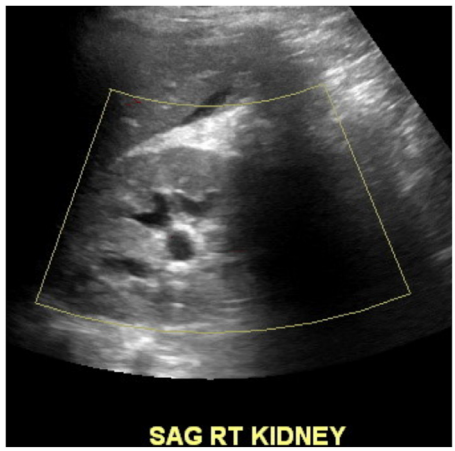
A 14-year-old male with history of acute lymphoblastic leukemia presented to the emergency department with increasing right flank pain which had been intermittent over the past 2 months, though acutely worsened in the past 24 hours. He was diagnosed at age 9 with ALL and first relapsed with a combined bone marrow and testicular relapse, then had a second relapse of central nervous system (CNS) and testicular involvement. He subsequently underwent cord blood transplant 18 months prior to presentation.

He was seen for a routine follow-up visit for ALL approximately 3 months prior to presentation in the ER. At that time, he noted some vague right flank pain, which was attributed to "sleeping on it funny." An abdominal radiograph was ordered at that time, however it was negative for any radiographic abnormality.

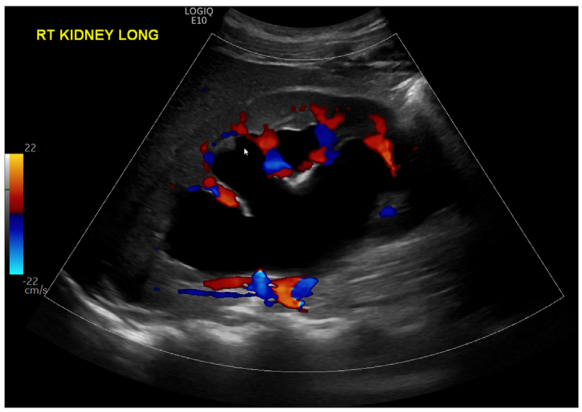
His review of systems was essentially negative, other than for the above mentioned right flank pain. On focused questioning, he denied any hematuria nor a history of nephrolithiasis. On physical exam, the patient was in no acute distress, and his vitals were within normal limits. He was able to ambulate on his own and demonstrated no weakness. However, the exam was significant for mild right paraspinal tenderness.

Medical history was significant for the above ALL along with relapse on 2 separate occasions. He also reports a history of asthma and prior chemotherapy. His surgical history is significant for prior marrow biopsies and port placements/removals as well as a prior cholecystectomy. Testicular biopsy was performed during a prior relapse.

Urinalysis showed microhematuria but no signs of an underlying UTI. Urine gram stain showed a few WBC's but no bacteria. Urine culture was negative. Additional laboratory results yielded no pertinent information, specifically his BUN and creatinine were normal.



(a)



(b)

Fig. 1 – (A) Sagittal ultrasound image of the right kidney and renal pelvis 1 year prior to presenting acutely in the emergency department demonstrating mild hydronephrosis. (B) Sagittal ultrasound image with color Doppler of the right kidney shows new, marked right hydronephrosis, dilated relative the exam 1 year prior. The left kidney, not shown, was normal.

Imaging findings and diagnosis

Prior ultrasound (US) performed 1 year earlier showed mild right hydronephrosis and cholelithiasis (Fig. 1a). Given the presenting symptoms, a repeat renal US was ordered in the emergency department. Renal US at this time demonstrated interval significant hydronephrosis as well as mass like replacement of a long segment of the distal right ureter with associated blood flow within the thickened ureteral tissue on Doppler imaging (Figs. 1b and 2). Differential considerations at the time of the renal US included relapse of ALL, infiltrating tumor or possibly atypical presentation of BK virus (though no longer immunosuppressed), with no associated sonographic abnormality of the bladder. The appearance did not suggest edema related to recent passage of a ureteral stone.

Given the findings, urology was consulted. Per urology request, additional lab work was ordered to assess renal function, and magnetic resonance imaging (MRI) was ordered in hopes to clarify the sonographic findings. MRI confirmed the US findings with right-sided hydronephrosis with proximal hydroureter, and abrupt transitioning of the mid right ureter (Fig. 3). There was some dilatation of the mid and distal ureter with wall enhancement and thickening (Fig. 4). With the imaging studies confirming a solid type lesion, cystoscopy with obtaining right ureteral tissue sample was recommended.

The patient subsequently underwent cystourethroscopy where a gentle right sided retrograde pyelogram was obtained (Fig. 5). Per the procedural notes, at the level of the mid-ureter there was a large, pedunculated papillary tumor that appeared to ball-valve when inflow was turned off. Beyond this, the entire ureter had small papillary tumors that did not appear to be obstructing the kidney. An N-gage grasper was used to remove the large pedunculated tumor off of its stalk. Initially there was a plan to laser the rest of the tumor. However, because of its extent and the concern for later stricture, in addition to its nonobstructive appearance, additional lasering was not performed.

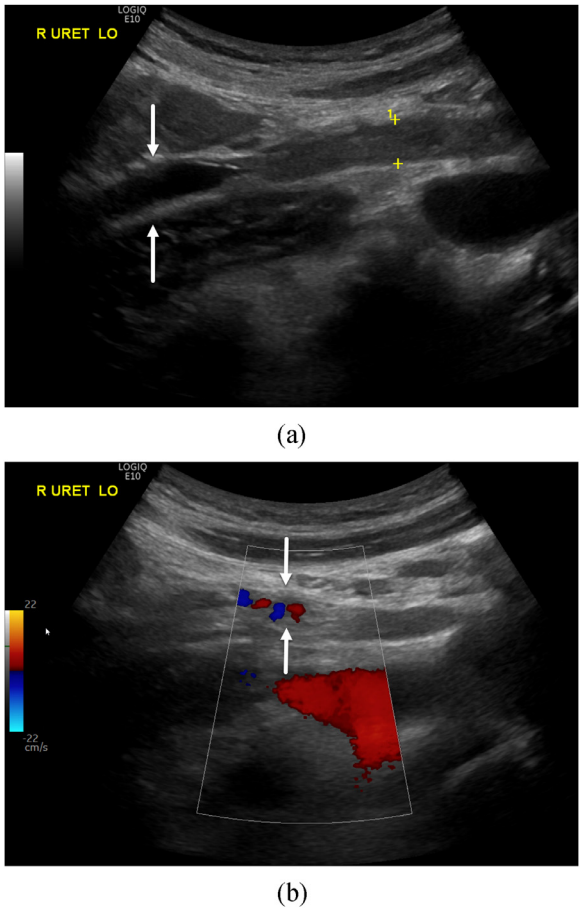


Fig. 2 – (A) Sagittal gray scale image shows a dilated, fluid filled proximal right ureter (arrow), with echogenic material distending the distal ureter (between marks). (B) Color Doppler showed perfusion within the mass-like material distending the distal right ureter (arrow).

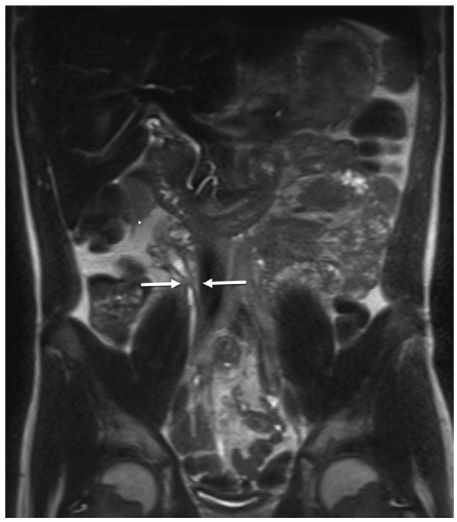


Fig. 3 – Coronal HASTE T2 MRI shows the previously noted transition and narrowing of the dilated ureter (arrow) but increased signal intensity of material resembling fluid within the ureter both proximal and distal to the transition.

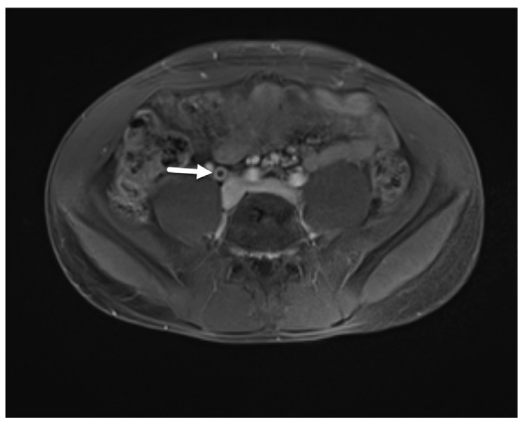


Fig. 4 – Delayed post contrast images only show thickening of the right ureter wall with enhancement (arrow).

Following this a semirigid ureteroscope was used to perform ureteroscopy, with washings biopsy forceps were used to take samples of the ureter at the site of the tumor. A stent was placed at this time to assist in decompressing the right sided hydronephrosis.

Ultimately the tissue diagnosis resulted in "nephrogenic adenoma of the right ureter." The hydronephrosis failed to resolve with stenting and given the size and growth of the adenoma, a right ureterectomy was performed with a right ileal-ureter replacement. Following this procedure, the patient's hydronephrosis resolved, and as of writing, the patient is free of any recurrence.

Discussion

Nephrogenic adenoma was initially described in 1949 as a hamartoma of the bladder (Davis), and it has also been referred to as mesonephric adenoma/metaplasia, adenomatoid tumor, and adenomatoid metaplasia [2]. As nephrogenic adenomas are rare lesions, they can easily be confused and/or misdiagnosed as a variety of other malignant lesions of the urinary system. These can be associated with various inflammatory processes, to include: recurrent urinary tract infections, urinary calculi, prior renal transplants, bladder wall diverticulum, radiotherapy as well as chemical agents and other irritative therapies [5,7].

Nephrogenic adenoma is more common in males in comparison with females, and there is a large range of reported age at diagnosis, from 4 years to 81 years [5,8]. While nephrogenic adenoma is more common in adults, there is a roughly 10% occurrence in pediatric patients [5,8]. Nephrogenic adenoma can be identified anywhere in the urinary tract, though it is most commonly encountered in the urinary bladder [9]. Of the multiple case reports of nephrogenic adenomas, lower than 20 have affected the ureter and ureteral involvement has been exclusive to adults [9].

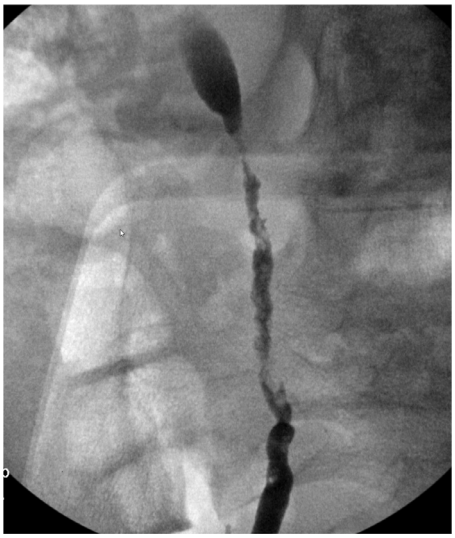


Fig. 5 – Fluoroscopic image from retrograde contrast injection via cystoscopy shows no obstruction but diffuse irregularity of the mid ureter.

Nephrogenic adenoma is still a rare entity, though reports of occurrence have increased since it was first described. These may mimic other urologic conditions, such as chronic cystitis or urothelial carcinoma. Most commonly, nephrogenic adenoma presents with lower urinary tract symptoms, such as hematuria, retention, dysuria or recurrent urinary tract infections [10].

There is some uncertainty about the origin of nephrogenic adenoma of the urinary bladder but a number of postulates exist regarding the pathogenesis of the disease and some of these include the following: it may be a metaplastic lesion; it may emanate from embryonic tissue; it may be a metaplasia that occasionally coexists with multifocal urothelial carcinoma; it may originate from embryonic mesonephroid tissue [5,11,12]. A number of reports had documented that cases of nephrogenic adenoma of the urinary bladder had emanated from urothelial injury pursuant to previous surgery or long-term inflammation. Immunosuppressive therapy in kidney transplant patients and intravesical instillations of Bacillus Calmette-Guérin have also been linked with nephrogenic adenoma of the urinary bladder [5].

As stated above, these lesions in the adult setting typically occur in the bladder and often in the setting of prior urinary tract surgery, chronic irritation from infection or stones. However, in children nephrogenic adenoma is almost exclusively seen in the urinary bladder, with the most frequent association being prior surgery, specifically ureteral reimplantation [6]. The most common subtypes are papillary, as in our case, tubulocystic and mixed papillary and tubulocystic.

Treatment is somewhat controversial, with complete resection being optimal, though this may further incite trauma, irritation and recurrence. Therapy may be directed at controlling bleeding and symptoms, as these lesions may remain silent for years [6]. It should be noted that the rate of recurrence in children is high, with some reporting a rate of 80% [12]. As these are rare lesions, there is little definitive guidance on management and imaging roles.

Conclusion

Nephrogenic adenomas are rare lesions of the urothelium, and are rarer in the pediatric population. When nephrogenic adenomas present in pediatrics, case reports have been limited to the urinary bladder, frequently with patients that have undergone prior bladder augmentation or ureteral reimplantation. Our case presents an exception to the rule as our patient presented with NA of the right ureter, which to our knowledge has not been reported in a pediatric patient. As these can be mistaken for neoplasia, appropriate diagnosis is crucial. Management at this time for our patient is unknown, but following resection there has been not reported recurrence as of case submission.

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