Chronic, Gross Hematuria Caused by Idiopathic Ureteric Stricture

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abstract

An otherwise healthy, 10-year-old boy presented with chronic, gross hematuria. This persisted daily for 5 years despite extensive multidisciplinary workup with renal biopsy and resulted in severe iron deficiency anemia. The extensive workup and requirement for routine follow-up, investigations, and procedures led to significant psychosocial distress for the patient. Initially, it was thought the patient had a nutcracker phenomenon, but on closer inspection of his ureters, an idiopathic, unilateral ureteric stricture was discovered and, after 8 weeks of stenting, resulted in complete resolution of the hematuria. Importantly, the patient’s psychosocial distress resolved after resolution of the hematuria and with the closure that came with a diagnosis.

Hematuria is defined as 5 or more red blood cells (RBCs) in a urine sample per high power field, observed on 3 separate occasions over the course of several weeks. Most often, there is a glomerular or genitourinary tract abnormality to accompany the hematuria, but in some instances, the discolored urine may in fact be hemoglobinuria, myoglobinuria, or food or medication related. Hematuria is most often recognized incidentally on screening urine studies. True hematuria can be separated on the basis of whether it is glomerular or nonglomerular in nature. Nonglomerular causes can include trauma, hypercalciuria, nephrolithiasis, cystitis, malignancy, and bleeding diatheses. Glomerular causes can be genetic in nature, including Alport syndrome and thin basement membrane disease, which oftentimes manifest with gross hematuria. Postinfectious glomerulonephritis (PIGN), vasculitides, and autoimmune glomerulonephritides, including immunoglobulin A (IgA) nephropathy and lupus nephritis, also present with glomerular hematuria. Benign urethrorrhagia is an important consideration; however, it is not true hematuria. To further aid in diagnosis, urine microscopy to look at RBC morphology is required. If they are eumorphic, considerations for underlying genitourinary pathology must be entertained. Meatal stenosis can be seen after hypo- or epispadias repair and can result in eumorphic microscopic hematuria. When dysmorphic RBCs are seen, glomerular disease must be considered and proteinuria screened for.

Idiopathic ureteric stricture is an apparently undescribed etiology of chronic, gross hematuria in pediatric patients. Ureteric stricture itself is usually associated with an underlying condition, with the most common etiology being urolithiasis, followed second by ureteric manipulation and previous radiation. Most episodes of gross hematuria associated with ureteric stricture are postinstrumentation bleeding.

The patient was 10 years old at the time of presentation with hematuria. He had a diagnosis of autism spectrum disorder but was otherwise healthy with no significant past medical history.
and no previous episodes of hematuria. He was given a presumptive diagnosis of PIGN; however, C3 complement was normal. IgA levels were within normal limits. The antinuclear antibody revealed a positive speckled pattern but was low titer; and native DNA antibodies tested negative. Urine for adenovirus resulted negative as did the urine culture. Urinalysis revealed 3+ blood, and microscopy showed erythrocytes packing the field of view. The erythrocytes were not described as dysmorphic, and no casts were noted. His urine calcium was <0.25 mmol/L, which, when used to calculate a urine calcium to creatinine ratio, was negligible. He was found to be normotensive with preserved renal function and had normal renal ultrasonography. His clinical examination revealed a well-nourished, otherwise healthy boy with no organomegaly or evidence of genital trauma.

Over the next year, the child had persistent, daily gross hematuria. His hematuria was always throughout the full stream, was not worse on initiation or termination, and there was no evidence of clots. If he was well hydrated, the color would occasionally be more red-pink; however, for the most part it resembled “tomato juice.” Because of this, he developed iron deficiency anemia, prompting further workup from a nephrologist. A tentative diagnosis of PIGN was investigated, but other considerations included IgA nephropathy, thin membrane disease, Alport syndrome, and foreign body. The patient did not have a course typical of IgA nephropathy, there was no history of sensorineural hearing loss, and ultrasonography confirmed no foreign body. The patient’s renal function remained normal, but his hemoglobin level continued to drop, and he required iron infusions because of poor response and poor tolerance to high doses (8 mg/kg) of daily oral iron supplements.

He underwent cystoscopy, which ruled out rhabdomyosarcoma and arteriovenous malformation (AVM). A computed tomography scan was performed and revealed normal corticomedullary differentiation, as was seen previously on ultrasonography, with the added observation of normal parenchymal enhancement without evidence of AVM. Almost 2 years after the initial presentation with hematuria, a renal biopsy was performed. An adequate sample with 28 glomeruli was obtained, and there was no evidence of sclerosis or segmental or interstitial fibrosis and no tubular atrophy. A hematologist ruled out a bleeding diathesis, and MRI ruled out nutcracker phenomenon. He was subsequently referred for a second opinion. Concurrently, the patient was having an increasingly hard time managing his medical condition, and it was having significant negative psychosocial effects manifesting as depressive symptoms.

After 3 years of gross hematuria with every void, he continued to have normal renal function as well as normal routine blood panels aside from anemia. He remained normotensive. His serial examinations in clinic did not reveal an etiology for his chronic hematuria. The second urology team requested an additional renal biopsy, which was undertaken and suspicious for IgA nephropathy but not confirmatory. Concurrently, hematology ruled out paroxysmal nocturnal hemoglobinuria.

A computed tomography scan with angiography of the kidneys and bladder was performed by interventional radiology. This revealed mild compression of the left renal vein as it passed over the anterior wall of the abdominal aorta, suggestive of nutcracker phenomenon. The computed tomography scan was sent to an additional center for reinterpretation, with the finding of presumed nutcracker phenomenon once again reported. Autotransplant on the affected side was discussed, but before this, full evaluation of the ureters was undertaken by direct visualization. This was >5 years after the initial discovery of hematuria.

Ureteroscopy was performed, with bilateral retrograde pyelography, and revealed a left ureteric stricture but normal ureterovesicular junctions (UVJs) bilaterally as well as a normal bladder. This stricture was noted ~2 to 3 cm from the UVJ, and the ureteroscope was unable to pass. There was frank blood noted coming from the left ureter before instrumentation. Given this, the stricture was stented. Around the time of this procedure, the patient began to experience symptoms of depression with superficial cutting. The patient suffered stent colic, which complicated this matter further; however, the stent remained in situ for the planned 8-week duration.

After stent removal, his urine cleared completely. He was quickly weaned from intravenous iron infusions with spontaneous normalization of his hemoglobin. Unfortunately, by this time, the patient was experiencing significant depressive symptoms and required referral to child and adolescent psychiatry for ongoing supportive care. He was seen 8 months later and again continued to have clear urine with no evidence of macro- or microscopic hematuria and had a normal hemoglobin level. He has ongoing follow-up with both his urologist and pediatrician. He was discharged from the child and adolescent psychiatry team given improvement in his depressive symptoms after diagnosis and resolution of his ureteric stricture.

Hematuria is a relatively common, incidental finding in pediatric patients and is often associated with an underlying urinary tract infection or postinfectious cause. When gross in nature, it is commonly associated with...
with trauma. Indeed, a recent study of the etiology of hematuria in 342 children revealed that over a 10-year period, 14% were associated with trauma, whereas 19% of patients had benign urothrorrhagia. Additionally, 14% had urinary tract infection. Of the 342 patients, 45 children had underlying congenital abnormalities, including vesico-ureteral reflux (22 children), posterior urethral valves (10 boys), and ureteropelvic junction obstructions (8 children). Some of the boys enrolled in the study also had proximal hypospadias repairs previously, which is a known risk factor for gross hematuria. Five percent of children had urolithiasis. None of the children had ureteric stricture. Lastly, for 34% of the patient cohort, there was no known etiology. The authors comment that because of their inability to perform cystoscopy or imaging on all patients, it is possible the cause of gross hematuria in those patients was self-limited nutcracker phenomenon or uretero-vascular malformation. In fact, uretero-vascular malformation, including uretero-iliac artery fistula and AVM, represent life-threatening conditions characterized by significant gross hematuria. Although our patient had significant, gross, and chronic hematuria, early imaging studies did not reveal any evidence of AVM. Additionally, there were several ultrasonograms performed that never revealed calculi, ureteropelvic junction, or UVJ abnormalities. Urethrorrhagia was not observed on cystoscopy.

Ureteric stricture can cause kidney damage, leading to significant morbidity or mortality. Its presence in the literature is limited, but a case series of congenital midureteric stricture exists as well as several case reports of varying etiologies. What is common among these studies is the rarity of isolated ureteric stricture in pediatric patients. In a recent case report, a 73-year-old woman was shown to have bilateral, progressive ureteric stricture requiring surgical management. She presented with lumbar pain and microscopic hematuria, not gross hematuria. She had previous hysterectomy and hernia repair and a past-treated multiple myeloma. An etiology for her strictures was never determined. Bhatta Dhar et al reviewed 2 patients with apparently idiopathic ureteric stricture, both of whom were adult patients, 1 with preexisting hypertension. One of the patients had a single event of gross hematuria. Lastly, Smith et al described 4 cases of congenital midureteric stricture and reviewed 13 additional cases from the literature. Important to note, none of the patients were noted to have hematuria, and almost all cases were associated with an underlying urogenital malformation.

In another study, a clear etiology for ureteric stricture was identified in 24 of 25 patients. The most common cause of ureteral stricture was impacted calculi (60%). Additionally, 5 of the patients with impacted calculi had iatrogenic injuries during stone removal, which may have led to variations in stricture severity. Other etiologies for stricture included previous radiotherapy, endometriosis, and non–calculus-related iatrogenic injury. The patient described in this case report did not have a history of urolithiasis, and each of his ultrasounds and scans revealed no evidence of calculi, hydronephrosis, or hydrourereter. He did not have any of the additional risk factors for ureteral stricture mentioned previously. Interestingly, once stented, and with no additional instrumentation, there was complete resolution of the hematuria, again suggestive that this isolated stricture was the cause of this patient’s chronic, gross hematuria.

Gross hematuria in children is a relatively uncommon finding when an etiology is not readily apparent. Ureteric stricture can cause significant kidney injury with associated morbidity and mortality. Interestingly, our patient presented with an uncommon finding in idiopathic ureteric stricture: isolated gross hematuria. Given the protracted course and significant psychosocial impacts this diagnostic journey had on the patient, it is important to consider ureteric stricture in the otherwise healthy patient with chronic, gross hematuria when all diagnostic modalities point to normal findings.

**ABBREVIATIONS**

AVM: arteriovenous malformation  
IgA: immunoglobulin A  
PIGN: postinfectious glomerulonephritis  
RBC: red blood cell  
UVJ: uretero-vesicular junction

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