A Child With Recurrent Gross Hematuria Caused by the Nutcracker Syndrome: Lessons Learned

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Recurrent gross hematuria in children requires a well thought-out evaluation to address a long list of glomerular and extraglomerular etiologies, among which the nutcracker syndrome is usually included.[1] Some authors have reported that this condition may be easily missed and underreported when hematuria is evaluated by routine diagnostic criteria.[2] The child reported in this report was diagnosed with the nutcracker syndrome by specific imaging techniques only after an extensive investigation to address his hematuria, including a kidney biopsy and a cystoscopy, was negative. The authors raise the question of whether diagnosing the nutcracker syndrome early on in the evaluation of recurrent gross hematuria may spare some children prolonged, expensive, and invasive diagnostic procedures.

Case Summary

A 10-year-old African American male presented with a history of 6 bouts of painless gross hematuria each one lasting 3 to 5 days in the last 1½ years. There was no history of trauma, urinary tract infection, edema, dysuria, urinary frequency, arthralgias, or skin rashes. Evaluation by a pediatric urologist, which included a cystoscopy, was normal. Past medical history was significant for acute lymphoid leukemia in remission for 3 years. Neonatal history was unremarkable. Family history was negative for hematuria, deafness, or end-stage renal disease. Physical examination was entirely normal. Blood pressure was 115/69 mm Hg and heart rate was 72 beats/min. Laboratory results were as follows: white blood cell $2.7 \times 10^3/mm^3$, hemoglobin 13.1 g/dL, platelets $275 \times 10^3/mm^3$, glucose 75 mmol/L, Na 139 mmol/L, K 4 mmol/L, chloride 101 mmol/L, CO_2 26 mmol/L, blood urea nitrogen 13 mmol/L, creatinine 0.6 mg/dL, Ca 9.1 mmol/L, total protein 6.7 g/dL, albumin 4 g/dL, SGPT 13 U/L, SGOT 20 U/L, alkaline phosphate 207 U/L, partial thromboplastin time 34.3 seconds, prothrombin time 13.9 seconds, international normalized ratio 1.1, C3 147 mg/dL, C4 33 mg/dL, ANA negative, urine pH 6.5, SG 1015 large blood negative protein, urine Ca/creatinine ratio 0.07, urine culture negative, and sickle cell screening negative. Kidney–bladder ultrasound was normal. Kidney biopsy performed under computed tomography scan guidance showed normal glomeruli and well-preserved tubules and interstitial compartment. Immune fluorescence was negative. Electron microscopy was normal. Computed tomography scan showed no kidney anatomical abnormalities. A magnetic resonance angiography was consistent with the nutcracker syndrome. Figure 1 shows a parallel orientation of the superior mesenteric artery running at a closer angle in relationship with the aorta. Figure 2 shows bright blood sequence depicting severe narrowing of the left renal vein between the superior mesenteric artery and the aorta.

Discussion

This child's history of recurrent gross hematuria prompted a comprehensive evaluation to rule out its list of customary glomerular and extraglomerular causes. The normalcy of this evaluation, which included a kidney biopsy and cystoscopy, raised the possibility of the nutcracker syndrome. This diagnosis was clearly demonstrated by a kidney magnetic resonance angiography. The nutcracker phenomenon was coined by De Schepper[3] in 1972 when reporting 2 patients presenting with hematuria and left renal vein entrapment. Since that time, this syndrome has been recognized as a valid clinical entity causing diverse symptoms, including nonglomerular recurrent gross hematuria, left flank pain, left varicocele, dysuria, dysmenorrhea, dyspareunia, orthostatic proteinuria, and fixed proteinuria.[4] Although considered to be a rare cause of hematuria, the true incidence of nutcracker syndrome may be underreported.[2] Shin et al[5] recently reported that more than 40% of patients

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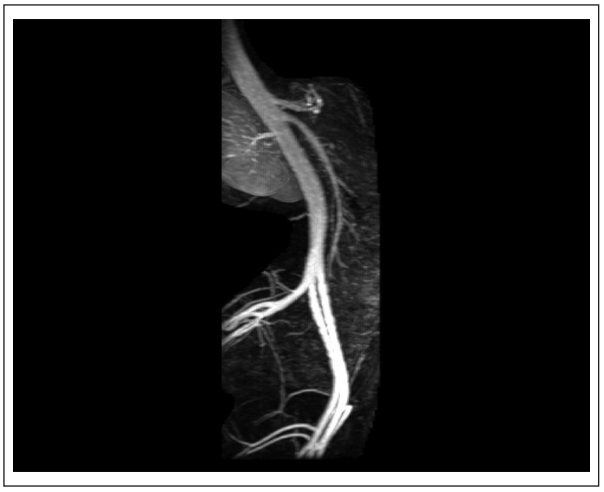

Figure 1. Parallel orientation of the SMA running at a closer angle in relationship to the aorta

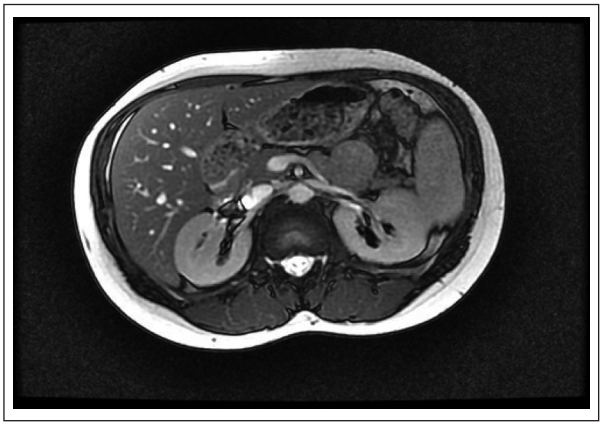

Figure 2. Bright blood sequence depicting severe narrowing of the left renal vein between the SMA and the aorta

with hematuria were diagnosed with the nutcracker syndrome.

The pathogenesis of nutcracker syndrome is still controversial. Some authors suggest that abnormal branching of the superior mesenteric artery from the aorta resulting in a narrower angle between these vessels can lead to left renal vein entrapment, increased venous pressure, and formation of renal hilar and gonadal collaterals. The venous congestion may cause pain referred to the flank, loin, or perianal areas. Rupture of the thin-walled septum that separates the veins from the renal collecting system results in hematuria.[6]

The most accurate diagnostic tool to diagnose nutcracker syndrome is renal venography combined with measurement of the pressure gradient between the inferior vena cava and left renal vein.[7] Other, less invasive imaging studies have also shown to be reliable to diagnose nutcracker syndrome. In experienced hands, Doppler sonography, including the measurement of the mesenteric angle, peak velocity and anterior–posterior diameter of the left renal vein in both supine and upright positions, has shown promise to detect nutcracker syndrome reliably.[7,8] Computed tomography and magnetic resonance angiography are also sensitive procedures to diagnose this syndrome.[9]

The treatment of nutcracker syndrome depends on the severity of the symptoms. Most patients presenting with mild to moderate symptoms and can be managed conservatively. Invasive procedures aimed at reducing the pressure within the left renal vein area have been attempted in patients manifesting with severe and frequent bleeding, significant proteinuria, and pain. These procedures have included excision of the renal varicosities, venous embolization, renal auto transplantation, gonadal–caval bypass, left renal vein transposition, and renal venous stenting.[4]

Our patient had a history of recurrent gross hematuria. Traditional etiologies of hematuria, including urinary tract infection, renal and lower tract malformations and tumors, coagulation disorders, sickle cell, urolithiasis, hypercalciuria, exercise-induced trauma, and glomerulonephritis, particularly IgA nephropathy and basement membrane related diseases, were ruled out by the appropriate investigations. Magnetic resonance angiography confirmed the diagnosis of nutcracker syndrome. In hindsight, we wonder whether having considered the nutcracker syndrome by the appropriate specific imaging studies earlier may have prevented this child from undergoing unnecessary invasive procedures such as cystoscopy and kidney biopsy.

The nutcracker syndrome should be considered in patients presenting with recurrent gross hematuria not due to unmistakable causes of glomerular and nonglomerular hematuria. Magnetic resonance angiography with venous phase imaging is a good, noninvasive tool to diagnose nutcracker syndrome. Supine and standing Doppler sonography is becoming a promising noninvasive, safe, and less expensive technique in centers experienced with this procedure. In light of the reported higher incidence of nutcracker syndrome attributed to cause gross hematuria, it is reasonable to think that in the future an increased awareness of this condition and mastery of its diagnosis by suitable imaging techniques such as Doppler sonography may help identify children presenting with recurrent gross hematuria associated with the nutcracker syndrome before invasive procedures are performed unnecessarily.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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