

CASE REPORT

Gross Hematuria of Uncommon Origin: The Nutcracker Syndrome

Domenico Russo, MD, Roberto Minutolo, PhD, Vittorio Iaccarino, MD, Michele Andreucci, PhD, Alfredo Capuano, MD, and Francesco A. Savino, PhD

● Left renal vein hypertension, also called “nutcracker phenomenon” or “nutcracker syndrome,” is a rare vascular abnormality responsible for gross hematuria. The phenomenon is attributable to the idiopathic decrease in the angle between the aorta and the superior mesenteric artery with consequent compression of the left renal vein. The entrapment of the left renal vein is not easily detectable by ordinary diagnostic procedures. We report two cases of gross hematuria (persistent in one patient and recurrent in the other) caused by “nutcracker phenomenon.” In both cases, no remarkable findings were obtained from medical history, urinary red blood cells morphology, repeated urinalysis, pyelography, cystoscopy, or ureteroscopy. Left renal vein dilation in one case was found with a computed tomography (CT) scan performed on the venous tree of left kidney. The diagnosis of “nutcracker phenomenon” was confirmed by renal venography with measurement of pressure gradient between left renal vein and inferior vena cava in both cases. In one case, the diagnosis was complicated by the presence of *Mycobacterium tuberculosis* in urine. The “nutcracker phenomenon” is probably more common than thought. Early diagnosis is important to avoid unnecessary diagnostic procedures and complications such as the thrombosis of the left renal vein. Many procedures are available to correct the compression of the left renal vein entrapped between the aorta and the superior mesenteric artery: Gortex graft vein interposition, nephropexy, stenting, and kidney autotransplantation. After surgery, gross hematuria ceases in almost all patients.

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INDEX WORDS: Hematuria; left renal vein hypertension; nutcracker syndrome.

SHORT-LIVED, recurrent, or persistent gross hematuria is observed in clinical practice as expression of some kidney diseases. We report two cases of gross hematuria (persistent in one patient and recurrent in the other) caused by the “nutcracker phenomenon,” which probably is the rarest cause of gross hematuria.

CASE REPORT

Patient 1

A 20-year-old woman was hospitalized in our unit for persistent gross hematuria of 6 months' duration. During this time, the patient had undergone repeated cultures of urine and excretory urography, with negative results.

On admission, gross hematuria was still present. The patient had no relevant medical history before the onset of gross hematuria: no renal colic, no urinary tract or upper respiratory tract infection, no use of nephrotoxic medications, no past abdominal trauma, surgery, or any other urinary alteration. Her family history was negative for renal diseases. Blood chemistry was normal. No casts were observed in repeated microscopic examinations of urinary sediment. Urine dipstick showed 1+ proteinuria. Urinary protein excretion ranged from 0.5 to 1.0 g/d. Urinary red cell morphology showed 90% isomorphic cells. Repeated cultures of urine did not show growth of common pyogens and fungus. Antinuclear antibody, anti-double-strand DNA, and anti-neutrophil cytoplasmic antibodies (ANCA) were negative; serum immunoglobulin (Ig) A, IgG, and IgM and complement concentration, erythrocyte sedimentation rate, tests for ASLO titer, and rheumatoid factor were in normal range. Kidney ultrasonography and renal parenchymal com-

puted tomography (CT) scan did not give evidence of any of the most common causes of gross hematuria. Cystoscopy showed bleeding from the left ureter and multiple petechiae on bladder mucosa; urinary cytology was negative for malignancy. One of five 24-hour urine collections grew *Mycobacterium tuberculosis*; thus, rifampicin, isoniazide, and ethambutol were administered.

The patient was again hospitalized 4 months later. Gross hematuria was still present, but *M tuberculosis* were not detected in urine samples. Renal arteriography did not show arteriovenous malformations or neoplasms; the left kidney, however, appeared not to be uniformly opacified during the venous phase of the arteriography. The subsequent venography showed dilatation of the left main renal vein and of its intrarenal branches (Fig 1). Venous pressure was measured, and a high-pressure gradient (5 cm H₂O) was found between the left renal vein and the inferior vena cava; this gradient clearly showed the presence of hypertension in the left renal vein and led to the diagnosis of “nutcracker phenomenon.” The patient refused surgery.

Gross hematuria was still present on August 1997 (date of the last visit), 3 years after its first appearance. At that time,

From the Division of Nephrology and Istituto di Scienze Radiologiche, School of Medicine, University “Federico II,” Naples, Italy.

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Address reprint requests to Domenico Russo, MD, Division of Nephrology, School of Medicine, University “Federico II,” Via Marconi 80, 80024, Cardito (Naples), Italy. E-mail: sbf004@sbf.it

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Fig 1. Venography shows dilatation of left renal vein and of intrarenal venous tree.

CT scan of the venous renal tree clearly showed dilation and intrinsic filling defects of the left vein (Fig 2); the latter were caused by parietal thrombi. Once again, the patient refused surgery.

Patient 2

A 20-year-old woman was admitted to our unit because of 3 months' intermittent gross hematuria.

On admission, gross hematuria was not present. The patient's medical history was negligible: there were no past renal diseases, no use of nephrotoxic drugs, no renal stones, no urinary tract or upper respiratory tract infection. Blood chemistry was normal. Casts were not found at repeated

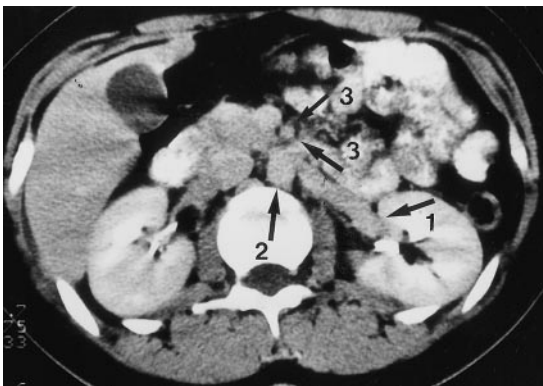


Fig 2. CT scan shows (1) the dilatation of left renal vein where it crosses between (2) the aorta and (3) the superior mesenteric artery.

urinalysis. Urine dipstick showed 1+ proteinuria and 2+ hematuria. Urinary red cell morphology showed 50% isomorphic red cells. Urinary protein excretion ranged from 0.5 to 0.7 g/day. Urine cultures were negative. Serum complement, IgA, IgG, IgM concentration, test for ASLO titer, antinuclear antibody, anti-double-strand DNA, rheumatoid factor, and ANCA were in normal range. Ultrasonography of kidneys and pyelography were normal. CT scan showed normal renal parenchyma but a narrowed left ureter. Cystoscopy showed light bleeding from the left ureter, but ureterography did not show abnormality. Renal arteriography was negative; selective left renal venography showed a dilation of the left renal vein, which appeared entrapped between the aorta and the superior mesenteric artery; the pressure measured in the left renal vein and the inferior vena cava exhibited a high gradient (7 cm H₂O).

The patient refused surgery.

DISCUSSION

We describe two cases of gross hematuria caused by left renal vein hypertension, which is also called "nutcracker phenomenon" or "nutcracker syndrome." This phenomenon is attributable to the idiopathic decrease in the angle between the aorta and the superior mesenteric artery with consequent compression of the left renal vein.

The hematuria is the result of the hypertension in the left renal vein and the development of collateral venous pathways with thin-walled veins close to calyceal fornices.^{1,2}

The "nutcracker phenomenon" is rare,¹⁻³ painless, and difficult to diagnose. In fact, the patient's clinical characteristics and medical history, biochemistry, and urinalysis are usually not remarkable. In addition, the left renal vein hypertension may not be easily detected by radiographic procedures, if it is not carefully sought. Because of these characteristics, the "nutcracker phenomenon" is probably more common than previously thought.

In our cases, several procedures (pielography, cystoscopy, ureteroscopy) were performed, and more common causes of long-lasting or intermittent unilateral gross hematuria (vascular abnormalities, urinary tract malignancy, or stones) had to be excluded before the diagnosis of "nutcracker phenomenon."

CT of renal parenchyma and of urinary tract did not evidence "nutcracker phenomenon" in both cases. The procedure did not show abnormalities in one case (case 2), whereas in the other it evidenced only imprint on the left ureter because of peri-ureteral varices; the latter finding is

not pathognomonic of “nutcracker phenomenon,”^{1,2} but it is frequently observed in diseases causing extrinsic urinary tract compression.⁴⁻⁶ However, CT scan proved useful when performed on the left renal vein, as observed in case 1; unfortunately, a CT scan of the left renal vein was not performed in case 2.

In the cases herein described, we found contrasting results in the red cell morphology test; in fact, urinary red cells were isomorphic (90%) in one case and mixed in the other. The red cell morphology test has been strongly suggested for the screening of patients and regarded as very helpful for the diagnosis of “nutcracker phenomenon.”⁷ However, the role of urinary red blood cell morphology needs to be better ascertained, because no relation was found between isomorphic/dysmorphic urinary red blood cell ratio and “nutcracker phenomenon” in a larger study.³

On the contrary, our cases underline that the measurement of pressure gradient between the left renal vein and the inferior vena cava is an important tool for the diagnosis of “nutcracker phenomenon.” In fact, both cases had high pressure gradient (5 and 7 cm H₂O in cases 1 and 2, respectively); in normal conditions, the gradient is either absent¹ or lower than 3 cm H₂O.^{2,3}

Because there is not a distinctive sign, it is likely that the “nutcracker phenomenon” may not be distinguished among more frequent causes of intermittent or persistent gross hematuria. The diagnosis of “nutcracker phenomenon” is even more difficult in concomitance with other renal diseases responsible for gross hematuria. In the first case of this report, in fact, the presence of *M tuberculosis* in urine was initially misleading. However, the persistence of gross hematuria after 4 months specific therapy required further procedures that finally led to diagnosis of left renal vein hypertension. IgA nephropathy⁸ or membranous glomerulonephritis⁹ associated with “nutcracker phenomenon” was previously reported.

Another possible misleading factor may be the presence of proteinuria that may postpone the diagnosis of “nutcracker phenomenon.” Proteinuria in hematuric patients with left renal vein hypertension is caused by lysis of red blood cells in urine. It has been calculated that proteinuria can increase up to 2+ (dipstick method) or up to 1 g/24 hr when hemolysis of red cells occurs in

timed urinary specimens of hematuric patients, and that massive bleeding may elevate urinary protein concentration up to 300 mg/dL.¹⁰ In our cases, proteinuria was below 1 g/24 hr; others have reported similar values in patients with “nutcracker phenomenon” but without renal disease.^{3,8,9}

In some cases, renal biopsy^{8,9,11} was performed before the final diagnosis of “nutcracker phenomenon.” In our patients, medical history, laboratory, and radiographic findings reasonably excluded a renal parenchymal disease: long-lasting (3 years) persistent gross hematuria (case 1), urinary red cell morphology, absence of urinary casts, unilateral bleeding (from left ureter) at cystoscopy, unilateral radiographic alterations (filling defect of left renal vein, varices of left ureter). Thus, renal biopsy was not performed.

The early diagnosis of “nutcracker phenomenon” is mandatory to promptly remove the venous compression and thus to avoid complication such as the thrombosis of the left renal vein. In one patient of the current study, CT scan showed intrinsic filling defects of left renal vein attributable to parietal thrombi 3 years after the onset of gross hematuria.

Many surgical procedures are available to correct the compression of the left renal vein between the aorta and the superior mesenteric artery: Gortex graft vein interposition, nephropexy, stenting, and kidney autotransplantation.^{12,13} After surgery, gross hematuria usually ceases.^{12,13} Unfortunately, our patients did not give consent to surgery even when warned of the presence of thrombi and of the risk of complete left renal vein thrombosis (case 1).

The cases of this report show that “nutcracker phenomenon” should always be sought in the presence of gross hematuria of unknown origin. Although less invasive procedures such as Doppler ultrasonography³ or intraarterial digital subtraction angiography¹¹ are suggested as diagnostic tools, CT scan of renal venous tree and left renal retrograde venography with measurement of pressure gradient remain, in our opinion, the main procedures leading to a final diagnosis of “nutcracker phenomenon.”

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