

The Nutcracker Syndrome

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ABSTRACT

Nutcracker syndrome (NCS) is a rare condition caused by the compression of the left renal vein between the abdominal aorta and the superior mesenteric artery. NCS may present with unexplained hematuria. This case report presents a 43-year-old healthy female without any complaints who had newly-detected hematuria in urinalysis during her annual examination. Her physical examination and the whole abdominal ultrasonography failed to explain the cause of hematuria. Further investigation with contrast-enhanced upper abdominal computed tomography revealed a NCS. In unexplained cases of asymptomatic hematuria NCS should be taken into account after excluding other preliminary diagnoses.

CASE REPORT

CASE REPORT

A 43-year-old healthy female without any complaint was found to have new hematuria in urinalysis during her annual examination. Her arterial blood pressure measurement (ABPM) was: 100/70 mmHg, Pulse: 61 bpm, Height: 162 cm, Weight: 56 kg, BMI: 21.33 kg/m². Her physical examination was normal, and her abdominal ultrasonography (USG) revealed no abnormality other than minimal hepatosteatosis.

An annual follow-up was planned due to the incidental hematuria. Next year, her urinalysis showed the same abnormality, indicating persistent hematuria. On her second abdominal USG, a plump appearance was noted in the calyx structures of both kidneys and renal pelvis (Figure 1). Neither physical examination nor other laboratory tests, including routine biochemistry (kidney and liver function tests, uric acid, fasting glucose), sedimentation rate, whole blood count, and urinalysis, explained the hematuria found in the case.

With these tests and the USG, potential causes such as urinary tract infections, urolithiasis, nephrolithiasis, or anemia were ruled out. Therefore, to explain the etiology of hematuria and to investigate a possible nutcracker syndrome (NCS), a nephrology consultation followed by an upper abdominal computed tomography (CT) was further planned.

On the contrast-enhanced upper abdominal CT, the angle between the superior mesenteric artery (SMA) and the aorta was measured as 17° (Figure 2). It was noticed that the left renal vein (LRV) was compressed at this level which is called the "Beak sign," indicating the nutcracker phenomenon (NCP, Figure 2). Both kidneys were of average size and configuration, parenchymal thicknesses were normal, no dilatation was detected in the collecting systems, and both ureters were normal without a filling defect in the lumen. However, the renal hilum-aortomesenteric diameter ratio was calculated as 5.24, higher than the suggested cutoff for the NCS (Figure 3).

The remainder of the examination was unremarkable. Since the patient did not have any subjective complaints and no

accompanying laboratory findings other than hematuria were detected, no treatment was planned.

In her subsequent annual follow-up visits, the hematuria continued without any abnormality in the physical examination. Also, in the annual controls, no additional abnormality was observed in the abdomen USG. The previously detected plump appearance in kidneys and renal pelvis calyx structures continued unchanged (Figure 1). Her routine annual visits are ongoing.

DISCUSSION

Etiology & Demographics:

In 1937 an anatomist, Grant, described the position of the LRV between the aorta and SMA as resembling that of a nut between the jaws of a nutcracker [1]. In 1950, El-Sadr and Mina illustrated the first clinical report of this syndrome, but the NCS nomenclature was first used by de Schepper in 1972 [2]. The NCS is a rare disorder that may affect children or adults with an unknown cause. It is characterized by the compression of the LRV, compromising the venous drainage and subsequently causing dilatation of the LRV [3]. Despite several diagnostic criteria, the prevalence of the NCS is unknown, probably due to the variety of symptoms, including hematuria, proteinuria, flank pain, and pelvic congestion in women (dyspareunia, dysmenorrhea, chronic pelvic pain), and varicocele in men [4]. In a study of 1000 abdominal CTs with contrast, anterior NCP was detected in 4.1% [5]. It has been reported that NCS is more common in women, especially in the third and fourth decades of life, as in our case [6,7]. In addition to that, the syndrome predominantly affects female patients of all ages [8]. Affected individuals are thought to be generally tall and slim, with low intra-abdominal mesenteric and retroperitoneal adipose tissue that contributes to narrowing the angle between the aorta and the SMA [7]. Thus, patients may have symptom alleviation with weight gain. The BMI of our patient was 21.33, normal but close to the lower threshold. On the other hand, it should be emphasized that many individuals with relatively low BMI have no manifestation of NCP [8]. Also, symptoms may appear after rapid weight loss.

Clinical & Imaging findings:

In the NCS, the distinctive clinical demonstration is hematuria (either gross or microscopic) which cannot be explained by other potential etiologies. It has been considered that hematuria is caused by the rupture of the thin-walled veins through the collecting system of the left kidney [7]. Also, proteinuria detected by urinalysis may be a possible sign of the NCS, which was absent in our case. Moreover, anemia may be present due to gross hematuria, which was also missing in our patient (Table 1). Our case presented without any clinical manifestation except for an abnormal urinalysis, which is an essential part of routine laboratory testing.

Although the NCS and NCP may incorrectly be used interchangeably in the literature, the NCP appears as a radiological finding, which is the asymptomatic compression of the LRV between the aorta and the SMA [3]. On the other hand, the NCS may manifest with different complaints, mainly

hematuria and left flank pain [3]. The NCS is often an "anterior" NCS, indicating the compression of LRV between the abdominal aorta and the SMA [9]. Rarely, the NCS may also appear as a posterior NCS with the compression of the LRV between the abdominal aorta and the spinal column, indicating a retro-aortic involvement [9]. The "posterior" NCS has also been reported as around 20% of all NCSs [8].

For diagnosis on imaging, the accepted average angle between the SMA and the aorta is commonly 38°-60°, with a mean of 45°, for normal individuals in CT and magnetic resonance imaging (MRI) [6]. Other studies also reported similar values for the degree of aortomesenteric angle (AMA) for NCS diagnosis in CT [3, 7-9]. The gold-standard method for the diagnosis of NCS is venography which scores the renal vein pressure gradient. However, it is an invasive technic that is often unnecessary [4]. Therefore, Doppler USG, CT, or MRI are better choices for the diagnosis. In our case, the absence of venography or Doppler USG, which could confirm the increase in renal vein pressure gradient, is a limitation. Nonetheless, late studies suggest that CT is the first choice of diagnosis due to its better efficiency in addition to allowing an expanded evaluation of abdominal organs [9]. Therefore, in our patient, we performed a CT which demonstrated that the AMA between the aorta and SMA was slightly decreased to 17°, indicating NCS. Also, another important finding of CT for the diagnosis of NCS is the renal hilar to aortomesenteric LRV ratio of ≥ 4.9 , indicating a NCS [10]. In our case, this ratio was 5.24 supporting NCS.

Treatment & Prognosis:

The treatment of choice in NCS is controversial. It depends on the severity of the clinical presentation. Conservative management is recommended for cases presenting with mild hematuria or no major complaints [8]. Surgical treatment is usually considered for patients with severe anemia (due to severe hematuria), serious pain despite analgesic use or deterioration of renal function [11]. Our case was managed conservatively with observation because no serious symptoms were described. For medical treatment, angiotensin-converting enzyme inhibitors can be used against proteinuria, and (although controversial) acetylsalicylic acid may be used to enhance renal perfusion in NCS [8]. Our case is followed annually for NCS, her hematuria persisted without anemia or any additional symptoms, including a normal ABPM.

The prognosis of NCS depends on the presence of clinical findings. In patients requiring treatment but not treated, the NCS may predispose to thrombosis of LRV, resulting in kidney damage. Additionally, the NCS presenting with hematuria may lead to anemia results requiring blood transfusion and result in anemia-related complications [12].

Differential Diagnoses:

The most important causes of hematuria are urinary tract infection, nephro/uroolithiasis, and neoplasms in the adult population, which were excluded by laboratory and imaging tests in our case. Besides, other possible less common causes such as drug-induced hematuria, trauma, glomerulonephritis, hypercalciuria, and endometriosis were also excluded. The second most frequent symptom of the NCS is pain, either left

flank or abdominal, which was absent in our case [8]. Pelvic congestion syndrome and Loin pain-hematuria syndrome are other entities that should be considered [13,14]. Due to compression of LRV, flank pain and hematuria can also be seen in other less common causes such as pancreatic neoplasms, para-aortic lymphadenopathy, overarching testicular artery, retroperitoneal masses, lordosis, and in conditions with reduced retroperitoneal and mesenteric fat between the SMA and aorta. [12]. Pelvic congestion disease is accompanied by complaints including pelvic pain, dysmenorrhea, dyspareunia, post-coital pain, dysuria, pelvic, vulvar, gluteal, or thigh varices which were all not present in our case. Also, the CT showed no ipsilateral tortuous and dilated parauterine or gonadal veins (unilateral or bilateral). With regard to the Loin pain-hematuria syndrome, which should also be counted in the differential diagnosis of the NCS, our case was free of nausea, vomiting, or flank pain.

Conclusion:

The purpose of this case is to demonstrate the importance of the simple urinalysis and imaging to detect asymptomatic patients with NCS, which is an infrequent cause of hematuria. The NCS is an exclusion diagnosis. Therefore, firstly, one has to rule out other potential causes of hematuria. In patients without any complaint, hematuria in the simple urinalysis should alert physicians for a possible NCS, which could be confirmed with routine imaging methods such as Doppler USG, CT, or MRI.

TEACHING POINT

Nutcracker syndrome should be considered in patients with hematuria with an unknown cause. In Nutcracker syndrome, abdominal imaging reveals compression of the left renal vein, most frequently between the aorta and the superior mesenteric artery.

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FIGURES

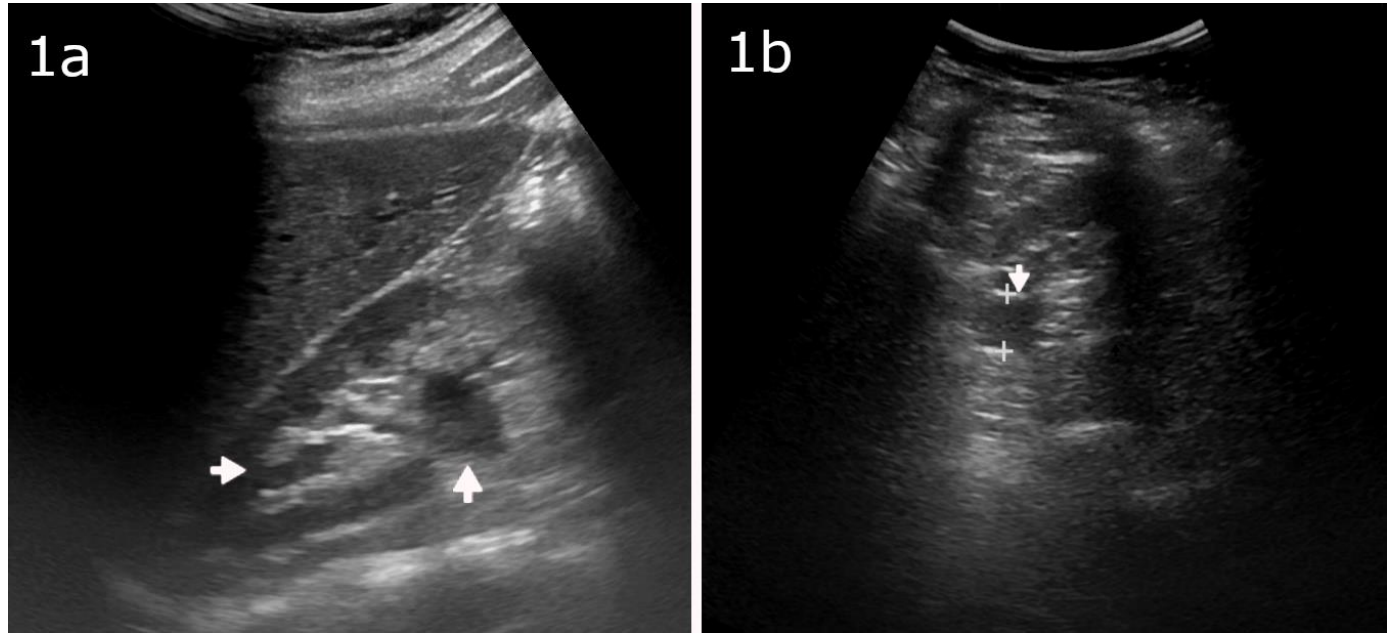


Figure 1: 43-year-old woman diagnosed with Nutcracker syndrome.

Findings: Ultrasonography demonstrates (1a) the plump appearance in the calyx structures in the right kidney (horizontal arrowhead) and renal pelvis (vertical arrowhead) on sagittal view. (1b) shows the plump appearance in the left renal pelvis on axial view.

Technique: Abdominal B-mode ultrasound with 2.5-6 MHz convex transducer showing sagittal view (1a) and axial views (1b) of the kidneys.

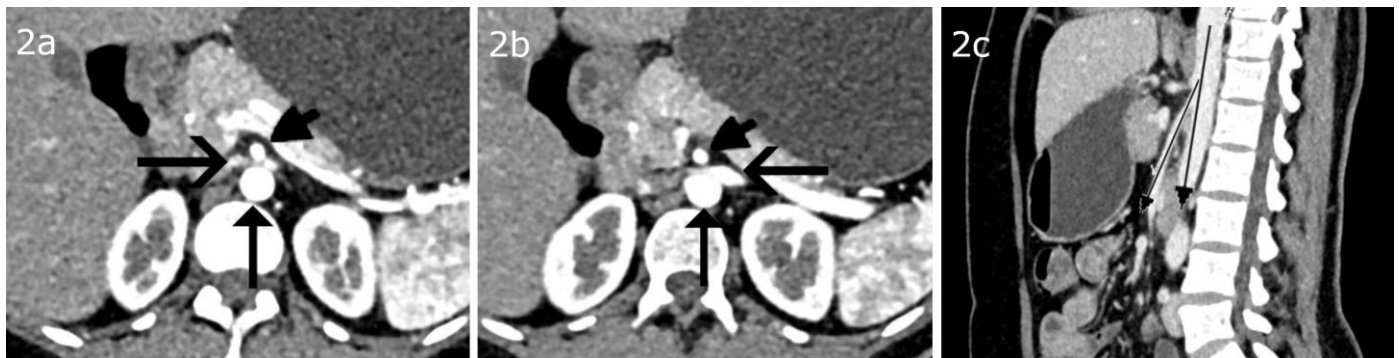


Figure 2: 43-year-old woman diagnosed with Nutcracker syndrome.

Findings: Contrast-enhanced upper abdominal computed tomography (CT) demonstrates (2a) the compression of the left renal vein (LRV, horizontal arrow) between the superior mesenteric artery (SMA, arrowhead) and the aorta (vertical arrow) on axial view. (2b) depicts the dilatation of the LRV (horizontal arrow) between the SMA (arrowhead) and the aorta (vertical arrow) on axial view. (2c) sagittal view of the abdominal CT scan. Arrows depict the aortomesenteric angle (AMA) between the SMA and the aorta. In this case, it is 17°, indicating the compression of LRV.

Technique: Contrast-enhanced CT in axial and sagittal planes. Arterial phase, slice thickness= 1 mm. 120 mA, 90 kV. Intravenous contrast: = Iohexol 350mg/100 ml.

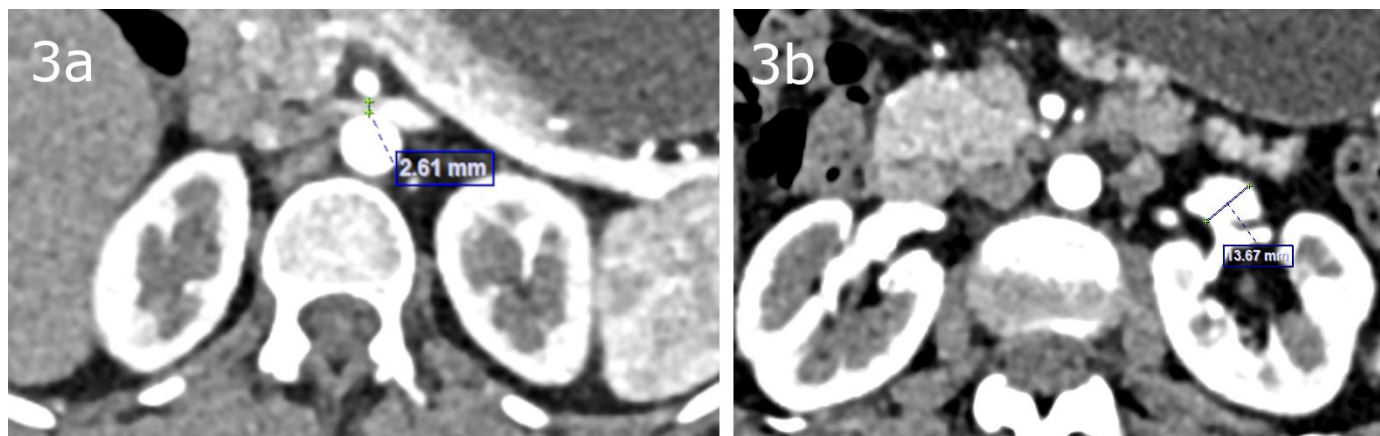


Figure 3: 43-year-old woman diagnosed with Nutcracker syndrome.

Findings: Contrast-enhanced upper abdominal computed tomography (CT) demonstrates (3a) the compression measurement of the aortomesenteric LRV (2.61mm). (3b) demonstrates the enlargement of the hilar LRV (13.67mm). The compression ratio is 5.24 indicating a NCS.

Technique: Contrast-enhanced CT in axial planes. Arterial phase, slice thickness= 1 mm. 120 mA, 90 kV. Intravenous contrast: = Iohexol 350mg/100 ml.

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Reference Range
Complete Blood Count							
Hemoglobin, g/dl	13.8	14	14.2	14.2	14.2	14.0	12.0-16.0
RBC, M/mm ³	4.8	4.9	4.9	4.8	4.8	4.7	4.00-5.20
MCV, fL	88.9	89.8	87.7	89.6	89.2	90.8	80.0-92.0
WBC, K/mm ³	6.4	8.0	7.6	5.8	9.2	5.7	4.5-11.0
Thrombocyte, K/mm ³	301	266	293	316	291	310	130.0-400.0
Biochemistry							
Creatinine, mg/dL	0.71	0.76	0.69	0.73	0.65	0.68	0.44- 1.00
BUN, mg/dL	13.80	12.80	19.50	12.80	13.10	16.80	6.00-20.00
Sedimentation rate, mm/h	22	16	14	16	13	11	0-20
Complete Urine Analysis							
Chemical analyses							
Density	1015	1015	1015	1015	1010	1015	1010-1030
Protein	Negative	Negative	Negative	Negative	Negative	Negative	<0.14
Blood, Ery/microL	250 (+++)	250 (+++)	150 (++)	150 (++)	250 (+++)	250 (+++)	Negative
Nitrite	Negative	Negative	Negative	Negative	Negative	Negative	Negative
Microscopic Evaluation							
Erythrocytes	20-25	30-35	8-10	8-10	20-25	15-20	0-3
Leukocytes	6-7	2-3	trace	1-2	trace	1-2	0-5

Table 1: Biochemical and urinalysis data of the case between first and latest follow up year. RBC, red blood cell; MCV, mean corpuscular volume; WBC, white blood cell; BUN, blood urea nitrogen.

Etiology	Unknown.
Incidence	Unknown. (But one study revealed that 1000 abdominal CTs with contrast anterior NCP was detected in 4.1%).
Gender ratio	NCS is more common in women, principally in the third and fourth decades of life. The syndrome affects predominantly female patients of all ages.
Age predilection	Patients' age can range from childhood to the seventh decade of life.
Risk factors	Slim and tall body habitus.
Treatment	Most patients are managed conservatively. If the patient is symptomatic, angiotensin-converting enzyme inhibitors may be used against proteinuria. Surgical treatment is usually considered for patients with severe anemia (due to severe hematuria), serious pain despite analgesic use, or deterioration of renal functions.
Prognosis	In most cases, (especially in children) spontaneous resolve can be seen. In patients requiring treatment but not treated, the NCS may predispose to thrombosis of LRV, resulting in kidney damage. Additionally, the NCS presenting with hematuria may lead to anemia and complications related to anemia.
Findings on imaging	CT: AMA lower than 35° with sagittal reconstruction (Beck sign). LRV diameter ratio > 4.9 (in contrast arterial and portal venous phase, axial reconstruction).

Table 2: Summary table of Nutcracker Syndrome.

	Symptoms	CT findings	MRI findings	USG findings
Nutcracker syndrome	Hematuria, left flank and abdominal pain.	AMA < 35° (in contrast arterial and portal venous phase, sagittal). The Beck angle < 35 and (hilar and aortomesenteric) LRV diameter ratio > 4.9 (in contrast arterial and portal venous phase, axial). LRV compression at the AMA portion. The beak sign of the LRV and the contrast-jetting phenomenon.	AMA <35° (in MRA, sagittal). The Beck angle < 32 and (hilar and aortomesenteric) LRV diameter ratio >4.9 (in MRA, axial). Dorsolateral torsion of the left kidney, compression and pre-stenotic dilatation of the LRV, abnormal configuration of SMA, and peri-renal or gonadal vein varices.	The ratio of the LRV diameters and peak velocities at the hilar and aortomesenteric regions > 5.
Pelvic congestion syndrome	Pelvic pain, dysmenorrhea, dyspareunia, post-coital pain, dysuria, pelvic, vulvar, gluteal, or thigh varices.	Four ipsilateral tortuous and dilated parauterine veins (at least one >4 mm) gonadal vein (>8 mm, unilateral or bilateral) Absence of obstructing mass or structural obstruction.	Retrograde caudal flow of contrast material at MRA, dilated parauterine varices. Heterogeneous or T2-hyperintensity due to slow flow, presence of an arcuate vein crossing the midline, vulvar and/or thigh varices, Polycystic ovarian configuration, absence of a structural obstruction or endometriosis.	First choice for pelvic congestion syndrome. USG helps to rule out pelvic masses or uterine problems. Retrograde flow in a dilated right or left gonadal vein (>5 mm).
Loin pain hematuria syndrome	Nausea, vomiting, flank pain, microscopic or gross hematuria.	In at least two episodes of loin pain, imaging (CT or USG) must be obtained to demonstrate an absence of urolithiasis or urinary tract obstruction.	Not visible.	In at least two episodes of loin pain, imaging (CT or USG) must be obtained to demonstrate an absence of urolithiasis or urinary tract obstruction.

Table 3: Differential diagnosis table for Nutcracker Syndrome.

ABBREVIATIONS

ABPM = Arterial blood pressure measurement
AMA = Aortomesenteric angle
CT = Computed tomography
LRV = Left renal vein
MRA = Magnetic resonance angiography
MRI = Magnetic resonance imaging
NCP = Nutcracker phenomenon
NCS = Nutcracker syndrome
SMA = Superior mesenteric artery
USG = Ultrasonography

KEYWORDS

Nutcracker syndrome; rare disease; hematuria; left renal vein compression; renal vein entrapment

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