Case Report

Nutcracker syndrome presenting as recurrent hematuria

Blessing Ose-Emenim Igbinedion, Festus Oghanina Ehigiamusoe, Stanley Ngoka[1]

Department of Radiology, University of Benin, University of Benin Teaching Hospital, [1]Department of Internal Medicine, Nephrology Unit, University of Benin Teaching Hospital, Benin, Edo, Nigeria

Abstract

Nutcracker syndrome (NCS) occurs from compression of the left renal vein between the abdominal aorta and the superior mesenteric artery. It is rare and commonly presents with hematuria, flank pain, and dysuria. A 27-year-old male with sickle cell trait presented with a 9-month history of total hematuria complicated with anemia necessitating blood transfusion. He had no overt signs of urogenital infestation, renal impairment, or trauma. Genotype was AS. Intravenous urography was normal. On cystoscopy, the bleeding was seen to be coming through the left ureteral orifice. Renal angiography showed left renal venous stasis and contrast extravasation into the upper calyces. An impression of NCS was made. Other imaging modalities (computed tomography and ultrasound) supported NCS. NCS should be suspected in cases of recurrent hematuria.

Keywords: Hematuria, nutcracker phenomenon, nutcracker syndrome, nutcracker

Address for correspondence: Dr. Blessing Ose-Emenim Igbinedion, Department of Radiology, University of Benin Teaching Hospital, Benin, Edo, Nigeria.
E-mail: blessing.igbinedion@uniben.edu

INTRODUCTION

Nutcracker syndrome (NCS) occurs from the compression of the left renal vein (LRV) between the abdominal aorta and the superior mesenteric artery (SMA) as a result of reduced angle between the abdominal aorta and SMA. Other terms for NCS are renal vein entrapment syndrome and mesoaortic compression of the LRV. Consequently upon this compression, there is left renal venous hypertension with backflow pressure and venous stasis which may lead to varicosities around the left renal pelvis and ureter and gonadal veins.[1] Such varicosities may present with congestion syndrome and varicoceles. This abnormality can be congenital or associated with left renal ptosis, reduction of perirenal fat, accentuated lumbar lordosis, pregnancy, abnormal high course of LRV, and abnormal branching of the SMA from the aorta.[2,3]

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El-Sadr and Mina were the first to clinically describe the phenomenon in the year 1950.[4-6] The prevalence of NCS is unknown. It can occur at any age; however, there is a slight increase of NCS in females and it is common in adolescents, although another peak in prevalence occurs between the 3rd and 4th decades of life.[7] It is worthy of note that most symptomatic patients are in their second decade of life.[8]

NCS can be anterior or posterior. Anterior NCS refers to compression of the LRV between the aorta and the SMA, whereas posterior NCS occurs if the LRV is compressed between the aorta and the vertebral column due to its retro-aortic position.[6] In some instances, the 3rd portion of the duodenum may be compressed by the aorta and SMA which is called SMA syndrome (Wilkie syndrome).[5] SMA syndrome may coexist with anterior NCS,[5] but such coexistence has not being seen in literature.[2] However,

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it is definite that SMA syndrome and anterior NCS are different entities.

The symptomatology of NCS is variable and can be asymptomatic even when the anatomical findings in NCS are present. In addition, there is a diagnostic dilemma which further delays early and prompt management of this condition. Consequently, a high index of suspicion should be entertained followed by necessary evaluation. We report this case of anterior NCS whose diagnosis was delayed due to poor clinical suspicion.

CASE REPORT

The patient was a 27-year-old man with hemoglobin AS trait who presented with 9-month complaints of passage of bloody urine and right flank pain of 2-week duration. He received multiple blood transfusions (amounting to a total of 15 units) at the primary care center on account of the recurrent hematuria, which resulted in anemia. The right flank pain was dull in nature, noncolicky, nonradiating, and aggravated by prolonged sitting, but relieved by rest. He was not a known hypertensive or diabetic.

On examination, he was acutely ill looking, not pale, anicteric, acyanosed, not dehydrated, and with no peripheral edema. Pulse rate was 80 beats/min and blood pressure was 120/70 mmHg. On auscultation, first and second heart sounds were present without cardiac murmurs. The abdomen was flat, soft, and moved with respiration but with right renal angle tenderness. The liver and spleen were not enlarged and the kidneys were not ballotable. Nervous system examination revealed a conscious and alert young man with no focal neurological deficit. Laboratory evaluation results are listed in Table 1.

He was reviewed at the renal unit of consultant outpatient clinic with initial assessment of hematuria from unknown cause to rule out bleeding dyscrasia/hemoglobinopathy, which may be complicated by right pyelonephritis. He was then placed on tablets augmentin for 14 days due to urinary tract infection and continued on hematinics. Abdominal ultrasound scan, chest X-ray, and intravenous urography (IVU) were normal. He was advised to do a cystoscopy and a computed tomography (CT) of the abdomen. On cystoscopy, the bleeding was observed to be arising from the left ureteric orifice which led to the suggestion of papillary necrosis. Initial CT abdomen report was normal. However, a second opinion review of the CT images by the authors led to the suspicion of a slightly distended LRV. The aortomesenteric angle (AMA) was then calculated and found to be 17.3° [Figure 1], and a diagnosis of NCS was entertained.

Renal angiography was done using GE Fluorostar™ C-arm fluoroscopy machine, 5 Fr cobra angiography catheter, and sheath. A right transfemoral artery approach was used employing single puncture Seldinger technique to insert the sheath. The cobra catheter was introduced and guided to the ostium of each renal artery after which contrast was injected to demonstrate the renal vasculature and followed to the venous phase. Venous stasis was demonstrated in

Table 1: Laboratory results of the patient

Laboratory test	Result
Urinalysis	Bloody appearance, pH of 8.0, specific gravity of 1.005, protein+++, blood+++, nitrite++
Urine microscopy	RBCs of 7–8 cells/high-power field with up to 50% of fragmented RBCs
Urine culture	*Klebsiella* species sensitive to meropenem, ceftriazone, and augmentin
Serum electrolyte/ urea and creatinine	Urea – 15 mg/dl, creatinine – 0.9 mg/dl, Na^+ – 139 mmol/l, K^+ – 3.8 mmol/l, HCO_3 – 22 mmol/l, Cl – 104 mmol/l
Full blood count	White blood cells – $5.1\times10^3/\mu L$; lymphocytes – 34.3%, monocytes – 7.9%, granulocytes – 57.7%, hemoglobin - 10.8 g/dl, hematocrit – 33.2%, mean corpuscular volume – 94.5 fl, mean corpuscular hemoglobin – 30.7 pg, platelets – $325\times10^3/\mu L$
Erythrocyte sedimentation rate	54 mm/h
Clotting profile	PT – 15.0 s (control – 14.0 s), PTTK – 28.0 s (control – 22.0 s), INR – 1.14
HIV status	Negative
Hepatitis screening	HBsAg and anti-HCV were negative
Hemoglobin electrophoresis	AS
Mantoux test	5 mm

RBCs – Red blood cells; PT – Prothrombin time; INR – International normalized ratio; HCV – Hepatitis C virus; HBsAg – Hepatitis B surface antigen; PTTK - Partial Thromboplastin Time Activated with Kaolin; AS - Sickle cell trait

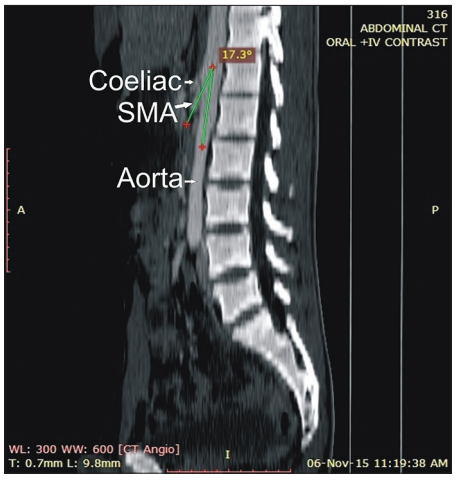

Figure 1: Sagittal reformatted computed tomography image showing the aortomesenteric angle of 17.3°

the LRV [Figure 2a]. Extravasation of contrast into the left upper renal calyces was seen in the delayed angiographic images [Figure 2b].

The patient was then referred to the cardio-thoracic and vascular surgery unit for surgical repositioning of the LRV which was planned for while on conservative management. However, the recurrent hematuria persisted. Last urine analysis and microscopy still showed significant hematuria. Serum electrolyte, urea and creatinine.

DISCUSSION

Patients with NCS can be asymptomatic. However, presentations vary and they include hematuria, flank pain (typically left sided), dyspareunia, dysmenorrhea, dysuria, varicocele, orthostatic proteinuria, orthostatic intolerance, and gonadal vein syndrome.[2,5] Hematuria is the most commonly reported symptom and it can be microscopic or macroscopic and may necessitate recurrent transfusion, especially if it is recurrent. In NCS, the hematuria is attributed to rupture of thin-walled variceal septum separating the intrarenal veins from the collecting system.[9] The rupture is due to elevated venous pressure as a result on the LRV compression and causes bleeding into the collecting system.[10] In this patient, we visualized the region where the bleeding occurred into the left renal upper calyces in the delayed venous phase of the angiography [Figure 2]. It may be the first case that the bleeding region was demonstrated on imaging. It is our belief that this bleeding site into the calyceal system acts as a pressure-releasing valve which may account for the observation that this patient does not have pronounced radiological findings, especially varices and markedly distended LRV.

Left ureteral orifice bleeding into the urinary bladder as seen during cystoscopy further helps in arriving at the diagnosis of NCS. Hematuria is reported to be exacerbated with orthostatism or exercise.[11] However in this case it is exacerbated by feeding which can be explained by the increased postprandial blood flow through the SMA to the bowels that may worsen the pinching effect in NCS. Similarly, a case of recurrent hematuria of 7 months duration in a 21-year-old woman which required repeated blood transfusion was reported by Xu *et al*.[1] Collaterals can be formed involving the tributaries of the LRV. The left gonadal vein is one such collateral and may lead to pelvic congestion with its associated complication which includes varicoceles in males. Varicocele in NCS almost always occurs on the left side and affects up to 9.5% of males.[5]

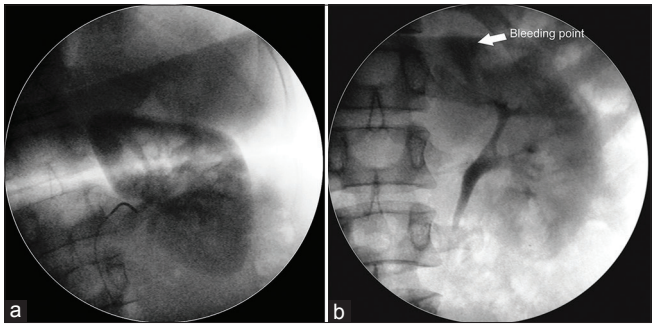

Figure 2: Delayed-phase angiographic image showing venous stasis (a); and a focus of bleeding (white arrow) at the left renal superior pole into the calyces (b).

In arriving at a diagnosis of NCS other ailments that can cause pain and hematuria has to be excluded. These differentials includes lithiasis, congenital vascular malformations, tumors, infections, parenchymal or urinary tract abnormalities and painful pelvic syndromes must be excluded.[2] Consequently to exclude all possible differentials barrage of investigations are usually ordered and the investigation request may continue until a suspicion of NCS is made. Unfortunately, algorithm for NCS diagnosis is not standardized as some patients may have anatomical characteristics without any clinical sign or symptom of NCS and may not be considered to have NCS. As a result, delay in the diagnosis occurs with attendant increased likelihood of complication that may lead to some morbidity or mortality. Early diagnosis is further worsened by there been no clear-cut criteria to diagnose NCS.

Radiological evaluation plays a pivotal role in both the diagnosis and management of NCS. Radiological investigation undertaken depends on the presentation, clinical suspicion, availability of imaging facilities and expertise. Ultrasound may demonstrate the acute projection of the mesenteric artery from the aorta, distended LRV and collaterals, as well as thin aorto-mesenteric fat tissue layer that was demonstrated in this case [Figure 3]. Doppler application may help visualize any complicating intraluminal LRV thrombus, detect waveform changes and evaluate pressure differences which are useful information in the diagnosis of NCS and in monitoring management. Sensitivity of 78% and specificity of 100% for NCS detection has been reported using Doppler ultrasound scan.[12]

CT and MRI are also useful imaging modalities which can demonstrate the anatomy and varices as well as other features and complications of NCS. The angle subtended by the SMA to the aorta can be calculated on Sagittal reformatted images called the AMA. AMA <45° calculated on CT is a useful criterion in making an

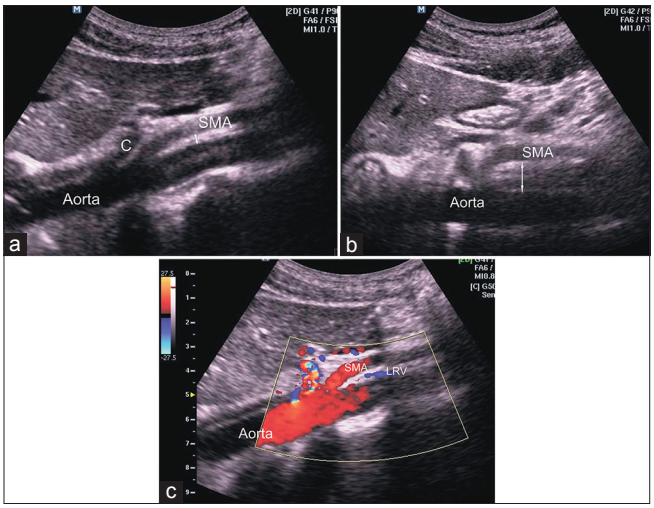

Figure 3: (a) Longitudinal ultrasound images showing the aorta, coeliac, and mesenteric arteries. The acute aortomesenteric angle and thin tissue layer between the superior mesenteric artery and aorta are appreciated; (b) Comparison with the almost right angle aortomesenteric angle projection and thicker tissue layer in another 26-year-old male patient; (c) Doppler image showing the left renal vein (blue) located between the superior mesenteric artery and aorta

impression of NCS with normal values in the range of 38°–65°.[5] IVU is usually normal in most individuals, but extrinsic compression of the ureter or renal pelvis may be seen from collateral varicosities.[11] Angiography is the gold standard and it has a dual role in both diagnosis and treatment. The bleeding point may be demonstrated as in this case report. This bleeding point may be embolized but we decided against doing so as it may open up collateral channels which may cause other complications. Contrast opacification of the calyces from the bleeding vessels may be visualized subsequently. Venous stasis and visualization of the varices are seen in the venous or delayed phase. Catheter LRV venography is also useful and may demonstrate the stasis and collateral circulation and the pressure difference between the LRV and IVC in excess of 3 mmHg suggests NCS (normal renocaval pressure gradient is 0–1 mmHg).[13]

The management of NCS ranges from conservative management to nephrectomy in very severe cases. It has been reported to resolve spontaneously in some cases, especially children and in an adult.[5] Consequently there should be some restraints in rushing to aggressive management. Hence conservative management should be attempted first while other treatment options should be entertained only if it fails or if the symptoms are severe or the condition persists/deteriorates. The patient was advised to gain weight with the hope that it will increase the aorto-mesenteric tissue bulk which will aid elevation of the aorta with consequent increase in the AMA. The patient in this case report could not do so as the hematuria was worsened by meals. Management options includes endovascular interventions (external and internal stenting), left renal transposition, renal autotransplantation of the left kidney, venolysis and anterior nephropexy, renal vein bypass or interposition grafting, renocaval reimplantation, autotransplantation.[14] There are various reasons to opt for any of these treatment options such as patient's preference, availability of treatment option and skill/man-power. In this case report the patient refused renal vein stenting due to the potential complication of shunt migration and opted for surgical management instead.

CONCLUSION

A high index of suspicion is required in making a diagnosis of NCS especially in patients with recurrent hematuria (and right flank pain rather than left which reduces the chances of considering NCS). Multiple investigations may be required in cases of NCS to make the diagnosis and the treatment options are variable.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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