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Review Article

Nutcracker syndrome: a review

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ABSTRACT

Left renal vein (LRV) entrapment is an anatomic condition characterized by extrinsic compression of the renal vein and consequent impaired inferior vena cava (IVC) outflow. Nutcracker syndrome (NCS) can be caused by compression of the LRV between the aorta and the superior mesenteric artery or by compression of LRV between vertebral bodies and the aorta. The most common presentations in NS include pelvic or left flank pain, hematuria, gonadal varices, thus the hallmark manifestations of NCS may be related to renal venous congestion and increased pressure within the venous structures. Computed tomography, magnetic resonance imaging and doppler ultrasonography are reasonable imaging studies in patients with suspected NCS, but invasive evaluation with catheter venography and pressure measurement is often required to the definitive diagnosis. For now, it is not possible to standardize a treatment modality, although the trend towards endovascular management is clear; therapeutic strategies with open surgery should not be lost for those cases that correspond to this.

Keywords: NCS, Nutcracker phenomenon, LRV entrapment, LRV compressions

INTRODUCTION

Left renal vein (LRV) entrapment is an anatomic condition characterized by extrinsic compression of the renal vein and consequent impaired IVC outflow, with demonstrable dilatation of the hilar region and narrowing of the LRV. the para-aortic region of the renal vein.[1] NCS can be caused by compression of the LRV between the aorta and the superior mesenteric artery (SMA) in this case it will be appropriate to speak of anterior NCS, or by the rarer compression of the LRV between vertebral bodies and the aorta, posterior nutcracker or pseudo-NCS.[2] NCS was first described by grant in 1937 also known as LRV entrapment syndrome.[3] The LRV, being between the aorta and the superior mesenteric artery SMA, resembles a walnut that is between the extensions of a nutcracker.[4] This condition leads to stenosis of the aorto-mesenteric region of the LRV, with dilatation of the distal portion of the vessel.[3]

Although in some cases the term is used interchangeably with the nutcracker phenomenon, it is essential to know that these changes in the aortomesenteric anatomy do not always lead to clinical symptoms, so the term NCS should be limited to patients who present clinical signs and symptoms characteristics such as hematuria, proteinuria, flank pain, pelvic pain, congestion in women, and varicocele in male patients, in addition to diagnosis by imaging studies of the aortomesenteric anatomy associated with the syndrome.[5,6] On the other hand, the findings by ultrasound and/or tomography in asymptomatic patients where a dilation of the LRV is visualized can be considered as a normal anatomical variant (Figure 1).[7] There are different conditions that can result in compression of the LRV such as pancreatic neoplasms, para-aortic lymphadenopathy, retroperitoneal tumors, abdominal aortic aneurysms, superior testicular artery, strangulation of the fibro lymphatic tissue between the aorta and SMA, high origin of the LRV, decreased

retroperitoneal / mesenteric fat and pregnancy with a gravid uterus compressing the renal vasculature.[3] Even rarer etiologies of LRV compression include severe lordosis intestinal malrotation and fast weight loss.[8-10]

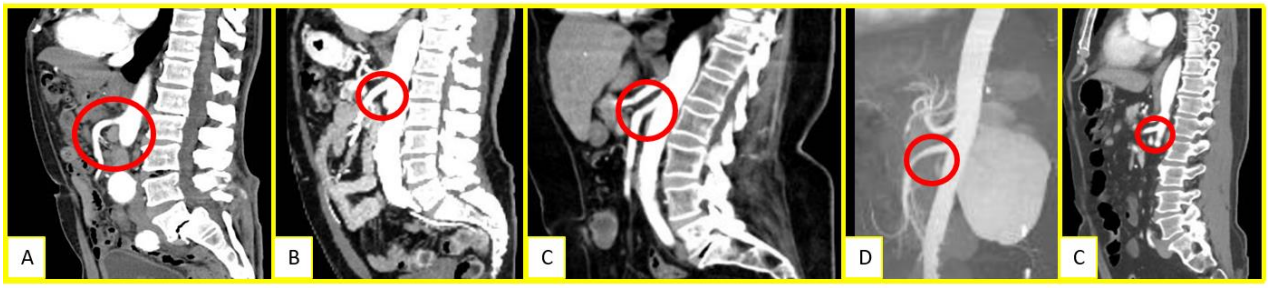

Figure 1 (A-D): Normal variants in the aortomesenteric angle (red circle).

EPIDEMIOLOGY

Buschi et al reported up to a 40% presentation of NCS in patients with hematuria, no association by age was found, so it can occur in any age range, although a higher prevalence has been reported between the second and third decade of life equally prevalent among both sexes.[7,11,12] Due to the variety of diagnostic criteria, the exact prevalence is unknown and it is considered underdiagnosed, as it is often pauci-symptomatic or completely asymptomatic.[1,13]

NCS pathophysiology

The LRV is between 6 and 10 cm long, and receives blood from the ipsilateral adrenal gland, gonadal vein(s), and lumbar veins. Along its course (in most cases), the LRV passes inferiorly to the SMA and anterior to the aorta. Anatomic variants of this vascular configuration must be taken into account, since these vessels have valves that prevent blood reflux, allowing the flow only toward the IVC. Incompetent valves or absent or ectopic venous outlets may increase the pressure within the LRV favoring the reflux.[1] Elevated pressure in the stenosed LRV as a consequence of aortomesenteric clamping results in the formation of venous reflux, venous hypertension, and thus variceal formation within the renal collecting system, the periureteral and peri pelvic varices swell and rupture, which become it manifests depending on the stage with microhematuria or macrohematuria.[14,15]

The pressure gradient between the LRV and the IVC is normally less than 1 mmHg but can increase to +3 mmHg in cases of decreased aorto-mesenteric angle which would increase the pressure directly in the LRV and therefore within the nephron, this venous hypertension is thought to induce a subclinical immune cascade in the vessel wall and predisposes to greater local release of norepinephrine and angiotensin II when standing.[16-18] This exaggerated physiologic response to abrupt changes in renal hemodynamics is thought to cause orthostatic proteinuria and severe systemic hypertension has been reported in association with NCS.[19-21] Concomitant NCS has been described in up to 18% of patients with pelvic venous congestion syndrome.[22]

ETIOLOGY

NCS is suspected to correlate with a low body mass index (BMI), with some authors suggesting that symptoms may resolve with increasing BMI, one possible explanation is that the lack of mesenteric fat removes support and decreases the SMA angle and otherwise lifts the intestine and raises the SMA angle.[13,23] It is rarely called anterior NCS to differentiate from a less common variant, posterior NCS, which occurs in the presence of a retro-aortic LRV compressed by the spinal column posteriorly and the aorta anteriorly and produces similar symptoms.[13,24,25] Combined (anterior and posterior) NCS, as a result of a circumaortic or duplicate LRV with both components stenosed by extrinsic compression, has also been reported (Figure 2).

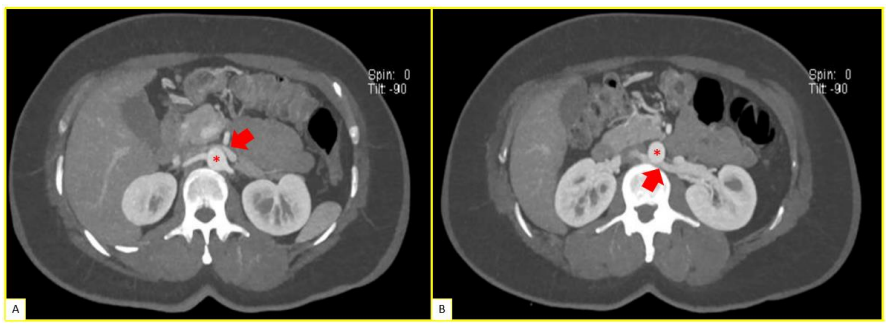

Figure 2 (A and B): Aorta with an asterisk and the red arrow indicates anterior compression of LRV between aorta and superior mesenteric artery. (The beak sign). Red arrow indicates posterior compression of LRV, between aorta (asterisk) and vertebral body.

The angle between the SMA and the aorta should be less than 45º in a sagittal cut, and authors such as Polguj et al. consider that an angle less than 35º is sufficient for a definitive diagnosis due to initial impingement and the acute angle with the origin of the SMA (Figure 3).[27,28] The rapid increase in height and development of the vertebral bodies at puberty can result in a narrowing of the aortomesenteric angle.[29]

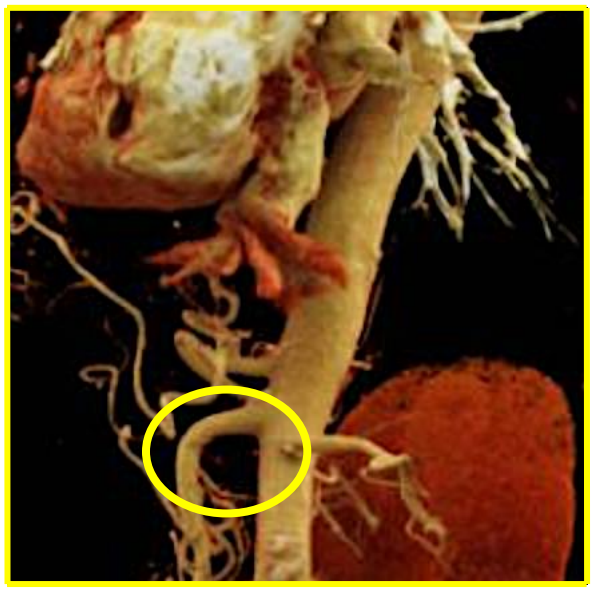

Figure 3: Aortomesenteric angle within yellow circle.

Anterior NCS

The anterior presentation is the most common form and corresponds to compression of the LRV between the aorta and superior mesenteric artery.

Posterior NCS

There are very few cases reported less than 30 in all medical literature, it occurs when the renal vein, which can be retro aortic or circumaortic, is compressed between the aorta and the vertebral bodies (Figure 2).

Clinical features

The hallmark manifestations of NCS (hematuria, proteinuria, and flank/pelvic pain) they may be related to renal venous congestion and increased pressure within the venous structures. The most common presentations in NCS include pelvic or left flank pain, hematuria, gonadal varices.[2,3,30,31] Isolated left-sided hematuria, identified on cystoscopy as hematuria of the left ureteral orifice only, supports the diagnosis.[32]

DIAGNOSIS

Computed tomography (CT), magnetic resonance imaging (MRI), and Doppler ultrasonography (DUS) are reasonable imaging studies in patients with suspected NCS, but invasive evaluation with catheter venography and pressure measurement is often required to the definitive diagnosis.[12] A study carried out by Kim et al demonstrated that an aortomesenteric angle of less than 39º in the sagittal plane has a sensitivity of 92% and a specificity of 89% in patients with symptoms of NCS in comparison with the measurement of the pressure gradient of the LRV and vena cava by venography.[33] The diagnosis of NCS may include imaging results such as DUS, real time DUS has a high sensitivity and specificity, of 69-90% and 89-100%, respectively or CT, MRI, phlebography, IVUS. Where DUS is not diagnostic, axial imaging may be required; both CT and MRI can demonstrate compression of the LRV in the fork formed by the SMA and abdominal aorta, gonadal vein distension, and pelvic congestion. The most specific finding with CT for NCS was a LRV diameter ratio (hilar to-aorto-mesenteric ratio) >4.9 (specificity 100%). However, the highest diagnostic accuracy observed in axial CT images is “the beak sign” with abrupt narrowing of the LRV at the SMA is reported to have a sensitivity of 91.7% and specificity of 88.9% (Figure 2).[3,34] Cross-sectional imaging with CT and MRI relies on vessel diameter and, to a lesser extent, SMA angle to identify pathologic narrowing of the LRV. A normal aorta-to-SMA angle is between 45 and 90 degrees. An angle of 35 degrees in sagittal dimension suggests NCS (Figure 3).[27]

Although tomography is a non-invasive technique, it is not exempt from the risk of allergy to the contrast medium and radiation, so the use of MRI can be an excellent alternative with similar results. The gold standard for NCS is considered to be the use of phlebography (specificity 62%), measurement of the pressure gradient between LRV and IVC (+3 mmHg diagnostic of NCS), or with the use of intravascular ultrasound (specificity 90%).[30, 35]

Conservative treatment

The treatment of NCS remains a controversial issue, in cases that present with mild hematuria or with mild and tolerable symptoms, it has been suggested as a recommendation to maintain conservative management.[36] Since in individuals under 18 years of age or who are still growing, due to the fact that mesenteric fat reserves can increase, it is possible to resolve the aortomesenteric clamping in approximately 30% of these patients and complete resolution of symptoms in 24 months.[36,37]

SURGICAL TREATMENT

Open surgery

The first surgery reported on a case of NCS dates from 1974 where Pastershank operated on a 34-year-old male with hematuria and flank pain. The surgery he performed consisted of releasing the fibrous entrapment that compressed the LRV between the aorto-mesenteric angle, the patient evolved asymptomatic in a two-year follow-

up.[38] Open surgery also considers transposition of the LRV and renal auto transplantation, due to which transposition of the LRV involves excision of the vessels at the IVC junction with reimplantation distal to the SMA by means of a transperitoneal approach on the midline, carries the risks of paralytic ileus, hemorrhage and venous thrombosis mainly.[35,39,40] Renal auto transplantation implies a greater approach with increased trans-surgical and post-surgical risks of nephrectomy and lower renal transplantation or in the right iliac fossa.[11] Other surgical interventions include proximal testiculariliac-saphenous anastomosis involving the use of the saphenous vein as a conduit to link the testicular and iliac veins, gonado-caval bypass, peri-pelvic varicosity excision and renocaval venous bypass.[4,14,35,41]

Laparoscopic surgery

The literature on laparoscopic surgery in NCS is largely limited to case reports; these include laparoscopic spleno-renal venous bypass and laparoscopic LRV-IVC transposition.[42] Laparoscopic auto transplantation was first performed in 1995 and within a decade became common practice.[43]

Endovascular stenting

Use of endovascular stenting (Figure 4) is not free of risks such as incorrect stent placement, stent migration, partial displacement of the stent towards the IVC, so it is of great importance to determine the appropriate size of the stent. Other less common complications include stent embolization, in-stent restenosis, and thrombosis. These complications are mainly attributed to the type and size of the stent and the degree of experience of the operator in performing this procedure.[3,30,44-47] Over the years, more successful cases of NCS successfully treated with EVS have accumulated and trend is very clear as treatment modality of choice since it generally avoids the additional requirements of open surgery; there is no risk of anastomosis/dissection surgery and the large difference in surgical time associated with adjacent complications.[12,45,48] However, there clear disadvantages due to antiplatelet and anticoagulation required after stent placement and that may limit the selection of some patients. Recommended regimen consists of 3 days of low molecular weight heparin, 30 days of oral clopidogrel, and 3 months of aspirin.[3]

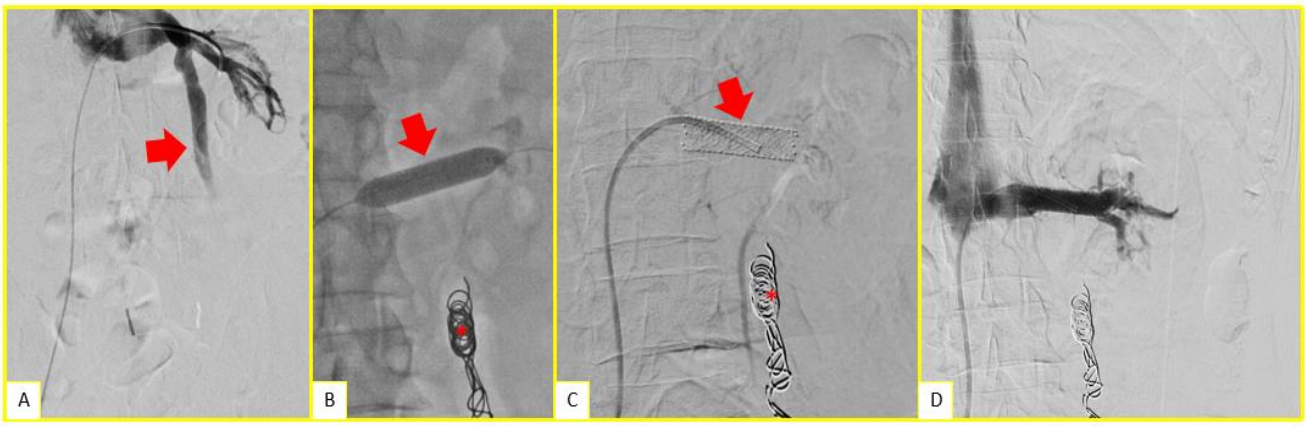

Figure 4 (A-D): Reflux into the gonadal vein in arrowhead. Asterisk embolization with gonadal vein coils and LRV angioplasty (red arrow). Post stent and coil placement control.

CONCLUSION

It is crucial to carry out a complete study protocol in patients with characteristic symptoms of NCS for an assertive early diagnosis and treatment, as well as to evaluate the need for screening tests to detect microhematuria and/or asymptomatic stenosis by imaging studies. For now, it is not possible to standardize a treatment modality, although the trend towards endovascular management is clear; therapeutic strategies with open surgery should not be lost for those cases that correspond to this.

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