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Review

Nutcracker syndrome: A rare cause of left flank pain that can also manifest as unexplained pelvic pain

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ABSTRACT

Nutcracker syndrome (NCS) is symptomatic unilateral renal venous hypertension due to compression of the left renal vein between the superior mesenteric artery and aorta (anterior NCS) or between the aorta and spine (posterior NCS). The left ovarian or spermatic vein empties into the left renal vein and is an additional site of venostasis in about half the cases of NCS. The presenting symptom of NCS in about half the cases is atypical left flank pain suggesting a disorder of the lower ribs or thoracolumbar spinal junction, particularly as the pain worsens with standing and increased lumbar lordosis. NCS may be suggested by any combination of the following manifestations: hematuria, which is often only microscopic; orthostatic proteinuria; varicocele and infertility; dyspareunia and other gynecological symptoms; varicose veins in the pelvis, buttocks, or upper thighs; orthostatic hypotension and fatigue; and abdominal pain. Narrowing of the left renal vein on imaging studies is required but far from sufficient to establish the diagnosis. Several converging clinical findings and a marked pressure gradient between the left renal vein and inferior vena cava must be present also. Urological procedures and vascular surgery are being superseded by endovascular stenting with or without simultaneous treatment of the acquired gonadal vein insufficiency by embolization.

Nutcracker syndrome (NCS) is the set of clinical manifestations of venostasis induced by left renal vein (LRV) compression (nutcracker phenomenon) between the superior mesenteric artery (SMA) and aorta (anterior NCS) (Fig. 1) or between the aorta and spine when the LRV is retroaortic (posterior NCS syndrome [1]). In about half the cases, pelvic venostasis develops due to distension of the left ovarian or spermatic vein, which empties into the LRV (Fig. 2). The azygos and neighboring lumbar veins may also be distended [2], contributing to patterns of pain that may result in rheumatologist visits.

NCS was first described in 1950 and is well known to urologists and nephrologists given its impact on the left kidney (hematuria, proteinuria, and orthostatic hypotension). Increasing the awareness of NCS among rheumatologists would be useful, as the symptoms often lead to diagnostic wanderings for many years. Thus, atypical left flank pain often suggests an abnormality at the thoracolumbar junction (e.g., Maigne syndrome or ilioinguinal neuralgia) or lower ribs (e.g., disorders of the costovertebral joints or rib cartilage dislocation) or leads to a wastebasket diagnosis of neuropathic pain [3]. Patients may also experience buttock or thigh pain, which may lead to a mistaken diagnosis of disk disease.

1. Anatomy

The LRV courses in front of the aorta to the inferior vena cava (IVC), behind the SMA and third portion of the duodenum. As the IVC is in the right side of the abdominal cavity, the LRV is considerably longer (6–10 cm) than the right renal vein (Fig. 1). Afferents to the LRV include the left adrenal vein, left gonadal vein (ovarian or spermatic vein), ureteral vein, second lumbar vein and, in some individuals, third lumbar vein (Fig. 1). These veins typically have anti-reflux valves (ostial, inconsistent), whose efficiency may be impaired in the event of LRV hypertension [4] or after multiple pregnancies.

NCS correlates strongly with a low position of the liver and pancreas, at the level of the LRV [5]. In a CT study, the liver and pancreas were visible at the level of the LRV in 88% of 25 patients with NCS versus only 5% of patients with hematuria due to other causes; only 4% of patients with NCS had neither the liver nor the pancreas visible at the LRV level, compared to 80% of patients with other diagnoses [5]. Presence of the liver and pancreas at the LRV level

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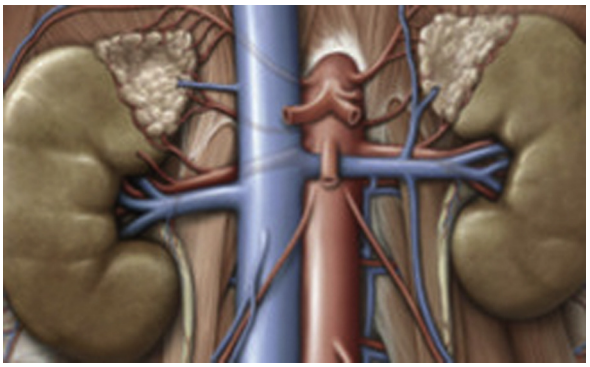

Fig. 1. Differences between the left and right renal veins. The renal vein is considerably longer on the left than on the right. Its course toward the inferior vena cava runs in front of the aorta and behind the superior mesenteric artery, which may put pressure on it. Another difference is that the left renal vein receives the left adrenal vein and, more importantly, the left gonadal vein (ovarian or spermatic vein), as well as veins draining the lumbar veins.

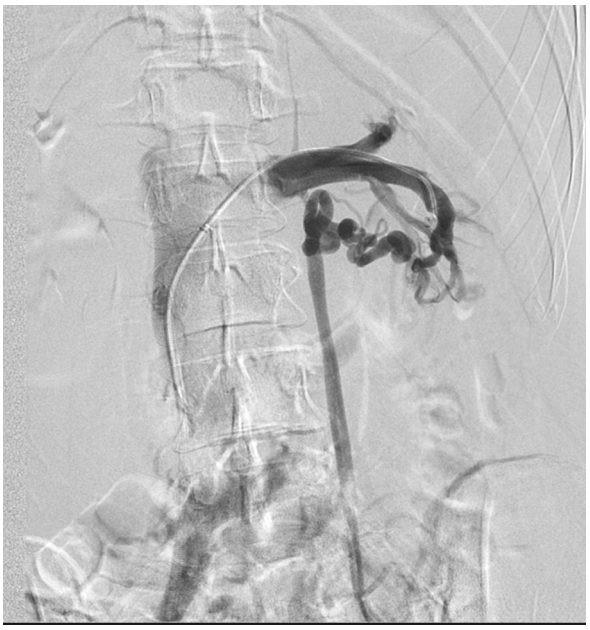

Fig. 2. Reflux into the ovarian vein during a retrograde injection into the left renal vein (selective venography) in a patient with nutcracker syndrome.

may reflect an unusually high position of the LRV origin, which may promote entrapment of the vein between the SMA and aorta.

2. Other anatomic variants possibly associated with nutcracker syndrome

LRV duplication with one vein coursing in front of, and the other behind, the aorta may result in concomitant anterior NCS and posterior NCS [6]. A horseshoe kidney or ectopic situation of the ovarian or spermatic veins may also cause LRV entrapment [2]. Right-sided NCS has been reported in a very small number of patients [7], most of whom had an aberrant position of the IVC in the left side of the abdominal cavity.

3. Non-anatomical factors that promote the development of symptoms

Constitutional leanness or marked weight loss are common in patients with NCS, reflecting the narrower space between the SMA and aorta in the absence of intraabdominal fat [8]. Marked lumbar lordosis and physical activity also promote LRV entrapment, raising diagnostic challenges for the rheumatologist [9].

Any situation associated with increased flow and pressure in the caval network (and to a lesser extent the portal vein) may contribute to the development or exacerbation of NCS. Retrograde venous blood drainage occurs through retroperitoneal collaterals to the ovarian or spermatic vein, pelvic venous network and, finally, IVC. Venostasis in the pelvic network is more a consequence than a cause of NCS but can exacerbate the symptoms. The female predominance of adulthood NCS may be related to impaired gonadal vein function caused by pregnancy [10]. During pregnancy, right-sided NCS may develop due to compression of the right renal vein by the gravid uterus [2]. However, NCS is more often diagnosed during the postpartal period than during pregnancy.

A single case of NCS due to an aortic aneurysm below the SMA has been reported [11]. All the causes of extrinsic renal vein compression can induce secondary NCS. Examples include pancreatic cancer, retroperitoneal tumors, and paraaortic lymphadenopathy [2].

4. Clinical manifestations

Symptoms (particularly hematuria) may develop in early childhood or later in life. They may be triggered by thrombosis of the LRV [12] or of the abdominal and pelvic venous network. The age at diagnosis varies considerably, from early childhood to 70 years of age, with two peaks, one before 10 years and the other between 20 and 30 years of age [13].

4.1. Hematuria, usually microscopic, less often macroscopic

Hematuria may be the presenting symptom of NCS and is usually microscopic. Macroscopic hematuria occurs in only one-fifth of cases [2] and is usually intermittent. The blood loss may be sufficient to induce anemia. Hematuria is not consistently present. Thus, in a retrospective study of 23 children and adolescents (mean age, 12 years) with imaging findings typical for nutcracker phenomenon, of the 17 symptomatic patients, 2 had microscopic and 9 macroscopic hematuria absent in 6 patients [14]. Hematuria triggered by exercise is highly suggestive of NCS [15]. Cystoscopy performed during a period with hematuria shows that the blood comes only from the left ureter. Intermittent hematuria coinciding with intermittent left flank pain may mistakenly suggest renal lithiasis. Another pitfall consists in ascribing the symptoms of unrecognized NCS to ureteropelvic junction obstruction on the same side or on the right side [16].

4.2. Orthostatic proteinuria

Standing can induce proteinuria, which may be massive (over 400 mg/dL after standing for at least 15 min) [7,17]. The mechanism involves exacerbation of the hematuria during standing with red blood cell lysis within the urinary collecting system [2]. Technetium-99m-labeled albumin scintigraphy has been suggested as a sensitive means of detecting NCS in children [18]. However, this test was positive only in children with macroscopic hematuria or orthostatic proteinuria in excess of 1 g/g of creatinine [18].

4.3. Varicocele and infertility

Varicocele is among the manifestations of NCS (2 of 11 adolescents in one study [14]). Anastomosing the spermatic vein to the