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Case Report

Diagnosis of Wilkie's Syndrome Associated with Nutcracker Syndrome: A Case Report and Literature Review

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Abstract: Superior mesenteric artery (SMA) syndrome or Wilkie's syndrome is a vascular compression disorder that causes abnormal compression of the third portion of the duodenum by the SMA. It has a low incidence rate, higher in young women, and is rarely associated with the Nutcracker phenomenon: a condition of compression of the left renal vein between the SMA and the aorta, which manifests as pain in the left flank and pelvis. Here we report the case of a 54-year-old woman with a history of repeated episodes of abdominal pain caused by the Nutcracker syndrome and Wilkie's syndrome.

Keywords: diagnosis; treatment; imaging; syndromes

1. Introduction

Superior mesenteric artery (SMA) syndrome is a rare disease in which, due to a lack of retroperitoneal fat, the third portion of the duodenum is compressed between the abdominal aorta and the SMA. Also known as Wilkie's syndrome, SMA syndrome is characterized by a group of symptoms that could mimic anorexia nervosa and functional dyspepsia: nausea, vomiting, "stabbing" postprandial abdominal pain, bloating, heartburn, and reflux. Over time, this can lead to a reduced caloric intake and weight loss, with a further reduction of the retroperitoneal fat and a consequent increase in duodenal compression, creating a vicious circle. The precise incidence of Wilkie's syndrome remains uncertain due to potential under- or over-diagnosis, but recent studies estimate it to be approximately 0.013%-0.3% among the general population [1]. When there is a suspicion of bowel obstruction, especially in the context of abundant weight loss, both these syndromes should be considered for differential diagnosis despite their rarity, especially considering their associated morbidity and mortality. Wilkie's syndrome is usually diagnosed via computed tomography (CT) scanning, which makes it possible to evaluate the SMA-aorta angle (normal values: 38°-65°) [2]. Using this method, Unal et al. reported a cut-off value at 22° on the SMA-aorta angle and at 8 mm on a distance, with 42.8% of sensitivity and 100% of specificity, respectively [3]. The barium X-ray examination, Wilkie's syndrome is characterized by some pathognomonic features. In particular, this condition presents dilatation of the first and second parts of the duodenum with or without gastric dilatation, abrupt vertical or oblique compression of the third part of the duodenum, reverse flow of the contrast liquid in the proximity of the obstruction, significant delay (4-6 hours) in gastroduodenal transit, and relief of obstruction after postural changes [4]. Nutcracker syndrome

(NCS) is a rare disease characterized by an extrinsic compression of the left renal vein (LRV) between the aorta and SMA. This leads to impaired blood flow and congestion, and, thus, to a dilation of the first part of LRV [5]. There are two types of NCS: the anterior, the most common, in which there is a compression of LRV between the abdominal aorta and SMA; and the posterior, which occurs when the retro-aortic or circum-aortic renal vein is compressed in the narrow gap between the aorta and the vertebral body [6]. The prevalence of NCS is still unknown, due to the variability of its symptoms and the absence of agreed-upon diagnostic criteria, but it is reported a higher incidence rate in female patients [7]. The pathologies and conditions associated with NCS are pancreatic neoplasms, para-aortic lymphadenopathy, retroperitoneal tumor, abdominal aortic aneurysm, overarching testicular artery, strangulating fibro lymphatic tissue between the aorta and SMA, high disposition of LRV, left renal ptosis resulting in the stretching of LRV over the abdominal aortae lordosis, reduced retroperitoneal and mesenteric fat, pregnancy with a gravid uterus compressing the renal vasculature [8]. NCS is clinically characterized by flank and abdominal pain, varicocele, fatigue, and orthostatic intolerance [9]. Retrograde venography, which measures the renal vein pressure gradient, is the gold standard in NCS diagnosis. However, its invasive nature often makes it a secondary option. Usually, diagnostic workup starts with a Doppler ultrasound (US) of the renal veins, which can describe the compressive process caused by SMA. CT and magnetic resonance imaging (MRI) should be considered as additional methods. Diagnostic criteria for NCS include the presence of a venous pressure gradient between the LRV and the inferior vena cava ≥ 3 mmHg, a maximum flow velocity five times higher than normal values in the LRV passing the SMA compared to the renal hilum, CT angiography or MRI angiography showing an angle between the aorta and the SMA of less than 45° [10]. However, the coexistence of both these two conditions can lead to difficult diagnostic and therapeutic management. For this reason, we report the case of a patient with Wilkie's syndrome combined with Nutcracker syndrome.

2. Case Report

This is the case of a 54-year-old woman with a body mass index of 23.2 kg/m^2 and a history of sub-continuous epigastric pain, not related to meals, radiating to the back, with associated retrosternal heartburn, nausea, and frequent belching for which she took antacids and prokinetics, with partial benefit. She underwent an esophagogastroduodenoscopy to have two hyperplastic gastric polyps removed. In addition, a diagnosis of diffuse atrophic gastritis with high titer anti-parietal cell antibodies (1:640) was made. Subsequently, she underwent a cholangio-MRI with no evidence of dilation of the intra- and extra-hepatic bile ducts or endoluminal stones. However, due to the persistence of symptoms, a cholecystectomy was performed. Postoperatively, the patient presented recurrent episodes of vomiting and an abdominal CT scan showed fluid overdistension of the stomach and abdominal adhesions, leading to a viscerolytic surgery. However, after discharge, abdominal discomfort persisted, though more mildly, and the patient was admitted to our center. A complete blood count with no evidence of laboratory parameters alterations, and subsequently, an upper gastrointestinal (UGI) series and a contrast-enhanced abdominal CT with contrast medium were performed. The UGI series showed a slowed-down progression of the contrast medium, which stagnated at the level of the third duodenal portion (Figure 1).



Figure 1. Antero-posterior projection of the UGI series showed a slowed gastric emptying time in later scans.

The diagnosis of Wilkie's syndrome (Figure 2) and NCS (Figure 3) was further confirmed via CT scan, with evidence of a significant restriction of the third duodenal portion as well as a compression with proximal dilatation of LRV.

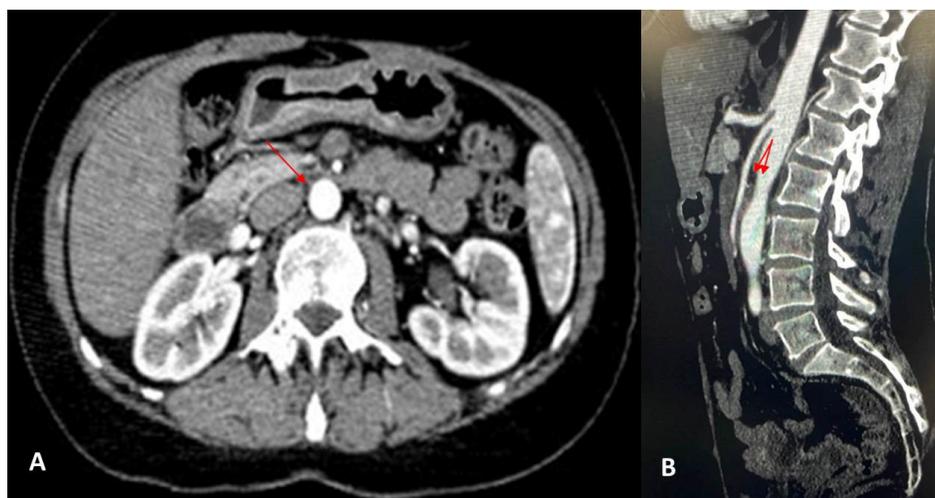


Figure 2. (A) Contrast-enhanced CT scan in axial projection showed the narrowing of the third duodenal portion between the aorta and the SMA, as indicated by red arrow (aorto-mesenteric distance of approximately 3 mm). (B) Contrast-enhanced CT scan in sagittal projection showed the narrowing of the third duodenal portion between the aorta and the SMA, with reduction of the aorto-mesenteric angle of approximately 13° , as indicated by red arrow (normal values: $28-65^\circ$).

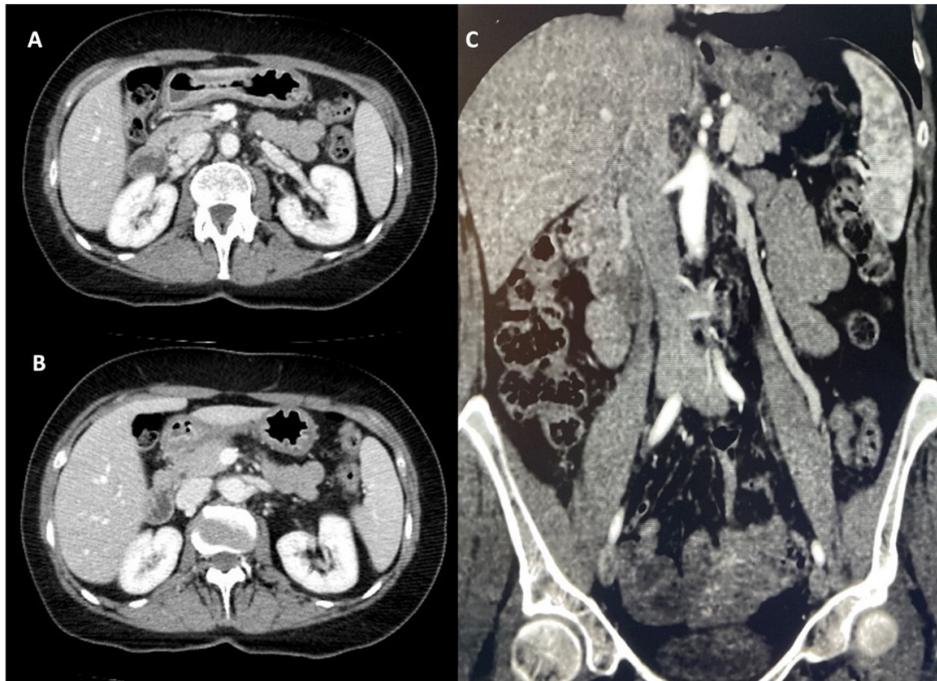


Figure 3. (A and B) Contrast-enhanced CT scan, in axial projection, showed the compression of the LRV. (C) Reversal flow from the left gonadal vein in a coronal projection.

Subsequently, the patient started a fodmap-free diet in combination with a treatment of trimebutyn maleate 150mg thrice a day, simethicone 80mg twice a day, and probiotic tablets once a day. This resulted in an improvement but not a reversal of the symptomatology due to the patient's poor therapeutic and alimentary compliance. Actually, considering the persistent symptomatology, and in particular persistent abdominal pain, the patient is under evaluation for a possible surgical approach.

3. Discussion

Considering the potentially associated life-threatening complications such as acute and chronic pancreatitis, severe malnutrition, duodenal and gastric ulcers, pneumoperitoneum and pneumomediastinum, Wilkie's syndrome and NCS should always be taken into consideration in differential diagnosis in case of patients with obstructive bowel symptoms. Both syndromes, although well described in the literature, are rare clinical pictures, usually presenting alone, and their coexistence is rare. Evidence described in the literature are summarized in Table 1.

Table 1. Summary of the different studies regarding the co-existence of Wilkie's syndrome and NCS.

Reference	Patient	Clinical manifestations	Diagnosis	Treatment
Barsoum <i>et al.</i> , 2008 [11]	29-year-old female	Early satiety and post-prandial epigastric abdominal pain	CT Upper GI gastrografin	Enteral nutrition
Vulliamy <i>et al.</i> , 2013 [12]	55-year-old male	Vomiting, epigastric pain and bloating	CT	N.A.

Inal <i>et al.</i> , 2014 [13]	28-year-old male	Cachexia and intermittent abdominal pain	CT	Enteral nutrition
Alenezy <i>et al.</i> , 2014 [14]	17-year-old male	Abdominal pain and intermittent vomiting	CT	Fluid and electrolytes replacement and nasogastric tube decompression
Nunn <i>et al.</i> , 2015 [15]	19-year-old female	Severe epigastric pain associated with emesis and anorexia	CT	Enteral nutrition
Iqbal <i>et al.</i> , 2016 [16]	62-year-old male	Cachexia	CT	Enteral nutrition
Heidbreder; 2018 [17]	20-year-old female	Severe left flank and lower left quadrant pain, abdominal pain, nausea, and vomiting	CT	Roux-en-Y duodenojejunostomy and LRV transposition
Al-Zoubi; 2019 [18]	38-year-old female	Intermittent left-sided loin pain	CT	LRV transposition
Shi <i>et al.</i> , 2019 [19]	32-year-old female	Severe bloating, epigastric pain, left flank ache, nausea and occasional vomiting	CT	Fluid resuscitation with parenteral and enteral nutritional support, plus mosapride citrate dispersible tablets 5 mg thrice a day
Diab <i>et al.</i> , 2020 [20]	18-year-old male	Crampy post-prandial abdominal pain associated with bilious vomiting, and signs of varicocele	CT	Regular assumption of a liquid diet
Lin <i>et al.</i> , 2020 [21]	15-year-old male	Postprandial discomfort, nausea, and vomiting	CT	Enteral and parenteral nutrition
Farina <i>et al.</i> , 2020 [22]	27-year-old male	Painful post-prandial crises at the sub-acute onset, located at the epigastrium	Doppler US CT	Endovascular stent grafting
Wang <i>et al.</i> , 2021[23]	15-year-old male	Hematuria, fatigue, anorexia, nausea, and recurrent abdominal distension	Doppler US Upper GI gastrografin	Pulse dose of methylprednisolone 500 mg daily for 3 days, followed by 1 mg/kg orally and mycophenolate mofetil 0.75 g twice a day

Suarez-Correa <i>et al.</i> , 2022 [24]	25-year-old male	Postprandial abdominal pain and distension, nausea, vomiting, and distension	CT Upper GI gastrografin	Enteral nutrition and surgery
Laskowski <i>et al.</i> , 2022 [25]	40-year-old female	Nausea, early satiety and diffuse abdominal pain	CT	LRV transposition
Khan <i>et al.</i> , 2022 [26]	25-year-old female	Abdominal pain associated with nausea, bilious emesis, and diarrhea	CT	Surgery and conservative therapy
Ober <i>et al.</i> , 2022 [27]	45-year-old female	Macroscopic hematuria, intermittent pain in the left flank and hypogastric region, postprandial nausea, and cachexia	Doppler US CT	Stent implantation in the LRV
Gungorer <i>et al.</i> , 2022 [28]	17-year-old male	Abdominal pain, nausea, and vomiting	Doppler US CT	Surgery
Castro <i>et al.</i> , 2023 [29]	18-year-old female	Epigastric pain and emesis	CT	Dietary changes
Pacheco <i>et al.</i> , 2023 [30]	26-year-old male	GI obstructive symptoms	CT	Enteral nutrition
Alonso-Canal <i>et al.</i> , 2023 [31]	24-year-old male	Functional dyspepsia	CT	Dietary changes
Brogna <i>et al.</i> , 2023 [32]	37-year-old female	Abdominal pain with sub-occlusive episodes, nausea, and vomiting	CT	Periodic insertion of a nasogastric tube to decompress the stomach, along with a high-protein diet and parenteral nutritional supplements

Abbreviations: CT: computed tomography; GI: gastrointestinal; N.A: not available; LRV: left renal vein; US: ultrasound.

In summary, according to the reported evidence, the mean age at diagnosis of patients with both syndromes was $28,72 \pm 12,85$ (mean \pm standard deviation), with a higher prevalence of males (12/22; 54%). Furthermore, these patients showed one to five clinical manifestations associated with both conditions. Regarding the patients' management, CT scanning was the most used technique for diagnosis (16/22; 72%; Figure 4A), while nutritional therapy was the preferred treatment (11/22; 50%; Figure 4B).

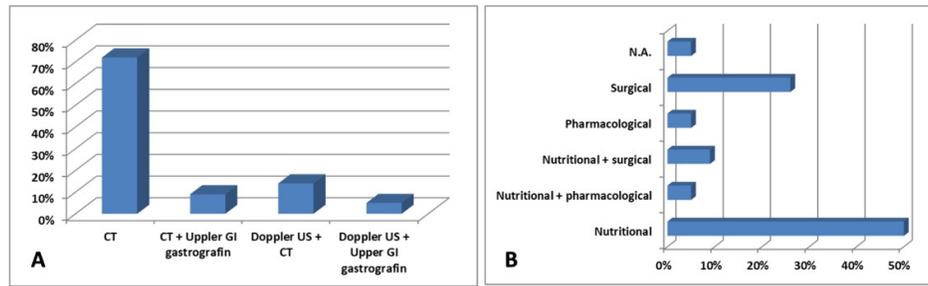


Figure 4. Different (A) diagnostic approaches, and (B) treatment according to the studies in the literature.

Regarding the diagnosis, although the US has been proposed as a diagnostic exam, poor patient cooperation and intestinal meteorism may hinder the correct viewing of abdominal structures. Using the echo-color-Doppler modality, US is also useful for showing bright colors of high velocity due to the aliasing artifacts from the jetting flow immediately distal to the AM portion of the LRV. Thus, for both Wilkie's syndrome and NCS, the definitive diagnosis is made with contrast-enhanced CT scanning or the MRI, which make it possible to detect the compression of the duodenum and LRV and accurately measure the SMA-aorta angle [33,34]. In terms of treatment options, the conservative one is the most widely adopted, especially because of the frequently associated benefits and the absence of related complications. Conversely, surgery is reserved for clinical cases characterized by a chronic persistence of symptoms unresponsive to conservative strategies. More specifically, surgical treatment is indicated in patients with the following clinical picture: 1) failure of the conservative treatment, 2) long-standing disease with progressive weight loss and duodenal dilatation with stasis, and 3) complicated peptic ulcer secondary to bile stasis and reflux [35]. Surgical interventions to consider include the Strong's procedure, gastrojejunostomy, and duodenojejunostomy (even through a laparoscopic approach). Duodenojejunostomy appears to be the best procedure, with a success rate higher than 90%, while Strong's procedure (lysis of the ligament of Treitz) showed a success rate of 25% [36]. Regarding NCS, conservative treatment must be preferred in young subjects given the higher probability of spontaneous remission, due to the increase in retroperitoneal fat and the formation of a collateral venous circulation [37]. Surgery is indicated in the presence of intolerable symptoms or after the failure of conservative treatment. Among the many surgical interventions, we mention LRV transposition, LRV transposition with patch venoplasty, patch venoplasty without LRV transposition, LRV transposition with saphenous vein cuff, gonadal vein transposition, and saphenous vein bypass. Among these, LRV transposition is the most common and effective approach [37,38]. Observational studies on large cohorts of patients are necessary to define appropriate guidelines on the subject of diagnosis, and to describe the possible treatment options to be adopted based on the clinical picture.

4. Conclusions

This case report highlights the diagnostic and therapeutic complexities associated with the coexistence of Wilkie's syndrome and NCS. Although these conditions are usually present alone, their simultaneous occurrence presents unique challenges, underscoring the importance of considering both in differential diagnosis. The patient in this case report showed persistent gastrointestinal symptoms despite multiple interventions, leading to the ultimate diagnosis through advanced imaging techniques. CT and MRI remain the most used diagnostic tools for these syndromes, providing detailed anatomical insights necessary for accurate diagnosis. Conservative management, including dietary modifications and pharmacological therapy, often serves as the initial approach, although patient compliance can significantly impact the effectiveness of this strategy. In refractory cases or when conservative treatment fails, surgical interventions such as duodenojejunostomy for Wilkie's syndrome and LRV transposition for NCS offer promising outcomes. The decision to proceed with surgery must be carefully weighed against the severity of

symptoms, the patient's overall health status, and the potential for spontaneous resolution, particularly in younger patients. This case report underscores the necessity for further research to establish comprehensive guidelines and optimize treatment protocols. Larger cohort studies are essential to better understand the pathophysiology, improve diagnostic accuracy, and refine both conservative and surgical treatment strategies for these complex syndromes.

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