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ISSN: 0015-5659

e-ISSN: 1644-3284

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DOI: 10.5603/fm.102679

Article type: Original article

Submitted: 2024-09-19

Accepted: 2024-10-30

Published online: 2024-11-18

ORIGINAL ARTICLE

Eray Atli et al., Prevalence of the Nutcracker phenomenon

Prevalence of left kidney vein entrapment signs on computed tomography angiography images of kidney donors

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ABSTRACT

Background: The Nutcracker phenomenon (NC-P) is the entrapment of the left kidney vein (LKV) between the superior mesenteric artery and the abdominal portion of the aorta. We aimed to evaluate the frequency of significant left renal vein compression in a healthy population.

Materials and methods: The computed tomography angiography images of the 131 healty patients who underwent living kidney donor nephrectomy at our institution were enrolled in this retrospective, descriptive anatomic study.

Results: Three (2.3%) cases had severe, 26 (19.8) had moderate stenosis. The mean aorto-mesenteric angle was more narrow in females ($p < 0.05$). The mean LKV diameter ratio and beak angle were shorter and more narrow in females ($p < 0.05$, $p < 0.01$; respectively). Thirteen cases (9.9%) showed three or four positive criteria for NC-P. As patients got younger and had body mass index (BMI) < 30 kg/m^2, the rate of positive criteria determination was increased ($p < 0.05$, $p < 0.01$; respectively).

Conclusions: The NC-P criteria were seen with a high frequency in healthy individuals. Female and younger individuals with less BMI showed a greater prevalence of positive

criteria. Revision of the current standards for NC-P with a distinct classification between sex, age, and BMI is required to assess LKV compression better.
Keywords: kidney, nutcracker, transplantation, entrapment, anatomy

INTRODUCTION

The Nutcracker phenomenon (NC-P) is the entrapment of the left kidney vein (LKV) between the superior mesenteric artery and abdominal segment of aorta (Fig. 1), which should be differentiated from its symptomatic form, Nutcracker syndrome (NC-S) [1]. The characteristic presentations of this syndrome are gross or microscopic hematuria and proteinuria, flank pain, gastrointestinal symptoms, arterial hypertension in both genders, pelvic congestion and dyspareunia, dysuria, dysmenorrhea in females, and varicocele in males [2–4].

Diagnosis of this rare anatomic condition is based on history, physical examination, and laboratory tests to exclude other reasons for haematuria [5]. The imaging series has been explained to doppler ultrasonography, computed tomography or magnetic resonance angiography imaging, and phlebography with renal and inferior caval vein manometry to confirm the diagnosis [6–8]. However, the underlying pathophysiology of this syndrome still needs to be wholly understood, and the prevalence is unknown. Moreover, most of the literature comprises case reports and retrospective heterogeneous studies, making it difficult to calculate its occurrence in the general population.

During the preoperative radiological evaluation of the vascular anatomy of the donors, we noticed the presence of NC-P was not well investigated. This study assesses the commonness of computed tomography angiography findings that would show significant compression on the LKV in kidney donors in the asymptomatic population.

MATERIALS AND METHODS

The patients who underwent living kidney donor nephrectomy from July 2018 through January 2022 at our institution were enrolled in this retrospective research.

The kidney donor candidates were selected or excluded, as we reported in our previous studies [9, 10].

With the theory that venous hypertension on LKV may cause more prominent hemodynamic results with a more significant number of meaningful symptoms, we asessed the prevalence of the association of various symptoms of compression (the presence of ≥ 3 criteria) regarding the left gonadal vein (LGV) diameter (Fig. 2), hematuria, distribution according to sex and body mass index (BMI).

Radiologic evaluation

All donors underwent abdominal computed tomography angiography. We received images as we presented in our previous study focusing on vascular variations of kidney, and a single radiologist (12 years experienced) evaluated computed tomography images using CT-software (GE-AW-4.7 Workstation, Volume&Threshold tools, GE Healthcare, Chicago, IL, USA).

Evaluation of computed tomography angiography images

The diameter and anteroposterior length of the LKV were measured on an axial image nearest to the centerline of the LKV as it transits among the aorta and the superior mesenteric artery. Between this aorto-mesenteric axis and the left kidney, the radiologist measured the maximum axial diameter of the LKV. The radiologist assessed the LKV for the LGV and a lumbar vein diameter, if identifiable at computed tomography angiography images. All measurements were completed on thin-section 2.5-mm thick axial images during the venous phase. The stenosis ratio of the LKV was calculated by accepting the diameter of the LKV as it intersects between the aorta and superior mesenteric artery and dividing it by the maximum LKV diameter upstream to this spot per the generally accepted norm [12]. For this study, we classified stenosis as less than 50%, 50% to 70%, and higher than 70%, corresponding to no significant stenosis, moderate stenosis, and severe stenosis, respectively. Diagnostic CT criteria [1, 13, 14] for NcP are:

- narrowing of the LRV at the aortomesenteric portion (the beak angle < 32°);
- beak sign: Severe form of narrowing of the LRV at the aortomesenteric portion;
- left renal vein diameter ratio (hilar to aorto-mesenteric) ≥ 4.9 mm;
- angle between the SMA and aorta < 41°.

An LGV was accepted as dilated if it measured greater than 5 mm in diameter [15–17]. A lumbar vein communicating with the LKV was assumed as dilated if it measured greater than 3 mm in diameter [17].

Ethical approval

Ethics committee of our institution approved the research protocol (No: 104, Date: March 13, 2019). We also procured informed consent from all individuals for using data and CT images.

Statistical analysis

We used the MATLAB-R2020b® (MathWorks Inc., Natick, MA, USA) software for statistical evaluation of the data. Quantitative variables were characterized using mean, maximum, and minimum values. Percentages were used for qualitative variables. Normal distributions were expressed as mean. If the distributions were normal, Student's t-test was used for comparison between groups. Pearson Chi-square test was used for comparative analysis of qualitative variables; however, if the sample size was ≤ 5, the Fisher-Irwin test was used. We accepted $p < 0.05$ as statisticallly significant.

RESULTS

One hundred sixty-one donor nephrectomy cases were included in to study protocol. Eleven individuals were excluded from the study due to lost follow-up visits, and seven were excluded due to having computed tomography angiography at another institution. Since having variant vascular anatomy, twelve cases also were not included in the evaluation, including seven circumaortic left kidney veins and five left retro-aortic veins. After excluding unappropriate patients, a total of 67 female and 64 male patients included to the study protocol who had no symptoms associated with NC-P. Table 1 demonstrates the clinical characteristics and anatomical measures in three groups of cases in the present research, divided by the degree of venous stenosis (< 50% stenosis, 50–70% stenosis, and > 70% stenosis). The mean aorto-mesenteric angle was 48.3° ± 20.6° in females and 52.8° ± 23.4° in males ($p < 0.05$). The mean LKV diameter ratio and beak angle were 1.43 ± 0.42 and 21.3° ± 13.7° in females ($p < 0.05$), and 1.67 ± 0.83 and 22.8° ± 15.1°, in males ($p < 0.01$).

Thirteen cases (9.9%) showed three or four positive criteria for NC-P (male/female: 5/8). Statistical analysis stratified by positive criteria for the NC-P (3 or 4) demonstrated no difference between males and females, and a meaningful correlation was noticed as patients got younger ($p < 0.01$) (Tab. 2). Additionally, the frequency of criteria for NC-P in the study population is shown in Table 3.

Beak sign, beak angle ≥ 32 and aortomesenteric angle < 41° were positive in all cases with severe left renal vein stenosis. Additionally aortomesenteric angle < 41° is the most observed CT finding in cases with no significant stenosis (Tab. 4).

In patients having a BMI less than 30 kg/m^2, the rate of having three or more positive criteria for the NcP was higher than in patients with a BMI between 30–35 kg/m^2 ($p < 0.05$). Also Additionally, right donor nephrectomy surgery was performed in 6 patients with positive criteria for the NC-P. In the postoperative follow-up, the nephrologist detected stage 1 hypertension in only one (16%) of these six patients, and medical treatment (Amlodipine 5 mg) was initiated; no other symptoms of NC-P were observed during six-month follow-up.

DISCUSSION

The present study showed that the most accepted computed tomography angiography diagnostic criteria for the NC-P and NC-S were notably prevalent in our healthy patient group. Although obvious clinical symptoms, such as hematuria and proteinuria, can be seen in some patients, NC-S is unique and commonly associated with less characteristic signs [18, 19]. LRV compression can typically be present in the aorto-mesenteric space; this typical presentation makes diagnosing abnormal LRV compression difficult. This difficulty in diagnosing irregular LRV compression from imaging studies has translated into the proposal of many criteria to determine the diagnosis [1, 4, 20–23].

Because of the close correlation between the NC-P and syndrome, it is crucial to define the specificity of the radiologic findings related to the diagnosis in kidney donor candidate patients. We saw the prevalence of the NcP to be 9.9% using computed tomography angiography in our patient population. This finding is less than previously reported studies in adults [15, 18, 24]. The present study only analyzed the patients who underwent donor nephrectomy, which was a narrow study group instead of the general population; this may have led to this different outcome.

The significant stenosis of LRV generally provokes eventual enlargement of collateral veins, and venous collateralization from the LRV emerges over time [17]. Such venous collateralization originating from the LRV has been documented as affirmative proof of NC-S [17, 25].

In the present analysis, dilation of the LGV or lumbar vein originating from the LRV was present in 14.5% and 24%, respectively. Previous researchers have documented that LGV dilation ranges from 5% to 47% [17, 26–29]. In the present study, we saw that the number of cases having left gonodal and lumbar venin dilatation raised as the percentage of LRV stenosis increased, which was an anticipated outcome; nevertheless, we saw that this increase was not statistically meaningful. We think this insignificance is caused by the low number of patients with advanced stenosis compared to the general patient population.

The beak sign has been applied in radiodiagnostics to identify the NC-P. And the beak angle expresses the objective/numeric presentation of the beak sign [18, 30]. Kim et al. [30] assessed twenty-seven cases presenting with hematuria who had a venographic evaluation with reno-caval pressure gradient measures. The outcomes showed a correlation between the beak sign and a reno-caval gradient higher than 3 mm Hg, with more than 90% sensitivity and 88.9% specificity. The present investigation revealed a frequency of 22.9% for the beak sign and 24.4% for a beak angle ≥ 32. Although, some investigators have subjectively thought this to be the computed tomography angiography images with the most satisfactory clinical relevance, superior diagnostic accurateness, and uncomplicated diagnosing with computed tomography angiography [1, 4, 23, 30]. Our results showed consistency with the findings of the previous analyses. These definitive criteria are widespread in the average population. And these criteria should be meticulously examined in the asymptomatic population because their existence might not show a reliable correlation with the LKV pressure gradient. The reno-caval pressure gradient has high specificity but low sensitivity because the maturation of collateral vessels can bypass this gradient increase, despite significant symptoms. This reinforces the finding that LRV compression can cause complex hemodynamic changes that are still poorly understood.

In this present research, there was a significant association between the cases having three or four positive NC-P criteria with younger age and a lower BMI. Various factors could cause this correlation, including lower body weight, an indirect sign of lower visceral fat level, which would alter the conformation of the aorto-mesenteric angle [31]. Some investigations have demonstrated that NC-S can be diagnosed at any time of life, from childhood to the seventh decade, with a top peak in the second-third decades. The rapid growth in the adolescence period is a possible triggering factor for SMA angle narrowing. As one ages, the anatomic characteristic of the aorto-mesenteric axis shifts, becoming more open, suggesting that the NC-P and NC-S might be temporary events in some cases. This time depended change in the aorto-mesenteric axis provokes the discussion of a more conservative therapeutic approach for symptomatic patients [1, 18, 32].

Limitations of the study

This analysis had various limitations. First, this study is a retrospective examination of kidney donor patients. Second, we did not use other imaging techniques, such as duplex ultrasonography, to asses the aorto-mesenteric axis and LKV, which can give better information about abdominal compressive venous alterations; we analyzed only the computed tomography angiography signs of compression at the LKV. Nevertheless, our investigation aimed to assess the data on the computed tomography angiography findings of the NC-P and syndrome in an average, asymptomatic population. The scarcity of diagnosed cases did not provide the best definition of the computed tomography angiography criteria for the NC-S or more acceptable criteria for determining NC-S from the NC-P. Since the high incidence in our asymptomatic patient population has suggested that the known criteria are not enough to define computed tomography angiography signs with clinical repercussions, the outcomes of the current investigation imply the necessity for reevaluating the currently accepted standards. Also, the results could encourage more researchers to explain better the standard parameters for the aorto-mesenteric axis and LKV.

CONCLUSIONS

We found that the most used diagnostic computed tomography angiography criteria for the NC-P and NC-S were notably prevalent in our healthy population group (living kidney donors).

Compression symptoms on the aorto-mesenteric axis are more likely observed in females and less BMI and younger patients. Our results imply the necessity for revising the NC-P and NC-S computed tomography angiography criteria. A distinct classification between sex, age, and BMI might also be practical to assess LKV compression events better.

ARTICLE INFORMATION AND DECLARATIONS

Data availability statement

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics statement

Ethics Committee of Istanbul Okan University approved the research protocol (No: 104, Date: March 13, 2019). We also procured informed consent from all individuals for using data and CT images.

Author contributions

M. Ferhat Ferhatoglu: project development, data collection and managements, manuscript writing and editing. **Eray Atlı:** project development, data collection and managements, manuscript writing and editing. **Alp Gurkan:** data analysis and managements, manuscript writing and editing.

Funding

The authors received no funding for this project.

Conflict of interest

The authors declare that they have no competing interests.

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Table 1. Clinical characteristics and anatomical measures among the degree of stenosis.

	Study group	**< 50% stenosis‡**	**50–70% stenosis‡**	**> 70% stenosis‡**	**P**
Patients, n [%]	131 (100)	102 (77.8)	26 (19.8)	3 (2.3)	0.214[b]
Age (years) (Mean ± SD) (min–max)	46.4 ± 12.1 (20–71)	39.4 ± 10.6 (20–67)	40.1 ± 9.7 (29–69)	42.3 ± 14.6 (39–71)	0.335[b]
Gender (male/female), n	64/67	43/59	18/8	3/0	0.327[b]
Ao-SMA LRV* diameter, mm (Mean ± SD) (min–max)	6.3 ± 2.2 (4.6–8.1)	7.7 ± 1.3 (6.2–8.1)	4.3 ± 1.1 (4.9–6.6)	3.6 ± 1.3 (4.6–5.9)	0.379[b]
Maximum LRV**, mm (Mean ± SD) (min–max)	9.9 ± 3.1 (7.1–14.3)	10.3 ± 2.6 (7.1–12.3)	10.8 ± 1.7 (8.9–12.7)	14.9 ± 9.6 (8.2–14.3)	0.619[b]
Dilated gonodal vein†, n [%]	19 (14.5)	15 (14.7)	4 (15.4)	0 (0)	0.886[b]
Dilated lomber vein††, n [%]	27 (20.6)	21 (20.5)	6 (23.1)	0 (0)	0.268[b]
Hematuria/proteinuria, n [%]	0 (0)	0 (0)	0 (0)	0 (0)	0.498[b]
Unspescific flank/abdominal pain, n [%]	3 (2.3)	1 (1)	0 (0)	2 (66)	0.274[b]

*Aorta-SMA left renal vein diameter, **Left renal vein, †If gonodal vein diameter > 5 mm, ††If lomber vein diameter > 3 mm; [a]Student's t-test, [b]Fisher Irwin test, [c]$p < 0.05$, [d]$p < 0.01$; ‡The authors classified stenosis as less than 50%, 50% to 70%, and higher than 70%, corresponding to no significant stenosis, moderate stenosis, and severe stenosis, respectively. LRV — left renal vein.

Table 2. Patients presenting with ≥ 3 positive criteria for nutcracker phenomenon stratified by sex and age.

Variable	**Number of positive criteria***	
	≥ 3	**< 3**
Women, n	8	59
Age (years), (Mean ± SD) (min–max)	38.7 ± 10.1	41.1 ± 10.9
Men, n	5	59
Age (years), (Mean ± SD) (min–max)	41.6 ± 11.3	54.1 ± 10.2
Total, n	13	118
Mean age, years (min–max)	40.7 ± 10.6	48.6 ± 10.4

Table 3. Frequency of main computed tomography criteria for nutcracker phenomennon according to gender.

Criteria	**Female, n [%]**	**Male, n [%]**	**Total, n [%]**
Beak sign			
Present¥	14 (20.9)	16 (25)	30 (22.9)
Absent¥	53 (79.1)	48 (75)	101 (77.1)
Beak angle			
Positive*	16 (23.9)	16 (25)	32 (24.4)
Negative**	51 (76.1)	48 (75)	99 (75.6)
Aortomesenteric angle			
Positive†	37 (55.2)	39 (60.9)	76 (58)
Negative††	30 (44.8)	25 (39.1)	55 (42)
LRV diameter ratio			
Positive‡	3 (4.4)	1 (1.5)	4 (3.
Negative‡‡	0 (0)	0 (0)	0 (0)

¥A ratio of peak systolic velocity of the aortomesenteric segment to the hilar portion of > 4.2 to 5.0 is considered as diagnostic criteria; *Beak angle ≥32 °; **Beak angle < 32°; †Aortomesenteric angle < 41°; ††Aortomesenteric angle ≥41 °; ‡Left renal vein diameter ratio ≥ 4.9 mm; ‡‡Left renal vein ratio < 4.9 mm; LRV — left renal vein.

Table 4. Frequency of main computed tomography criteria for nutcracker phenomennon according to stenosis degree.

	< 50% stenosis[‡] (n = 102)	50–70% stenosis[‡] (n = 26)	> 70% stenosis[‡] (n = 3)
Criteria			
Beak sign			
Present, n [%]	6 (5.9)	21 (80.8)	3 (100)
Absent, n [%]	96 (94.1)	5 (19.2)	0 (0)
Beak angle			
Positive[*], n [%]	12 (11.7)	17 (65.4)	3 (100)
Negative[**], n [%]	90 (88.3)	9 (34.6)	0 (0)
Aortomesenteric angle			
Positive[†], n [%]	47 (46.1)	26 (100)	3 (100)
Negative[††], n [%]	55 (53.9)	0 (0)	0 (0)
LRV diameter ratio			
Positive[‡], n [%]	1 (0.9)	1 (3.8)	2 (66.6)
Negative[‡‡], n [%]	101 (99.1)	25 (96.2)	1 (33.3)

[*]Beak angle ≥32 °, [**]Beak angle < 32°, [†]Aortomesenteric angle < 41°,[††]Aortomesenteric angle ≥41 °; [‡]Left renal vein diameter ratio ≥ 4.9 mm; [‡‡]Left renal vein ratio < 4.9 mm; LRV — left renal vein.

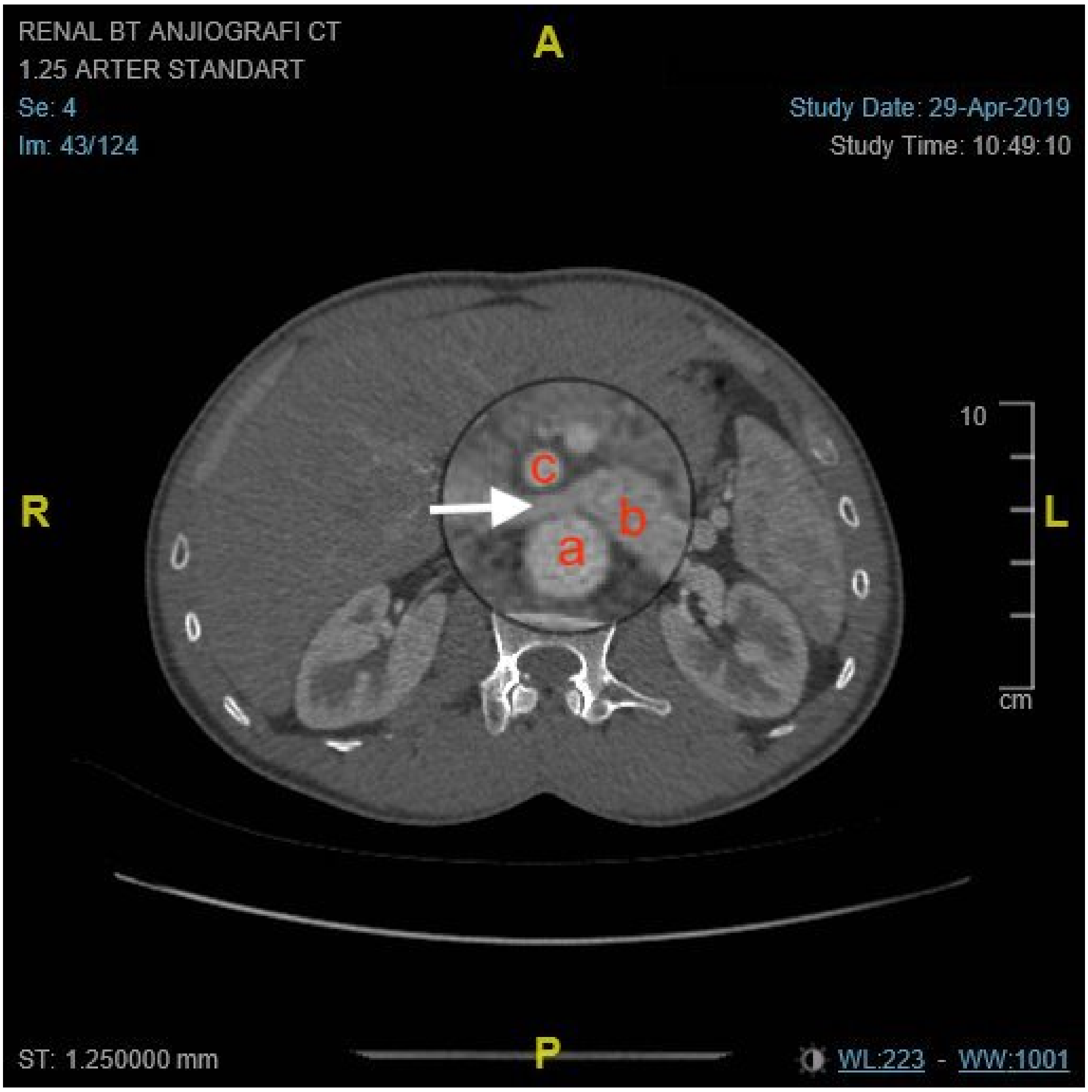

Figure 1. Computed tomography image of entrapment of the left kidney vein (white arrow) between the superior mesenteric artery and abdominal segment of aorta; a — abdominal part of the aorta; b — left kidney vein; c — superior mesenteric artery.

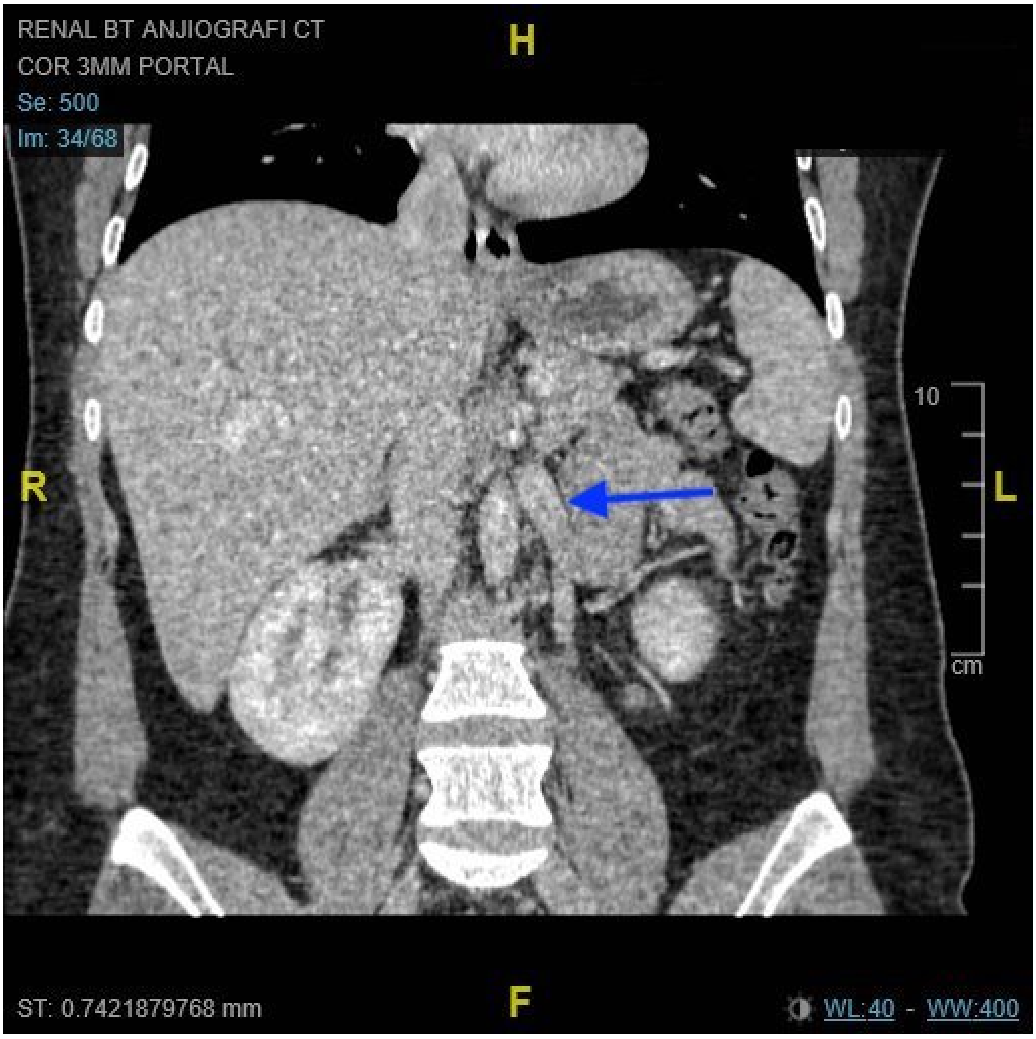

Figure 2. Dilated left gonodal vein (blue arrow).