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Polymorphism of Clinical Manifestations in Patients with "the Nutcracker Syndrome"

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Resume

Introduction. "The nutcracker syndrome" occurs due to abnormal compression of the left renal vein (LRV) between the superior mesenteric artery and the aorta. Clinical manifestations range from hematuria, proteinuria, pain in the left lumbar region, left sided varicocele in men, and left sided pudendal varicosity in women to the development of severe anemia and renal failure in some cases due to progressive phlebohypertension.

Materials and methods. The study included 210 patientswith suspected "nutcracker syndrome" . The age of the patients ranged from 12 to 52. All patients were interviewed for specific complaints. All referred patients underwent color Doppler ultrasound. The patients with confirmed left renal vein stenosis underwent CT angiography.

Results of the research

According to color Doppler ultrasound, different degree of aorta mesenteric clamp (AMC) was confirmed in 138 (65.7%) patients, critical LRV stenosis was observed in 35 of them. The predominant complaints of the patients with AMC included pain in the left half of the abdomen and left lumbar region, left sided varicocele and left sided pudendal varicosity, hematuria.. More than half of the patients with AMC complained of dysmenorrhea, and one in four patients with AMC complained of erectile dysfunction.

Conclusions. There is no consensus on the diagnostic algorithm for this pathology detection. There is a lack of evidence base (multicenter clinical randomized trials) regarding the clinical selectivity of treatment approaches. The pathology is rarely diagnosed due to a number of objective and subjective reasons, nonspecific symptoms, and therefore it deserves special attention in the study of pathogenesis, diagnosis and choice of treatment approach.

Key words: "the nutcracker syndrome", phlebohypertension, aorta mesenteric clamp.

Introduction. “The nutcracker syndrome” is a rarely diagnosed pathology. The disease occurs due to abnormal compression of the left renal vein (LRV) between the superior mesenteric artery and the aorta, which is accompanied by the development of phlebohypertension in the left renal vein system. Clinical manifestations range from hematuria, proteinuria, pain in the left lumbar region, left sided varicocele in men, and left sided pudendal varicosity in women to the development of severe anemia and renal failure in some cases due to progressive phlebohypertension. Although the pathogenesis is based on vascular-compression syndrome, the abovementioned symptoms make patients first consult urologists and gynecologists and very rarely angiologists,.

The objective of the research was to analyze the clinical course and its features in the patients with “the nutcracker syndrome”.

Materials and methods. The study included 210 patients (142 men and 68 women) with suspected “nutcracker syndrome” who were referred to vascular surgeons for a consultation by urologists and gynecologists during the period from 1999 to 2020, mainly from the western regions of Ukraine (about 11 million population). The age of the patients ranged from 12 to 52. All patients were interviewed for specific complaints: pain in the left lumbar region and left half of abdomen, inability to eat large amounts, hematuria, proteinuria, hemospermia, erectile dysfunction, left sided varicocele in men, and left sided pudendal varicosity and dysmenorrhea in women. All referred patients with suspected “nutcracker syndrome” underwent color Doppler ultrasound to determine the presence of pathological reflux in the left renal and gonadal veins by measuring peak systolic velocities in order to confirm or rule out that pathology. The patients with confirmed left renal vein stenosis underwent CT angiography.

Results of the research

According to color Doppler ultrasound, different degree of aorta mesenteric clamp (AMC) was confirmed in 138 (65.7%) patients (83 men and 55 women), critical LRV stenosis was observed in 35 of them. Particular attention was paid to the difference in the diameters of LRV in the distal part and in the aorto-mesenteric segment, as well as to the difference between the peak blood flow velocities in those areas.

The ultrasound pattern of “the nutcracker syndrome” was characterized by a sharp narrowing of the LRV diameter in the aorto-mesenteric segment and prestenotic expansion in the distal part, which correlated with a corresponding increase in peak systolic velocity in the stenosed part of the LRV.

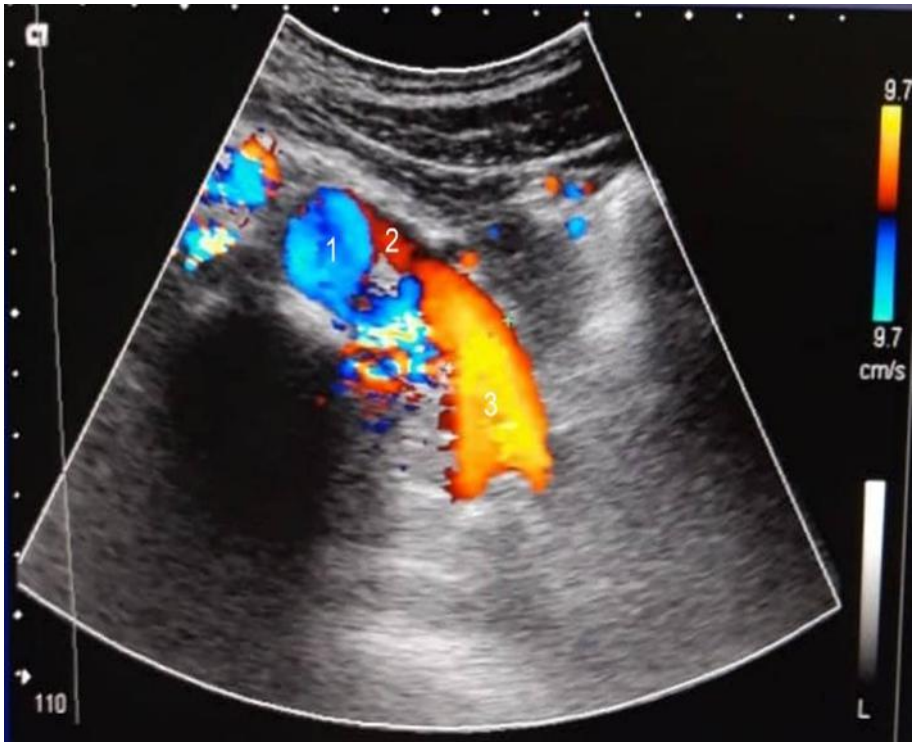

Figure 1. Ultrasound pattern of “the nutcracker syndrome” (1 – aorta, 2 – stenosed part of LRV, 3 – dilated part of LRV).

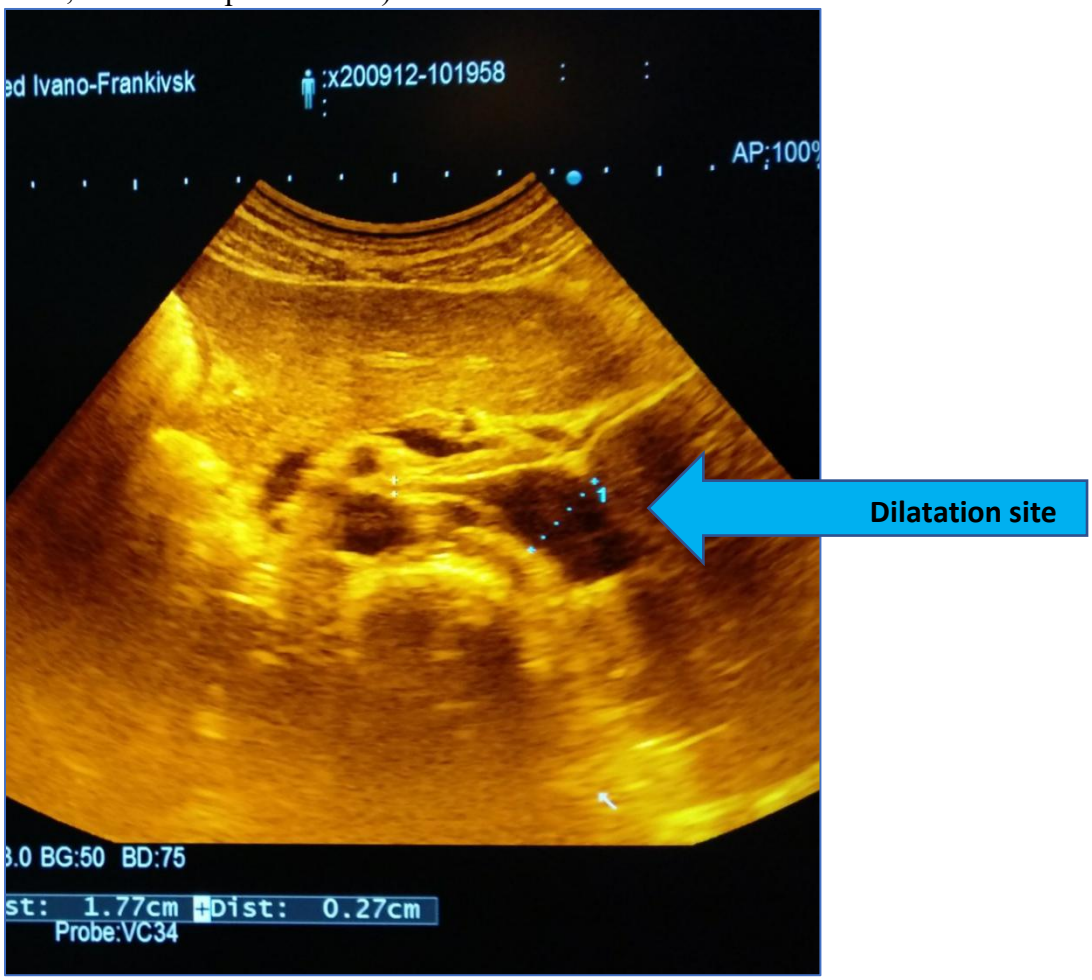

Figure 2. Ultrasound pattern of “the nutcracker syndrome” (B - mode).

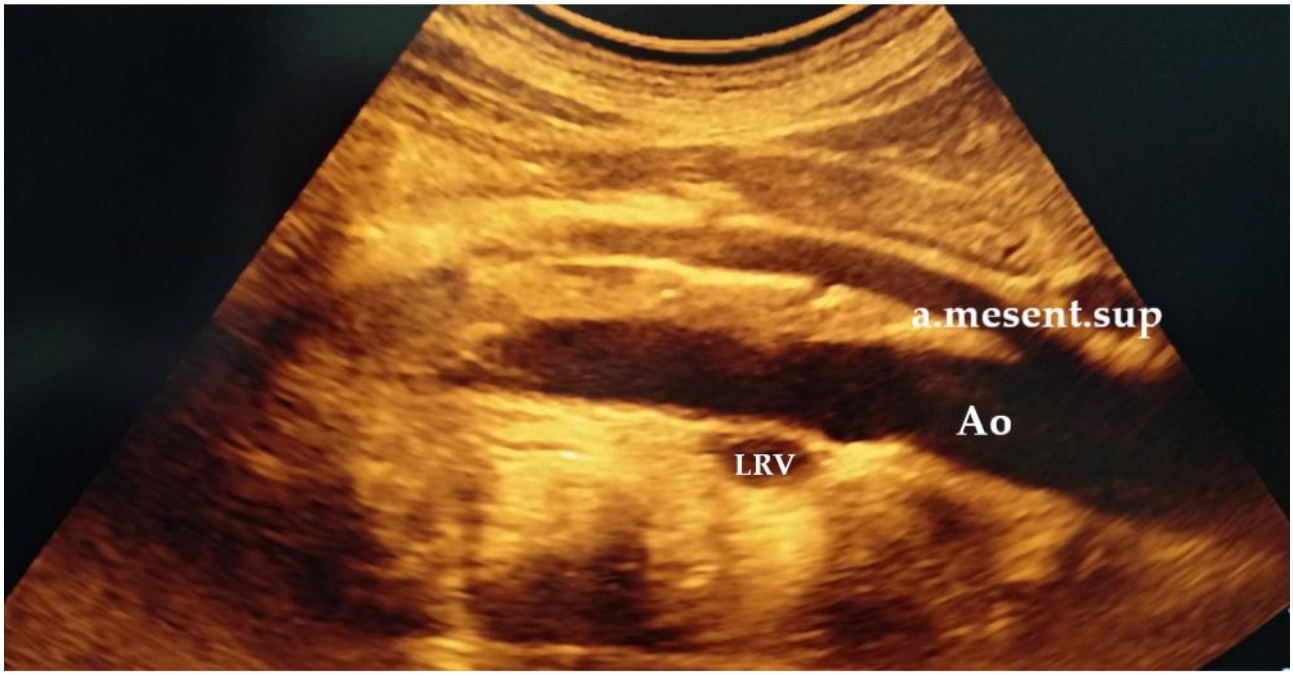

Figure 3. Ultrasound pattern of "the posterior nutcracker syndrome" (B - mode).

According to observations, clinical manifestations of severe forms of AMC syndrome occurred in case of an increase in the diameter of the distal (prestenotic) part of the LRV compared to its proximal (aorto-mesenteric) segment by 3-6 times as well as in case of an increase in peak systolic velocity in the stenosed proximal (aorto-mesenteric) segment by 6-14 times (by 8.7 times on average) compared to the LRV distal segment. Indices of the ratio of the diameters of LRV distal and proximal segments ≥ 3 and the ratio of peak systolic velocities in the proximal and distal segments ≥ 6 were evaluated as critical LRV stenosis.

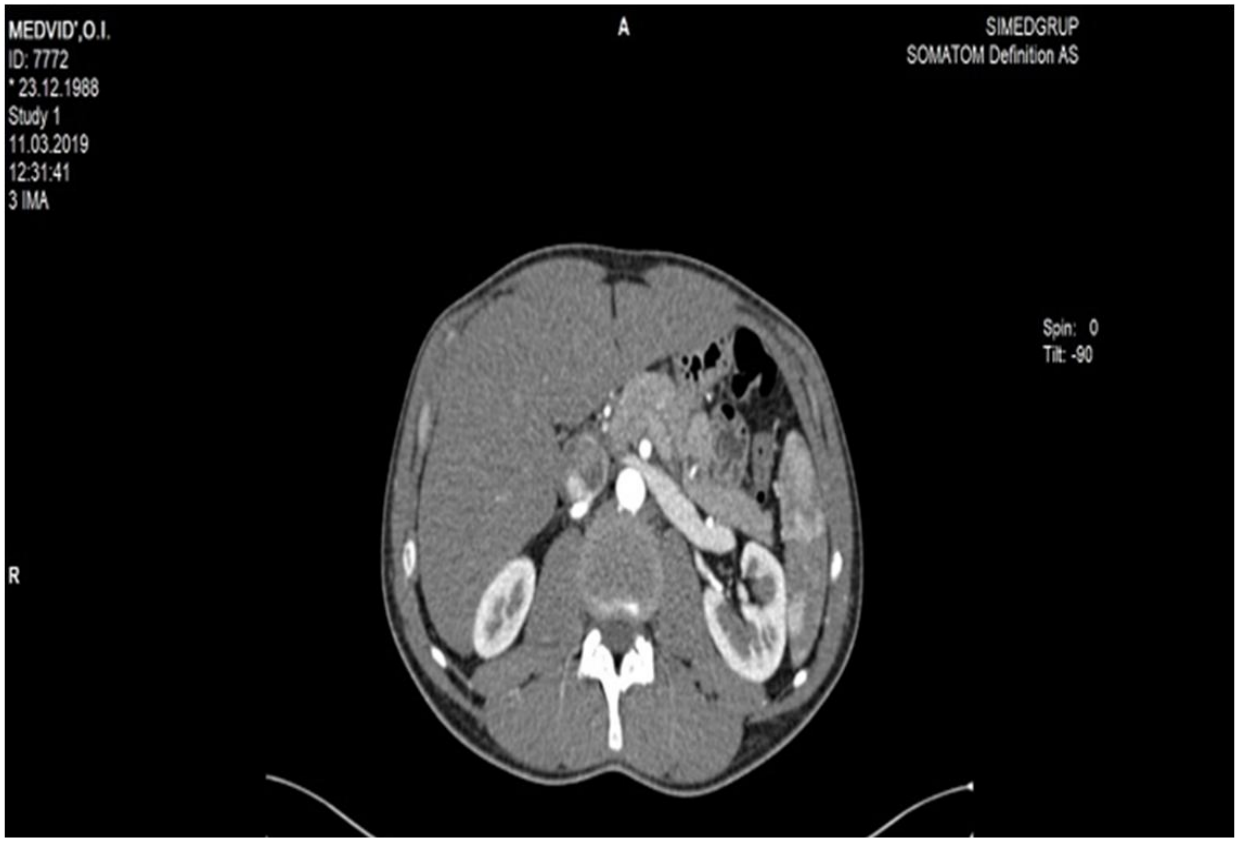

Figure 4. CT angiography of a patient with “the nutcracker syndrome”

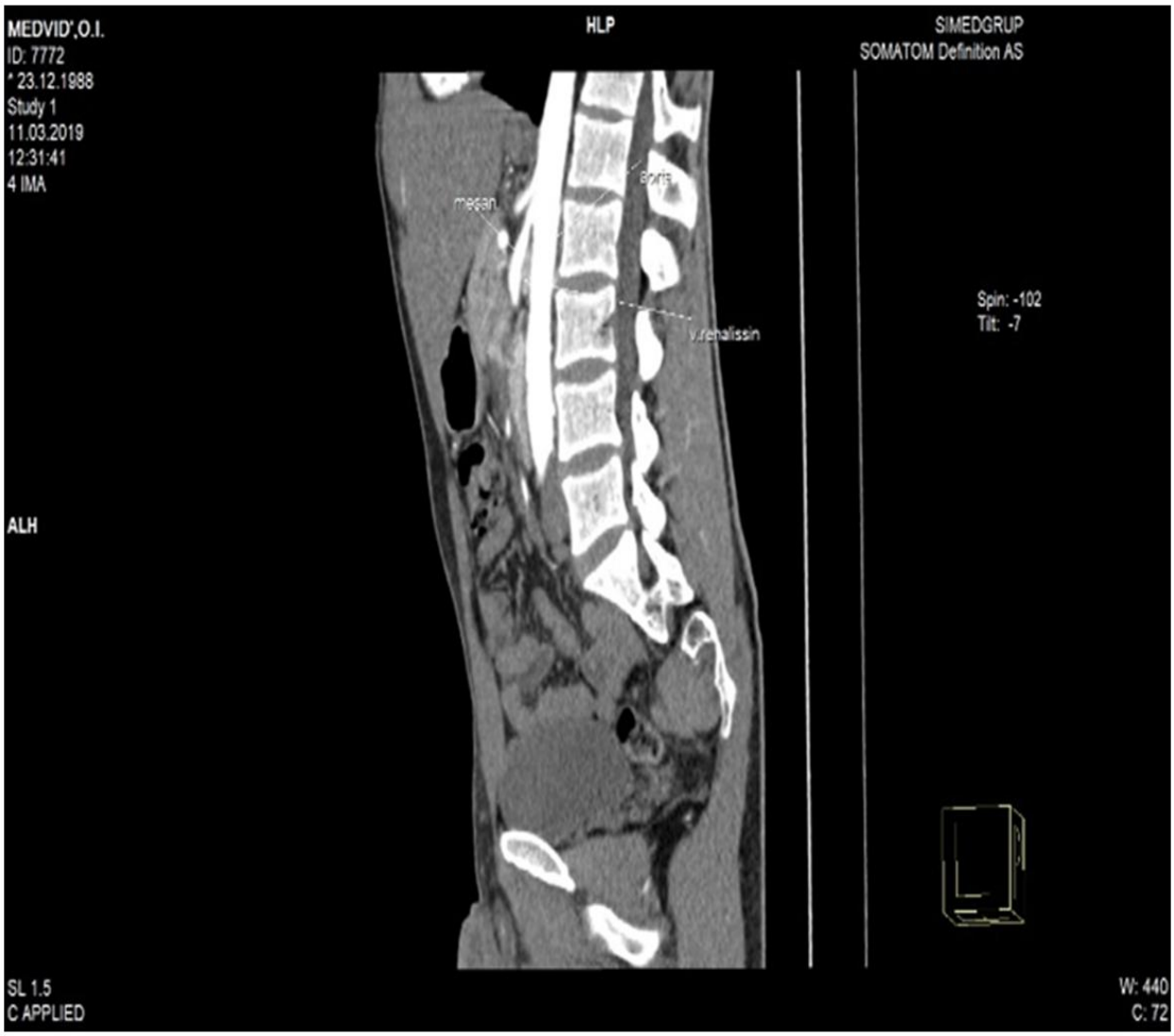

Figure 5. CT angiography of a patient with “the nutcracker syndrome” (sagittal plane)

The patients were divided into 3 groups: Group 1 included the patients without ultrasound evidence of AMC; Group 2 consisted of the patients diagnosed with AMC without critical LRV stenosis; Group 3 included the patients with critical LRV stenosis. The results are presented in Figure 5.

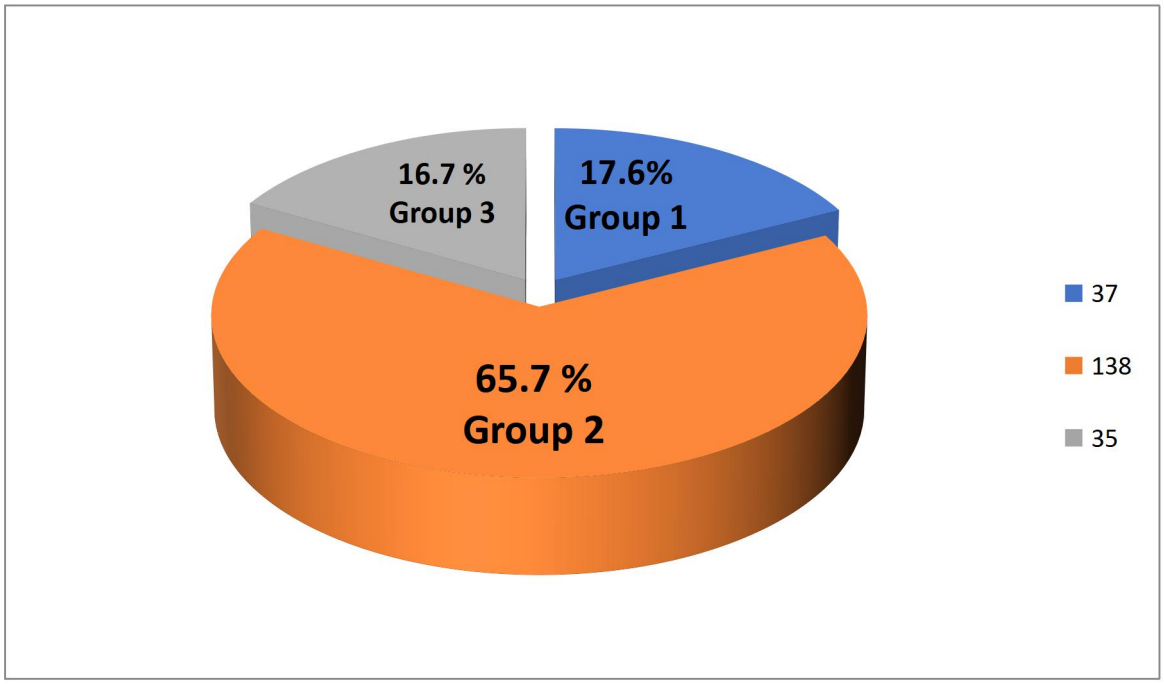

Figure 6. Distribution of patients by ultrasound signs of aorto-mesenteric clamp

The predominant complaints of the patients with AMC included pain in the left half of the abdomen and left lumbar region which increased in a sitting position and during exercise, left sided varicocele and left sided pudendal varicosity, hematuria (macro- or micro). Hematuria was mostly episodic and occurred at the peak of physical activity. The onset of the disease occurred in childhood and puberty in most of the examined patients. More than half of the patients with AMC complained of dysmenorrhea, and one in four patients with AMC complained of erectile dysfunction. All patients had an asthenic type of constitution (BMI ≤21).

Table 1

Pathological changes detected during the interview and examination of men with AMC (n = 83)

№	Symptoms	Abs.	%
1.	Hematuria	16	19.2
2.	Proteinuria	6	7.2
3.	Anemia	4	4.8
4.	Hemospermia	3	3.6
5.	Pain in the left half of abdomen	68	81.9
6.	Pain in the left lumbar region	62	74.7
7.	Erectile dysfunction	28	33.7
8.	Left sided varicocele	48	57.8
9.	Pain in the epigastrium, inability to eat large amounts of food	10	12

Table 2

Pathological changes detected during the interview and examination of women with AMC (n = 83)

№	Symptoms	Abs.	%
1.	Hematuria	6	10.9
2.	Proteinuria	Not found	
3.	Anemia	1	1.2
4.	Pain in the left half of abdomen	48	87.3
5.	Pain in the left lumbar region	52	94.5
6.	Dysmenorrhea	38	69
7.	Left sided pudendal varicosity	7	12.7
8.	Arterial hypertension	4	7.3
9.	Pain in the epigastrium, inability to eat large amounts of food	4	7.3
10.	Dyspareunia	6	11

In addition to functional changes, phlebohypertension in the LRV system leads to a number of structural changes, namely, an increase in the left kidney size, thickening of its cortical layer, the development of stagnant venous congestion of the left kidney. Disturbed outflow through the adrenal vein in some patients leads to hyperaldosteronemia with the development of arterial hypertension and, in some cases, to adrenal adenoma.

Patients with left-sided varicocele, with the recurrent one in particular, deserve special attention. According to Sagalevych AI, more than 74% of patients with left sided varicocele have different AMC degrees, and in 2016 Kapto AA offered the classification of varicocele taking into consideration anatomic features of a reno-caval segment [1,3].

Table 3

Classification of varicocele according to Kapto AA (2016)

VARICOCELE				
Present arteriovenous conflicts			**Absent arteriovenous conflicts**	
Hypertensive one of the upper level		**Hypertensive one of the lower level**	**Hypertensive symptomatic**	**Idiopathic**
Nutcracker syndrome	Posterior nutcracker syndrome	May-Thurner syndrome	Testicular vein compression by the contents of the inguinal canal or elements of the spermatic cord (inguinal hernia, cyst, lipoma)	Connective tissue dysplasia, congenital failure of the valvular apparatus of the veins
Type 1	Type 2	Type 3	Type 4	Type 5

Based on this classification, 4 types of varicocele are accompanied by vascular compression. Impaired venous outflow is believed to affect only the scrotum; however, in case of varicocele, blood containing testosterone flows excessively into the pelvis with the concentration of free and total testosterone in these patients in the testicular vein and in

prostate veins 100 times higher than in peripheral venous blood (according to Gat et al.) [5]. High local concentration of testosterone causes benign and malignant prostatic hyperplasia and, in its turn, exacerbates varicose veins of the pelvis due to its vasodilating effect. According to Kapto AA, two pathogenetic mechanisms develop in case of varicocele and they determine the range of clinical manifestations: 1) venous congestion of the scrotum as a cause of pathospermia and testicular hypotrophy; 2) venous congestion of pelvic organs as a cause of prostatitis, dysuria, pelvic pain, erectile dysfunction and hemorrhoids.

AMC syndrome is often combined with superior mesenteric artery syndrome (Wilke's syndrome, duodenal obstruction syndrome). The angle of the superior mesenteric artery origin from the aorta less than 25° causes not only compression of the left renal vein but also compression of the lower horizontal part of the duodenum, which, in its turn, causes a number of gastrointestinal complaints of patients, namely increased pain after eating, nausea, less often vomiting, inability to take a larger amount of food at once, sometimes patients suffer from intestinal obstruction. Patients often keep consciously to a strict diet due to the intensification of pain, thus resulting in an even greater weight deficit and the aorto-mesenteric angle becoming more acute.

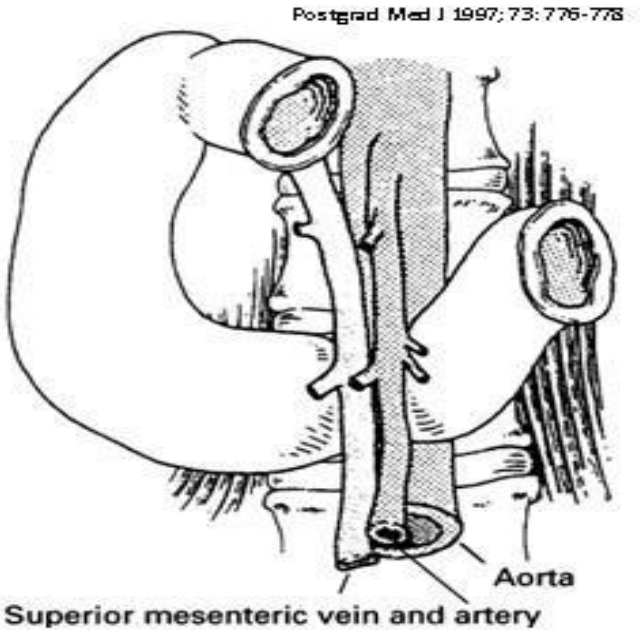

Figure 7. Duodenal obstruction syndrome (compression of the lower horizontal part of the duodenum)

Clinical variants of the course can be classified as follows:

1) Hematuric form: the patient indicates episodes of macro- or microhematuria of different duration, the size of the left kidney is usually not changed or is slightly increased, the thickening of the cortical layer is almost absent, the pain is usually significant;
2) The form of "stagnant venous congestion" of the left kidney: the left kidney veins are enlarged, the cortical layer of the left kidney is thickened to 2-2.5 cm, the size of the left kidney is increased, the pain is usually less intense, hematuria is not typical;
3) The form of pelvic venous congestion with a predominant pathological venous shunt into the pelvis is accompanied by the development of pelvic varicosity, left pudendal varicosity, algodismenorrhea, dyspareunia in women and left sided varicocele, erectile

dysfunction in men. May-Thurner syndrome as the main pathogenetic mechanism of phlebohypertension development in the pelvis should be excluded.

4) Epigastric form: increased pain after eating, inability to eat large amounts of food, severe pain syndrome, severe asthenization in patients.
5) Adrenal form: it usually debuts in the form of idiopathic hypertension, pain is not significant or is absent, increased levels of aldosterone and blood cortisol are noted.

One variant of the course is seldom noted, there is usually a combination of several clinical forms with dominance of one variant or another.

Discussion

The low frequency of "the nutcracker syndrome" detection is explained by the relatively short period of its study. Anatomist Grant was the first to describe this anomaly in 1937 [8]. The syndrome was described clinically for the first time in 1950 by physicians El.-Sadr AR, Mina E. [6]. In 1971, Chait et al. described the abdominal aorta and the superior mesenteric artery as two arms of the "nutcracker" compressing the LRV, which suggested an idea to the Belgian doctor De Schepper to describe this pathology as "the nutcracker" phenomenon [4, 5]. Lopatkin NA indicated the connection between LRV stenosis and varicocele recurrence [2].

According to Sagalevych AI, 83.3% of patients with left-sided varicocele have left-sided renal venous hypertension due to the pathology of the reno-caval segment (different variants of "the nutcracker syndrome" – anterior, posterior and combined) [3].

Attention to this pathology has increased significantly with the expansion of diagnostic capabilities. Today, color Doppler ultrasound, computed tomography with angiography, MRI, phlebography is used to make the diagnosis. Takebayashi S, Ueki T, Ikeda N et al. consider Doppler ultrasound to be the method of choice for patients with suspected "nutcracker syndrome" due to the high specificity and sensitivity of this method constituting 78-100% 10]. Thus, Takahashi Y, Sano A, and Matsuo M believe that ultrasound Doppler can clearly assess the degree of the left renal vein stenosis and blood flow velocity in it [9].

Conclusions. Analyzing the literature data on diagnostic and treatment approach to "the nutcracker syndrome", we can draw the following conclusions. Firstly, today there is no consensus on the diagnostic algorithm for this pathology detection. Secondly, there is a lack of evidence base (multicenter clinical randomized trials) regarding the clinical selectivity of treatment approaches. Thirdly, the pathology is rarely diagnosed due to a number of objective and subjective reasons, nonspecific symptoms, and therefore it deserves special attention in the study of pathogenesis, diagnosis and choice of treatment approach.

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