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# RAPIDLY PROGRESSIVE COURSE OF NONSPECIFIC AORTOARTERITIS: A CLINICAL CASE

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***Background.*** *Nonspecific aortoarteritis, or Takayasu's disease, is one of the most complex and rare pathologies in modern clinical practice. It is the orphan nature of the disease, along with non-specific clinical manifestations, that causes a large number of clinical and diagnostic errors that lead to an unfavorable prognosis and early disability of patients. Despite the development of modern methods of treatment of nonspecific aortoarteritis, in some cases it is not possible to achieve a stable remission, which leads to a steady progression of the pathological process.* ***Clinical case description.*** *The article presents a case of a rapidly progressing course of Takayasu's disease in a young woman with multiple arterial vascular lesions that developed during the first year after the onset of arterial hypertension, while the narrowing of the carotid arteries (75–85%) was not accompanied by signs of cerebral ischemia. The follow-up period was 10 years.* ***Conclusion.*** *Given the peculiarities of this nosology, each identified case of Takayasu's disease is of great clinical and practical interest. The disease peculiarity in thise patient is that during the first year from the onset of arterial hypertension, the main occlusive lesions of the aorta and arterial vessels were identified. At the same time, the narrowing of the carotid arteries (75–85%) was not accompanied by signs of cerebral ischemia. It should be noted that often the symptoms of non-specific aortoarteritis appear under the "masks" of other diseases, which requires a careful differential search. A correct diagnosis and timely treatment can prevent the development of complications and slow the progression of the disease.*

***Keywords:*** *nonspecific aortoarteritis, Takayasu's disease, aorta, systemic diseases, pathomorphology, diagnostics, clinical case.*

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## BACKGROUND

To date, the diagnostics of some systemic diseases is not particularly difficult. However, blurred clinical symptoms and orphan pathology registered often prevent from making timely the correct clinical diagnosis, which affects the prognosis of life and the success of treatment of such patients. Nonspecific aortoarteritis (syn. Takayasu disease, Takayasu arteritis, pulseless disease) is a chronic granulomatous inflammation of the aorta and its large branches, less often the branches of pulmonary vessels and coronary arteries, leading to stenosis and ischemic damage to the corresponding tissues [1, 2].

## NONSPECIFIC AORTOARTERITIS

### Epidemiology

The incidence of the disease varies from 1.2 to 2.6 cases per 1 million population per year, depending on the region of residence and ethnic group. Thus, among Asian patients, the incidence of Takayasu arteritis is 10 times higher than among other populations. Unfortunately, in the Russian Federation, there are no exact data on the prevalence of aortoarteritis, therefore we can not suggest the epidemiological aspects of this pathology in our region [1]. Takayasu disease develops mainly in young people, and about 70% of cases are registered in patients under the age of 20 years, up to 30% of cases in patients under 40 years of age. The medical literature also comprises information on diagnostics of nonspecific aortoarteritis at a later age [1, 3]. The ratio of male and female patients, according to different authors, varies from 1:1.3 in Israel to 1:6.9 in Mexico and 1:8 in Japan [2–4].

### Pathogenesis and aspects of the clinical course

Until now, the disease etiology remains unclear. Some researchers suggest that the initiation of the pathological process is induced by various stress factors, the most significant of which are psychoemotional stress, pregnancy, chronic and acute intoxication, as well as infectious diseases in history. It should be noted that for a long time a lot of attention has been paid to the theory of an infectious trigger. Thus, according to

the references to the studies by S. Kinare, more than 30% of cases of lesions of the branches of the aorta were registered in patients with tuberculosis [3, 5].

In recent decades, critical importance is attached to various genetic factors, including the detection of HLA alleles, namely HLA-DHO, HLA-DR2, HLA-DR4, HLA-A10, HLA-B*52:01, HLA-B*67:01, HLAB/MICA, HLA-DQB1/DRB1, IL12B [3, 5]. Susceptibility to Takayasu arteritis increases in individuals with polymorphisms of the HLA-B protein with histidine at position 171 and phenylalanine at position 67, as well as when the FCGR2A/FCGR3A locus is detected on the chromosome 1 [1, 2, 6]. However, the most convincing theory of the pathogenesis of nonspecific aortoarteritis belongs to autoimmune mechanisms. This is also evidenced by the presence of circulating immune complexes in the acute phase of the disease, anti-aortic antibodies in blood serum and vascular walls, as well as the positive effect of cytostatics and glucocorticosteroids on acute manifestations of the disease [3, 5].

The inflammatory process affects the aorta and the orifices of the great vessels extending from it. Pathomorphologically, panaortitis is noted with damage to all layers of the vascular wall, mainly media, where a presentation of productive inflammation develops. In the vascular wall itself, cell adhesion molecules and neovascularization processes are activated. Cellular infiltration is an accumulation of CD4+ T-lymphocytes, macrophages, giant cells, and B-lymphocytes. In addition, the deposition of immune complexes in the intima and tunica media of the affected vessels is noted. In general, the acute phase of the pathological process is characterized by infiltration of mononuclear immune cells into the adventitia and then into the tunica media which thickening is facilitated by the proliferation of fibroblasts. In the chronic phase, noticeable fibrotic changes appear. It should also be remembered that damage to the intima often contributes to the development of aneurysms and the formation of parietal blood clots. Fibrotic changes in the vessels lead to complete or partial occlusion of the arteries [3, 5, 6].

### Treatment

In most patients, under the influence of appropriate pathogenetic therapy, the course of the pathological process is replaced by remission. In 20% of patients with nonspecific aortoarteritis, spontaneous recovery and cessation of aggravation of vascular lesions are registered. However, in some patients, despite the ongoing treatment, the course of the disease is steadily progressing, involving new vessels in the pathological process and aggravating the severity of damage to already altered arteries [3].

**The work aimed** to demonstrate one of the variants of the steadily progressive course of nonspecific arteritis.

## CLINICAL CASE

### Patient information

Female patient T, 32 years old, was admitted to the department with complaints of intermittent short-term semi-fainting, lasting up to several seconds, as well as shortness of breath when walking at 100 m, which is accompanied by pain behind the sternum irradiating to the left arm. The patient also suffered from the arising intermittent lameness, decreased visual acuity, frequent increase in blood pressure (up to a maximum of 200/100 mm Hg.) and general asthenia.

*Case history*. In March 2009, the patient noted the occurrence of a stabbing headache. The ambulance team registered an increase in blood pressure up to 180/100 mm Hg. During an outpatient examination by a cardiologist, in addition to high blood pressure (200/140 mm Hg), during auscultation, a protodiastolic murmur was heard above the aorta; and a significant (up to 38 mm/h) increase in the erythrocyte sedimentation rate (ESR) was noted. The echocardiographic examination revealed dilatation (up to 4 cm in diameter) of the aortic root due to the left coronary sinus with the development of moderate aortic valve insufficiency (++), while the dimensions of the heart cavities and myocardial thickness were not changed, myocardial contractility was satisfactory (35%), and the ejection fraction was normal (63%). The patient was consulted by a cardiac surgeon, and a murmur was detected in the projection of the abdominal aorta and the left renal artery; murmur was not heard over other arteries. Study of the abdominal aorta and renal arteries was recommended.

In October 2010, multispiral computed tomography of the thoracic and abdominal aorta, as well as the iliac arteries, was performed, which revealed an uneven circular thickening of the aortic wall (0.4–0.6 cm) from Th11 thoracic to L3 lumbar vertebrae, with uneven narrowing of the lumen from 0.7 to 1.1 cm; at the level of vertebra L3, there was a sharp narrowing of the aortic lumen to 0.3–0.4 cm (70–80%) up to 0.6 cm long, and more distally the lumen of the aorta was 1.5 cm. The renal arteries extended from the aorta at the level of the vertebra L2. Directly at the orifice of the lumen of the left renal artery, its lumen narrowing to 70–80% over 0.2 cm was determined, then early branching of the re-


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nal artery (developmental variant) was visualized, and the diameter of its two branches was 0.5 cm.

*Conclusion*. Changes in the aortic wall at the level of Th11–L3 vertebrae with extension to the left renal artery and narrowing of their lumen are of inflammatory nature (Fig. 1).

Considering the nature of changes in the abdominal aorta and renal artery in combination with high arterial hypertension, signs of inflammation (ESR 45 mm/h), the patient was diagnosed with occlusive thromboaortopathy, Takayasu disease with lesions of the abdominal aorta and left renal artery, relative aortic valve insufficiency of the degree 2, secondary arterial hypertension, chronic heart failure stage I.

In November 2010, in the Department of Cardiac Surgery of the Donetsk Clinical Territorial Medical Association (DCTMA), surgical intervention was performed in the scope of stenting of the abdominal aorta, and bifurcation stenting of the renal arteries on the left (Fig. 2, 3).

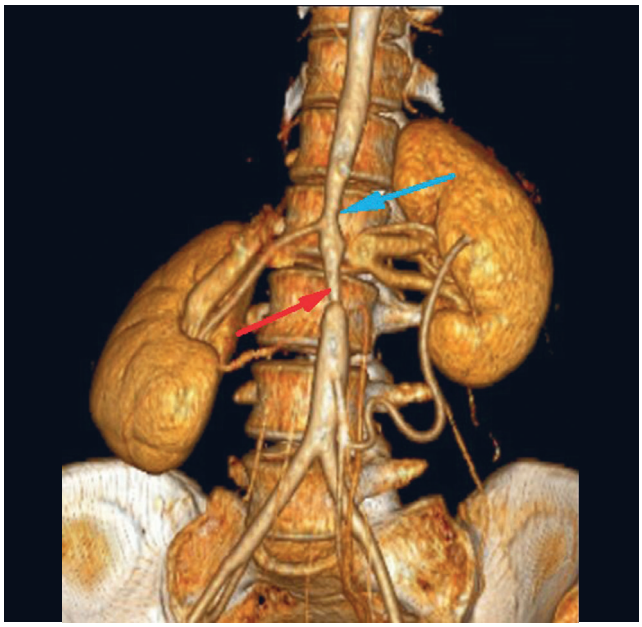
In the postoperative period, there was a persistent decrease in blood pressure to 110/50 mm Hg. The patient was consulted by a rheumatologist and transferred to the rheumatology department of DCTMA for further examination and clarification of the diagnosis.

In the rheumatology department, a Doppler study of the neck vessels was performed (January 2011) which revealed echo signs of structural changes in the brachiocephalic arteries of the type of vasculitis, stenosis of the common carotid arteries on the right (up to 75%) and on the left (85%), stenosis of the orifice of the right internal carotid artery (up to 50%), stenosis of the brachiocephalic trunk (up to 55%) and the right subclavian artery. The diameter of the right subclavian artery at the point of branching from the brachiocephalic trunk was 0.5 cm, the velocity was 200 cm/sec, in the proximal section 0.5–0.8 cm and approximately 250 cm/sec, respectively. The parameters of the vertebral arteries were within the normal range.

The clinical analysis of blood showed signs of moderate anemia (hemoglobin 90 g/l, erythrocytes $3.2 \times 10^{12}$/l), and increased ESR up to 45 mm/h.

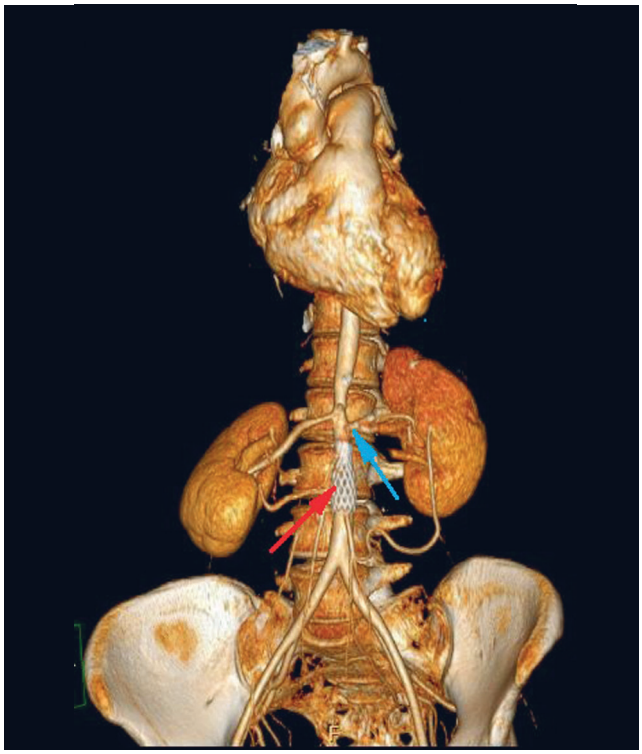
Repeated echocardiography revealed that the aortic root remained enlarged due to non-coronary and left coronary sinus; there were areas of marginal induration of the aortic valve cusps, heterogeneity and minimal fragmentary deflection of the segment of the anterior mitral valve cusp with the development of moderate mitral valve insufficiency. Pulmonary artery pressure was 17 mm Hg.

**Fig. 1.** Patient T, 32 years old, with a steadily progressive course of nonspecific aortoarteritis: multislice computed tomography of the thoracic and abdominal aorta (3D reconstruction).



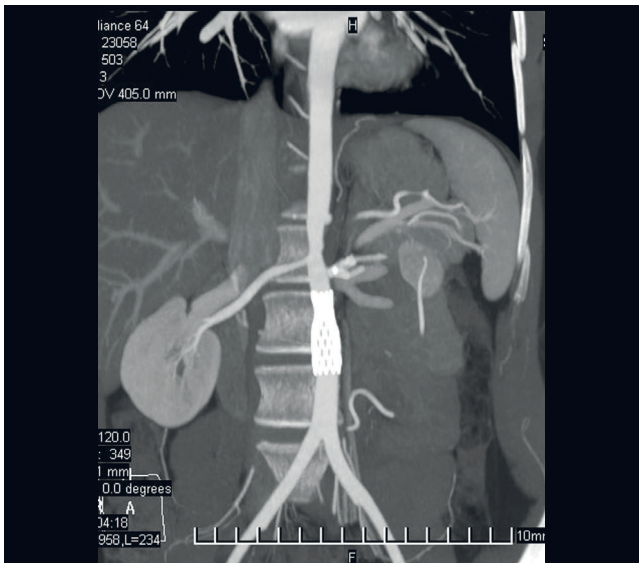
***Note.*** Uneven circular thickening of the aortic wall with narrowing of its lumen at the level of vertebrae Th11–L3 (blue arrow). A site of sharp narrowing of the aortic lumen at the level of L3 (red arrow).

**Fig. 2.** The same patient: multislice computed tomography of the thoracic and abdominal aorta (3D reconstruction) after surgery



***Note.*** Red arrow — abdominal aortic stent; blue arrow — stent in the renal artery.

**Fig. 3.** The same patient: visualization of stents during computed tomography.




**Provisional diagnosis**

Nonspecific aortoarteritis, type III, grade 3 activity, chronic course with lesions of large and medium-sized vessels (stenosis of the abdominal aorta and renal arteries, condition after stenting of the abdominal aorta, renal arteries on the left in 2010; stenosis of the carotid arteries on the right and left, stenosis of the brachiocephalic trunk and right subclavian artery); aortic valve insufficiency degree 2, secondary arterial hypertension, stage I chronic heart failure, functional class II.

The therapy performed in the department included methylprednisolone at a dose of 16 mg/day, pentoxifylline 600 mg/day, perindopril 5 mg/day, amlodipine 5 mg/day, bisoprolol 5 mg, cardiomagnyl 75 mg/day, and clopidogrel 75 mg/day. Blood pressure persisted at 130/90 mm Hg. Surgery for stenotic lesions of the neck vessels was offered to the patient, however she temporarily refused it.

However, three years after the surgery, the patient again felt a significant deterioration in general health, general asthenia increased; she had pains in the left half of the neck, left arm, and interscapular space. In addition, the patient began to notice interruptions in the work of the heart and dizziness. And she had a tendency for blood pressure increase to 170/90 mm Hg.

In March 2014, the patient consulted an angiosurgeon, and aortography was performed in the vascular surgery department, which revealed occlusion of the common carotid artery on the right and left, stenosis of the brachiocephalic trunk up to 50–60%; stents in the infrarenal aorta and left renal artery were satisfactorily patent. Subclavian-carotid shunting on the left was performed. The patient was discharged from the department in a satisfactory condition with appropriate recommendations. Control angiography in December of the same year revealed occlusion of the subclavian-carotid shunt. In December 2014, a subclavian-carotid prosthetics with a synthetic prosthesis was performed on the right.

In the future, the patient constantly took the recommended therapy. She underwent treatment at the rheumatology department annually. She noted the condition deterioration for the last 3 months, dyspnea increased during physical exertion which was accompanied by pain behind the sternum radiating to the left arm.

**Diagnostic procedures**

***Physical diagnostics***

The general condition of the patient is satisfactory. The patient has a normosthenic physique, satisfactory nutrition (body mass index 20.3), and moon-shaped face. The skin and visible mucous membranes are moderately pale and clean. She has postoperative scars on the neck, in the area of clavicles and abdomen. Peripheral lymph nodes are not enlarged. The thyroid gland is not palpable. Respiratory rate is 18/min. Above the lungs, there is a percussion clear pulmonary sound; she has auscultatory weakened vesicular breathing; additional respiratory rales and murmur are not heard. Borders of relative cardiac dullness on the right are along the right edge of the sternum, upper at the rib III, and the left is 1 cm outward from the left mid-clavicular line. The activity of the heart is rhythmic, the heart rate is 88 beats/min, the tones are preserved at the apex. The weakening of the tone II above the aorta is determined, and a protodiastolic murmur is heard at the Botkin-Erb point. Also, a murmur is heard over the carotid arteries, the abdominal aorta and in the projection of the renal artery on the left. Blood pressure indices are 120/75 mm Hg. in the right hand, and 140/80 mm Hg. in the left hand. The pulsation on the right radial artery is weakened to some extent. The abdomen is soft, painless; the liver is at the edge of the costal arch, the kidneys and spleen are not palpable. There is no peripheral edema. The joints are not changed externally, with full range of motion.

***Instrumental and laboratory diagnostics***

*Data from additional research methods*. In the analysis of blood, mild anemia persists (hemoglobin 95 g/l, erythrocytes 3.3 × $10^{12}$/l), leukocytosis (10.9 × $10^{9}$/l), ESR 11 mm/h, leukocyte count has no abnormalities,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hypochromia, moderately pronounced anisocytosis.

Renal and liver function test results are normal, C-reactive protein test result is positive.

Electrocardiogram (on admission) showed sinus regular rhythm, heart rate of 80 bpm, vertical position of the electrical cardiac axis. Segment ST-T is on the isoline.

Echocardiogram revealed persisting grade 2 aortic insufficiency and local dilatation of the left coronary sinus; the cavities of the heart were not dilated, the myocardium was not thickened, and contractility was satisfactory. Minor functional mitral and tricuspid regurgitation was registered.

Results of Doppler ultrasound of the brachiocephalic arteries showed no negative changes, there was occlusion of the subclavian-carotid shunt to the left of the orifice, subclavian-carotid prosthesis to the right, and satisfactory blood flow. The subclavian arteries were thickened, indurated, the walls had signs of loss of layers differentiation, and there was narrowing of the lumen throughout.

Doppler imaging of the arteries of the upper and lower extremities revealed a moderate thickening of the arterial walls without disorders of blood flow.

Doppler imaging of renal vessels showed significant disorders of blood flow in the renal artery basins. There is a significant increase in the resistance index at all levels, an increase in systolic blood flow velocity, mainly in the main trunks. There is a pronounced unevenness, in some places narrowing of the diameter of the main trunks of the renal arteries and the abdominal aorta.

The patient was consulted by a neurologist, and discirculatory encephalopathy with bilateral reflex pyramidal insufficiency in the extremities, and vestibulopathy was diagnosed.

The patient was consulted by an endocrinologist, and hypoplasia of the thyroid gland with nodulation, symptoms of mild hypothyroidism were detected (Euthyrox 25 mg/day was prescribed).

**Final diagnosis**

Nonspecific aortoarteritis, type III, activity of the degree 1, chronic course, with lesions of large and medium-sized vessels (stenosis of the abdominal aorta of the renal arteries, condition after stenting of the abdominal aorta, renal arteries on the left in 2010; stenosis of the carotid arteries on the right and on the left, stenosis of the brachiocephalic trunk and right subclavian artery, condition after subclavian-carotid bypass on the left in March 2014, subclavian-carotid prosthetics on the right with a synthetic prosthesis in December 2014); degree 2 aortic valve insufficiency. Secondary arterial hypertension, chronic heart failure stage I, ejection fraction 60%, grade II.

**Treatment and outcomes**

In the department, the patients received methylprednisolone 6 mg/day, omeprazole 20 mg/day, nebivolol 5 mg/day, amlodipine 5 mg/day, clopidogrel 75 mg/day, levothyroxine sodium 25 μg/day, pentoxifylline 600 mg/day, Vazaprostan 1 vial (20 μg) with intravenous drip-feed No. 10.

During the therapy, intermittent lameness, asthenia, and dizziness decreased; blood pressure stabilized at 130/80 mm Hg.

## DISCUSSION

There are four anatomical variants (types) of late stages of nonspecific aortoarteritis. Type I presents isolated lesion of the aortic arch and arteries extending from it; type II presents isolated lesion of the thoracic or abdominal aorta and its branches; type III indicates combined lesion of the aortic arch and its branches with changes in the thoracic or abdominal aorta; type IV indicates damage to the pulmonary artery and any part of the aorta [3, 4].

It should be remembered that the diagnostic concept of nonspecific arteritis is based on a complex of basic and additional research methods, anamnestic data, as well as the results of instrumental and laboratory research methods, namely the angiographic data, computed and magnetic resonance imaging. The presence of corresponding angiographic lesions, including dilation and/or occlusion of the aorta and its main branches in young people, even in the absence of any signs of an inflammatory process, suggests nonspecific aortoarteritis in the patient. However, any diagnostic search requires a thorough differential diagnostics. First of all, the presence of other systemic diseases of the connective tissue should be ruled out. The lesion of the great vessels of the aorta and vessels of the extremities requires ruling out of thromboangiitis obliterans, Behcet's disease, bacterial aneurysms, congenital abnormalities, and syphilitic mesaortitis. Involvement of the renal arteries requires ruling out of atherosclerotic lesions and their fibromuscular hyperplasia [3, 5].

Therapeutic approach for such patients includes basic steroid therapy using a personalized approach. Conservative therapy does not exclude the use of surgical methods for the correction of hemodynamically significant stenosis of the affected arteries.

## CONCLUSION

The complexity of diagnostics of nonspecific arteritis consists in the absence of pathognomonic signs and specific research methods that enable to establish timely correct diagnosis of the pathological process. The symptoms of such a disease often appear under the guise of other diseases, which requires a careful differential search. In the presented clinical case, Takayasu disease is described in a young woman with multiple lesions of arterial vessels and a rapidly progressive course of the disease. The peculiarity of the patient's disease is that during the first year after the onset of arterial hypertension, the main occlusive lesions of the aorta and arterial vessels were revealed, while narrowing of the carotid arteries (75–85%) was not accompanied by signs of cerebral ischemia. Correct diagnosis and timely treatment helped prevent the development of complications and slow down the disease progression.

Thus, each detected case of Takayasu disease is of great clinical and practical interest, and given the peculiarities of the nosology itself, nonspecific aortoarteritis should be considered as a major multidisciplinary problem affecting many medical and social aspects.

## INFORMED CONSENT

Written voluntary informed consent was obtained from the patient to publish the description of the clinical case.

## ADDITIONAL INFORMATION

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**Competing interests.** The authors declare that they have no competing interests.

## AUTHOR CONTRIBUTIONS

M.V. Grushina developed the concept and design of the article, collected and processed the material, wrote and edited the text; I.S. Grekov prepared the layout of the article text, worked with literature, collected and processed the material, wrote and edited the text; K. D. Arkhipova worked with literature, wrote the text. All authors made a significant contribution to the search and analytical work and preparation of the article, read and approved the final version before its publication.

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