

EARLY DIAGNOSIS OF TAKAYASU ARTERITIS

S. Emin, V. Boyadzhieva, Zh. Dimova, R. Stoilov, N. Stoilov

Clinic of Rheumatology, University Hospital "Sv. Ivan Rilski" – Sofia

Abstract. Systemic vasculitis is a group of heterogeneous diseases characterized by inflammation of the vascular wall. They can be primary or arise in the context of another disease. Blood vessels of different sizes are affected, being mainly divided into small, medium and large vessels. Takayasu arteritis is a vasculitis of the large blood vessels, most often affecting the aorta and its branches, subclavian arteries, iliac, femoral arteries and others. The presented clinical case concerns a woman with non-specific symptoms – low fever, sweating, weight loss, fatigue. After excluding an infectious genesis of the complaints, a diagnosis of Takayasu arteritis was made in the early phase of the disease as a result of positron emission tomography. Corticosteroid and immunosuppressive therapy was started. After performance of follow-up PET scan 20 months after the start of the therapy, a significant regression to the absence of the findings from the imaging study was observed.

Key words: aortoarteritis, vasculitis, Takayasu, early diagnosis, PET-CT

INTRODUCTION

Systemic vasculitides represent a group of heterogeneous diseases characterized by inflammation of the vascular wall [1]. They are relatively rare, with a worldwide incidence estimated at about 20-40 cases per 1 million people [2]. There are different classifications of vasculitis. According to the size of the affected vessels, they are mainly divided into three groups – vasculitis of the large, medium and small vessels [3]. Takayasu arteritis is a systemic vasculitis of an unknown etiology that mainly affects large and medium vessels.

It occurs in the pediatric population and adults [4, 5]. The symptoms are diverse and the disease can begin with non-specific manifestations such as fatigue, myalgia, arthralgia, fever [6].

Cardiovascular manifestations such as claudication of upper or lower limbs, as well as a difference in systolic arterial pressure of both arms or both legs, noise in some of the affected arteries and others are typical [4-8]. Cutaneous and/or neurological manifestations may also be present [9, 10].

Diagnosis is based on clinical symptoms and arteriographic findings. The most commonly used in routine clinical practice are the classification criteria of the American College of Rheumatology (ACR) from 1990 (Table 1) [11]. In November 2022 the new validated classification criteria of the American College of Rheumatology/European League of Rheumatology (EULAR) for Takayasu arteritis were published (Table 2). They have high sensitivity (93.8%) and specificity (99.2%). They consist of 10 clinical

signs, each of which carries a different number of points (+1 to +3), and ≥ 5 points are required to classify the disease. There are two mandatory criteria – age up to 60 years and evidence of vasculitis on imaging study. Unlike the previously used criteria from 1990, the new criteria are oriented to modern clinical practice, with a great weight in the direction of modern imaging studies. Another big difference is that the study was conducted on a larger population of patients, who are from different countries and continents [11, 12].

Treatment of the disease usually begins with intravenous corticosteroids and immunosuppressants. If there is no improvement and the symptoms persist as a result of conventional therapy, surgical revascularization of the affected vessels is the means of choice [13].

CASE REPORT

A 62-year-old white female patient was admitted to UMHAT „Sv. Ivan Rilski“ in the Rheumatology Clinic in July 2020 due to complaints of fever 37.5-38.2°C, fatigue, weight reduction by 6 kg and sweating for the past 4 months. Due to clinical and radiographic evidence of pneumonia, the patient was treated with Augmentin 2 x 1 tablet/day for 7 days, and then replaced with Avelox 1 tablet/day for 7 days. Despite the therapy (and the absence of inflammatory changes from follow-up radiography), the patient's symptoms persisted. Consultations with a gynecologist and a gastroenterologist were conducted, from which

no significant pathological findings were established, except chronic gastritis. Microbiological tests of throat and nasal samples, as well as blood and urine cultures remained negative over time (they were tested repeatedly), therefore an infectious process was excluded. More than 20

PCR tests for Covid-19 infection have been performed, with negative results.

The patient did not reported any family history, as well as allergies.

Concomitant diseases: arterial hypertension, chronic gastritis, type 2 diabetes mellitus.

Laboratory tests

Test Name	Result	Unit	Reference Range
Biochemistry			
ALAT	7.50	U/l	0-41.00
Alb	38.7		
ALP	122.00	U/l	0-140.00
ASAT	15.80	U/l	0-40.00
Cholesterol	5.07	mmol/l	0-5.20
CPK	100		
Crea	74.00	μmol/l	0-104.00
CRP	90.80		
Iron	4.10	μmol/l	6.60-36.00
GGT	24.00	U/l	0-60.00
Gluc	5.38	mmol/l	3.50-6.70
LDH	296		
TG	1.32	mmol/l	0-2.00
TP	80.60	g/l	64.00-83.00
UA(S)	360.00	μmol/l	142.00-420.00
Urea	2.90		
Iron+TIBC			
Iron(S)	4.10	μmol/l	6.60-36.00
TIBC	39.20	μmol/l	42.00-78.00
UIBC	35.1		
Hematology			
CBC EDTA - 20			
WBC	9.09	x10 ⁹ /L	3.50-10.50
RBC	4.83	x10 ¹² /L	3.70-5.90
HGB	113	g/l	120.00-180.00
HTC	0.385	l/l	0.36-0.53
MCV	79.8	fl	80.00-96.00
MCH	23.5	Pg	27.00-33.00
MCHC	294	g/l	300.00-360.00
PLT	492	x10 ⁹ /L	130.00-360.00
LYM%	30.4	%	20.00-48.00
MONO%	6.7	%	1.00-11.00
EO%	2.4	%	0-6.50
BASO%	0.5	%	0-2.00
NEUT%	58.8	%	40.00-70.00
LYM#	2.76	x10 ⁹ /L	1.00-4.00
MONO#	0.60	x10 ⁹ /L	0-0.80
EO#	0.22	x10 ⁹ /L	0-0.50
BASO#	0.04	x10 ⁹ /L	0-0.14
NEUT#	5.34	x10 ⁹ /L	2.00-7.00
RDW	12.50		
MPV	8.9	fl	6.10-12.50
ESR/ Sedimentation Rate			
ESR/ Sedimentation Rate	100	mm/h	0-30.00

Rheumatology Clinic due to high disease activity and a single infusion of Methylprednisolone 1000 mg intravenously was performed. Azathioprine dose was increased to 150 mg/day. The patient continued outpatient treatment with Dehydrocortisone 5 mg – 4 tablets/day for a period of 1 month, after which the dose was gradually reduced to 2 tablets/morn-

ing in combination with Azathioprine 150 mg/day. Three months later or 1 year after initiation of treatment, the patient underwent a follow-up PET/CT scan. Normalization of the metabolic of the affected vessels and absence of underlying morphological changes in their walls from the native examination was established.

Table 1. ACR criteria for classification of Takayasu's arteritis. A diagnosis of Takayasu arteritis requires that 3 of the 6 criteria are met [Arend WP, 1990]

Sr. No.	Criteria
1.	Age at disease onset ≤ 40 years
2.	Claudication of extremities
3.	Decreased brachial artery pulse
4.	Blood pressure difference >10 mmHg
5.	Bruit over subclavian arteries or aorta
6.	Arteriogram abnormality

Table 2. 2022 American College of Rheumatology/EULAR classification criteria for Takayasu arteritis [Grayson PC, 2022]

2022 AMERICAN COLLEGE OF RHEUMATOLOGY / EULAR

CLASSIFICATION CRITERIA FOR TAKAYASU ARTERITIS

CONSIDERATIONS WHEN APPLYING THESE CRITERIA

- These classification criteria should be applied to classify the patient as having Takayasu arteritis when a diagnosis of medium-vessel or large-vessel vasculitis has been made
- Alternate diagnoses mimicking vasculitis should be excluded prior to applying the criteria

ABSOLUTE REQUIREMENTS

- Age ≤ 60 years at time of diagnosis
- Evidence of vasculitis on imaging¹

ADDITIONAL CLINICAL CRITERIA

Female sex	+1
Angina or ischemic cardiac pain	+2
Arm or leg claudication	+2
Vascular bruit ²	+2
Reduced pulse in upper extremity ³	+2
Carotid artery abnormality ⁴	+2
Systolic blood pressure difference in arms ≥ 20 mm Hg	+1

ADDITIONAL IMAGING CRITERIA

Number of affected arterial territories (select one) ⁵	
One arterial territory	+1
Two arterial territories	+2
Three or more arterial territories	+3
Symmetric involvement of paired arteries ⁶	+1
Abdominal aorta involvement with renal or mesenteric involvement ⁷	+3

Sum the scores for 10 items, if present. A score of ≥ 5 points is needed for the classification of TAKAYASU ARTERITIS.

1. Evidence of vasculitis in the aorta or branch arteries must be confirmed by vascular imaging (e.g., computed tomographic/catheter-based/magnetic resonance angiography, ultrasound, positron emission tomography).
2. Bruit detected by auscultation of a large artery, including the aorta, carotid, subclavian, axillary, brachial, renal, or iliofemoral arteries.
3. Reduction or absence of pulse by physical examination of the axillary, brachial, or radial arteries.
4. Reduction or absence of pulse of the carotid artery or tenderness of the carotid artery.

5. Number of arterial territories with luminal damage (e.g., stenosis, occlusion, or aneurysm) detected by angiography or ultrasonography from the following nine territories: thoracic aorta, abdominal aorta, mesenteric, left or right carotid, left or right subclavian, left or right renal arteries.
6. Bilateral luminal damage (stenosis, occlusion, or aneurysm) detected by angiography or ultrasonography in any of the following paired vascular territories: carotid, subclavian, or renal arteries.
7. Luminal damage (stenosis, occlusion, aneurysm) detected by angiography or ultrasonography involving the abdominal aorta and either the renal or mesenteric arteries.

DISCUSSION

The clinical signs and symptoms of Takayasu's arteritis can vary widely. In most cases, the first manifestations of the disease are non-specific. Arthralgia, myalgia, fatigue and malaise, subfebrile and febrile conditions are observed. In case of clinically significant involvement of the vascular wall of the aorta and its branches, complaints are corresponding to the affected region such as absent or reduced pulse, difference in systolic arterial pressure in both arms, new-onset arterial hypertension with involvement of the retinal arteries, neurological manifestations with involvement of the carotid arteries such as headache and transient ischemic attacks and other symptoms [6-10].

The most widely used criteria in the diagnosis of the disease are the classification criteria of the ACR from 1990, as it is necessary to fulfil 3 out of 6 criteria [11]. At the onset of the disease, the criteria are usually not met and the clinical feature may be dominated only by non-specific symptoms, as it is in our case. Imaging studies of the vessels are crucial for the diagnosis of Takayasu arteritis, especially in the early phase of the disease. CT and magnetic resonance tomography-angiography are most often used, with the help of which lesions on the examined vessels such as stenoses, obturation and aneurysms can be visualized [14]. Ultrasound is also the method of choice for carotid and subclavian arteries, but it is limited to the study of superficial vessels and the impossibility of studying the aorta and its proximal branches [15]. Conducting PET with radiolabeled deoxyglucose is used both in the diagnosis of the disease and in screening. This methodology allows visualization of an inflammatory process in the vessels through the uptake of radiolabeled glucose by the inflammatory cells in the vessel wall, even before the presence of morphological changes that occur in the late phase of the disease [16, 17, 18]. In the 2018 EULAR Guidelines, the recommendations for suspicion of vasculitis of the large vessels are in the direction of conducting ultrasonography and MRI as the means of first choice, and PET and Computed tomography as an alternative option for early diagnosis [19]. In our clinical case, PET was performed to exclude malignancy and screen for large vessel vasculitis, and a diagnosis of Takayasu's arteritis was made. Positron emission tomography, due to the high sensitivity of the methodology and the mechanism of vessel

imaging, is the means of choice for monitoring disease activity and the possibility of evaluating the therapeutic effect.

CONCLUSION

Due to suspicion of vasculitis of the large vessels in the differential diagnostic plan, the patient underwent a highly specialized imaging study – PET-CT, thanks to which a diagnosis of Takayasu's arteritis was made in the early phase of the disease. Imaging studies play a key role in the diagnostic process, especially when the clinical picture does not present with typical symptoms.

Библиография / References

- Guillevin L, Dörner T. Vasculitis: mechanisms involved and clinical manifestations. *Arthritis Res Ther*. 2007;9 Suppl 2(Suppl 2):S9. doi: 10.1186/ar2193.
- Jatwani S, Goyal A. Vasculitis. [Updated 2022 Aug 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK545186/>
- Jennette JC, Falk RJ, Bacon PA et al. 2012 revised International Chapel Hill Consensus Conference nomenclature of vasculitides. *Arthritis Rheum*. 2013;65:1-11. doi: 10.1002/art.37715
- Kerr GS, Hallahan CW, Giordano J et al. Takayasu arteritis. *Ann Intern Med*. 1994 Jun 1; 120 (11): 919-29. doi: 10.7326/0003-4819-120-11-199406010-00004.
- Brunner J, Feldman BM, Tyrrell PN et al. Takayasu arteritis in children and adolescents. *Rheumatol (Oxford)*. 2010 Oct;49(10):1806-14. doi: 10.1093/rheumatology/keq167.
- Hall S, Barr W, Lie JT, et al. Takayasu arteritis. A study of 32 North American patients. *Med*. 1985;64:89-99.
- Lupi-Herrera E, Sánchez-Torres G, Marcushamer J et al. Takayasu's arteritis. Clinical study of 107 cases. *Am Heart J*. 1977 Jan;93(1):94-103. doi: 10.1016/s0002-8703(77)80178-6.
- Subramanyan R, Joy J, Balakrishnan KG. Natural history of aortoarteritis (Takayasu's disease). *Circulation*. 1989 Sep;80(3):429-37. doi: 10.1161/01.cir.80.3.429.
- Li-xin Z, Jun N, Shan G et al. Neurological manifestations of Takayasu arteritis. *Chin Med Sci J*. 2011 Dec;26(4):227-30. doi: 10.1016/s1001-9294(12)60005-4.
- Francès C, Boisnic S, Blétry O et al. Cutaneous manifestations of Takayasu arteritis. A retrospective study of 80 cases. *Dermatologica*. 1990;181(4):266-72. doi: 10.1159/000247820.
- Arend WP, Michel BA, Bloch DA et al. The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. *Arthritis Rheum*. 1990 Aug;33(8):1129-34. doi: 10.1002/art.1780330811.
- Grayson PC, Ponte C, Suppiah R For the DCVAS Study Group, et al 2022 American College of Rheumatology/EULAR classification criteria for Takayasu arteritis. *Ann Rheumatic Dis*, 2022;81:1654-1660.

13. Trinidad B, Surmachevska N, Lala V. Takayasu Arteritis. [Updated 2022 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan. Available from: [https:// www.ncbi.nlm.nih.gov/books/NBK459127/](https://www.ncbi.nlm.nih.gov/books/NBK459127/)
14. Schmidt WA, Nielsen BD. Imaging in large-vessel vasculitis. Best Pract Res Clin Rheumatol. 2020 Dec;34(6):101589. doi: 10.1016/j.berh.2020.101589.
15. Nielsen BD, Hansen IT, Keller KK et al. Diagnostic accuracy of ultrasound for detecting large-vessel giant cell arteritis using FDG PET/CT as the reference. Rheumatol (Oxford). 2020 Aug 1;59(8):2062-2073
16. Balink H, Bennink RJ, van Eck-Smit BL, Verberne HJ. The role of 18 F-FDG PET/CT in large-vessel vasculitis: appropriateness of current classification criteria? BioMed Res Int 2014;1e13.
17. Writing group, Reviewer group Slart RH, et al. FDG-PET/CT(A) imaging in large vessel vasculitis and polymyalgia rheumatica: joint procedural recommendation of the EANM, SNMMI, and the PET Interest Group (PIG), and endorsed by the ASNC. Eur J Nucl Med Mol Imag 2018;45:1250e69.
18. Grayson PC, Alehashemi S, Bagheri AA, et al. 18 F-Fluorodeoxyglucose-Positron emission tomography as an imaging biomarker in a prospective, longitudinal cohort of patients with large vessel vasculitis. Arthritis Rheum 2018;70: 439e49.
19. Dejaco C, Ramiro S, Duftner C, et al EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice. Ann Rheumatic Dis, 2018;77:636-643.

Постъпил за печат: 11.02.2023 г.

Submitted: 11.02.2023

✉ Адрес за кореспонденция:

Д-р С. Емин, дм
Клиника по ревматология
УМБАЛ "Св. Иван Рилски"
Медицински университет – София

✉ Correspondence address:

S. Emin, MD, PhD
Clinic of Rheumatology
UMHAT "Sv. I. Rilski
Medical University – Sofia