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Takayasu's arteritis - a summary of current, clinically relevant knowledge of the disease

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ABSTRACT

Takayasu's disease, also known as pulseless disease or aortic arch syndrome, is a rare inflammation of the aorta and its branches, and sometimes the pulmonary arteries, which, according to studies, occurs most frequently in people from the Far East and Asian countries. In addition, its incidence is significantly higher in women, and the mean age of affected patients is 45.4 years [1]. The first official clinical case report of the disease by Shimizu and Sano appeared in 1951, while the name of the disease was proposed by Cassamise and Okuda in 1954 to honour the first clinician, Mikito Takayasu, who as early as 1908 presented a case of a young female patient with characteristic fundus lesions associated with pulse disturbances [2].

KEY WORDS: Takayasu's arteritis (TA), pulseless disease, aortic arch syndrome.

INTRODUCTION

The aetiology and pathogenesis of this disease entity are still unknown. What is known, however, is that the cellular inflammatory infiltrate involves the vascular endothelium and the middle membrane of the affected vessels. In the next stage of the disease, aneurysms as well as stenosis, occlusion and dilatation of various vessel segments occur due to endothelial cell proliferation and fibrosis of the middle membrane [3]. The consequence of these changes is the formation of thrombosis and peripheral embolism.

An autoimmune basis is suspected in the development of the disease. Its incidence also apparently correlates with genetic conditions, as suggested by the fact that the disease is much more common in people with particular antigens, such as the tissue compatibility antigens HLA-B*52 or HLA-B39 [4].

SYMPTOMS

The symptomatology of this disease varies widely and is closely dependent on the location and severity of the stenosis, obstruction and aneurysms that have developed, which influences the varying haemodynamic significance of the lesions.

The initial period of the disease usually lasts a long time (even several years) and does not manifest itself with any serious symptoms on the part of the inflamed vessels or ischaemic organs. However, symptoms such as weakness, loss of weight and appetite, night sweats, fever or muscle and joint pains often appear. Patients also sometimes develop non-specific lesions on the skin which, as the disease progresses, most commonly take the form of erythema nodosum [5]. Of the more advanced symptoms observed in this disease entity, there is a characteristic absence or asymmetry of the pulse and a pressure differential in the upper limbs [6]. The disease can also manifest with a number of disorders resulting from impaired cerebral circulation, such as headaches and dizziness, syncope, seizures, TIA, stroke and blindness. The latter, together with other visual impairment, may be a consequence of the formation of multiple anastomoses between arterial and venous vessels in the retina [7]. Another symptom is renal vascular hypertension, which develops as a result of a narrowing of the diameter of the renal arteries [8]. Arterial hypertension is also the most common complication occurring in the course of this disease. Lesion involvement of the mesenteric arteries and visceral trunk will result in diarrhoea, abdominal pain and gastrointestinal bleeding, while chest pain, dyspnoea and haemoptysis will be seen if pulmonary artery lesions are present [9][10]. One of the most characteristic symptoms of Takayasu's disease is so-called carotidism, which is pain or tenderness in the neck corresponding to the location of the affected vessels. Another symptom is chroma usually affecting the upper limbs, lower limbs and mandible [11][12].
In addition to dilatation and the appearance of aneurysms on the aorta, dissection of the aortic wall may also occur. Dilation may also affect the aortic valve annulus, resulting in aortic regurgitation, which is a significant risk factor for death in patients with this disease.

DIAGNOSIS

Various types of imaging are widely used in the diagnostic process of Takayasu's disease. Sometimes it is possible to reveal aortic or mediastinal dilatation with a chest X-ray. It is also sometimes helpful to use ultrasound , which allows assessment of thickening of the entire vessels, together with the constrictions within them, in vessels such as the subclavian, carotid or sometimes lower limb arteries. However, the most relevant imaging studies are angio-CT, classic angiography and angio-MR, which highlight arterial stenosis in more advanced stages of the disease [13]. Another tool for more accurate detection and control of the course of inflammatory changes in the vessel walls is PET [14].

Patients with imaging-diagnosed endovascular lesions are often classified according to the table below on the basis of the vessels involved, which can be helpful in the context of potential surgeries planned for the future, as well as more accurately predicting possible complications as a result of further disease progression [15][16].

Type	**Vessel involvement**
I	Branches from aortic arch
IIa	Ascending aorta, aortic arch and its branches
IIb	Ascending aorta, aortic arch and its branches, thoracic descending aorta
III	Thoracic descending aorta, abdominal aorta and/or renal arteries
IV	Abdominal aorta and/or renal arteries
V	Combined features of types IIb and IV

Among the abnormalities in the basic laboratory tests, these patients have elevated CRP and a2-globulin protein levels and accelerated ESR. In addition, normocytic anaemia and reduced plasma albumin levels are also found in some cases.

Based on the 1990 American College of Rheumatology (ACR) guidelines, Takayasu's disease can be diagnosed by fulfilling at least three of the six criteria, which include the presence of the arteriographic abnormality found, impaired limb function, a diagnosis of onset before the patient's 40 years of age, an upper limb systolic blood pressure difference of more than 10 mm Hg, significant weakening or complete loss of the brachial artery pulse and an audible murmur over the subclavian artery or aorta.

A different method of diagnosis is to follow the Ishikawa criteria, which distinguishes between obligatory criteria (necessary for the diagnosis of the disease), major and minor criteria, of which two major criteria, one major and two minor criteria or four minor criteria must be met.

Obligatory criterion:
1. Age < 40 years
Major criteria:
1. Left mid subclavian artery lesion
2. Right mid subclavian artery lesion
Minor criteria:
1. High ESR
2. Carotid artery tenderness
3. Hypertension
4. Aortic regurgitation or Annuloaortic ectasia
5. Pulmonary artery lesion
6. Left mid common carotid lesion
7. Distal brachiocephalic trunk lesion
8. Descending thoracic aorta lesion
9. Abdominal aorta lesion

For the Sharma criteria, the quantities of large and small criteria required for diagnosis are the same as for Ishikawa, but there is no obligatory criterion.

Major criteria
1. Left mid subclavian artery lesion
2. Right mid subclavian artery lesion
3. Characteristic signs and symptoms of at least one month duration
Minor criteria
1. High ESR
2. Carotid artery tenderness
3. Hypertension
4. Aortic regurgitation or Annuloaortic ectasia
5. Pulmonary artery lesion
6. Left mid common carotid lesion
7. Distal brachiocephalic trunk lesion
8. Descending thoracic aorta lesion
9. Abdominal aorta lesion
10. Coronary artery lesion

[1][2][3][9]

However, in 2022, a new classification was created in collaboration between the ACR and EULAR to diagnose the disease more accurately and efficiently. According to this method, a score equal to or greater than 5 points from the following criteria outlined below is needed to make a diagnosis of the disease [17].

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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 imaging[1]	

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.

In the context of differential diagnosis in younger patients in particular, it is important to consider the possibility of disease entities such as tumour fever syndromes, chronic secondary hypertension, bacterial and viral infections, coarctation of the aorta, Ehlers-Danlos syndrome, systemic cellulitis or other systemic vasculitis.

TREATMENT

The treatment of patients with Takayasu's disease is aimed at preventing irreversible damage to the organs and blood vessels. Its selection is based on the correct determination of the degree of disease activity.

The basis of treatment is the use of oral corticosteroids (prednisone) at a dose of approximately 1-2 mg/kg of the patient. This action is meant to bring the disease into remission and then maintain it. Once the patient's inflammatory exponents have normalised, the dose should be slowly and gradually reduced, aiming for complete withdrawal [18].
In cases of steroid dependence and rapid relapses with lower doses of the drug, immunosuppressive preparations are added to the therapy. Among the most commonly used drugs in this group are cyclophosphamide, methotrexate, azathioprine, mycophenolate mofetil and cyclosporine. If good results are observed with such therapy, it can be used for long periods of time. In the context of the above-mentioned drugs, it is worth

remembering that their long-term use may contribute to some of the symptoms or complications observed in this disease.

However, in situations of persistent unsatisfactory results of therapy, there is the possibility of alternative treatment in the form of biological drugs. These include IL-6 inhibitors (tocilizumab) and TNF-alpha inhibitors (infliximab and adalimumab) [19].

There are also various surgical treatments, in the form of surgery or endovascular procedures. The use of the second method is more common due to its less invasive nature and includes procedures such as endovascular aneurysm repair or angioplasty. Invasive treatment is currently used as soon as possible after the diagnosis of the disease or during periods of low disease activity and clinical remission [20].

SUMMARY

TA is a recurrent disease whose prognosis is closely related to the degree of ischaemia of the various organs of the body as a result of the vascular lesions that have developed. Its biggest problem is the still too late diagnosis in patients suffering from it. This is certainly partly due to the very wide range of symptoms with which it manifests itself. This problem could largely be solved by greater availability and referral to imaging, and by raising clinicians' awareness of the very characteristic symptoms that can be detected by a simple physical examination [2].

Perhaps a breakthrough in the detection and early treatment of this disease entity would be further research into its still very poorly understood aetiology and pathogenesis with a view to more accurately uncovering the genetic factors and autoimmune mechanisms involved.

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