



## Case Report

<http://crp.tums.ac.ir>**Takayasu Arteritis: Diagnosed and Treated as Labyrinthitis**

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**ABSTRACT**

The objective of this paper is to report a case of a patient with Takayasu arteritis (TA), diagnosed and treated as labyrinthitis for two years, with brief review of the literature. A 36-year-old woman, who presented vertigo, falling on the ground for losing consciousness for a few seconds, and progressive loss of left vision, was admitted to the emergency with headache and impalpable carotid pulses. The erythrocyte sedimentation rate (ECR) and C-reactive protein (CRP) serological tests were increased; however, the ANF (Antinuclear factor), venereal disease research laboratory (VDRL) and fluorescent treponemal antibody absorption (FT-ABS) were negative. After aortography, she developed convulsive seizures, loss of consciousness, hemodynamic instability, and death. The cause of death was distributive shock.

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**Introduction**

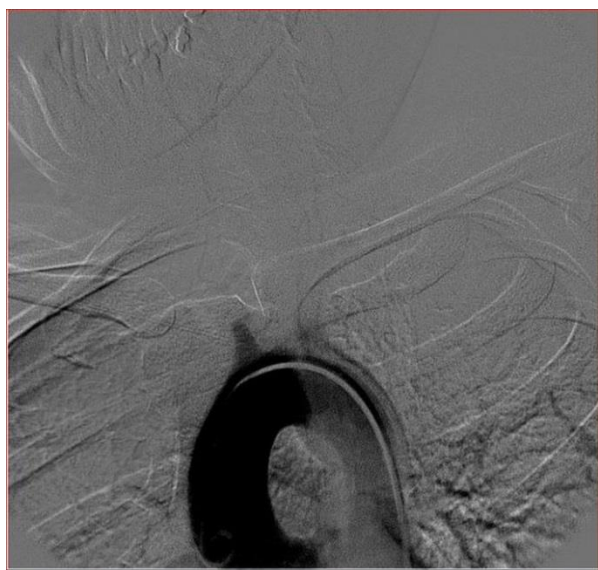
**T**akayasu arteritis (TA) is a chronic inflammatory disease that affects the wall of large vessels, and therefore has a variety of clinical presentations which may confuse the attending physician, a priori, delaying the diagnosis and consequently the treatment. Mikito Takayasu described the first case of TA in 1905. The objective of this paper is to report a case of a patient with TA, diagnosed and treated as labyrinthitis.

**Case Report**

A 36-year-old Caucasian woman reported daily symptoms of resting tremor followed by dizziness, weakness in the limbs, difficulty in walking, loss of balance and falling on the ground for losing consciousness for a few seconds during the preceding two years. Concomitantly, the patient experienced progressive vision loss in the left eye, and later in the right eye. During this period, the patient reportedly attended several medical

services, and was diagnosed and treated for labyrinthitis and systemic hypertension. However, the symptoms worsened over time, with the addition of frontal and retro orbital pulsating headache, photophobia, and nausea. Common analgesics (dipirona and paracetamol) were ineffective.

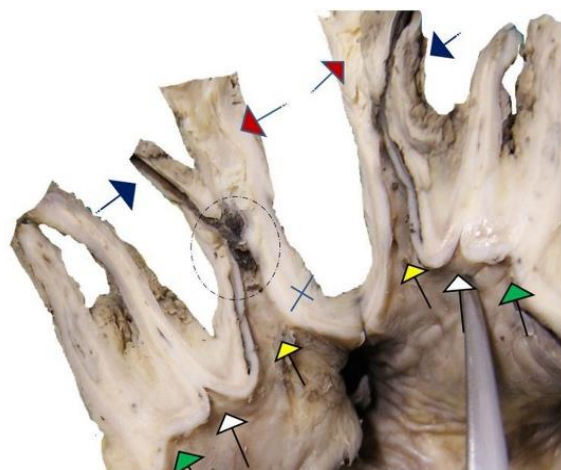
The patient was admitted to the emergency with clinical findings included facial mask of pain, impalpable radial, brachial and carotid pulses, and an arterial blood pressure of 140 x 90 mmHg (measured in the right and left thigh). Several laboratory tests were performed including serology for toxoplasmosis and cytomegalovirus (CMV), anti-human immunodeficiency virus (HIV) antibodies, antinuclear antibodies (ANA), perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA), cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA), venereal disease research laboratory (VDRL), and fluorescent treponemal antibody absorption (FTA-ABS), all of which were negative. There was an increase in erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP). On aortography, all vessels of the aortic arch were obstructed, with involvement of the brachiocephalic trunk and the carotid arteries (Figure 1).



**Figure 1.** Obstruction of the brachiocephalic trunk on aortography

Collateral pathways of the vertebral artery maintained cerebral circulation, and the right renal artery was partly occluded. Based on these findings, the patient was diagnosed with TA). Following arteriography, the patient had three episodes of seizure at 10-min intervals, and her blood pressure was 220 x 120 mmHg (measured in the right and left thigh). Intracranial hypertension was the only finding on computed tomography (CT). Subsequently, the patient experienced loss of consciousness, bradypnea, bronchoaspiration during orotracheal intubation, hemodynamic instability, areflexia, brain death, and death.

On autopsy, the brain was swollen and the right lung was augmented, with the middle and lower lobes congested and friable upon cutting. The endothelium of aorta and pulmonary artery were displaying thickening, fibrosis and retraction. The vessels of the aortic arch were completely obstructed from the emergence of the left subclavian artery, the left common carotid and the right subclavian artery. The brachiocephalic trunk was pervious, but a small thrombus occluded the vessel at the emergence of the right common carotid and the right subclavian artery (Figure 2).



**Figure 2.** Complete obstruction of left subclavian artery (green arrow); left common carotid artery (white arrow); right subclavian artery (yellow arrow); right common carotid artery (blue arrow); right subclavian artery (red arrow); small thrombus (line-drawn circle)

The coronaries were unobstructed. Fatty streaks were visible on the aorta, and the right renal artery was narrowed on arteriography. The kidneys displayed severe cortical pallor. Diffused hepatic congestion was also evident. On microscopy, inflammatory infiltrate (lymphocytes and rare plasmocytes) was observed on the walls of the aortic, pulmonary, carotid, and subclavian arteries, in addition to areas occluded by fibrous tissue. An organized thrombus and fibrosis were seen in the right subclavian artery. The liver displayed signs of necrosis, hemorrhage, cholestasis and centrilobular steatosis. Both kidneys presented cortical and medullar necrosis. The right lung was affected with bronchopneumonia.

## Discussion

Takayasu disease is a clinicopathologic term to designate one noninfectious aortitis. TA is a chronic inflammatory disease involving the aorta, the main aortic branches and the pulmonary arteries, starting with the tunica media and tunica externa. The disorder affects primarily Asian and South American women (1).

The pathogenesis and progression of TA are not fully understood, but the vascular inflammatory process appears to be triggered by factors such as genetic predisposition (as in relatives sharing HLA-B\*52). HLA-B\*52:01 is associated with TA beyond population. It is associated not only with TA susceptibility, but also with clinical phenotypes (2). The matrix metalloproteinase-2 (MMP-2) can be helpful in diagnosing TA, and MMP-3 together with MMP-9 can be used as activity markers for TA (3).

As a large-vessel vasculitis, TA has a highly variable clinical presentation, potentially delaying diagnosis and treatment, as in the case reported here. TA may present unspecific inflammatory symptoms such as fever, weight loss, loss of appetite, fatigue, myalgia, and arthralgia (4). More specific presentations include vascular tissue involvement with increased demand/supply

ratio (angina pectoris and acute myocardial infarction) and cerebrovascular disease. On physical examination, pulses may be weak or impalpable. According to our patient's relatives, this parameter was not evaluated during previous consultations.

The carotid arteries may also be involved, producing symptoms of carotidynia, fainting, and blurry vision (4).

Cardiac manifestations are main cause of morbidity and mortality in TA, as pericarditis, myocarditis, coronary arteritis with myocardial ischemia, valve disease (aortic regurgitation is the most common, followed by mitral regurgitation) or intracardiac thrombus, valvulopathy and acute pericarditis (5, 6).

Other signs include mucocutaneous pallor (due to anemia) and abnormal blood pressure. The variation in pressure is a result of the involvement of the subclavian arteries and the augmentation of systemic arterial pressure in the upper and lower limbs (4).

Other manifestations such as vertigo, syncope, orthostasis, headache, convulsions, visual impairment, and dementia may present clinically due to the involvement of the carotid and vertebral arteries. The rare phenomenon called subclavian steal syndrome (SSS) can be manifested due to retrograde flow through the vertebral artery that supplies the subclavian distal to the stenosis, and vasodilation of the arterial bed in the upper limb with exercise compromises posterior cerebral blood flow (7).

Moreover, clinical manifestations may include skin lesions such as inflammatory nodes, erythema nodosum-like lesions, pyoderma gangrenosum, and livedo reticularis. Raynaud's phenomenon may also be observed (8-11).

TA may not represent a major problem during pregnancy, although it increases the risk of complications, especially eclampsia and hypertension (12).

The histopathological findings in TA are not specific to TA; thus, when suspecting TA, the clinical diagnosis can be established based on Ishikawa's diagnostic criteria, which

consist of clinical, image and laboratory findings. The set includes one obligatory criterion (age  $\leq$  40 years), two major criteria (left mid-subclavian artery lesion, right mid-subclavian artery lesion) and nine minor criteria (ESR  $>$  20 mm/hour, common carotid artery tenderness, hypertension, aortic regurgitation or annuloaortic ectasia, pulmonary artery lesion, mid-common carotid artery lesion, distal brachiocephalic trunk lesion, descending thoracic aorta lesion, abdominal aorta lesion). In addition to the obligatory criterion, the presence of two major criteria or one major plus two or more minor criteria, as well as four or more minor criteria suggests a high probability of the presence of TA (13).

Another way to establish the diagnosis of TA is through the American College of Rheumatology (ACR), according to which six criteria were selected for the traditional form of classification: onset at age under 40 years, claudication of extremities, decreased brachial artery pulse, blood pressure difference between arms more than 10 mmHg, bruit over subclavian arteries or the aorta, and arteriographic evidence of narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities. The presence of 3 or more of these 6 criteria demonstrates a sensitivity of 90.5% and a specificity of 97.8% (14).

Sharma et al. proposed a modification of Ishikawa's diagnostic criteria for TA. The criteria proposed consists of three major criteria including left and right mid subclavian artery lesions, characteristic signs and symptoms of at least one month duration, and ten minor criteria: a high ESR, carotid artery tenderness, hypertension, aortic regurgitation or annuloaortic ectasia, pulmonary artery lesion, left mid common carotid lesion, distal brachiocephalic trunk lesion, descending thoracic aorta lesion, abdominal aorta lesion, and coronary artery lesion. To establish a diagnosis, there should be two major criteria or one major plus two or

more minor criteria, or four or more minor criteria. The sensitivity and specificity of Sharma's diagnostic criteria for TA is 92.5% and 95.0%, respectively (15).

The differential diagnosis of TA includes an array of disorders affecting the aorta and its main branches. These may be grouped in two major categories: non-infectious (isolated aortitis and giant-cell aortitis) and infectious (mainly syphilitic aortitis) (16). From the clinical-epidemiological point of view, it should be kept in mind that TA is most common in young women with vascular occlusion, while isolated aortitis has no evident age or sex preference, and is usually discovered incidentally on imaging. On the other hand, giant-cell aortitis typically presents as aortic insufficiency with or without temporal arteritis (16). Moreover, it may be distinguished from TA by the fact that it classically affects patients over 60 years of age (17).

Treatment of TA usually consists of oral corticosteroids; preferably, prednisone at a dose of 45-60 mg per day to control the disease.

The patient met the diagnostic criteria (both Ishikawa's and Ishikawa's modified) for TA: age under 40 years, left and right mid-subclavian artery lesions (major criteria), increased ESR and hypertension, pulmonary and common carotid artery involvement, brachiocephalic trunk lesion, descending thoracic aorta lesion, and abdominal aorta lesion (minor criteria). Having met two major and several minor criteria, a diagnosis of TA was established. According to ACR, the patient met 5 criteria. However, the lack of proper medical evaluation contributed to the delayed diagnosis of the disease, which only occurred in an advanced stage, led to patient death. Cause of death was distributive shock.

### **Conflict of Interests**

Authors have no conflict of interests.

### **Acknowledgments**

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