THE NEW ARMENIAN MEDICAL JOURNAL
Vol.5 (2011), N 1 , p.43-47

TO THE ISSUE OF RARE PATHOLOGIES: THE EXAMPLE OF TAKAYASU'S DISEASE

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Abstract

The purpose of the work is representation of clinical, laboratory and tool examination results (X-ray, echocardiographic and MRT data) of a patient with Takayasu's disease, whose diagnosis has been put at University Hospital "Muratsan" for the first time.

The aneurysm of aorta was revealed through cardiac ultrasound when the Takayasu's disease was suspected for the first time. This diagnosis was confirmed at the Research Center of Cardiovascular Surgery after A.N. Bakulev (Moscow, Russia). The patient was diagnosed for nonspecific aortoarteritis: Takayasu's arteritis type III, connective tissue dysplasia syndrome.

Overall prognosis in individuals with Takayasu's arteritis relates to the degree of vascular and end-organ damage, specifically retinal vasculopathy, aortic insufficiency, aortic aneurisms, and hypertension; 15 years survival rate is high and makes 95%. Takayasu's arteritis is a life threatening and a heavy relapsing disease. Early diagnosis can be difficult due to nonspecific early symptoms; consultations of a wide range of professionals (pediatric rheumatologist, ophthalmologist, pediatric cardiologist, vascular surgeon, and interventional radiologist) are required in order to exclude other diseases. Early diagnostics of the given disease and treatment initiated in due time will allow to improve the quality of patients' life, to prolong remission, to stabilize the pathological process. This is the reason why the given problem is a matter of urgency today.

Keywords: aneurysm of aorta, arteritis, artery stenosis, artery occlusion, granulomatous vasculitis.

INTRODUCTION

Last years interest to rare diseases has sharply increased in the medical world. Takayasu's disease refers to such pathologies. Takayasu's arteritis (also known as "Aortic arch syndrome", and "Pulseless disease" [*James W. et al., 2006*] is an inflammatory disease with an unknown cause. It affects the aorta, the main blood vessel from the heart, as well as the blood vessels, which are attached to it. Takayasu's arteritis is a granulomatous vasculitis of unknown etiology that commonly affects the thoracic and abdominal aorta. It causes intimal fibroproliferation of the aorta, great vessels, pulmonary arteries, and renal arteries and results in segmental stenosis, occlusion, dilatation, and aneurismal formation in these vessels. Takayasu's arteritis is the only form of aortitis that causes stenosis and occlusion of the aorta. About half of all patients develop an initial systemic illness. The other half of patients with Takayasu's arteritis present only with late vascular changes. The inflammation of the aorta and its branch arteries can lead to poor blood supply to tissues of the body in patients with Takayasu's disease. This can cause painful, cool, or blanched extremities, dizziness, headaches, chest pain, and abdominal pain. Other early symptoms can include fatigue, weight loss, and low-grade fever.

Classification criteria for Takayasu's arteritis are established:

- Age of 40 years or younger at disease onset;
- Claudication of the extremities;
- Decreased pulsation of one or both brachial arteries;

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Difference of at least 10 mm Hg in systolic blood pressure between arms;

Bruit over one or both subclavian arteries or the abdominal aorta;

Arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the upper or lower extremities that is not due to arteriosclerosis, fibromuscular dysplasia, or other causes.

Three of 6 criteria are necessary for diagnosis of Takayasu's arteritis. The presence of any 3 or more criteria yields a sensitivity of 90.5% and a specificity of 97.8%.

Early corticosteroid therapy may lead to improvement in clinical findings and may aid in subsidence of the active inflammatory process of Takayasu's arteritis. Prednisone is usually effective in controlling the clinical symptoms of Takayasu's arteritis, as well as controlling and decreasing the progression of active disease [*Weyand C., Goronzy J., 2003; Park M. et al., 2005; Phillip R., Luqmani R., 2008*].

Although it has been reported worldwide, it is more common in young Asian women. Takayasu's arteritis is observed more frequently in Asian countries such as Japan, Korea, China, India, Thailand, Singapore, Israel, and Turkey, as well as Central and South America. About 100-200 new cases of Takayasu's arteritis are registered each year in Japan. Females are about 8-9 times more likely to get it than males [*Abularrage C. et al., 2008; Akar S. et al., 2008*]. People usually get the disease between 10 and 30 years of age. The 5- and 10-year survival rates are approximately 69% and 36%, respectively, in patients with two or more complications. The 5- and 10-year survival rates associated with one or fewer complications are 100% and 96%, respectively.

About the half of all patients develop an initial systemic illness with symptoms of malaise, fever, night sweats, weight loss, arthralgia, and fatigue. There is often an anemia and marked elevation of the erythrocyte sedimentation rate (ESR). This phase gradually subsides and is followed by a more chronic stage characterized by inflammatory and obliterative changes in the aorta and its branches. The other half of patients with Takayasu's arteritis present with only late vascular changes, without an antecedent systemic illness. In the late stage, weakness of the arterial walls may give rise to localized aneurysms. Raynaud's phenomenon is commonly found in this disease. The doctor can find elevated blood pressure in over half of the patients with Takayasu's disease. Abnormal sounds of blood movement through blood vessels can sometimes be heard with a stethoscope. Small notches in the ribs of the back of the chest have sometimes been detected on routine chest X-rays and are felt to be a result of abnormal pulsations of blood vessels in these areas.

The diagnosis is supported by the blood tests, such as the erythrocyte sedimentation rate (sed rate) that suggests inflammation in the body. In fact, elevated blood pressure with an elevated sedimentation rate is distinctly uncommon in children and very helpful in suggesting Takayasu's disease as a possible cause. Anemia (low red blood cell count) is frequent [*Schmidt W., Blockmans D., 2005; Andrews J., Mason J., 2007*].

Takayasu's arteritis is ultimately diagnosed with an angiogram of the arteries (arteriogram), whereby a contrast material is injected into the blood vessels and it makes them visible by X-ray. With the arteriogram, the doctor can visualize the abnormally narrowed and constricted arteries. Studies have shown a successful diagnosis of Takayasu's disease using magnetic resonance angiography (MRA). MRA, the combination of magnetic resonance tomography (MRT) scan with angiogram, could be used as a noninvasive method of diagnosing and monitoring patients with Takayasu's disease.

Takayasu's arteritis has early and late phases. The early phase is inflammatory and has been called the prepulseless phase; the late phase, called the pulseless phase, is characterized by occlusion. Patients may present with nonspecific signs and symptoms such as fever, arthralgias, and weight loss.

During the acute inflammatory stage, Takayasu's disease causes a low-grade fever, tachycardia, and pain adjacent to the inflamed arteries (e.g., carotodynia) [*Seo P., Stone J., 2004*]; in addition, 50% of patients experience fatiga-

bility. Carotid and clavicular bruits, asymmetric upper-extremity blood pressures, hypertension, diminished or absent upper-extremity pulses, and ischemic symptoms may suggest the diagnosis. A 5- to 20-year interval may separate the acute inflammatory stage and the symptomatic arterial occlusive stage. Neurologic symptoms are present in 80% of patients with Takayasu's disease that involves the brachiocephalic arteries [*Seo P., Stone J., 2004; Yagi K. et al., 2004*].

Four types of late-phase Takayasu's arteritis have been described based on the sites of involvement; those types are as follows:

Type I: Classic pulseless type that involves the brachiocephalic trunk, carotid arteries, and subclavian arteries;

Type II: Combination of types I and III;

Type III: Atypical coarctation type that involves the thoracic and abdominal aortas distal to the arch and its major branches;

Type IV: Dilated type that involves extensive dilatation of the length of the aorta and its major branches.

The purpose of this study is to present clinical, laboratory results and X-ray, echocardiographic and MRT data of a patient who appealed for medical aid to the University Hospital "Muratsan". Takayasu's illness was diagnosed in our clinic for the first time and then confirmed in Moscow.

MATERIAL AND METHODS

The patient L., who is 26 years old, came to our clinic with complaints of general weakness, painful joints, tingling in her heart, fluctuation of blood pressure. The girl was born from the first normal pregnancy (delivery at term, weight at birth 3700 g, stature 51 cm). The child was breastfed; she was not vaccinated. She did not fall ill until the age of 1 year old. Later she often had acute tonsillitis. When she was 15 years old, she was treated at the Medical Center "Arabkir", and diagnosed for rheumatoid arthritis, Wisler-Fankoni subsepsis. At the age of 18 years, a high level of c-O (1000-2500) was marked in the patient. She received antirheumatic treatment (retarpen), after which the anti-streptolysin O (ASL-O) level decreased. The patient had no complaints for two years. She had a plastic surgery, later the ASL-O level was increased (1:3000). The general condition included the following symptoms: weakness, paleness of skin, hipermobility of wrist joint and the little finger, heart sounds were muffled, middiastolic and midsystolic murmur, which was maximally heard under the aorta, intermittent claudication, she had a bad eye-sight and lumbar hernia. Other systems did not have pathologic changes. The patient had the high risk of thromboses formation, since a homozygous mutation was observed (C677T).

The aneurysm of aorta was revealed on the cardiac ultrasound and the Takayasu's disease was diagnosed for the first time. This diagnosis was confirmed in Moscow at the Research Center of Cardiovascular Surgery after A.N. Bakulev, where our patient was examined. The complete blood count (CBC) revealed a normochromic normocytic anemia (Hb 115 g/L, erythrocytes 3.8 x 1012/L, farbindex 0.9), insignificant leukocytosis (9.4 x 109/L) and thrombocytosis, elevated ESR (35 mm/h). Biochemical blood analysis included the following changes: kreatinin level was elevated (98.3 mmol/L), C-reactive protein (CRP) 23-33 mg/L; increased level of ASL-O: 225-452 and the immune complex (330 U). Antituberculosis antibody and rheumatoid factor were negative. The urine analysis did not have any pathology changes. β-hemolytic streptococcus was found in the throat swab. The hormones of thyroid gland were within normal limits. Retinal artery spasm was also revealed.

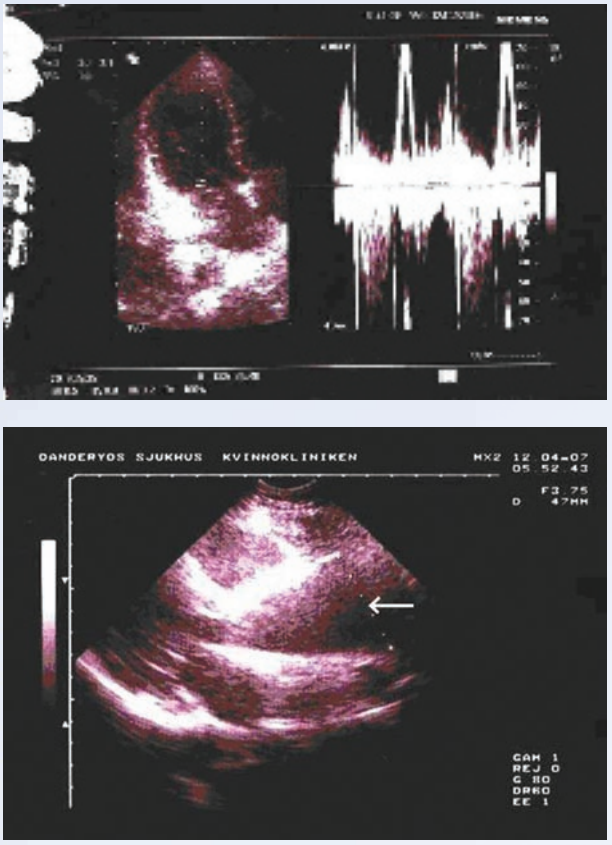
There were no pathologic changes on chest X-ray, but only a right superior area of the vascular fascicle dilated, there was ascending aortic aneurism, aortic and mitral insufficiency.

Right kidney was rotated, asymmetric kidneys (L>R); decreased renal blood flow on the right side, bilateral renal artery stenosis were observed on the ultrasound.

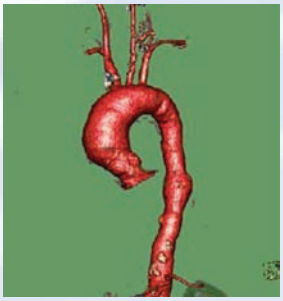
The aneurysm of ascending aorta, aortal insufficiency (2+), symmetrical insignificant hypertrophy of the left ventricle of heart, mitral valve prolapse (1+) with regurgitation were detected at echocardiography.

Picture 1 shows patient's echocardiography, when she was 15 years old and echocardiography with the aneurism of ascending aorta in three years.

Duplex Doppler revealed a homogenous atherosclerotic thickening (arteriosclerosis). Computed tomography (CT) scan revealed the changes, appropriate to Takayasu's arteritis, type III, progressive course with development of complete occlusion of right external iliac artery. Right lower extremity blood supply was maintained because of multiple collaterals formed, right renal artery stenosis with progressively worsening right kidney parenchimal atrophy, and left kidney hypertrophy. There was an early damage of proximal left renal artery. Stenosis of celiac artery was observed and superior mesenteric arteries were unchanged. Dilation of ascending aorta was recorded, aneurism of middle third of thoracic descending aorta and calcifications of middle and lower parts of thoracic aorta unchanged. Picture 2 demonstrates CT scan examination of aorta branches.



Picture 1. *Echocardiography with aneurism of ascending aorta.*
a) *no aneurism;* **b)** *with aneurism of ascending aorta.*



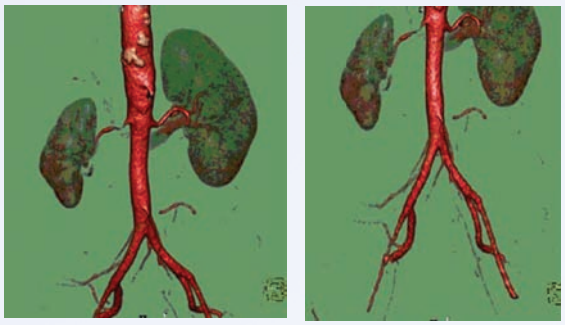
Picture 2. *CT scan examination of aorta branches.*

Picture 3 demonstrates CT scan of the right renal artery stenosis and asymmetric kidneys (right kidney is smaller than the left one), the occlusion of right external iliac artery, the occlusion of right external iliac artery.

The patient was diagnosed for nonspecific aortoarteritis: Takayasu's arteritis, type III, connective tissue dysplasia syndrome.

Our patient received the following therapy: minimal dose of prednisone 5 mg/day, retarpen 2.4 g/day, dilitrend 12.5 mg twice per day, ibuprofene 200 mg twice per day, hypotensive therapy, trental 400 mg three times per day, methotrexate 2.5 mg twice per day, and one course of plasmapheresis.

Endovascular stenting is used in patients with severe stenoses, hypertension, or ischemia during the fibrotic phase of the disease. Multiple stents have been used to relieve long-segment renal artery stenosis and attendant renovascular hypertension. Takayasu's arteritis patients with implanted stents have lowered arterial blood pressure and decreased requirement for antihypertensives. Immunosuppressant-eluting stents could potentially deliver local treatment at sites of inflammation. Our patient's stent was in the



Picture 3. *Right renal artery stenosis and the occlusion of right external iliac artery.*
a) *right renal artery stenosis;* **b)** *the occlusion of right external iliac artery.*

right renal artery. As the blood pressure of the patient still remained high,remicad should be prescribed. Afterwards, in 6 months, she should undergo a complete examination.

Conclusion

Takayasu's arteritis is a life-threatening disease. Overall prognosis in individuals with Takayasu's arteritis relates to the degree of vascular and end-organ damage, specifically retinal vasculopathy, aortic insufficiency, aortic aneurysms, and hypertension; 15 years survival rate is high and makes 95%.

Thus, Takayasu's arteritis is a heavy relapsing disease. Early diagnosis can be difficult due to nonspecific early symptoms. Consultations of a wide range of professionals (pediatric rheumatologist, ophthalmologist, pediatric cardiologist, vascular surgeon, and interventional radiologist) are required in order to exclude other diseases. Early diagnostics of the given disease and treatment initiated in due time will allow to improve the quality of the patients' life, to prolong remission, to stabilize the pathological process. This is the reason why the given problem is a matter of urgency today.

REFERENCES

1. *Abularrage C.J., Slidell M.B., Sidawy A.N., Kreishman P., Amdur R.L., Arora S.* Quality of life of patients with Takayasu's arteritis. J. Vasc. Surg. 2008; 47(1): 131-136; discussion 136-137.

2. *Akar S., Can G., Binicier O., Aksu K., Akinci B., Solmaz D. et al.* Quality of life in patients with Takayasu's arteritis is impaired and comparable with rheumatoid arthritis and ankylosing spondylitis patients. Clin. Rheumatol. 2008; 27(7): 859-865.

3. *Andrews J., Mason J.C.* Takayasu's arteritis – recent advances in imaging offer promise. Rheumatology (Oxford). 2007; 46(1): 6-15.

4. *James W.D., Berger T.G., Elston D.M.* Andrew's Diseases of the Skin. Clinical Dermatology. 10th edition. Canada. Saunders Elsevier. 2006. 1210p. ISBN 0-7216-2921-0.

5. *Park M.C., Lee S.W., Park Y.B., Chung N.S., Lee S.K.* Clinical characteristics and outcomes of Takayasu's arteritis: analysis of 108 patients using standardized criteria for diagnosis, activity assessment, and angiographic classification. Scand. J. Rheumatol. 2005; 34(4): 284-292.

6. *Phillip R., Luqmani R.* Mortality in systemic vasculitis: a systematic review. Clin. Exp. Rheumatol. 2008; 26(5; Suppl 51): S94-104.

7. *Schmidt W.A., Blockmans D.* Use of ultrasonography and positron emission tomography in the diagnosis and assessment of large-vessel vasculitis. Curr. Opin. Rheumatol. 2005; 17(1): 9-15.

8. *Seo P., Stone J.H.* Large-vessel vasculitis. Arthritis Rheum. 2004; 51(1): 128-139.

9. *Weyand C.M., Goronzy J.J.* Medium- and large-vessel vasculitis. N. Engl J. Med. 2003; 349(2): 160-169.

10. *Yagi K., Kobayashi J., Yasue S. et al.* Four unrelated cases with Takayasu arteritis and CD36 deficiency: possible link between these disorders. J. Intern. Med. 2004; 255(6): 688-689.