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Case Report

Nonspecific Aortoarteritis, Case Presentation and Literature Review

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Abstract

We present a case of delayed diagnosed aortoarteritis who respond dramatically to immunosuppressive therapy stressing the needs of early diagnosis of such cases.

Keywords: *A Nonspecific Aortoarteritis; Takayasu's Disease*

Abbreviations

CBC: Complete Blood Count; Er: Erythrocytes; Hb: Hemoglobin; CP: Color Index; Tr: Platelets; Ht: Hematocrit; Leu: Leukocytes; Eo: Eosinophils; P: Bacilli; S: Segments; L: Lymphocytes; M: Monocytes; ESR: Sedimentation Rate of Erythrocytes; CT: Computed Tomography; MRI: Magnetic Resonance Tomography; TD: Takayasu's Disease; NSAIDs: Non-Steroidal Anti-Inflammatory Drugs

Introduction

Takayasu's disease (TD) is a nonspecific autoimmune lesion predominantly of the vessels of the upper half of the body and manifests itself with a variety of clinical symptoms, often simulating various diseases. TD is a rare disease and is diagnosed on average 2 cases per million population per year [14,26]. In 90% of cases, it occurs in female patients, the peak of the disease occurs at the age of 15 to 19 years [20,34]. In adolescence, mortality reaches 35% [7,9,23,31]. This is partly due to the fact that doctors often neglect auscultation of the vessels, and if they listen to the vessels, they do not always listen to pathological noises due to the inflammatory nature of the changes in the walls of the vessels. On average, the diagnosis is established after 2 years and in one third in the stage of stenosis of the affected vessels [7,9,12,13,31]. Patients during this time undergo numerous expensive examinations and consultations of specialists. During this time, irreversible complications often develop - strokes, loss of vision, myocardial infarction.

In recent years, modern, high-tech methods for studying various human systems and organs have been introduced, but the doctor's ability to correctly, systematically examine the patient, evaluate symptoms, logically compare them with the study data and correctly compose the study algorithm still remains in the first place.

We present a case of successful diagnosis of nonspecific aortoarteritis in a patient with severe headaches is presented, which allowed timely initiation of immunosuppressive therapy.

Case Presentation

Patient S., born 03.08.1992 was hospitalized in the therapeutic department of City Clinical Hospital №12, Kazan on November 10, 2017. Complaints at admission: headaches mainly in the left half, dizziness when standing up, malaise; pain in the left side of the neck, dull, aching; general weakness, fever to febrile figures with chills; weight loss of 3 kg in 3 weeks.

Her symptoms dated back to the end of October 2017, when she had diffuse pain in the right ear. She went to an otolaryngologist, then to a neurologist. She was treated with NSAIDs with a positive effect. The resumption of pain has been noted since the end of October 2017 - a diffuse headache with irradiation to the cheekbones and lower jaw, accompanied by a rise in temperature to 39 degrees and increased sweating, reduced by taking acetylsalicylic acid and NSAIDs, was treated on an outpatient basis by a therapist with antibiotics for a week without effect. On 11/08/2017, thermometry revealed a temperature of 39.5 degrees, she was examined by an ENT doctor, a general practitioner, an infectious disease specialist, a gynecologist. On November 10, 2017, she was referred to a neurologist at City Clinical Hospital No. 12 with a suspected diagnosis of: Thrombosis of the venous sinus? Trigeminal neuropathy 2-3 branches on the right? When examining data for thrombosis was not revealed, she was hospitalized in the therapeutic department of City Clinical Hospital №12 with a diagnosis of fever of unknown origin.

The patient past history was insignificant apart from urgent delivery in June 2016, followed by curettage 10 days later, in July 2017 she suffered bilateral adnexitis (treated on an outpatient basis by a gynecologist with gentamicin and ampicillin). Transferred infectious diseases denies. Viral hepatitis, AIDS virus, tuberculosis, venereal diseases denies. She was not in contact with infectious patients, she did not travel abroad, she did not drink raw water. Heredity is not burdened. Allergological anamnesis: allergic reactions denies. Bad habits: denies.

On admission the patient was in State of moderate severity due to febrile syndrome. Consciousness is clear. Height 150 cm, weight 46 kg, BMI 20 (normal). The skin is dry, physiological color. There are no rashes. Visible mucous membranes of normal color. There are no edema. Peripheral lymph nodes are not enlarged. The musculoskeletal system is without pathology. Breathing through the nose is free. Respiratory rate 18 per minute. Pulmonary percussion sound over the lung fields. Breathing is vesicular, no wheezing. Pulse 102 beats per minute of satisfactory filling. BP on the right arm 110/70 mm Hg, BP on the left arm 100/60 mm Hg. The borders of the heart are within the normal range. Heart sounds are clear, rhythmic. The abdomen is soft and painless. The size of the liver according to Kurlov is 9 x 8 x 7 cm. The spleen is not enlarged. Pasternatsky's symptom is negative on both sides. The thyroid gland is not enlarged.

She was diagnosed as a case of fever of unknown origin.

Data of laboratory and instrumental studies: Complete blood count (CBC) on 10/11/2017: erythrocytes (Er.): 3,9 x 1012/l (3.7 - 4.7 x 1012/l), hemoglobin (Hb): 91 g/l (120 - 140 g/l), color index (CP): 0.71 (0.85 - 1.05), platelets (Tr.): 549 x 109/l (200 - 400 x 109/l); Leukocytes (Leu.): 10.9 x 109 (4.0 - 9.0 x 109/l), eosinophils (Eo.): 1% (0 - 5%), bacilli (P.): 2% (1 - 6%), segments (S.): 74% (47 - 72%), lymphocytes (L.) - 14% (18 - 38%), monocytes (M.): 9% (3 - 11%), Sedimentation rate of erythrocytes (ESR): 55 mm/hour (2 - 15 mm/hour).

Complete blood count 5 days latter showed elevation of leukocytes from 10.9 to 12 and an increase in sedimentation rate from 55 to 67 mm/ hour.

Biochemical blood test dated 11/15/2017: ALT - 62 U/l (N ≤ 40 U/l), AST - 40 U/l (N ≤ 40 U/l), CRP - 200.8 mg/l (N ≤ 5 mg/l), RF - 1.7 IU/ml (N up to 14 IU/ml), fibrinogen 7.8 g/l (N2-4 g/l), ASL-O 100 IU/ml (N up to 200 IU/ml).

Uranalysis dated 11/17/2017: urine specific gravity 1011, transparent, color - straw-yellow, acid reaction, protein - negative, Leukocytes 1-2 in the field of view, Erythrocytes 0 in the field of view, epithelium 1- 3 in the field of view.

Immunogram 11/17/2017: IgA-1.8 g/l (N1.1 - 3.1 g/l), IgG- 21 g/l (N6.9 - 17.5 g/l), IgM- 1.1 g/l (N0.75 - 2.2 g/l). Proteinogram dated November 17, 2017: albumins - 38 g/l (N35- 50 g/l), β-globulins - 9 g/l (N5-11 g/l), γ-globulins - 24 g/l (N5 - 16 g/l).

Fibroesophagogastroduodenoscopy on 11/13/2017: The esophagus is freely passable throughout, the cardiac sphincter closes completely. Stomach: the contents are mucus, the mucosa is moderately hyperemic, the folds are not thickened. Bulb duodenum without features. Conclusion: Superficial gastritis.

Spiral computed tomography of the head on November 15, 2017: The shape and dimensions of the skull are within normal limits. Focal changes are not defined. The ventricles are not dilated. Median structures are not displaced. The region of the Turkish saddle and the trunk without features. Conclusion: no focal changes were detected.

Spiral computed tomography of the cervical spine dated November 15, 2017: The tomogram shows some straightening of the lumbar lordosis, subchondral sclerosis of the endplates, a decrease in the height of the intervertebral disc at the level of L4-L5, L5-S1, signs of deforming spondylosis at the level of L3-L5, Th11 -Th12. On a series of tomograms at the level of L4-L5: a circular protrusion of the intervertebral disc by 0.4 cm is determined, the protrusion narrows the intervertebral foramens completely on both sides. At the L5-SI level: against the background of uneven circular protrusion of the intervertebral disc by 0.4 - 0.6 cm, a posterior-central hernia with lateralization to the right-left side is determined, a right-sided formal hernia of the intervertebral disc protruding into the lumen of the spinal canal at see the intervertebral foramen by 0.5 cm. The hernia fills the lumen of the right left lateral pocket, causing partial calcification of the posterior longitudinal ligament. The right spinal root is compressed, thickened compared to the opposite. The volume and distribution of epidural fatty tissue is normal. The position and shape of the dural sac was not changed.

Conclusion: Degenerative-dystrophic changes in the intervertebral discs at the studied levels, manifested in protrusion of the intervertebral discs, right-sided left-sided formal hernia at the level of L4-L5, L5-SI.

Gynecologist's consultation: Chronic endometritis. Functional cyst of the left ovary.

The patient was examined by the staff of the Department of Hospital and Polyclinic Therapy of the KSMA - Branch Campus of the FSBEI FPE RMACPE MOH. A thorough examination of the patient revealed a systolic murmur over the left and, to a greater extent, over the right carotid artery. Taking into account the laboratory signs of systemic inflammation (leukocytosis, accelerated ESR up to 55 - 67 mm/h, increased CRP up to 200 mg/ml, fibrinogen up to 7.8 g/l, increased IgG, γ-globulin), a preliminary diagnosis was made: nonspecific aortoarteritis (Takayasu's disease), type 1, affecting both carotid and subclavian arteries (without hemodynamic disturbances). Iron-deficiency anemia, mild severity, Chronic endometritis. Functional cyst of the left ovary. The diagnosis of nonspecific aortoarteritis was confirmed by ultrasound examination of extracranial vessels. A thickening of the walls of the right external carotid artery with some narrowing of the lumen of the vessel was revealed.

Immunosuppressive therapy was recommended. However, the patient was discharged from the hospital on 11/17/2017 on a personal request.

From 11/18/17 to 12/08/17 she was in the Interregional Clinical and Diagnostic Center in the cardiology department, an additional examination (computed tomography of the chest cavity, echocardiography, ultrasound of the uterus and appendages, kidneys, adrenal glands, spleen, lymph nodes, esophagogastroduodenoscopy) did not reveal any pathology. Repeated extracranial duplex scanning visualized a compacted, thickened intima-media complex without a clear differentiation into layers, predominantly in the common carotid artery and subclavian artery, on both sides there are signs of non-specific aorto-arteritis with stenosis of the right common carotid artery and the right subclavian artery by 20%. Treatment was carried out: Metipred 1000g IV drip No. 3, followed by a transition to oral prednisolone 60 mg per day (30 mg in the morning, 20 mg in the afternoon, 10 mg in the evening). The patient was discharged for outpatient treatment with a recommendation for re-hospitalization.

On March 30, 2018, she was admitted for inpatient treatment to the rheumatology department of the Medical and sanitary department of Kazan Volga Federal University. Against the background of immunosuppressive therapy, the patient's temperature returned to normal, headaches disappeared, her general condition improved significantly, and her immune status returned to normal.

KBC dated 03/27/18: erythrocytes 4.29 x 1012/l, hemoglobin 128 g/l, color index 0.9, platelets 180 x 109/l, leukocytes 13.4 x 109/l, ESR - 19 mm/h, Eo - 2%, P.-6%, S.-60%, L.-22%, M.-8%, P.-2%. CRP from 04/02/18: less than 6 mg/l. ELISA CEC - 93 U (norm up to 120 U). Rheumatoid factor negative. Biochemical blood test dated 03/30/18: ALT - 17 U/l (N ≤ 40 U/l), AST - 15 U/l (N ≤ 40 U/l), creatinine - 56 μmol/l (30 - 110 μmol/l l), cholesterol - 5.4 mmol/l (2.2 - 5.7 mmol/l), glucose - 4.0 mmol/l (3.8 - 6.0 mmol/l) total protein - 64 g/l (64 - 84 g/l), uric acid - 295 μmol/l (202 - 416 μmol/l). Immunogram from 04/01/2018: IgA-1.6 g/l (1.1 - 3.1 g/l), IgG- 16.1 g/l (6.9 - 17.5 g/l), IgM - 1.4 g/l (0.75 - 2.2 g/l). Proteinogram dated April 1, 2018: albumins - 42 g/l (35 - 50 g/l), β-globulins - 10.5 g/l (5 - 11 g/l), γ-globulins - 14.2 g /l (5 - 16 g/l).

Discussion

In the presented case, the development of the disease began with neurological symptoms: severe headaches, mostly in the left half with irradiation to the cheekbones and lower jaw, dizziness, chills and weight loss, which are the most common non-specific clinical symptoms of the onset of TD. According to the literature, in most patients, the first clinical symptoms in decreasing frequency are: headache (31%), shortness of breath (23%), weight loss (22%), vomiting (20%), musculoskeletal symptoms (myalgia, arthralgia, arthritis (14%)) [15,31]. Therefore, initially a lot of laboratory and clinical studies were carried out in an unsuccessful search for neurological diseases.

Suspicion of TD arises when noise is detected on the carotid arteries, vessels of the extremities, or in the absence of a pulse on the extremities. In our case, due to a thorough sequential examination of the patient, systolic murmurs were detected in the projection of the carotid arteries. After that, the diagnosis of nonspecific aortoarteritis was suspected, and then confirmed by targeted laboratory and instrumental studies.

Nonspecific aortoarteritis is an autoimmune disease characterized by granulomatous inflammation of the aorta and main arteries. Takayasu's arteritis is characterized by multiple segmental lesions of the aorta and its branches with the presence of stenosis, occlusion, and aneurysm formation. Initially, the inflammatory process is localized in the media and adventitia of the vessel, and then passes to the paravasal tissue. The intimal lesion has a secondary reactive-hyperplastic character.

Diagnosis of TD remains a difficult task due to the non-specificity of many symptoms of the onset of the disease in half of the patients and, therefore, more than 12 months, an average of 24 months, elapse from the onset of the first symptoms to the diagnosis of aortoarteritis [12,13,23,31].

During this period, it is necessary to exclude many diseases that occur with similar symptoms, such as systemic infections (AIDS virus, brucellosis, endocarditis), autoimmune systemic diseases (Kawasaki disease, polyarteritis nodosa, rheumatic fever, systemic lupus erythematosus, sarcoidosis, spondyloarthropathies, Behçet's disease), non-infectious diseases (Ehlers-Danlos disease, congenital coarctation of the aorta, fibromascular dysplasia, Marfan's syndrome).

To date, in the world practice, when making a diagnosis of TD, the criteria of the American College of Rheumatology (The American College of Rheumatology) are widely used [3]:

1. Age less than 40 years,
2. The presence of symptoms of limb ischemia,
3. Decrease in the amplitude of the pulse on the limb

4. Pressure gradient between the upper limbs >10 mm Hg, systolic blood pressure
5. Systolic murmur in the projection of the carotid or subclavian arteries or aorta
6. Angiographic signs of narrowing or occlusion of the aorta, or its branches, or large proximal vessels of the upper or lower extremities.

The presence of 3 or more of the 6 criteria means 90.5% sensitivity and 97.8% specificity of these criteria in the diagnosis of TD, which was demonstrated in our patient (age, systolic murmurs in the projection of the carotid arteries and ultrasound and MRI of vessels).

Approximately 30% of patients on examination have elevated indicators of blood inflammation, such as ESR, C-reactive protein, which can also be used to control the dynamics of disease activity, although only in a fraction of patients [10,14,19,29]. Serum antibodies such as Pentraxin 3 [11], as well as the ratio of platelets to lymphocytes and neutrophils to lymphocytes, have been found to reflect disease activity [25].

Of the instrumental methods of diagnosis, a combination of radiation methods of research is recommended, such as color duplex scanning [17,30] and CT/MR angiography or radiopaque angiography [5,21], which makes it possible to clarify the localization and prevalence of damage to the arterial bed.

Taking into account the poor and unspecific clinical picture in Takayasu's arteritis, a number of authors recommend screening duplex scanning of the arteries of the aortic arch and abdominal aorta to all persons under 50 years of age with elevated erythrocyte sedimentation rate and/or C-reactive protein in the absence of obvious reasons for their increase [28].

Treatment of aortoarteritis is aimed at suppressing active inflammation in the vessel wall. According to the EULAR 2009 recommendations, early initiation of corticosteroid therapy in order to quickly achieve remission and the use of immunosuppressive drugs as additional therapy was proposed [24]. Various schemes of immunosuppressive therapy have been proposed. They are based on glucocorticoids (prednisolone, methylprednisolone), cytostatics. One of the highly effective treatment regimens is the method of pulse therapy with methylprednisolone and cyclophosphamide. Azathioprine, mycophenolate mofetil, leflunomide, cyclophosphamide are the most widely used drugs to achieve and maintain disease remission [6].

In recent years, encouraging results have been oTDained on the use of biological preparations. A particularly pronounced effect was found in the drugs tocilizumab, rituximab, which have become widely used in pediatric practice [4,5,8,18,22,28,32,33,36].

In the presence of indications resort to surgical methods of treatment. These indications include: cerebrovascular disease due to cerebrocranial stenosis, coronary ischemic disease, coarctation and aortic aneurysm, renovascular hypertension, limb ischemia, increased risk of vascular dissection ruptures [16].

Conclusion

Objective examination of a patient with fever of unknown origin should be carried out carefully and include auscultation of vessels (carotid arteries, subclavian arteries). The presence of noise allows to suspect, and then prescribe extracranial duplex scanning of blood vessels, timely confirm the diagnosis of nonspecific aortoarteritis and prescribe early treatment.

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