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Стаття надійшла до редакції 22.04.2024;
затверджена до публікації 30.11.2024



UDC 616.132-002.6-02-036-07-08

<https://doi.org/10.26641/2307-0404.2024.4.319405>

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SYPHILITIC AORTITIS: FROM THE PAST TO THE PRESENT (view of a dermatovenerologist)

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Цитування: *Медичні перспективи.* 2024. Т. 29, № 4. С. 264-271

Cited: *Medicni perspektivi.* 2024;29(4):264-271

Key words: *clinic, complication, diagnosis, syphilitic aortitis*

Ключові слова: *діагностика, клініка, сифілітичний аортит, ускладнення*

Abstract. *Syphilitic aortitis: from the past to the present (view of a dermatovenerologist). Zakharov S.V., Svyatenko T.V., Zakharov V.K., Gorbuntsov V.V., Pohrebniak L.A. In order to improve the diagnosis and treatment of syphilitic aortitis, an analysis of known data on the clinical manifestations, course and diagnosis of this pathology was conducted, illustrating our own observations with the subsequent implementation of recommendations in clinical practice. The problem of syphilitic aortitis - the most frequent manifestation of late syphilis - was considered. Current data on clinical manifestations, possibilities and problems of diagnosing this pathology were presented. Modern methods of serological research used in the diagnosis of syphilitic aortitis were analyzed in detail; the course, complications and*

prognosis of this pathology were separately considered. All these aspects were illustrated by our own observations of clinical cases of syphilitic aortitis, which are of interest due to their rarity in clinical practice and demonstrate the importance of correct diagnosis and appropriate treatment. Serological tests for syphilis, ultrasound examination of the heart, extracardiac vessels and internal organs; X-ray examinations were used when examining patients. It was concluded that lesions of the cardiovascular system are currently among the most common forms of visceral syphilis. Syphilitic aortitis with symptoms of cardiovascular damage, which are caused by aortic valve insufficiency, narrowing of the ascending coronary arteries, aneurysmal dilatation of the ascending part and aortic arch, occurs in the late stages of syphilitic infection. Even in patients with syphilis who have been treated in the past with penicillin drugs, cardiovascular damage may occur, namely aortitis with aortic valve insufficiency. The most informative methods for detecting late cardiovascular damage are: enzyme-linked immunosorbent assay, passive hemagglutination reaction, immunoblotting and computed tomography of the heart and echocardiography. Special attention is paid to the fact that the uniqueness of the above observations lies in the fact that complicated forms of aortitis began to occur more often and also in treated syphilis patients who had previously been treated with water-soluble penicillin. Aortitis also occurs against the background of seroconversion (positivity) of non-treponemal tests, which were previously negative after treatment.

Реферат. Сифілітичний аортит: від минулого до сьогодення (погляд дерматовенеролога). Захаров С.В., Святенко Т.В., Захаров В.К., Горбунцов В.В., Погребняк Л.А. З метою покращення діагностики та лікування сифілітичного аортиту проведено аналіз відомих даних щодо клінічних проявів, перебігу та діагностики цієї патології з ілюстрацією власних спостережень з подальшим упровадженням рекомендацій у клінічну практику. Розглянуто проблему сифілітичного аортиту – найбільш частого прояву пізнього сифілісу. Наведено сучасні дані щодо клінічних проявів, можливостей та проблем діагностики цієї патології. Докладно проаналізовано сучасні методи серологічного дослідження, які застосовуються при діагностиці сифілітичного аортиту; окремо розглянуто перебіг, ускладнення та прогноз цієї патології. Усі ці аспекти проілюстровано власними спостереженнями клінічних випадків сифілітичного аортиту, які викликають зацікавленість через рідкісність у клінічній практиці та демонструють важливість правильної діагностики та відповідного лікування. При обстеженні хворих використовувались серологічні дослідження на сифіліс, ультразвукове дослідження серця, екстракардіальних судин та внутрішніх органів; рентгенологічні дослідження. Зроблено висновки про те, що ураження серцево-судинної системи до цього часу відносяться до форм вісцерального сифілісу, що зустрічаються найбільш часто. Сифілітичний аортит із симптомами ураження серцево-судинної системи, які зумовлені недостатністю клапанів аорти, звуженням висхідних отворів коронарних судин, аневризматичним розширенням висхідного відділу та дуги аорти, виникає на пізніх стадіях сифілітичної інфекції. Навіть у хворих на сифіліс, які були ліковані в минулому препаратами пеніциліну, можуть виникати ураження серцево-судинної системи, а саме аортит з недостатністю стулок аортального клапана. Найбільш інформативними методами для виявлення пізніх уражень серцево-судинної системи є: імуноферментний аналіз, реакція пасивної гемаглютинації, імуноблотинг та комп'ютерна томографія серця й ехокардіографія. Звернуто особливу увагу на унікальність наведених спостережень, яка полягає в тому, що ускладнені форми аортиту стали зустрічатись частіше і також у лікованих хворих на сифіліс, які раніше отримували лікування водорозчинним пеніциліном. Аортит також виникає на тлі сероконверсії (позитивації) нетрепонемних тестів, які раніше після лікування були негативними.

Visceral syphilis (VS) is a clinical form of syphilis in which internal organs are affected. Most often, syphilis affects those organs that have the greatest functional load; this includes the heart. Early and late forms of visceral syphilis are distinguished. In particular, early forms occur in patients with primary and secondary syphilis, and only the function of the affected organs is impaired; late forms of visceral syphilis are changes in internal organs of a destructive nature, namely, specific granulomatous inflammation: in late visceral syphilis, in more than 90% of cases, this is syphilis of the cardiovascular system (CVS) [1, 2, 3].

In the world literature over the past 30-40 years, one can find only isolated scientific works devoted to the damage to the cardiovascular system in syphilis, which are based on isolated clinical observations without taking into account the modern results of instrumental and serological examination (western-

blot, *Treponema pallidum* hemagglutination assay (ТРНА), ELISA, computed tomography).

Modern cardiology made it possible to detect early specific signs of heart and vascular lesions, which can be a guarantee of effective treatment and a decrease in the number of late complications of syphilitic infection [4-15].

A fairly typical localization of syphilitic aortitis (SA) is the ascending part of the aorta, located outside the sternum, mainly in the valve rings and in the area of the exit of the coronary arteries. In this regard, syphilitic aortitis is often complicated by aortic valve insufficiency and narrowing of the coronary artery outlet openings up to their complete obliteration; this is observed in almost a third of cases of syphilitic aortitis (according to autopsy data). Both of the above complications lead to the development of heart failure [16, 17].

It is known that the syphilitic process in the aorta proceeds asymptotically for a long time. Often the diagnosis of complicated aortitis is established by chance [1, 3, 18].

Syphilitic aortitis is the most frequent manifestation of late syphilis, the diagnosis of which occurs during life in about 25% of patients [19, 20]. The period from primary infection to initial clinical manifestations in most patients ranges from 10 to 20 years and can vary from three to five to 40-50 years. By gender distribution, men over the age of 60 are more often affected; in women, syphilitic aortitis also occurs at the age of over 60 years [1, 3, 20]. According to the clinic of skin and venereal diseases of the Dnipro State Medical University, until 2017 we observed isolated cases of late syphilis of the cardiovascular system; over the past three years, the number of such patients has increased significantly – to 8-11 cases each year.

The purpose of the article was to improve the diagnosis and treatment of syphilitic aortitis (SA) by analyzing the known data on the clinical manifestations, course and diagnosis of this pathology with the illustration of own observations with further implementation of recommendations in clinical practice.

MATERIALS AND METHODS OF RESEARCH

When monitoring patients, clinical, anamnestic, laboratory (serological tests for syphilis (micro-precipitation reaction (MRP)), *Treponema pallidum* hemagglutination assay (TPHA), enzyme immunoassay (ELISA) method were used: *Treponema pallidum*, IgM antibodies; *Treponema pallidum*, IgG antibodies (rea-gent Euroimmun); bioimmunochemistry: *Treponema pallidum* antibodies (Roche Diagnostics reagents); IgM antibodies to Tr15, IgG antibodies to Tr47); ultra-sound of the heart, extracardial vessels and internal organs, X-ray examination (X-ray and computer tomography of the chest, magnetic resonance imaging of the ascending part, arch and descending part of the aorta).

The study was approved by the Commission on Biomedical Ethics of the Dnipro State Medical University and was conducted in accordance with the ethical principles outlined in the Helsinki Declaration “Ethical Principles of Medical Research Involving Humans” and the “General Declaration on Bioethics and Human Rights (UNESCO)”.

Patients provided written consent to participate in the study and to publish the data.

RESULTS AND DISCUSSION

Patient P., 76 years old, was referred for consultation and examination from the Regional Clinical Center of Cardiology and Cardiac Surgery, where she was being treated with a diagnosis of coronary artery

disease. Stable angina pectoris, II functional class. Condition after coronary angiography:

- aneurysmal expansion of the ascending aorta;
- severe insufficiency of the aortic valve;
- dilatation of the cavity of the left ventricle;
- heart failure of the 1st degree;
- NYHA II;
- hypertensive disease III stage. 2nd degree; the risk is very high.

The result of serological tests for syphilis (the test was carried out three times with an interval of 10 days):

- complement binding reaction (RW) is positive (4+) at a titer of 1 : 5;
- TPHA is positive at a titer of 1 : 5120;
- ELISA IgG is positive.

She complained of:

- stabbing pain in the area of the heart, with irradiation in the area of the neck;
- shortness of breath under slight physical exertion;
- rapid fatigue, weakness;
- interruptions in the work of the heart;
- dizziness;
- headache.

She considers herself sick for many years, as she suffers from hypertension and coronary heart disease. The current deterioration was about 6 months ago, when she felt intense anginal pain in the heart area. Planned hospitalization for further examination and the decision of further treatment.

Comprehensive scanning of extracardial vessels:

- ultrasound signs of:
 - 1) structural changes in the vessel wall;
 - 2) vascular deformation;
 - 3) fibrosis, mitral valve calcinosis;
- tricuspid aortic valve:
 - 1) ring diameter 21 mm;
 - 2) ascending aorta diameter 60 mm.

Conclusion:

- aneurysmal expansion of the ascending part of the aorta;
- expansion of the aortic arch;
- insufficiency of the aortic valve leaflets – from significant to severe.

Ultrasound examination of internal organs – ultrasound signs of:

- diffuse changes in the liver;
- chronic cholecystitis;
- diffuse changes in the pancreas;
- atherosclerosis of the abdominal aorta.

X-ray of the chest (Fig. 1):

- lung fields – without infiltrative and focal changes;
- the roots of the lungs – structural *Cor pulmonale* are normal;
- the shadow of the aorta is expanded, elongated, dense.

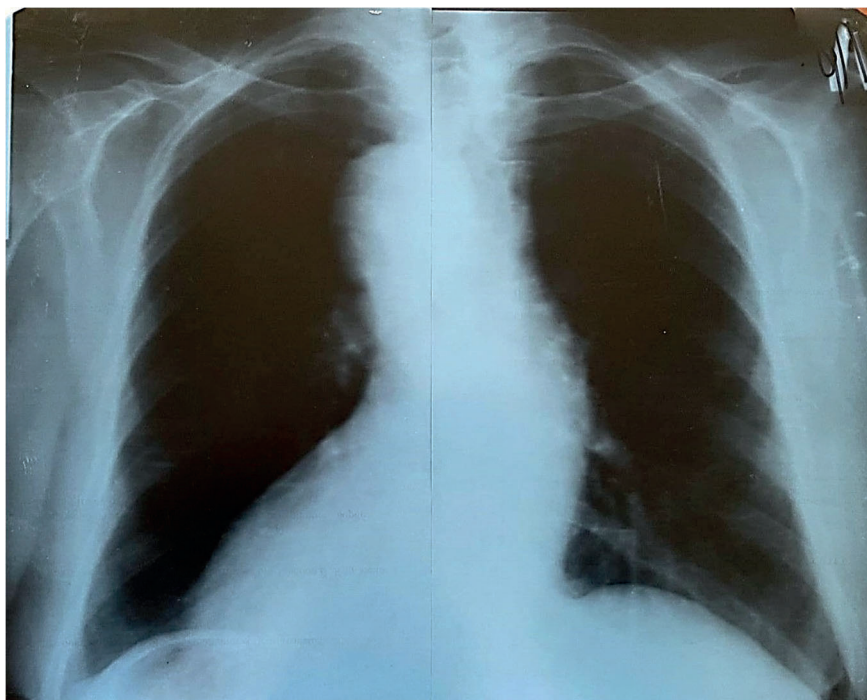


Fig. 1. Patient P., 76 years old. X-ray of the chest

Computed tomography of the chest (Fig. 2) – aneurysmal expansion of the thoracic aorta:

- the diameter at the level of the sinuses of Valsalva – 37.5 mm;
- the root of the aorta – 45 mm;
- the beginning of the arch – 49 mm;
- the middle of the arch – 31 mm;
- the ascending part – 61 mm;
- the beginning of the part directed downward – 34 mm; the S-shaped bend of this department;
- calcination in S6 of the left lung;
- an area of linear pneumofibrosis in S5 of the left lung.

Coronary angiography was performed. Aortography:

- backflow of blood on the aortic valve 3+;
- diameter of the aortic opening 60 mm.

Conclusion:

- aortic insufficiency 3+;
- arterial opening – 60 mm;
- no atherosclerotic changes have been detected.

A clinical diagnosis was made: syphilitic aortitis complicated by aortic valve insufficiency and aortic aneurysm.

Three courses of treatment with the sodium salt of benzpenicillin were prescribed.

A 54-year-old patient was diagnosed based on the results of an X-ray examination during a professional examination in the district hospital at his place of residence. The radiologist recommended the patient to consult a dermatovenerologist, as the aortic configuration of the heart, which had the appearance of a

"duck", was visible on the X-ray image. The patient's blood test revealed positive serological reactions to syphilis. In this regard, he was sent for consultation to the Department of Skin and Venereal Diseases of the Dnipro State Medical University.

From the anamnesis: the patient never had syphilis before.

The patient was consulted in the cardiology center. Echocardiography:

- fibrosis of the aorta and leaflets of the aortic valve;
- dilatation of the ascending aorta;
- moderate insufficiency of the aortic valve leaflets;
- regurgitation in the aortic valve leaflets of the 1st degree.

Left ventricular hypertrophy. The function of diastolic relaxation of the myocardium of the left ventricle is impaired.

Magnetic resonance imaging (MRI) of the ascending, arch and descending part of the aorta:

- the diameter of the ascending part of the aorta is 47 mm;
- the diameter of the aorta arch and the initial section of its descending part is 53 mm.

Conclusion: signs of dilatation of the exit part of the aorta and its arch.

Consultation of a cardiac surgeon:

- aortitis;
- aneurysm of the ascending part, arch and initial part of the descending aorta;
- aortic valve insufficiency of the 1st degree, mitral valve – of the 2nd degree;
- heart failure of the 1st degree.

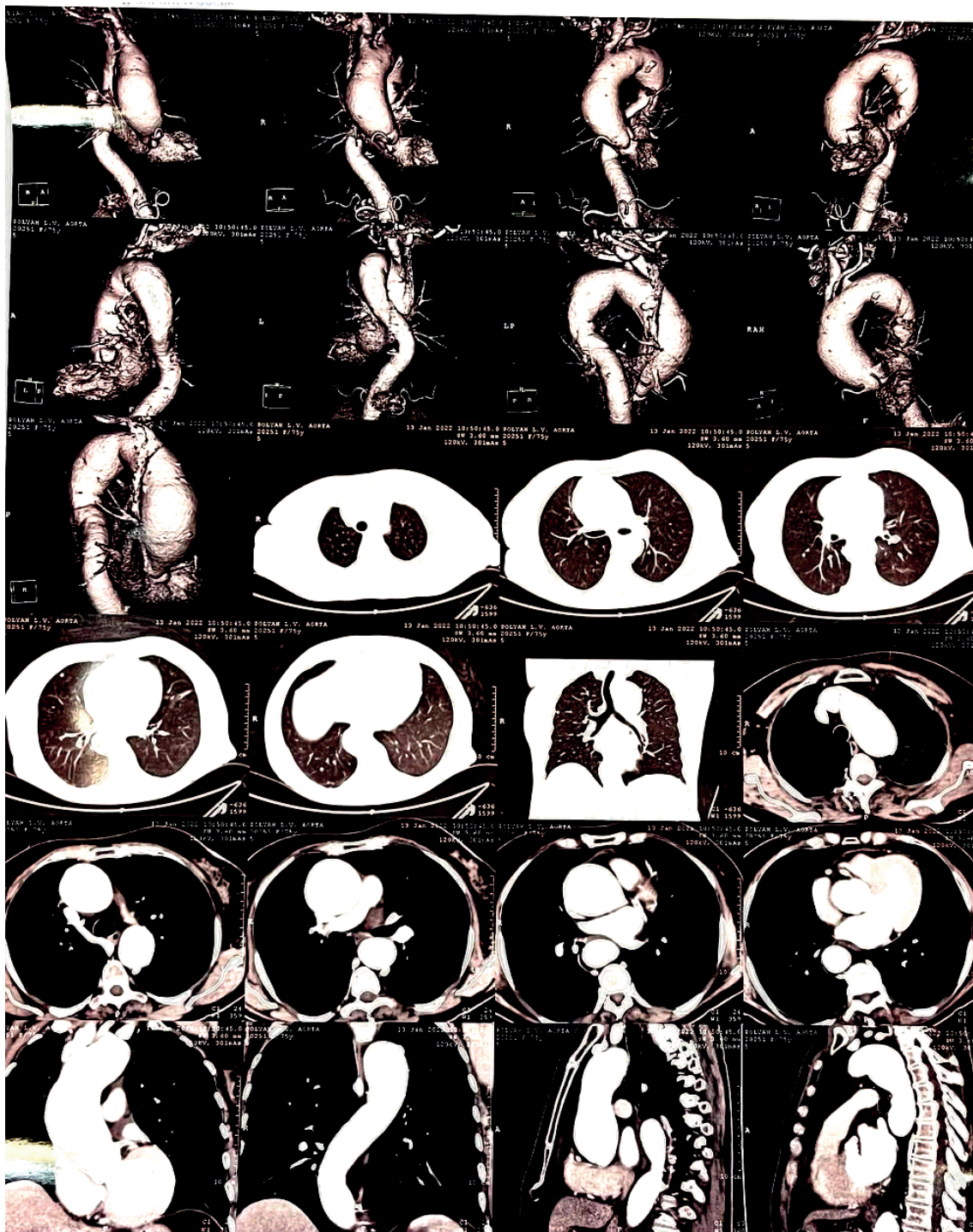


Fig. 2. Patient P., 76 years old. Computed tomography of the chest

The result of serological tests for syphilis (the test was carried out three times with an interval of 10 days):

- MRP (micro-precipitation reaction) is positive (4+) in titers 1 : 4 – 1 : 16 – 1 : 16;
- TPHA (*Treponema pallidum* hemagglutination assay) is positive (4+) at a titer of 1 : 1280
- ELISA:
 - 1) *IgM* – negative result.
 - 2) *IgG* – positive result.
- Immunoblotting:

– *Treponema pallidum IgM* antibodies – negative result.

– *Treponema pallidum IgG* antibodies to:

- 1) Tr-15 – negative result;
- 2) Tr17 – positive result;
- 3) Tr47 – positive result;
- 4) Tr45 – positive result.

Clinical diagnosis:

- syphilitic aortitis;
- insufficiency of aortic valves;

– aortic aneurysm.

Appointment of treatment with the sodium salt of benzylpenicillin in three courses.

The patient, 42 years old, was sent for a consultation with a dermatovenerologist from the cardiology center, in connection with interruptions in the work of the heart. During the examination at the cardiology center, she was found to have positive microprecipitation reaction (MPR) results.

From the anamnesis:

– 20 years ago she was treated in a hospital for hidden syphilis with penicillin; curability was monitored irregularly;

– 17 years ago she gave birth to a child, the child is healthy.

Interruptions in the work of the heart have worried for several months. She examined in the cardiology center:

– computed tomography of the heart;

– echocardiography.

Cardiac surgeon's conclusion:

Aortitis;

Insufficiency of aortic valves of the 1st degree, mitral valve – of the 2nd degree;

Aneurysm of the ascending aorta;

Heart failure of the 1st degree.

In the subsequent serological examination, the results were as follows (blood tests were carried out three times with an interval of 10 days):

– MRP (micro-precipitation reaction) is positive (4+) in titers 1 : 4 – 1 : 8 – 1 : 4;

– TPHA (*Treponema pallidum* hemagglutination assay) is positive in titers T 1 : 5120 – T 1 : 10240;

– ELISA:

1) *Treponema pallidum IgM* antibodies 0.36 – negative result;

2) *Treponema pallidum IgG* antibodies 8.2 – positive result (Euroimmun reagent);

– bioimmunochemistry: total *Treponema pallidum* antibodies – 249 (Roche Diagnostics reagents);

– immunoblotting – *Treponema pallidum* antibodies:

1) *IgM* – negative result;

2) *IgG* to Tr15 – negative result;

3) *IgG* to Tr17 – positive result;

4) *IgG* to Tr47 – positive result.

Clinical diagnosis:

– syphilitic aortitis;

– insufficiency of aortic valves;

– aortic aneurysm.

It is prescribed for treatment with the sodium salt of benzylpenicillin.

The clinical experience shows that sometimes in medical institutions, syphilis is detected accidentally during an X-ray or serological examination, and only

then a detailed examination, additional instrumental and laboratory tests are carried out [2, 3].

The highest percentage of diagnostic errors occurs in cases of SA with progressive cardiac decompensation, which masks its clinical manifestations, and, in this connection, cardiac decompensation is mistakenly assessed as a complication of atherosclerotic cardiosclerosis. Clinical manifestations of the aorta atherosclerosis and atherosclerotic cardiosclerosis, on the one hand, and SA, on the other hand, have many common features. In favor of a syphilitic lesion of the aorta is evidenced by:

– the uneven expansion of its ascending part, which is usually detected only during X-ray examination;

– the emphasis of the II tone on the aorta with a metallic shade;

– the presence of aortic insufficiency, which is often combined with coronary disorders, – which in the literature is called "aortic root syndrome" [3, 4].

The diagnosis of syphilitic lesion of the aorta becomes:

– probable – when there is a triad of symptoms characteristic of aortitis in combination with insufficiency of arterial valves;

– reliable – when it is combined with aortic disease and insufficiency of coronary vessels; the most advantageous is the presence of the aorta aneurysm [2, 6].

The diagnosis of SA must be confirmed by anamnestic data (treatment of syphilis in the past) as well as positive non-treponemal and treponemal tests.

In middle-aged people, an unmotivated circulatory disorder should lead the internist to suspect a syphilitic lesion of the aorta complicated by the narrowing of the ascending openings of the coronary vessels, and should be the reason for a detailed clinical, radiological, instrumental and serological examination of the patient.

Under SA complicated by insufficiency of the aortic valves, differential diagnosis with rheumatic lesions of the aortic valves or septic endocarditis is a very difficult diagnostic problem.

Treponemal tests, which are almost 100% positive in late forms of syphilis, take a very important stand in the differential diagnosis of this issue. Syphilitic aneurysm of the aorta should be distinguished from tumors of the mediastinum, lung cancer, dermoid cyst and others [1, 3, 10].

The diagnosis of aortic aneurysm should be based on a detailed comprehensive examination of the patient – clinical, instrumental, radiological, serological one.

X-ray examination, in which a pulsating shadow corresponding to the affected part of the aorta can be seen, is of certain importance; in such cases this examination should be supplemented with tomography of the lungs [3, 19, 20].

Considering all of the above, it is recommended to pay attention to the following when diagnosing SA:

– complaints of shortness of breath, dull pains behind the sternum, coronary disorders, especially in young and middle-aged people;

– lesions of the aorta in persons younger than fifty years – require mandatory differential diagnosis between atherosclerosis and SA; with symptoms of damage of the aortic valves, it is necessary to rule out their syphilitic nature;

– the presence of stenocardia attacks, insufficiency of the aortic valves and expansion of the ascending part of the aorta, which makes it possible to diagnose SA (requires confirmation by positive treponemal tests) even in the elderly and middle-aged persons, since such a combination of symptoms in atherosclerosis is an exception.

Anamnestic data under SA indicate that most patients deny having syphilis in the past. The absence of a history of syphilis cannot be a reason to deny a syphilitic lesion of the aorta [2, 3, 6].

Early diagnosis and timely appointment of specific therapy are very important. The prognosis for patients with SA improves to a great extent with rational, systematic, specific treatment. Specific treatment significantly improves the prognosis under complicated forms of aortitis.

Early and complete treatment prolongs the life expectancy of patients with aortic valve heart failure and aortic aneurysm.

Specific rational therapy makes significant corrections in the prognosis of patients with complicated forms of aortitis and makes it less severe [12, 14, 16].

These two clinical cases of syphilitic aortitis are of interest due to their rarity in clinical practice and demonstrate the importance of correct diagnosis and appropriate treatment.

CONCLUSIONS

1. Damage of the cardiovascular system is currently one of the most common forms of visceral syphilis.

2. Syphilitic aortitis with symptoms of damage of the cardiovascular system, which are due to insufficiency of aortic valves, narrowing of the ascending openings of coronary vessels, aneurysmal expansion of the ascending part and the arch of the aorta, occurs in the late stages of syphilitic infection.

3. Even syphilis patients, who have been treated with penicillin in the past, can develop damage of the cardiovascular system, namely aortitis with insufficiency of the aortic valve leaflets.

4. The most informative methods for detecting late lesions of the cardiovascular system are: enzyme immunoassay (ELISA), *Treponema pallidum* hemagglutination assay, immunoblotting and computer tomography of the heart and echocardiography.

5. The practical significance of the observations lies in the fact that complicated forms of aortitis began to occur more often also in treated syphilis patients, who were previously treated with water-soluble penicillin. Aortitis occurs against the background of seroconversion/positivization/of non-treponemal tests, which were previously negative after treatment.

Contributors:

Zakharov S.V. – conceptualization, methodology;

Svyatenko T.V. – conceptualization, validation;

Zakharov V.K. – research, resources, data curation, writing;

Gorbuntsov V.V. – conceptualization, supervision, review and editing.

Pohrebniak L.A. – resources, data curation.

Funding. This research received no external funding.

Conflict of interests. The authors declare no conflict of interest.

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Стаття надійшла до редакції 18.06.2024;
затверджена до публікації 22.10.2024

