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Analysis of own observations of visceral syphilis lethal outcomes

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Abstract

The epidemiological situation of the syphilis incidence in the modern world is characterized as a "hidden" epidemic, which manifests itself in latent and late forms of the disease. Despite the general trend towards a decrease in the incidence of syphilis, there are some specific features in many regions of Russia. Deaths from visceral syphilis are now rare. The article presents data on the epidemiology, nosological forms of visceral syphilis, and describes two lethal outcomes. In observations, late syphilis was characterized by damage to several organs (liver, lungs, heart, brain), but the leading clinical manifestations were neurosyphilis (syphilitic meningoencephalitis) and cardiovascular syphilis (syphilitic mesaortitis, interstitial myocarditis). Damage of the respiratory and digestive organs (stomach, liver) are rare forms of visceral syphilis. In the presented observations, gummas in the lungs and liver, which were not clinically diagnosed, were detected. In all cases, the diagnosis of visceral syphilis was established at autopsy on the basis of a characteristic morphological picture (detection of gummas) and positive results of the Wassermann reaction.

Keywords: tertiary syphilis, cardiovascular syphilis, neurosyphilis, liver gumma, lung gumma, lethal outcomes.

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Background

The epidemiological situation of the incidence of syphilis in the modern world is characterized as a hidden epidemic, manifesting itself in latent and late forms of the disease [1]. According to the time of onset of the infection, syphilis is conditionally divided into early (up to 2 years from the infection) and late (more than 2 years from the moment of infection) forms [1].

In the past few years, despite the preceding decade of a steady decline, syphilis has reemerged in the USA with outbreaks across the country [2]. The prevalence of syphilis varies by ethnic group and gender. Thus, among homo- and bisexual men, the incidence of primary and secondary syphilis throughout the USA was 228.8 cases per 100,000 population in 2013; among women, the disease was much less common (0.9 cases per 100,000 in 2013) and with single outbreaks [2]. In some African countries, the incidence of syphilis reached up to 2300 cases per 100,000 population [3]. In 2016, the incidence of syphilis in Ukraine was 3,200 cases (7.6 per 100,000 population) [4].

In the 1990s, Russia experienced an epidemic, and we are still facing its consequences. The incidence of syphilis among the population in the Russian Federation in 2017 was 19.5 cases per 100,000 population, which is 14 times less than the same indicator in 1997 [5].

Nevertheless, despite the general trend toward a decrease in the incidence of syphilis, there are some peculiarities in many regions of Russia [6–8]. Therefore, for the period of 2010–2017 in the Moscow region, the incidence of syphilis in the population of this region increased while there was an increase in the incidence of asymptomatic neurosyphilis [9]. In Dagestan, the low incidence of syphilis in the population (4.5 per 100,000 population) was accompanied by an increase in the incidence of late latent syphilis [5].

In Novosibirsk, from 2013 to 2017, there was a downward trend in the detection of new cases of syphilis, such that the incidence rate in 2013 was 28.2 cases per 100,000 population, and in 2017, it was 20.2 cases per 100,000 population. Over the same monitoring period (2013–2017), there was a persistent trend toward a decrease in the rate of early forms of syphilis (70.2% in 2013; 44.4% in 2017) and an increase in the rate of late forms of syphilis (6.7% in 2013 and 8.3% in 2017) and latent unspecified syphilis (23.1% in 2013 and 47.3% in 2017). In the structure of late forms of syphilis in 2013–2017, late latent syphilis prevailed (55%–76%), followed by neurosyphilis (20%–42% of all

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late forms of syphilis), which was most often detected in the age group of 40 years and older [10].

Tertiary syphilis develops in a few patients who have received insufficient or no treatment for syphilis [1, 10]. The onset of tertiary syphilis is often registered 4–5 years after infection, but in recent decades, it has more often manifested itself after 8–10 years, and sometimes even decades after infection. The development of tertiary syphilis is promoted by senile and childhood age, injuries (physical, mental, drug-induced), chronic diseases and intoxications, and alcoholism [1].

With syphilis, lesions of any internal organs and systems of the patient (heart and blood vessels, stomach, lungs, liver, kidneys, endocrine glands, etc.) can develop; they occur at any stage of the disease, do not have specific clinical manifestations, and can be completely resolved when using specific therapy in the early stages of the disease [3, 4, 11–13].

In early forms of syphilis, functional disorders of the affected organs were most often recorded, and the heart is predominantly involved in the pathological process (early cardiovascular syphilis). The formation of specific lesions of the nervous and cardiovascular systems is more characteristic of late syphilis, in which destructive and inflammatory changes in internal organs occur [1, 11, 14].

Thus, monitoring of the epidemiological situation of syphilis in Russia and worldwide remains an urgent problem of modern medicine.

Since deaths from visceral syphilis are rare, we present our own cases of two lethal outcomes over the past 10 years.

Case 1

A 54-year-old patient was admitted in a serious condition with a clinical presentation of a central nervous system disease of unclear etiology. The examination results revealed a positive Wasserman reaction (RW+++), which led to the suspicion of neurosyphilis. The patient was diagnosed with increased blood pressure of 150/90 mmHg. The leukocyte count was 13.3×10^9/L. Although treatment was initiated, the patient died due to increasing symptoms of cardiac and respiratory activity.

Final clinical diagnosis. The underlying disease was acute toxic (probably endogenous) encephalopathy associated with neurosyphilis, syphilitic vasculitis. Complications of the underlying disease were edema, dislocation of the brain, and acute cardiovascular and respiratory failure. A concomitant diagnosis was arterial hypertension.

Postmortem examination revealed that the brain weighed 1260 g and was flabby, with smoothed gyri and flattened sulci. The pia mater was moist, full-blooded, dimmed in places, and matted together. The gray matter and white matter were demarcated, with full-blooded vessels, and the brain pattern was somewhat erased in some places. The ependyma of the lateral ventricles was moist and focally dimmed. Vessels of the brain base were dense, gaping on the cut, and there was a significant number of atherosclerotic plaques in their intima. On the base of the brain, there was a circular impression from the edges of the great foramen. Histological examination in the pia mater showed plethora, inflammatory lymphoplasmacytic infiltration; in the substance of the brain, there were perivascular infiltrates of lymphocytes, macrophages, plasma cells, as well as perivascular and pericellular edema.

The heart weighing 490 g was enlarged and of elastic-flabby consistency, and its cavities were dilated, containing blood clots. The left ventricle wall thickness was 2.1 cm, and that of the right ventricle was 0.7 cm. The myocardium was brown, dull, with whitish layers and scars. The valves were thin, whitish, and smooth. The coronary arteries were tortuous, dense, with a moderate amount of atherosclerotic plaques in their intima. Histological examination showed plethora, focal lymphoplasmacytic infiltration in the interstitium, and sclerosis.

Liver weighing 1740 g was flabby, variegated, and brownish yellow. In the left lobe of the liver, there was a focus of 3.5 cm, in a capsule 1.0–1.5 cm thick, with whitish viscous contents. No similar foci were found in other parts of the liver. Histological examination revealed vacuolar dystrophy of a part of the hepatocytes. The focus had the gumma structure with the focus of caseous necrosis, and the capsule around the necrosis was represented by dense fibrous connective tissue infiltrated by lymphocytes, macrophages, and a large amount of plasma cells.

Based on the findings of macro- and microscopic examination, considering the clinical and laboratory data, a *postmortem diagnosis* was formulated. The underlying disease was A52.1, tertiary syphilis, syphilitic meningoencephalitis, syphilitic interstitial myocarditis, and liver gumma. There were complications of the underlying disease, including focal confluent bilateral abscess pneumonia, venous plethora and dystrophic changes in internal organs, pulmonary edema, and edema and dislocation of the brain. A concomitant disease was chronic coronary heart disease (CHD).

A 54-year-old patient with tertiary syphilis had a visceral encephalitic form with damage to the heart, liver, and brain. The disease course was complicated by bilateral abscess pneumonia, followed by progressive cerebral edema up to dislocation and wedging of the stem part into the great occipital foramen.

Case 2

A 61-year-old man was registered with a cardiologist at the dispensary "D" with a diagnosis of CHD, angina pectoris II, and chronic heart failure I. In April 2020, he underwent examination and treatment in the therapeutic department for an aneurysm of the ascending aorta. In June 2020, he was additionally examined at the central district hospital, and late syphilis, cardiovascular form, was detected. The patient also had grade 2 chronic obstructive pulmonary disease, emphysema, and pneumosclerosis. The patient had a long-standing history of smoking and alcohol abuse. He lost a lot of weight within six months. The patient was consulted by a vascular surgeon, and angiography was performed for aortic aneurysm. In August, the patient died at home.

Final clinical diagnosis. The underlying disease was late syphilis, cardiovascular form, and aneurysm of the ascending aorta. Complications were rupture of the ascending aorta, acute blood loss, and pulmonary edema. Concomitant diseases were chronic obstructive pulmonary disease II, pulmonary emphysema and pneumosclerosis, and CHD and atherosclerotic cardiosclerosis.

Postmortem examination revealed approximately 1200.0 ml of dark red blood in the left pleural cavity, in the form of clots and in a liquid state. The lungs were of doughy consistency as a whole; on sections, the lungs were light red, and a significant amount of foamy liquid flowed from the cut surfaces when squeezed. In the upper lobe of the right lung, there was a whitish induration focus with a diameter of up to 5 cm. Histological examination revealed gumma represented by a focus of caseous necrosis with peripheral diffuse and focal inflammatory infiltration, mainly from plasma cells, macrophages, and lymphocytes, as well as sclerosis and signs of endoarteritis (Figs. 1, 2).

Flabby heart. The wall thickness of the left ventricle of the heart was 1.8 cm, and that of the right one was 0.4 cm. The heart cavities were empty. The myocardium on sections had a uniform dark, brown-reddish color. The valves of the vessels of the heart were translucent and thin. On the inner surface of the coronary arteries, single atherosclerotic plaques were noted, protruding into the lumens of the arteries, and narrowing it in places up to one-third of the vessel diameter. Numerous atherosclerotic plaques were seen on the inner surface of the aorta. In the thoracic aorta, from the level of the descending section of the arch and downwards, aortic dilatation (aneurysm) of 9 × 6 cm in size was seen, with a thin wall at this level of 0.1–0.2 cm. On the posterior left surface of the aneurysm, a rupture was detected throughout the entire thickness of the wall for 2.0 cm; the edges of the rupture were uneven; in the rupture circumference, the wall was frayed to a width of up to 2–2.5 cm; in the surrounding soft tissues, there were dark red hemorrhages.

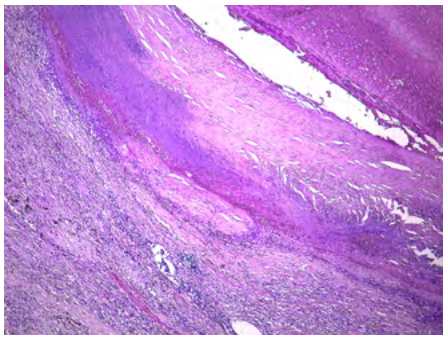

Fig. 1. Lung gumma: a focus of caseous necrosis surrounded by a bank of inflammatory cells. Stained with hematoxylin and eosin. Magnification ×50.

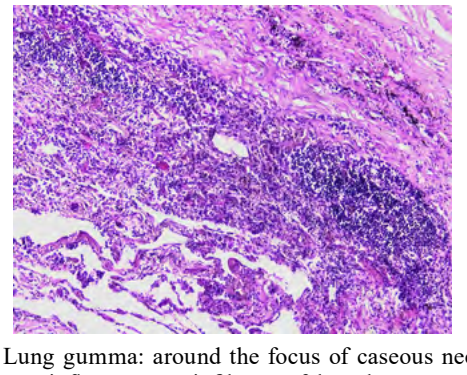

Fig. 2. Lung gumma: around the focus of caseous necrosis, there is an inflammatory infiltrate of lymphocytes, macrophages, plasmocytes, and endoarteritis. Stained with hematoxylin and eosin. Magnification ×200.

Histological examination revealed diffuse and focal inflammatory infiltration in the tunica media of the aorta, mainly from plasma cells, macrophages, and lymphocytes, as well as sclerosis (Fig. 3); when stained with resorcinol-fuchsin, the foci of destroyed elastic fibers were detected (Fig. 4).

Pathological diagnosis. The underlying disease was A52.0+I71.0, visceral syphilis, syphilitic mesaortitis, and gumma of the right lung. Complications included ampullary aneurysm of the thoracic aorta with wall rupture, massive bleeding, left-sided hemothorax, and hemorrhagic shock.

Discussion

Neurosyphilis is the most significant among lesions of organs in syphilis. The term "neurosyphilis" refers to an infection that affects the central nervous system. It can occur at any time after infection. Before the advent of antibiotics, neurosyphilis was common and reported in 25%–35% of patients with syphilis. It is now more common in patients with human immunodeficiency virus infection, espe-

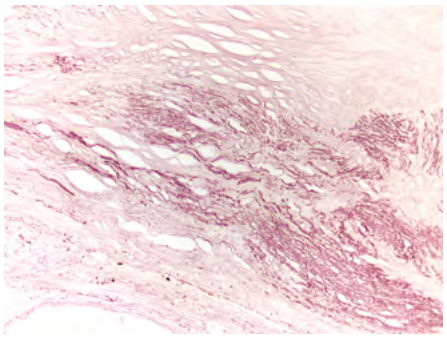

Fig. 3. Syphilitic mesaortitis: destruction of elastic fibers in the tunica media. Weigert's resorcinol-fuchsin stain. Magnification ×100.

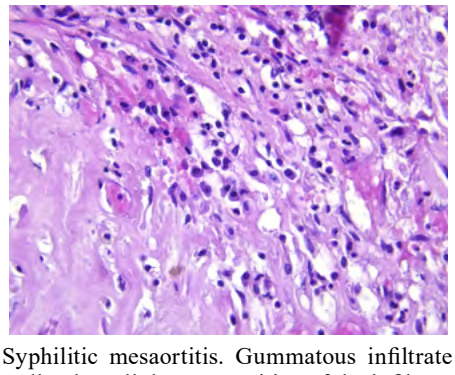

Fig. 4. Syphilitic mesaortitis. Gummatous infiltrate in the tunica media: the cellular composition of the infiltrate is represented by plasma cells, macrophages, and lymphocytes. Stained with hematoxylin and eosin. Magnification ×400.

cially those who are untreated and have low $CD4^+$ counts [15].

The lesions of the cardiovascular system in syphilis are very variable; most often, specific lesions of the aorta (mesaortitis), aortic valve insufficiency, aortic aneurysm, myocarditis, gummous endo- and pericarditis develop [3, 15]. The frequency of registration of cardiovascular syphilis varies widely. This is perhaps due to the fact that such lesions are diagnosed in only 10% of patients with syphilis during their lifetime. In 2014–2015, in Moscow and the Moscow region, specific aortic valve lesion was diagnosed in 91 patients, namely in 14 patients (9 men and 5 women) in Moscow and 77 patients (55 men and 22 women) in the Moscow region. Among the patients, men predominated in a ratio of 2.4:1. The age of patients at the time of diagnosis was within a wide range from 34 to 79 years (mean age, 52.8 years) [16].

According to the statistics of the Regional Dermatovenerological Dispensary of Novosibirsk, only two cases of cardiovisceral syphilis were registered for the period from 2013 to 2016 [10].

In their work, Drago et al. (2018) collected 44 articles over the past 6 years on 66 patients with cardiovascular syphilis. Aortic aneurysm was the most common lesion detected in 71% of patients. Fusiform or ampullary aneurysms often occurred in the thoracic aorta, mainly localized on its ascending segment. The second most common complication was aortic valvular insufficiency registered in 47% of patients. Stenosis of the ostia of the coronary arteries and aortic root dilatation were less common [14].

Lesions of the respiratory and digestive organs (stomach, liver) are rare forms of visceral syphilis [11]. In our case, gummas were detected in the lungs and liver, which were not clinically diagnosed.

Thus, in two cases, late syphilis in men was characterized by lesion of several organs, but the most common clinical manifestations were neurosyphilis and cardiovascular syphilis. The diagnosis of visceral syphilis was established only in the course of a postmortem examination.

Conclusion

Despite the downward trend in the incidence of syphilis in the Russian Federation, the incidence of late syphilis, characterized by damage to internal organs, primarily the central nervous and cardiovascular systems, has been increasing in several regions. The clinical presentation of visceral syphilis is nonspecific and often mimics other diseases (hence the name of syphilis, "great imitator"). The diagnosis of visceral syphilis in the fatal outcome in both cases presented was established at postmortem examination based on the characteristic morphological pattern and positive results of the RW test.

Author contributions. A.P.N. developed the study concept and design, collected and cleaned the data, performed statistical data analysis, and wrote and edited the manuscript; A.B.K. developed the study concept and design, collected and processed the data, and wrote the manuscript; A.E.P., M.A.T., and E.E.P. collected and processed the data.

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