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Tabes dorsalis на фоне прогрессирующей ВИЧ-инфекции: описание клинического случая и обзор литературы

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РЕЗЮМЕ

Описан редкий случай спинной сухотки у мужчины 66 лет с впервые выявленной ВИЧ-инфекцией (стадия 4В). Поздний нейросифилис (НС) и ВИЧ-инфекция были диагностированы у пациента одновременно при обследовании в связи с жалобами на снижение слуха, слабость мимической мускулатуры правой половины лица, нарушение походки. Спинная сухотка проявлялась невритами *n. vestibulocochlearis* и *n. facialis*, сухожильной гипорефлексией, положительным симптомом Аргайла Робертсона, статической и двигательной атаксией. Неврологическая симптоматика соответствовала началу атактической стадии спинной сухотки. Диагноз был подтвержден результатами исследования цереброспинальной жидкости. Пациенту было назначено лечение массивными дозами внутривенно вводимого пенициллина, однако возникшая на 12-й день лечения токсикодермия потребовала замены препарата на антибиотики резерва. На фоне специфического лечения было отмечено уменьшение неустойчивости при ходьбе, но положительной динамики со стороны органа слуха и симптомов прозопареза не было. ВИЧ-инфекция без антиретровирусной терапии прогрессировала, и спустя 3,5 мес пациент скончался вследствие двусторонней субтотальной пневмоцистной пневмонии.

Описанный случай представляет интерес в связи с редкостью *tabes dorsalis* и необычно быстрым нарастанием неврологической симптоматики на фоне прогрессирующей ВИЧ-инфекции. В ближайшие годы прогнозируется увеличение числа случаев коинфекции *Treponema pallidum* и ВИЧ и, следовательно, у ВИЧ-инфицированных пациентов возможно более частое развитие поздних форм НС.

Ключевые слова: поздний нейросифилис, спинная сухотка, исследование цереброспинальной жидкости, ВИЧ-инфекция, коморбидность ВИЧ-инфекции и сифилиса.

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Tabes dorsalis associated with progressive HIV infection: a case history and review of the literature

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ABSTRACT

A rare case of a tabes dorsalis in a 66-year-old man with a newly diagnosed HIV infection (stage 4B) is described. Late neurosyphilis (NS) and HIV infection were both diagnosed in the patient during an examination in connection with complaints of hearing loss, weakness of the mimetic muscles of the right half of the face, gait abnormality. Spinal troughs manifested as neuritis of vestibulocochlearis nervus and facialis nervus, tendon hyporeflexia, positive symptoms of Argyll Robertson syndrome, static and motor ataxia. Neurological symptoms corresponded to the onset of the atactic stage of the tabes dorsalis. The diagnosis was confirmed by the results of the study of cerebrospinal fluid. The patient was prescribed treatment with massive doses of intravenously injected penicillin, however, toxicoderma, which occurred on the 12th day of treatment, required replacement of the drug with reserve antibiotics. Against the background of specific treatment, a decrease in instability during walking was noted, but there was no positive dynamics on the part of inner ear and symptoms of paresis. HIV infection without an-

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tiretroviral therapy progressed, and after 3.5 months the patient died as a result of bilateral subtotal pneumocystis pneumonia.
This case is of interest in respect of the rarity of tabes dorsalis and because of the unusually rapid augmentation of neurologic symptoms in association with progressive HIV infection. In the coming years, the number of cases of co-infection of *Treponema pallidum* and HIV is expected to increase and, consequently, the late forms of neurosyphilis are more likely to develop in HIV-infected patients.

Key words: late-stage neurosyphilis, tabes dorsalis, cerebrospinal fluid testing, HIV infection, HIV and syphilis comorbidity.

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In recent years, a decrease in the incidence of early infectious forms of syphilis has been noted in the Russian Federation. However, the incidence of late forms of the disease, in particular, late specific lesions of the nervous system, is increasing. There were 220 cases of late neurosyphilis (NS) registered in 2002, with the number for 2016 being 1,159 (5 times higher) [1,2]. Late NS occurs mainly in the age groups of 30-39 years and ⩾40 years, it occurs 2 times more often in men than in women [1].

It is generally believed that late manifestation forms of syphilis develop in patients who have not received treatment at all or who have received inadequate treatment. However, there are NS cases among patients who received specific therapy for the early forms of syphilis that formally corresponded to accepted standards but in reality turned out to be insufficient [3—5]. For instance, the use of prolonged penicillin preparations is known to be insufficient for achieving the treponemocidal concentration of the antibiotic in the cerebrospinal fluid (CSF); for this reason, they are ineffective in NS [6,7]. Ideally, the administration of these drugs should be preceded by CSF analysis, even when it comes to the treatment of primary and secondary recent syphilis. Unfortunately, the currently widespread practice of outpatient treatment of syphilis implies neither CSF analysis nor examination of patients by a neurologist and ophthalmologist. Incomplete examination of patients and unjustified prescription of repository penicillin preparations, especially in a long (more than 6 months) or undetermined duration of the disease, are the basis for the observed increase in the incidence of NS and, in particular, its late forms.

Another major factor that will have a negative impact on the incidence of NS in the near future is the steady increase in the number of patients with *Treponema pallidum* and human immunodeficiency virus (HIV) co-infection. Thus, the proportion of HIV-infected individuals among the newly diagnosed syphilis patients in the Russian Federation was 2.3% in 2011, 3.3% in 2014 and 3.7% in 2015 [8]. Since, to date, the examination of syphilis patients for HIV infection is voluntary and not performed for all patients, the real prevalence of the co-infection is obviously much higher. It has been shown that the risk of NS in HIV-infected patients is 3 to 6 times higher than for HIV-negative patients [9—13]. Moreover, in more than half of the cases (57.8%), NS in HIV-positive patients is manifested in the form of asymptomatic meningitis, which can only be detected by CSF examination [9]. Meanwhile, HIV-infected patients refuse lumbar puncture in 47.4% of cases [9]. In this regard, the development of late NS forms in patients with HIV infection can be expected in the nearest future. Management of such patients who visit a wide variety of specialists (dermatologist, neurologist, ophthalmologist, infectious disease specialist, and etc.) will present certain difficulties, since nowadays doctors are not familiar with the clinical manifestations of late NS, and many aspects of its diagnosis and treatment have not been not fully developed yet.

Here we present a case of rapid development of tabes dorsalis (TD) following progression of HIV infection in a patient previously receiving treatment for syphilis.

Clinical case

Patient D., 66 years old, St. Petersburg resident, was urgently hospitalized in the Clinic of Otorhinolaryngology n.a. I.P. Pavlov with a diagnosis of bilateral conductive hearing loss on March 15, 2018.

During hospitalization, he complained of a pronounced hearing loss in both ears (almost completely deaf on the right side), right-sided facial muscle weakness, unsteady gait, instability when walking, decreased visual acuity, flickering spots in front of the eyes.

Anamnesis morbi. Medical history taking was complicated due to gross hearing impairment: the patient practically did not hear any questions, communication was conducted through correspondence. He considered himself ill from mid-December 2017 when his well-being changed to ear congestion and tinnitus followed by a sharp deterioration in hearing in both ears. An outpatient examination was performed by an otorhinolaryngologist at a private medical center on December 27, 2017, audiography was performed, which revealed a decrease in the air and bone conduction threshold to 75 and 55 dB on the right side and to 80 and 60 dB on the left side. The diagnosis of chronic bilateral sensorineural hearing loss of the III degree was made. The patient refused hospitalization. Parenteral dexamethasone was prescribed (according to the following scheme: 16 mg for 3 days, 8 mg for 4 days and 4 mg for 3 days), vasoactive and microcirculation drugs, anticoagulants, nootropic drugs, and B-group vitamins. The hearing loss gradually progressed despite the prescribed treatment.

In mid-January 2018, the patient noticed increasing gait instability, insecurity when walking, decreased vision in both eyes, and flickering spots in front of the eyes. Magnetic resonance imaging (MRI) of the brain without contrast administration was performed on January 18, 2018. Pronounced *ex vacuo* hydrocephalus and a discirculatory lesion focus in the brain substance were found. The neurologist diagnosed acute bilateral labyrinthopathy. The case remained diagnostically unresolved; differential diagnosis of either infectious and autoimmune injury of the VII cranial nerves on the right and the VIII cranial nerves on both sides, a space-occupying lesion in the region of the right cerebellopontine angle or paraneoplastic process was carried out. Due to the disease progression, the patient was prescribed methotrexate orally at a dose of 7.5 mg per week in February 2018. No positive effect of the therapy was observed.

Severe right-sided facial muscle weakness suddenly appeared on March 10, 2018. The patient was examined by a neurologist (March 14, 2018), and a diagnosis of "compression-ischemic neuropathy of the right facial nerve, vasoneural conflict in the right cerebellopontine angle?" was made on March 15, 2018. The patient was consulted at Pavlov St. Petersburg State Medical University and hospitalized for emergency examination, specification of the diagnosis and subsequent treatment in the Clinic of Otorhinolaryngology. The first serological examination for syphilis was performed only on March 19, 2018: 4+ (1:32) express test for rapid plasma reagins (RPR), 4+ passive hemagglutination reaction (PHA), negative *IgM*-ELISA, positive *IgG*-ELISA. The degree of positiveness (PD) was 2.5 (1:128). Due to the positive serological reaction to syphilis, the patient was transferred for further treatment to the Dermatology department at Pavlov Medical University of St. Petersburg on March 22, 2018.

*Anamnesis vitae***.** The patient is socially integrated. He held a managerial position at a construction company. The patient did not abuse alcohol, denies drug use. In 2008, he underwent diagnostic laparotomy for suspected acute intestinal obstruction. The patient denied any drug, food, or household allergy. No indications of penicillin intolerance were obtained from the medical history. The patient denied infectious hepatitis, tuberculosis, malaria, and HIV infection in the past. The patient received no blood transfusions.

The patient admitted suffering from syphilis (possibly primary, since he remembered the presence of a "sore" on the penis) about 20 years ago. According to the patient, he received intramuscular injections of some antibiotic prescribed by a private practitioner once a week, he could not name the number of injections. After treatment, he did not receive any clinical serological supervision. The wife was not examined and did not receive preventive treatment. He had been divorced for a year before the present disease and lived separately from his wife and two adult children. The ex-wife did not appear for examination despite the repeated calls.

Examination. The condition is satisfactory, consciousness is clear. No typical rash was detected on the skin and visible mucous membranes. A hyperpigmented patch was observed on the glans penis (the patient claimed that there was an ulcer at the site during syphilis infection 20 years ago). Inguinal and submandibular lymph nodes were enlarged to 1.5-2 cm on both sides, painless on palpation and mobile. No abnormalities were found upon examination of organs and systems.

Laboratory and instrumental examination. Clinical blood test (March 22, 2018) results are the following: $4.4 \cdot 10^{12}$/L red blood cells, 128 g/L hemoglobin, 37.4 hematocrit, $199 \cdot 10^{9}$/L platelets, $6.8 \cdot 10^{9}$/L white blood cells, 67.1% neutrophils, 26.6% lymphocytes, 4.8% monocytes, 0.1% basophils, 1.4% eosinophils, 29 mm/h ESR.

Urine analysis (March 22, 2018) results are as follows: urine is yellow, transparent, relative density is 1.017, pH 6.0, 0.3 g/L protein; glucose, hemoglobin, and bilirubin: none; leukocyte: 2 cells in the field of view; red blood cells and cylinders: none; flat epithelium: 1 cell in the field of view; mucus is present in a small amount; salts (oxalates) are present in a small amount; bacteria and yeast: none.

Blood biochemical analysis (March 22, 2018) showed 67 g/L total protein, 11.7 mmol/L total bilirubin, 4.4 mmol/L glucose, 0.097 mmol/L creatinine, 9 U/L alanine aminotransferase, 13 U/L aspartate aminotransferase, 3.7 mmol/L total cholesterol.

HBsAg (March 22, 2018) is negative, HCVAb (March 22, 2018) is negative.

Screening for HIV infection (March 22, 2018) by chemiluminescent microparticle immuno assay (ARCHITECT HIV Ag/Ab Combo assay, Abbot, Germany) revealed antibodies to HIV-1 and the viral antigen p24. Immunoblotting (linear immunoassay) using recombinant virus-specific polypeptides (Blot-HIV 1/2+0, Bioservice, Russia) confirmed the diagnosis of HIV infection.

CSF analysis (March 20, 2018) results are as follows: CSF is cloudy, transparent after centrifugation; color is bloody, slightly yellowish after centrifugation; Pandy reaction ++, Nonne-Apelt reaction ++, cytosis 1000/3 (752 neutrophils, 48 monocytes, 200 lymphocytes), 1.356 g/L protein, 17,800 in 1 mm^3 of fresh red blood cells, RPR 3+, RPGA 4+.

Brain MRI without contrast (March 16, 2018) revealed no focal changes and space-occupying brain lesions. Arachnoid cysts were observed. The structure of intracranial arteries is as follows: anterior trifurcation of the left internal carotid artery, posterior trifurcation of both internal carotid arteries.

Cone beam computed tomography of the temporal bones (March 19, 2018) showed no pathological changes in the area of the facial nerve canal.

Electrocardiography (March 23, 2018) revealed sinus rhythm, single ventricular extrasystoles, heart rate is 68 per minute, ECG signs of left ventricular hypertrophy.

Echocardiography (March 22, 2018) results are as follows: diameter of the aortic bulb is 38 mm, diameter of the ascending portion is 32 mm, aortic valve is tricuspid, valve opening is 23 mm. Thickening of the aortic wall is noted. The left atrium is 43 mm, slightly expanded. Diastolic and systolic size parameters of the left ventricle are 48 mm and 31 mm, respectively. Shortening fraction is 36%, global ejection fraction is 74%, end-diastolic volume is 122 mL, end-systolic volume is 32 mL. The thickness of the posterior wall in diastole is 7 mm. There were no mitral valve changes. Anterior wall thickness and diastolic diameter of the right ventricle are 4 mm and 35 mm (slightly expanded), respectively. The diastolic thickness of the interventricular septum is 8 mm. Right atrium is 46 mm (not enlarged). Pulmonary artery diameter is 19 mm. There are no changes in the atrial septum. The kinetics of the LV walls are normal. The inferior vena cava is not dilated, it dissipates well upon sharp breath. The estimated pressure in the pulmonary artery is up to 27 mm Hg (not increased). The conclusion of sclerotic changes in the aorta and I degree aortic insufficiency were made. The systolic function of the left ventricle is preserved, its relaxation is slightly impaired. Pressure in the pulmonary circuit is not increased.

Triplex ultrasound imaging (color-flow imaging) of extracranial regions of the brachiocephalic arteries and intracranial vessels (March 20, 2018) revealed signs of nonstenotic atherosclerosis of the carotid arteries.

Ultrasound examination of the abdominal cavity (March 26, 2018) showed a focal hepatic lesion (hemangioma?), sonographic signs of chronic cholecystitis, gallbladder polyps, right-sided nephroptosis, signs of chronic pyelonephritis, microliths in the right kidney.

Neurologist examination (March 23, 2018) results are as follows: consciousness is clear, no psychotic, emotional, or intellectual-mnestic disorders. Higher brain functions (speech, gnosis, praxis) are not disturbed. Examination of the cranial nerves revealed no hemianopsia. Pupils are of medium diameter, regular shape, D=S. The response of the pupils to light is sluggish, the reaction to convergence and accommodation is preserved. The movements of the eyeballs are not limited. No diplopia is noted. Nystagmus is absent. Face sensitivity is not impaired. Pronounced peripheral prozoparesis of the facial nerve is observed on the right side. Swallowing and phonation are not disturbed. There are no symptoms of oral automatism. Tongue is located in the midline. Motor system examination revealed normal muscle tone, D=S. There are no paresis. Brachioradial reflex, biceps and triceps reflexes are reduced, D=S. Knee and Achilles reflexes are reduced, D=S. There are no pathological carpal and foot symptoms. Extrapyramidal system is not affected. Finger-to-nose and heel-to-shin coordination test results are satisfactorily. Romberg's test demonstrated the patient falling to the right. Fukuda test is positive: he falls to the right. Meningeal symptoms are absent. No local myotonic syndrome is observed. There is no gross disturbance in the spinal statics and dynamics. The conclusion is late neurosyphilis (tabes dorsalis).

Examination by an ophthalmologist (March 23, 2018) revealed partial lagophthalmos. No changes in the anterior chamber of the eye are noted. The ocular media are transparent. The pupils are round, OD=OS. The response of the pupils to light (direct and consensual) is sluggish. Phacosclerosis of the lens is present. Examination of the fundus of the eye showed that the optic papilla are pale pink, their borders are shaded, the optic disc cupping is preserved. The vessel caliber is normal, the artery walls are thick. The Salus-Gunn sign is I. No focal pathology is detected. Intraocular pressure showed OD 15 mm Hg and OS 16 mm Hg. The conclusion is congestive disks of the optic nerves (advanced stage). Reduced pupil reaction to light, hypermetropia and presbyopia OU are observed. Spectacle correction is recommended.

Examination by a therapist (March 23, 2018) revealed stage II hypertension and left ventricular hypertrophy. The risk of cardiovascular complications was evaluated as 3 (high).

Antibiotic therapy was started on March 23, 2018 according to the treatment regimen for late NS: crystalline sodium salt of benzylpenicillin at a dose of million units 2 times a day intravenously. Two 20-day courses of treatment with a 2-week interval (total dose of penicillin is 480 million units) were planned. In order to prevent the progressive development of neurological symptoms due to exacerbation, oral prednisolone was administered to the patient at a dose of 90-60-30 mg daily (single dose in the morning) for the first 3 days of penicillin therapy. On day 12 (April 3, 2018), the patient's body temperature increased to 38.3°C, and itchy bright pink rash appeared in the form of individual spots on the skin of the face, trunk and extremities and subsequently merged into the foci of erythema with large festoon borders. The condition was regarded as penicillin toxicoderma (moderate to severe), and antibiotic therapy was interrupted. By the end of the

therapy, the patient received in total 288 million units of penicillin intravenously. During penicillin therapy, the patient noted a decrease in gait instability, but no positive dynamics were noted for the hearing organ; no symptoms of facial palsy were observed. In order to stop toxidermia, the patient underwent a short course of systemic therapy with prednisone, which yielded a quick positive effect.

Due to the detection of HIV infection and the need for a break in the specific syphilis therapy because of the developed toxidermia, the patient was discharged from the Dermatology department at Pavlov Medical University of St. Petersburg and transferred to the St. Petersburg Center for Prevention and Control of AIDS and Infectious Diseases for registration and antiretroviral therapy (ART) on April 6, 2018. He was recommended to continue the treatment of syphilis with the reserve antibiotic 2 weeks after discharge at a hospital.

Upon subjection to dispensary registration at St. Petersburg's AIDS Center, an immunological examination was conducted (April 11, 2018): 293 cells/mL CD4 T-helpers (normal range, 570-1,100), CD4 to CD8 cells ratio is 0.09 (normal range, 1-1.7), 9,114 copies/mL HIV-1 RNA (viral load). Results of a repeated serological examination (April 11, 2018) are as follows: the reaction of microprecipitation (RMP) yielded 4+ 1:32; *IgG*-ELISA is positive, 1: 640; total antibody ELISA is positive; PD is 20.26. Due to the obtained values for the immune status and viral load, the patient was prescribed ART, but thee therapy delayed until the NS treatment course is ended.

For further course of specific therapy, the patient was transferred to the hospital at St Petersbug Dermatovenerologic Center on April 19, 2018. At the Center, he received the following treatment: 100 mg of doxycycline 2 times a day for 14 days, then 1 g of ceftriaxone intramuscularly 2 times a day to a total dose of 21 g. Serological examination (April 23, 2018) revealed RMP of 4+ 1:64, immunofluorescence reaction with absorption (RIF-abs) of 4+, RIF-200 of 3+, *IgM*-ELISA is negative, *IgG*-ELISA is positive (1:1280), PD is 13.4.

During the hospital stay, on May 26, 2018, weakness, dizziness, cough with scanty sputum, temperature increase up to 39.3°C appeared. An X-ray examination of the thoracic organs was performed on May 30, 2018: an increased pulmonary vasculature was found in the central lobe of the right lung, in the middle lobe and S8 on the right. On the same day, the patient was transferred to the specialized department of the Clinical Infectious Disease Hospital n.a. S.P. Botkin with a diagnosis of acute right-sided pneumonia, respiratory failure I degree.

Upon admission to the infectious department, the patient's condition was moderate; lungs examination revealed hard breathing, dry rales in the lower sections on both sides. Treatment with ceftriaxone was continued: 1 g intramuscularly daily (received from May 30 to June 4, 2018), 100 mg of levofloxacin was prescribed 2 times daily intravenously by drop infusion, expectorant and antipyretic agents. Examination on June 1, 2018 revealed: 4+ 1:32 RMP, 4+ RPGA, ELISA test is positive, **215** cells/mL CD4 T-helpers, CD4 to CD8 cells ratio is **0.08**, HIV-1 viral load is **17,035** copies/mL. Despite the treatment, the pyretic fever remained, dyspnoea appeared and increased, the patient also suffered from weakness. Due to suspected pneumocystis pneumonia, the patient was prescribed prednisone intramuscularly at increasing doses (from 120 to 360 mg/day), Biseptol intravenously by drop infusion (from 15 mg/kg 2 times a day to 20 mg/kg 4 times a day), and oxygenation by moistened oxygen on June 4, 2018. Despite the treatment, on June 7, 2018, the patient died upon increasing symptoms of respiratory failure caused by pneumocystis pneumonia.

Final diagnosis: HIV infection, stage 4B, progression in the absence of ART. Complications include pneumocystis pneumonia, bilateral bacterial pneumonia, respiratory failure III degree, acute cardiovascular failure. Concomitant diseases included late neurosyphilis (tabes dorsalis), coronary heart disease, ventricular arrhythmia, chronic cholecystitis, chronic pyelonephritis.

Pathoanatomical diagnosis (June 9, 2018) is as follows: primary disease is HIV infection without ART, AIDS stage, lymphoid depletion of all groups of lymph nodes; secondary diseases include bilateral subtotal pneumocystic pneumonia, advanced pseudomembranous candidiasis of the mucous membranes of the mouth, pharynx and esophagus; complications include hyperplasia of the inferior tracheobronchial lymph nodes, parenchymal dystrophy of internal organs, pulmonary edema, acute cardiovascular and pulmonary failure; concomitant diseases are late neurosyphilis, left-sided hydronephrosis. The patient's death was caused by increasing intoxication in association with cardiopulmonary insufficiency.

Discussion

Tabes dorsalis (progressive locomotor ataxia, syphilitic myelopathy) is a form of late (parenchymal) NS characterized by a slowly progressive dystrophic process in the posterior roots and posterior columns of the spinal cord, usually at the lumbar and sacral levels. The processes of inflammatory proliferation and destruction (demyelination followed by fibrosis) occur simultaneously in these segments. Degenerative changes in the parenchyma of the spinal cord are accompanied by vasculitis and perivascular lymphocytic infiltration of the meninges. Syphilitic myelopathy, or tabes (the Latin word "tabes" means decay, shriveling), was considered a pathognomonic and the most common form of NS in the prepenicillin era. After introduction of penicillin into medical practice, TD cases were rarely recorded. However, in recent years, reports of these are increasing in both domestic [14-19] and foreign [20-22] literature. There are also few reports of TD in HIV-infected people [23, 24].

The first signs of TD develop on average 10-15 years after infection with syphilis. According to traditional believe, this form of late NS is characterized by staging with

a slow increase in neurological symptoms. Three stages of the disease are distinguished: neuralgia (preataxic), ataxic and paralytic degree.

The preataxic stage of TD is characterized with lesion of the posterior roots of the spinal cord (chronic meningoradiculitis). The disease usually begins with short recurring episodes of radicular pain, which is sharp, shooting and piercing in nature. Pain in the lower extremities, girdle sensation in the trunk and internal organs (tabetic crisis) are typical manifestations. In the same period, impairment of surface sensitivity appears: paresthesia and hyper- and hypoesthesia in the limbs and trunk. Impairment of tendon reflexes are among the earliest and persistent symptoms: knee and Achilles reflexes gradually decrease and eventually are not triggered anymore, then the same happens to the reflexes on the upper extremities. Pupillary disorders are observed at the initial stage of the disease. The most characteristic sign is lethargy or the lack of response to light while the response to convergence and accommodation (Argyll Robertson syndrome) is preserved. Along with the disturbed reaction of the pupils to light, paralytic miosis, anisocoria, a change in the shape can be observed as well: outline of the pupils acquire irregular or angular shape. In 10-15% of patients, optic nerves (n. opticus, II pair) are involved in the process gradually causing their primary atrophy. Paresis and paralysis of other cranial nerves may also occur: oculomotor (*n. oculomotorius*, III pair), abducens (*n. abducens*, VI pair) and hypoglossal (*n. hypoglossus*, XII pair) nerves. Lesions of the facial (*n. facialis*, VII pair) and auditory (*n. vestibulocochlearis*, VIII pair) nerves are relatively rare in TD. At the end of the neuralgic stage, pelvic organ dysfunctions often occur: difficulty urinating or urinary incontinence, cystic crisis; persistent constipation or fecal incontinence; impotence.

Disorders of the muscle and joint and vibrational sensitivity, progressive coordination disorders (sensitive ataxia) predominate in the clinical picture of the ataxic stage of TD. Static ataxia is manifested by instability in the Romberg position (we would like to note that M.N. Romberg first described the imbalance with eyes closed for patients with TD), while motor ataxia is characterized by unsteady gait, insecurity when walking and the gradual formation of the stamping gait. Muscle hypotension develops along with ataxia and grows at the same proportion, sometimes even resulting in atony. In addition to ataxia, the progression of the symptoms that occurred in the first stage of the disease is also observed.

The paralytic stage of TD is characterized by afferent paresis and paralysis of the limbs. Due to the aggravation of ataxia, patients lose the ability to move independently, cannot take care of themselves. Motor ataxia affects not only the lower but also the upper extremities as well as trunk and head. At this stage, trophic disorders occur: Charcot's arthropathy, osteopathy, perforating ulcers, loss of the teeth and hair, onychodystrophy, decreased sweating. The absence of pain is typical for all trophic disorders in tabes. At the late stage of the disease, skin and muscle atrophy with the development of cachexia is observed. For this reason, TD was called "a disease that dries up the whole body."

In the presented patient, at the time of admission to the Dermatology Center, TD manifested with neuritis of the VIII cranial nerves with almost complete hearing loss, pronounced peripheral prozoparesis of the facial nerve (VII) on the right, tendon hyporeflexia on the lower and upper extremities, positive Argyll Robertson syndrome, static and motor ataxia. Thus, all cardinal manifestations of tabes were observed. Neurological symptoms corresponded to the onset of the ataxic stage of TD. The diagnosis was fully confirmed by the results of the CSF study.

Detection of echocardiographic signs of the aortic wall thickening and I degree aortic insufficiency suggested syphilitic mesaortitis, but these changes could be also due to aortic atherosclerosis, especially since atherosclerotic plaques in the carotid arteries and II degree hypertension were diagnosed in a 66-year-old man. Thus, the presence of cardiovascular syphilis in the patient has not been unequivocally confirmed.

The rapid development of TD symptoms (there was a month interval between the first complaints of hearing loss and the onset of ataxia symptoms) is apparently due to the negative impact of progressive HIV infection, which was beyond the patient's knowledge. Paraphrasing the well-known statement on the mutual influence of syphilis and alcoholism, one can say that the patient with *Tr. pallidum* and HIV co-infection is like a "candle burning from both ends." The lethal outcome was due to cardiovascular and respiratory failure caused by an opportunistic infection: bilateral subtotal pneumocystic pneumonia and AIDS.

Our clinical observation emphasizes the difficulty in diagnosing TD due to the non-specificity of neurological symptoms; it shows the probability of a delayed diagnosis (in this case, both NS and HIV infection), which significantly limits the treatment options. In TD, specific therapy is ineffective, which is because the antibiotics are targeted at *Tr. pallidum* and the inflammation it causes, while degenerative-dystrophic processes predominate in TD, and the severity of inflammatory changes is minimal [14, 22]. Nevertheless, the "Clinical practice guidelines for the management of syphilis patients" recommends intravenous administration of the sodium salt of benzylpenicillin at a dose of 12 million units 2 times a day for 20 days in TD followed by a two-week break and the second course of treatment according to a same scheme [25]. The patient's toxicoderma did not allow him to complete the treatment with water-soluble penicillin and required the use of reserve drugs. However, now it is not possible to assess the extent to which it worsened the prognosis. There are no reliable data on the efficiency of ceftriaxone and other reserve antibiotics in TD. However, inferiority of the drug ceftriaxone to penicillin was shown for the treatment of another form of late NS: progressive paralysis [26].

Penicillin therapy for TD usually does not lead to regression of the existing clinical manifestations. An indicator of the treatment efficiency is the absence of new neurological symptoms and increase in the existing ones as well as normalization of the CSF parameters (6 months for cytosis 2 years after treatment for the protein level). CSF should be examined in patients after two courses of specific therapy, then once every 6 months during the first year of the follow-up period and once every 12 months in the subsequent years. Patients with NS, regardless of stage, should be under clinical and serological control for at least three years [25].

Along with the objective difficulties that arose in the diagnosis and treatment of NS in the presented patient, a number of medical errors, which ultimately led to a fatal outcome, should be also mentioned. These errors include, first of all, late examination of the patient for syphilis: serological tests were performed only 3 months after the first complaints, despite the fact that the patient repeatedly sought medical help at various specialists and medical institutions. If the routine screening for syphilis was performed in accordance with current instructions, specific therapy could be started earlier and probably be more successful. Finally, the origin of the adverse outcome of the disease is the inadequate syphilis therapy performed in the past by the patient, the lack of clinical and serological monitoring after treatment, the lack of examination and treatment of the patient's wife. In addition, the patient was not promptly offered and tested for HIV infection. The current epidemic situation on HIV infection in the Russian Federation requires caution regarding this disease. The state strategy to counteract the spread of HIV infection in the Russian Federation for the period till 2020 and the further prospects involve medical examination for HIV infection of all those who turn to medical centers for medical care, especially in regions with a growing increase in the incidence of the disease. Moreover, special attention is paid to medical examination of populations with increased risk of infection.

Conclusion

The similarity of conditions and the transmission mechanisms for HIV and syphilis pathogens, as well as subpopulations at risk of infection, assumes that more and more cases of the co-infection will be registered in the nearest years.

In HIV-infected patients with syphilis, the probability of specific neuronal damage, organs of vision and hearing is 3 to 6 times higher than in HIV-negative individuals. In case if NS is developed in the presence of HIV-induced immunosuppression, it can differ in the severity of clinical symptoms and rapid progressing. In this regard, one can predict an increase in the NS cases among HIV-infected patients.

Doctors of various specialties (dermatologist, neurologists, ophthalmologists, infectious disease specialists, and etc.) should be informed about the clinical manifestations of late NS and the examination algorithm in case if the disease is suspected. Strict compliance with the requirements for screening patients for syphilis will help avoiding mistakes in difficult-to-diagnose cases.

Due to the unfavorable epidemic situation, screening for antibodies to HIV should be mandatory for all patients with sexually transmitted infections.

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