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BEHCET'S DISEASE DIAGNOSTICS FEATURES

A clinical case of Behcet's disease has been described. The clinical picture and the course of the disease has been described, additional research methods results have been interpreted. An algorithm for diagnosis and treatment of the disease has been offered.

INTRODUCTION

Behcet's disease (Adamantiada - Behcet's disease, the Silk Road disease) is a systemic chronic idiopathic inflammatory disease of unknown etiology with recurrent course, manifested by a characteristic triad of recurrent aphthous stomatitis, ulcerative changes in the mucosa and genital skin, inflammation of eyes. Additionally, other organs may be affected - often there are arthritis, thrombophlebitis, colitis, neurological symptoms. The highest prevalence of Behcet's disease takes place in Turkey and is 80-370 cases per 100 thousand of population. The prevalence in Japan, Korea, China, Iran and Saudi Arabia ranges from 13.5 to 20 cases per 100 thousand, while in Western countries (Britain and the United States) it is lower - 0.64 and 0.33 per 100 thousand population, respectively. The prevalence in the countries of the former CIS makes 3 per 100 thousand. It is known that in Japan and Korea, Behcet's disease most often affects women, while in the Middle East it mostly affects men. The most frequently the disease's debut comes in the age of 30-40 years. Thus, epidemiological studies suggest that the disease development is influenced both by genetic and extrinsic factors [6, 8].

Behcet's disease etiology is currently unknown. The role of various etiological factors is assumed, such as infectious (streptococcus, herpes simplex virus type 1), hormonal disorders, and genetic factors.

The pathogenesis is the development of systemic vasculitis of immune complex nature. The main pathogenetic links of the process are: reduction of T-helper lymphocytes activity and increased circulating of autoantibodies to the cells of the mucous membranes; occurrence of circulating T-lymphocytes possessing cytotoxicity to the epithelium of the oral mucosa; reducing the amount of IL-2 receptors on T-lymphocytes; decrease in saliva of concentrations of secretory IgA; high chemotactic and phagocytic activity of segmented neutrophils. All these factors contribute to the damage of vascular endothelial with Behcet's disease. Histology of tissue damage is often presented perivascular lymphocytic infiltration, vasculitis. Blood vessels, both arterial and venous may be affected [1, 4, 6].

Behcet's disease is characterized by a triad of clinical signs: aphthous stomatitis, ulcerative changes in the mucosa and genital skin, eye damage in the form of uveitis or iridocyclitis. Ulceration of the oral cavity is observed in all patients and is considered one of the earliest symptoms, often outpacing the development of systemic symptoms for months and even years. The disease usually begins with the appearance on gums, tongue, and mucous membrane of cheeks and lips of aphtae with turbid contents, which then turn into sores with diameter of 2-12 mm of hot pink colour having round shape with an erythematous margin. Surface of ulcers may be covered with yellowish pseudomembranes. Ulcers tend to merge, and the affected area may be a continuous pitting surface. On the mucous membrane of a balanus, vagina, on the scrotum painful aphthae appear, transforming into ulcers, resembling ulcers in a mouth, but it is usually larger and deeper, irregularly shaped. Eye involvement is the first symptom of the disease in $\approx 10\%$ of patients, but more often develops after ulcerative stomatitis. Patients with affected eyes have a variety of complaints, among which the most frequent are vagueness of visual objects, eye pain, photophobia, lacrimation, periorbital congestion. Also frequently skin lesions occur in the form of erythema nodosum, papules, folliculitis. There can be a rash resembling erythema multiforme. Subungual abscesses and ulcers are also often present. Joint disease occurs in about half of patients and is characterized by predominantly mono- or oligoarthritis of large joints; less frequently, patients have polyarthritis. The defeat of gastrointestinal tract manifests abdominal pain and diarrhea. Development of gastrointestinal bleeding and perforation of intestine are possible. Ileocecal region of the intestine is affected most often, rarely esophagus, transverse and ascending colon are involved. Chronic, progressive damage to the central nervous system is seen in 10-20% of patients and occurs more frequently in men infected at a younger age. In the early stages of the disease in the acute phase aseptic meningitis or meningoencephalitis may develop, which are manifested by headache, fever, stiff neck. According to various studies, the incidence of lung involvement in Behcet's disease is from 1 to 7%. Possible manifestations of lung injury may be the pulmonary artery aneurysm, arterial and venous thrombosis, pulmonary infarction, recurrent pneumonia, bronchiolitis obliterans, pleural effusion. Kidney involvement in Behcet's disease happens much less than in other vasculitis and is accepted less hard. Sometimes proteinuria, hematuria, minor kidney failure are revealed. Cardiac involvement is rare and can be represented by pericarditis, myocarditis, koronariitom, endocarditis, mitral valve prolapse, etc. Vascular lesions of the small-caliber underlies many pathological processes in Behcet's disease

and is observed in 7-38% of cases. Typical symptoms include thrombosis of superficial and deep veins [3, 5, 7].

Given the fact that the etiology of Behcet's disease is unknown, but the pathogenesis is the development of systemic vasculitis of autoimmune nature, which may be manifested in clinical damage of any organs, diagnosis at an advanced stage of the disease should be based on the identification, review and consolidation into a single symptom the triad of symptoms: aphthous stomatitis, ulcerative changes in the mucosa and genital skin and eye damage in the form of uveitis or iridocyclitis.

The results of laboratory and imaging studies in Behcet's disease are not specific and sensitive. These laboratory studies usually indicate inflammatory processes. In clinical analysis of blood, the increase in erythrocyte sedimentation rate (ESR) is most often marked. General analysis of urine is usually uneventful, with involvement of kidneys, proteinuria and hematuria are possible. Biochemical and immunological assays may be not altered, except for increasing C-reactive protein and fibrinogen, reflecting the degree of activity and inflammation. One of the most important diagnostic criteria for establishing the diagnosis is positive pathergy test evidencing cutaneous hypersensitivity. Radiological methods of investigation have no independent value in establishing the diagnosis. However, the conventional x-ray, computed tomography and magnetic resonance imaging are important for assessing lung disease, and central nervous system. Ophthalmologic examination helps to clarify the nature of eyes involvement. Therefore, information obtained on the basis of additional research methods and conclusions of specialists, can confirm the presence and severity of inflammatory syndrome and clarify the involvement of a common pathological process of organs and systems with reflected nature of their injuries.

In 1990 international diagnostic criteria of Behcet's disease were developed (Internal Study group for Behcet's disease, 1990). These criteria are:

- Recurrent oral ulcers - small and/or large aphthas, herpetiform ulceration, recurrent at least 3 times during a year identified by a doctor or a patient.
- Recurrent genital ulcers - aphthous or scarring ulceration identified by a physician or by a patient.
- Eye lesion - anterior uveitis, posterior uveitis, cells in the vitreous body at the study with a slit lamp, retinal vasculitis identified by an ophthalmologist.
- Skin lesions - erythema nodosum, pseudofolliculitis, papulopustular rash, acne like nodules identified by a physician at patients using steroids in post-pubertal period of development.
- A positive pathergy test - estimated by a physician in 24-48 hours.

In accordance with these criteria, the diagnosis is considered valid if the ulcerative stomatitis is combined with two of the following features: recurrent genital ulcers, eye damage, skin lesions or a positive pathergy test [2].

Thus, clinical diagnosis of Behcet's disease is formulated on the basis of a preliminary diagnosis data (established in accordance with international criteria) identified characteristics of the disease and effectiveness of therapy in accordance with the protocols of treatment. Information obtained by using additional methods of research and opinion of domain specialists, helps to document the systemacity and nature of the lesion of a patient's organs.

MAIN PART

As an example of diagnostic features of Behcet's disease we present a clinical case. Patient K., 33 years old, on 11/10/2012 was enrolled in the rheumatology department of Luhansk City Clinical Hospital № 1 multi complaining of pain in mouth, throat, difficulty in swallowing food, eye redness and soreness, ulcers in the scrotum. The disease began to 14.09.2012 with the above complaints. Examination of the ENT doctor diagnosed "strep throat" and corresponding treatment was prescribed. Despite this, on 15/09/2012, the patient developed ulcers on the scrotum, and then - on the oral mucosa and trunk skin. He got consultation from a dermatologist who prescribed symptomatic treatment (rinsing, ointments). When the patient applied to a dentist, the latter diagnosed "thrush", treatment was ineffective. After 2 weeks from the onset of the disease the patient was consulted by the assistant professor of dermatology & venereology of SE "Lugansk State Medical University", who suspected Behcet's disease, and recommended medical check-up with a rheumatologist. For more accurate diagnosis and treatment strategies the patient was hospitalized in a rheumatology department. Consequently, the preliminary stage of diagnosis was 28 days.

On admission to the clinic, general condition of the patient was heavy. Asthenic physique (height - 172 cm, weight - 40 kg). Skin is dry, bloodshot eye sclera, on the oral mucosa - the numerous sores, destruction of palatal arches, multiple ulcerative defects on the trunk, scrotum. In the lower third of the right arm of there were a group of ulcers covered with scabs. In the scrotal there was a wound with areas of granulation. On the lower third of the leg there was a round ulcer in diameter up to 7 cm with purulent discharge.

Peripheral lymph nodes are not enlarged. Above lungs the sound was clear, vesicular breathing, respiratory rate 18 per minute. The boundaries of the heart are age appropriate, heart activity is rhythmic, sounds are clear, HR - 78 beats per min, pulse - 78 beats per min, blood pressure - 100/60. The abdomen was soft, painless, liver was at the costal margin. Urination is free, painless, the Pasternatsky symptom was negative on both sides.

When analyzing the patient's identified symptoms we can identify the major triad of syndromes caused by systemic vasculitis characteristic of Behcet's disease. These include:

- 1) the syndrome of lesions of oral mucosa and pharynx (multiple ulcers in an oral cavity and pharynx);
- 2) the syndrome of skin and genital organs lesions (sores on skin of the trunk, limbs, scrotum);
- 3) the syndrome of eyes lesions (acute uveitis).

To establish a clinical diagnosis, it is necessary to clarify the extent of the process and the severity of the current, consultations of related professionals are recommended: an ophthalmologist - for the diagnosis of eye damage, an otolaryngologist - to agree management of oropharynx lesions, a neurologist - to clarify the status of the central nervous system, a surgeon - to agree the tactics for treatment of the leg sore, a proctologist - to eliminate intestinal lesions. For this purpose, the patient underwent lab and instrumental tests, as well as microbiological swabs and crops from the discharge of wounds on the pathogenic flora, as well as screening for specific infections (tuberculosis, syphilis, and HIV).

The results of the survey. Complete blood test: RBC - $3.78 \times 10^{12}/L$, Hb - 101 g/l, color index - 0.8, WBC - $6.3 \times 10^9/L$ (E-1%, PA-15%, C-72%, LA-7%, MA-5%), ESR - 24 mm/h. Biochemical blood test: rheumatoid factor - negative; haptoglobin - 14.5 mm/l, total protein - 55 g/l, protein fractions: α - 33 g/l, β - 12 g/l, γ - 10 g/l; ALT - 0.58 IU/L, AST - 0.77 IU/L, thymol - 3.5 units.; urea - 3.7 mm/L, creatinine - 95 mm/l. Urinalysis, urine analysis according to Nechyporenko – acc. to the norm. Antibodies to HIV, syphilis were not identified. Scraping on the mushrooms from the mouth ulcers - identified yeasts; scraping on the flora of scrotal ulcers - no growth; scraping on the pale Trepanier of scrotal ulcers - negative. Analysis of the urethral organs: the WBC - 11-12, the epithelium - 2-4, mucus - a lot, microflora - rods/cocci, gonorrhea, chlamydia, trichomonas - not identified.

On the plain film of OGK of 05/10/12 focal changes have been identified, the roots are structural. In the lateral section, right side, interlobar pleura is thickened and sclerotic. The left hemidiaphragm is with an irregular outline due to pleural-phrenic adhesions.

Consultations of related professionals: eye specialist - retinoangiopathy of vessels of both eyes; ENT - affect of upper respiratory tract of a systemic nature, treatment of the underlying disease is recommended, antibiotic therapy - combination drug ceftriaxone and sulbactam, levofloxacin, anti-inflammatory therapy; proctologist - diseases have not been identified; surgeon - recurrent streptoderma, necrotic leg wound, recommended dressings with checking and appropriate drainage of streaks under general anesthesia. Neuropsychologist - revealed no pathology.

Thus, these preliminary diagnosis, the results of additional research methods that have established the degree of inflammatory activity, and the conclusion of narrow specialists indicate generalization and the severity of the disease process, enable us to establish a clinical diagnosis of Behcet's disease, the activity of the Ist stage, subacute, with a generalized form with skin lesions (ulcerative lesions of the skin of the lower limbs, forearm, upper arm, scrotum, right ankle, left leg, with gathering of ulcers of the right forearm and lower leg), mucosa of the mouth, nose and throat (thrush).

According to the minutes of treatment the patient received: basic therapy (glucocorticosteroids - methylprednisolone), anti-inflammatory (diclofenac sodium, meloxicam), antibacterial (combined drug of ceftriaxone and sulbactam, levofloxacin), anticoagulant therapy. Cytostatics were not appointed because of ulcerative lesions with suppuration. Comprehensive treatment with glucocorticosteroids significantly improved the health and condition of the patient. However, due to the prevalence of secondary effects in the form of septic wounds of the shoulder and arm, requiring surgery, the patient is transferred to the department of purulent surgery of Lugansk Municipal Multidisciplinary Clinical Hospital No.15. After providing appropriate medical care and treatment, the patient was discharged with improvement.

After being discharged from the hospital the patient receives 16 mg of methylprednisolone per day, is in a stable condition, is registered at the rheumatologist.

CONCLUSION

1. Behcet's disease is rarely diagnosed in the territory of Ukraine (3:100 thousand), a disease of unknown etiology, in a pathogenesis way is characterized by development of autoimmune systemic vasculitis.

2. The typical clinical picture of the disease is revealed by aphthous stomatitis, uveitis or iridocyclitis, ulcers of the mucosa and genital skin. Generalization of pathological process is manifested by defeat of large joints (50%), small-caliber vessels (38%) and central nervous system (up to 20%), lung (up to 7%), and much less - the heart, gastrointestinal tract and kidneys.

3. Doctors of narrow specialization have no suspicion in the recognition of Behcet's disease, interpretation and analysis of detected symptoms results in local perception of pathology that is unreasonably delaying a preliminary stage of diagnosis of the disease.

4. Feature of diagnosis of Behcet's disease is that it is based on the interpretation and analysis of symptoms the doctor reveals using survey methods and physical examination of a patient. The results of additional research methods, lacking specificity and sensitivity, can confirm the presence and severity of autoimmune systemic inflammation and to clarify the involvement of the patient's organs and systems in the pathological process with displaying the nature of their defeat.

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DIAGNOSTIC FEATURES OF BEKHCHET'S DISEASE

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Summary. *The clinical case of Behcet's disease is described. The clinical picture and the disease course are presented, results of additional investigations are described. The diagnostic and management algorithm are proposed.*

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