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ANALYSIS OF SOME CAUSAL FACTORS PROVOKING A SEVERE COURSE OF BEHCET'S DISEASE IN ADOLESCENT PATIENTS

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Abstract

Aim: The aim of our study was to conduct a comparative analysis of the factors leading to a further aggravation of the course of Behcet's disease in adolescent patients.

The authors examined and treated 8 persons of adolescent age diagnosed with Behcet's disease. Simultaneously with clinical and anamnestic observation, a thorough examination of the mucous membranes of the urogenital tract was carried out for the presence of urogenital infections of a bacterial-viral nature, a study of autoimmune antibodies (Anti-double-stranded DNA, IgG and Anti-single-stranded DNA, IgG) in the blood serum of patients, consultations of related specialists. It was found that among the features of the clinical course of Behcet's disease in adolescents, the prevailing symptoms are aphthous stomatitis, erosive and ulcerative lesions of the oral mucosa and eye lesions. Among infections of the genital mucosa, herpesvirus, papillomavirus, ureaplasma and candida infections are detected with an increased frequency. A 1.5-fold increase in the content of autoimmune antibodies (Anti-double-stranded DNA, IgG and Anti-single-stranded DNA, IgG) was noted, which indicates the beginning of the formation of an autoimmune component in the development of the disease. Connection of appropriate antiviral and antibacterial drugs to therapy significantly accelerates the recovery time and lengthens the recurrence intervals.

Keywords: Behcet's disease, causal factors, adolescent patients.

文摘

目的：我们研究的目的是对导致青少年白塞病病程进一步加重的因素进行比较分析。

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作者检查并治疗了 8 名被诊断患有白塞病的青少年。在临床和回忆观察的同时，对泌尿生殖道粘膜进行了彻底检查，以确定是否存在细菌病毒性质的泌尿生殖道感染，研究自身免疫抗体（抗双链 DNA、IgG 和抗-单链DNA，IgG）在患者血清中，请咨询相关专家。发现青少年白塞病的临床病程特征中，以口疮性口炎、口腔黏膜糜烂性和溃疡性病变以及眼部病变为主要症状。在生殖器粘膜感染中，疱疹病毒、乳头瘤病毒、脲原体和念珠菌感染的检测频率增加。注意到自身免疫抗体（抗双链 DNA，IgG 和抗单链 DNA，IgG）的含量增加了 1.5 倍，这表明在疾病的发展过程中开始形成自身免疫成分.将适当的抗病毒和抗菌药物与治疗相结合可显着加快恢复时间并延长复发间隔。

关键词：白塞病，致病因素，青少年患者。

Introduction

Behcet's disease is a multisystem recurrent chronic vasculitis of unknown etiology, accompanied by lesions of the mucous membranes, which explains the variety of clinical symptoms: recurrent erosive and ulcerative lesions of the oral mucosa and genital organs, involvement in the pathological process of the joints, central nervous system, organs of the gastrointestinal tract. The disease is widespread, but more common in the countries of the ancient Silk Road. [1,2]. There are certain differences in the clinical characteristics of the disease between ethnic groups living in different geographic regions. If in Turkey the prevalence of Behcet's disease is very high and ranges from 80/100000, then in the USA the disease is quite rare, amounting to 1/300000 [2]. Disease affects both men and women. But in different geographical points of the world, the prevalence of the disease in representatives of one or the other sex has been described. That is, a higher prevalence of Behcet's disease occurs in adult women in Korea [3], Israel [2], Singapore [4], while BD in men is more often observed in the West Indies [1], Spain [5], Japan [6], Jordan [7], Iran and Turkey [8].

Recent studies have shown that male sex and the onset of the disease at an early age are associated with more severe manifestations of Behcet's disease, for example, damage to blood vessels (thrombosis, etc.), eyes, gastrointestinal tract and central nervous system [3,7].

The peak onset of Behcet's disease usually occurs in the third decade of life, although the diagnosis is finally verified more often in the fourth decade of life. Behcet's disease is less common in children, even in high-risk countries. Few epidemiological studies have been conducted on Behcet's disease [8]. Albuquerque P. et al. [9] indicated that the prevalence of Behcet's disease in children is 1: 20,000. Most of the data is based on retrospective analysis. Among patients with Behcet's disease (meeting the criteria of the International Behcet's Disease Study Group [1]), approximately 2-3% are patients under the age of 16 years.

However, it should be noted that in a significant number of adult patients, the first symptoms of the disease appear in childhood, but only years later the full type of the disease develops. This, of course, is of no small importance for the prognosis of the disease, since there are reports that adult patients in whom the first symptoms of the disease appeared at a young age have a worse prognosis than patients with the onset of the disease after 40 years [8,10]. The influence of age on the course and prognosis of

the disease still remains one of the urgent problems in the study of BD.

The polysystemic nature of clinical manifestations, relatively rare occurrence, especially in childhood, low identification of the disease in adolescence, determines the difficulty of early verification of the disease. Diagnosis of Behcet's disease is based on a set of classification signs / symptoms, the formation of which takes 5-8 years or more [11].

The diagnosis of Behcet's disease is especially difficult in cases where eye or skin symptoms are presented as an isolated or predominant manifestation of the disease, and they are often mistakenly regarded as ordinary dermatoses or separate eye diseases. The absence of a leading etiological agent in the development of Behcet's disease leads to a lack of clarity in therapy and a long, progressive, recurrent course of the process, with the subsequent development of formidable complications in adolescents.

Purpose

Characteristics of factors leading to a more severe course of Behcet's disease in adolescents.

Material And Methods

The work is based on clinical, anamnestic and laboratory observation of 8 adolescent patients with various clinical manifestations of Behcet's disease, who were examined in the Department of Sexually Transmitted Infections and Reproductive Disorders of the Republican Specialized Scientific and Practical Medical Center for Dermatovenerology and Cosmetology of the Republic of Uzbekistan from 2017 to 2019 years. Their age varied from 15 to 18 years. Before starting treatment, all patients, with their voluntary consent and, if necessary, the consent of their parents, underwent the following research methods: clinical and laboratory examination of patients, including bacteriological examination of the detachable urinary tract, polymerase chain reaction for the diagnosis of infections of the urogenital tract, immunological studies for the presence of autoimmune antibodies (Anti-double-stranded DNA, IgG and Anti-single-stranded DNA, IgG), histological examination of material from lesions, as well as consultation of related specialists.

Results

The time interval from the onset of the disease to admission to the clinic of the Center and the establishment of a clinical diagnosis ranged from 3 to 5 years. In all patients, the primary symptom was most often aphthous stomatitis and accompanying fever. Erosive and ulcerative lesions of the genitals were observed in 6 out of 8 patients within 2 years after the onset of aphthous stomatitis. In 3 patients, skin manifestations in the form of papulopustular rashes were noted, in 4 erythema nodosum and in 1 patient a combination of erythema nodosum and acne-like rash was observed. Subsequently, other organs and systems were involved in the pathological process. In the advanced stage of the disease, there was already a clinical symptom complex, including aphthous stomatitis, ulcerative process on the genitals, damage to the skin, eyes, gastrointestinal tract and, less often, the central nervous system in the form of headaches. Before contacting the clinic of our Center, almost all 100% of patients received various therapies for a particular symptom of the disease with a temporary effect or without an effect.

Previously, patients mainly consulted ophthalmologists, dentists, pediatricians, pediatric gynecologists, and rheumatologists. The drugs prescribed were dominated by corticosteroid hormones, vitamin therapy, and antibiotics.

When studying the factors provoking a more severe course of Behcet's disease in adolescents, one can note, first of all, a burdened anamnesis: in 6 maternal patients episodes of recurrent aphthous stomatitis and conjunctivitis occurring with periodic exacerbations were observed. Studies have shown that among the examined patients with the bacterioscopic method of studying the discharge from the lesions, 8 (100%) revealed Candida albicans and 5 (62.5%) - Gardnerella vaginalis. In addition, cultural diagnostics of the lesion separated from the lesions showed that other bacterial pathogens were also detected in patients with Behcet's disease. So, in 4 (50.0%) patients, Staphylococcus epidermidis was inoculated, in 3 (37.5%) - Enterobacter, in 2 (25.0%) - Streptococcus haemolyticus. The study of the lesion separated from the lesions using the polymerase chain reaction showed that with this method of research, 5 (62.5%) of the 8 people examined with Behcet's disease had a positive result for the presence of Ureaplasma Urealyticum. A study in blood serum during PCR diagnostics for the presence of viruses revealed that in 8 patients with this pathology, in 5 (62.5%) cases, herpes simplex virus type I (HSV I) was detected, in 1 (11.1%) of patients diagnosed with herpes simplex virus type II (HSV II), 2 (25.0%) - Cytomegalovirus (CMV) and 2 (25.0%) - Human Papillomavirus (HPV). Also, in this group of patients, diseases of the genitourinary system were identified: urethritis in 8, vulvitis in 4, cystitis in 3 and pyelonephritis in one patient. In the majority of patients, the simultaneous presence of three or more infectious agents was noted, which in turn was characterized by a more protracted course of the process in the form of often recurrent aphthae of the oral and pharyngeal mucosa and erosive and ulcerative lesions of the genitals. These studies indicate the important role of viral-microbial associations in the development of protracted clinical symptoms and long-term healing of pathological elements. Detection of Cytomegalovirus infection, Herpes simplex virus and Human Papillomavirus may also become a risk factor for malignant transformation of erosions and ulcers in the future. We also studied the indicators of class G autoimmune antibodies (Anti-double-stranded DNA, IgG and Anti-single-stranded DNA, IgG), since the diagnosis of these antibodies also leads to a more severe course of the disease, and early diagnosis allows the choice of the correct therapy tactics. Thus, in the patients of the study group, a statistically significant increase in the content of Anti-double-stranded DNA (37.99 ± 1.29 IU) and Anti-single-stranded DNA (32.60 ± 1.51 IU, $p < 0.01$) was observed. compared with the data of the control group (23.14 ± 0.76 IU and 22.16 ± 1.02 IU, respectively).

Table 1. Indicators of double-stranded and single-stranded deoxyribonucleic acid (DNA) in patients with Behcet's disease and healthy controls (M ± m)

Disease duration	Number of examined persons	dsDNA (international unit)	ssDNA (international unit)

The control group	14	23,14 ± 0,76	22,16 ± 1,02
Patients with Behcet`s disease	8	37,99 ± 1,29**	32,60 ± 1,51**

Note: p - reliability of data in relation to control.

* - p <0.05; ** - p <0.01; *** - p <0.001

As can be seen from the data in Table 1, in patients with Behcet's disease with a disease duration of 3 to 5 years before the start of treatment, more pronounced changes in the indicators of class G autoimmune antibodies are detected in the blood serum. An increased content of the studied class G autoimmune antibodies in relation to the control may indicate on the severity of the inflammatory response, as well as on the activation of the autoimmune process, which must be taken into account when prescribing treatment. Taking into account the identified changes, drugs effective against herpes simplex viruses, Human Papillomavirus and concomitant microflora were added to the treatment of patients, which led to a more rapid relief of symptoms of the disease and a decrease in the number of relapses.

Discussion

Thus, the management of patients with Behcet's disease is a complex multicomponent medical problem. Of particular difficulty is the identification of this disease in adolescents. The task is complicated by the need to combine a comprehensive examination and taking into account the patient's financial capabilities. All of the above features should be taken into account in order to avoid unnecessary diagnostic interventions and iatrogenic complications. In this regard, a more thorough examination of patients with Behcet's disease using the most modern diagnostic capabilities, such as polymerase chain reaction, diagnostics of autoimmune antibodies, immunological diagnostics, the involvement of related specialists, will allow identifying and establishing the correct diagnosis at the early stages of the development of the disease, in order to prevent further development and complications of the disease.

Conclusion

1.The prevalence of aphthous stomatitis, erosive and ulcerative lesions of the oral mucosa and eye damage should be attributed to the modern features of Behcet's disease in adolescents and young adults. Among infections of the genital mucosa, Herpesvirus, Papillomavirus, Ureaplasma and Candida infections are detected with an increased frequency, which must be taken into account in the treatment of the disease.

2. Study of the content of autoimmune antibodies (Anti-double-stranded DNA, IgG and Anti-single-stranded DNA, IgG) can become an early prognostic criterion for the development of the autoimmune component of the disease and the basis for appropriate immuno-targeted therapy.

3. Connection to therapy of drugs effective against Herpes Simplex Viruses, Human Papillomavirus and concomitant microflora, possibly affecting the severity of the course, the progression of the disease, the severity of clinical manifestations, led to

accelerated healing of erosive and ulcerative processes and a decrease in the number of relapses of the disease.

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