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THE ROLE OF HERPESVIRUS REPRESENTATIVES IN OPHTHALMIC PATHOLOGY

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In the last decade the first place among the inflammatory diseases of the cornea was taken by viral diseases, mainly of herpes (HV) or adenovirus etiology. To date, herpetic keratitis (HK) are very widespread because of the tendency of relapse (in 50-80% of cases), difficulties in treatment and often severe consequences. The relevance of HK problem in practical ophthalmology is connected with disease relapsing, often leading to a decrease in vision, including blindness. There is also marked an increase of relative density and frequency of viral uveitis in both children and adults. Eye inflammatory diseases make up from 7 to 30% of the total clinical entities. Chronic and relapsing course of these diseases, the lack of effectiveness of symptomatic treatment often lead to severe outcomes. Thus, blindness in both eyes with the most severe forms reaches up to 10%, and disability on the loss of sight is about 30%. [1]

Etiological role in the occurrence of ocular pathology in 43.5% of cases is assigned to infectious agents. This figure can significantly increase when decrypting the diseases of unknown etiology, the percentage of which is ranging from 20 to 80%. There are a lot of data on affection of the uveal tract, retina and optic nerve, caused by viruses. According to some authors, the pathology of the virus is noted in 1,5-40% of cases of uveitis. Such variation in the number of detected viral agents is explained by ambiguous approach to the evaluation of their role and lack of use of methods of laboratory diagnosis.

Diagnostics of herpetic uveitis is extremely difficult due to the lack of specific clinical picture. Defining the etiology of herpes lesions of posterior eye part is rather ambiguous, since in some cases, the clinical picture is not very different from that in the other eye disease genesis.

Laboratory diagnosis of herpes virus infection (HVI) is necessary to confirm the pathogenesis of the disease, differentiation of active and chronic phases of infection, as well as choosing the most effective method of treatment. One of the serological markers of active stage of HVI are specific immunoglobulins of M class (IgM). However, no consensus yet has been found about the importance of detection of IgM to hepatitis for clinical ophthalmology. The question of their synthesis and duration of their detection in the blood during the exacerbation of persistent HBV infection still remains debatable. In addition, while formulating this test there could be received false-positive results for patients with rheumatoid diseases. The direct methods of diagnosis are preferred in this case. The serological analysis gives only

tentative answer. Immunofluorescence assay can detect viral antigens in the material (scrapings from the cornea, the conjunctiva, as well as in the blood cells) by using monoclonal antibodies; this reaction is the most revealing one. [2,3]

In the scientific literature they mainly describe the research on ophthalmologic herpes caused by HSV type 1, and there are almost no studies on the etiologic role of other representatives of Herpesviridae family. [4-6] In connection with this, it is advisable to provide some data on the role of different types of herpes viruses in the development of eye pathology.

In most cases, herpetic eye diseases are conditioned not by primary infection of HV, but by the reactivation of the virus persisting in the human body. Here-with, the role of HV in ophthalmopathy is very diverse. The relapse of HV infection can lead to a form of ophthalmic herpes (etiological factor) and induce (trigger factor) or make heavier (complicating factor) the disease of another etiology. Unlike the majority of opportunistic infections, reactivation of HV is observed even among immunocompetent individuals. [7]

And if the keratitis and keratoconjunctivitis caused by HSV, are clinically examined and are rather widely diagnosed, the uveitis and eye damage caused by the other members of this family in their turn are barely mentioned among the diagnoses in the practice of ophthalmologists. This is contributed by lack of awareness of practitioners of the role of HV in ocular pathology, polymorphism and low specificity of clinical manifestations and laboratory diagnosis complexity. Considering the above, we set a goal to establish a place of herpes viruses (HSV1, HSV2, HHV6, CMV, VZV, EBV) in the etiological structure of the eye lesions.

Materials and Methods

On the examination there were present 35 patients aged from 17 to 65 years who were on outpatient and inpatient treatment in the Kharkiv municipal ophthalmic Hirschman hospital № 14, as well as in the clinic № 6 of the Moscow district of Kharkiv.

After clinical examination all patients were diagnosed with recrudescing keratitis (15 patients) and viral uveitis (20 patients). The common characteristic features were as follows: 1) frequent contact with infectious diseases (influenza, SARS, etc.); 2) failure of antibiotic therapy and the activating effect of corticosteroids; 3) a tendency to relapsing. All the patients had a serous and seroplastic keratitis or iridocyclitis. In case of the infection anterior extension there often developed bullous kerato-iridocyclitis. When the inflammatory process passed into the posterior part of the eye there were observed the emergence of the clinical picture of optic neuritis (3 patients), chorioretinitis (2 patients). In order to establish the etiologic diagnosis a virological examination was carried out, including a chemiluminescence linked immunoassay (CLI), scrapings from the cornea and conjunctiva for the presence of HV antigen and identification in the blood leukocytes the viruses with the calculation of the fluorescence index (FI). There have been used a muscular polyclonal antibodies against HSV1, HSV2, HHV6, CMV, VZV, EBV

of the company Santa Cruz Biotechnology, Inc. To establish the persistence of HV a viral antigen was determined in blood lymphocytes for three times once a month.

Results and discussion

The examination revealed that viral antigens were detected in the scrapings of more than 85% of cases of keratitis and 35% of cases of uveitis. In case of keratitis in the corneal scrapings herpes antigens (usually it is - HSV1 and CMV) in 46% of the cases combined with adenovirus. Attention is drawn to the fact of the persis-

tence of HV in leukocytes in 95% of patients with viral uveitis and 32% of patients with keratitis. It should be noted that in every second patient with viral uveitis (10 persons) there were detected associations of three or more antigens of HV in the blood leukocytes. Most often in these associations there were found antigens of viruses EBV, CMV, and HHV6. If to place the representatives of the HV, persisting in the blood leukocytes of patients with uveitis in order of decreasing of detection frequency, we obtain: EBV, CMV, HHV6, HSV, VZV. Meanwhile IF ranged from 20% to 40% for each virus.

Table.- Identification of herpesvirus markers in different clinical forms of inflammatory eye diseases

Clinical groups	Herpes virus antigens (scrapping/ leukocytes)					
	HSV1	HSV2	HHV6	CMV	EBV	VZV
Uveitis	20	10/87	5/35	7/68	13/88	9/91
Keratitis	15	70/10	8/9	30/6	65/18	5/12

Conclusion

The data obtained supports the hypothesis that viral agents affect the uveal tract, penetrating through the blood aqueous barrier to blood cells. And also, persistent HBV infection is likely to support the chronization of eyes pathological process. This gives us grounds to recommend examining patients with virus nature uveitis on the presence of persistent herpes virus infections in leucocytes. In our opinion, it is the persistent HV infection that has a major influence on the immune status of patients studied. We can assume that for the clinician the detection of viral antigen in blood cells may be a measure of the functional state of the immune system, and the probable causative agent in diseases of the eye, especially uveitis.

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РОЛЬ ПРЕДСТАВИТЕЛЕЙ ГЕРПЕСВИРУСОВ
В ОФТАЛЬМОЛОГИЧЕСКОЙ ПАТОЛОГИИ

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Целью работы было установить место герпесвирусов (HSV₁, HSV₂, HHV₆, CMV, VZV, EBV) в этиологической структуре поражений глаз. Обследовано 35 больных с диагнозом рецидивирующий кератит (15 больных) и увеит вирусной природы (20 человек). Было проведено вирусологическое обследование, включающее в себя исследование методом флюоресцирующих антител соскобов с роговицы и конъюнктивы на наличие антигена герпесвирусов и определение в лейкоцитах крови антигенов вирусов с расчетом индекса флуоресценции (ИФ). Установлена персистенция различных герпесвирусов в лейкоцитах крови у 95 % пациентов с вирусными увеитами и у 32% пациентов с кератитами. У каждого второго пациента с вирусным увеитом (10 человек) обнаруживалась ассоциация 3 и более антигенов герпесвирусов в лейкоцитах крови. Чаще всего в этих ассоциациях встречаются антигены вирусов EBV, CMV и HHV₆.

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РОЛЬ ПРЕДСТАВНИКІВ ГЕРПЕСВІРУСІВ В
ОФТАЛЬМОЛОГІЧНІЙ ПАТОЛОГІЇ
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Метою роботи було встановити місце герпесвирусов (HSV₁, HSV₂, HHV₆, CMV, VZV, EBV) в етіологічній структурі уражень очей. Обстежено 35 хворих з діагнозом рецидивуючий кератит (15 хворих) і увеїт вірусної природи (20 осіб). Було проведено вірусологічне обстеження, що включало в себе дослідження методом флюоресцирующим антитіл зіскрібків з рогівки і кон'юнктиви на наявність антигену герпесвірусів і визначення в лейкоцитах крові антигенів вірусів з розрахунком індексу флуоресценції (ІФ). Встановлено персистенція різних герпесвірусів у лейкоцитах крові у 95% пацієнтів з вірусними увеїтами і у 32% пацієнтів з кератитом. У кожного другого пацієнта з вірусним

увеїтом (10 осіб) виявлялася асоціація 3 і більше антигенів герпесвірусів в лейкоцитах крові. Найчастіше в цих асоціаціях зустрічалися антигени вірусів EBV, CMV і HHV6.

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THE ROLE OF REPRESENTATIVES IN OPHTHALMIC PATHOLOGY HERPESVIRUS

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The goal was to establish a place of herpesviruses (HSV1, HSV2, HHV6, SMV, VZV, EBV) in the etiological structure of the eye's diseases. The study involved 35 patients diagnosed with recurrent keratitis (15 patients) and viral uveitis (n = 20). Was carried out virological examination, including a study using fluorescent antibody scrapings from the cornea and conjunctiva for the presence of herpesvirus antigen in leukocytes and determination of the blood antigens of viruses with the calculation of the fluorescence index (FI). Set of different herpesvirus persistence in leukocytes of blood in 95% of patients with viral uveitis and 32% of patients with keratitis. In the each second patient with viral uveitis (10) detected association of three or more herpesvirus antigens in blood leukocytes. Most often these associations are found antigens of viruses EBV, SMV, and HHV6.