IMMUNOLOGIC AND IMMUNOBIOCHEMICAL FEATURES OF UVEITIS AT VOGT-KAYANAGI-HARADA SYNDROME

The purpose of our research is to study immunologic and immunobiochemical indicators at patients with VKH syndrome. 35 pairs of eyes (21 patients aged from 16-42 years) with Vogt-Kayanagi-Harada (VKH) syndrome and 13 almost healthy faces were surveyed. At all patients along with the standard ophthamologic inspections there were investigated immunologic and immunobiochemical indicators of a peripheral blood. The uveitis at a syndrome of VKH is characterized by the changes of cellular immunity which were more expressed at an excavation and complication of inflammatory process. The significant role in a uveitis pathogenesis at a syndrome of VKH is played by autoimmune process that proves accumulation in blood serum of excess concentration of circulating immune complexes and immunoglobulins of classes G and M. Studying of immune mechanisms of a uveitis at VKH syndrome opens new opportunities for well-timed diagnostics and pathogenetically focused therapy of this disease.

Keywords: Immunologic and immunobiochemical indicators, VKH syndrome

UDC: 617.723-002:616.831.32-086.6-07:612-017.1

Introduction

It is known that Vogt-Kayanagi-Harada syndrome (VKH syndrome) is an idiopathic, multisystem disease, with which people of middle age are ill mainly, more often men (Zamanova, 2005; Starikova and Gvozdyuk, 2008; Fattakhov, Vavilova, Babushkin, and Syunyaev, 2003; De-Domingo, Blanco, Rodriguez-Cid, Pineiro, Mera, and Capeans, 2008). In development of uveitis the leading role belongs to the autoimmune reactions caused by the genetic status of the patient. Detection of antibodies to melanocytes and identification in a high antiserum capacity to external segments of photoceptors and Muller's cells at patients with an active uveitis at VKH syndrome, according to many authors, is a releaser in development of autoimmune reaction (see, e.g., De-Domingo et al., 2008; Sugita, Takase, Taguchi et al., 2006).

It is known that the HLA system provides interaction of all immunocompetent cells of an organism, recognition of own and foreign, including changed own cells, start and implementation of the immune answer (Katargina, Denisova, Starikova, and Gvozdyuk, 2008; Zhang, Qian, Guo, Yuan, and Xue, 2009).

However, parallel studying of immunologic and immunobiochemical features of uveitis at patients with a syndrome of VKH, wasn't carried out in the sufficient volume, which made a subject of our research.

Objective of this research was to study immunologic and immunobiochemical indicators at patients with VKH syndrome.

Materials and methods of research

There were observed 21 patients (35 pairs of eyes) with a VKH syndrome at the age of 16-42 years treated in Republican clinical ophthalmologic hospital. Ophthalmologic
inspection included biomicro- and an ophthalmoscopy, visual-and perimetry, A- and B-scanning.

Immunologic research of a peripheral blood consisted in determination of total of T- and V-lymphocytes in rosette formation reactions with erythrocytes of a ram and mice, the maintenance of subpopulations of T-lymphocytes monoclonal antibodies (anti-CD3, CD4, CD8) a method of the indirect immunofluorescent staining, (CIC, concentration and the size) investigated circulating immune complexes using polyethyleneglycol-600 in concentration of 7 and 3.5%. Concentration of S-reactive protein defined by an enzyme immunoassay (IFA: “Biomerica” IBL test systems) presented by “Biokhimmak” company (Russia). Class M and G immunoglobulins, and also component of a complement of C3 defined on the biochemical analyzer of “HUMAN” firm using reactants of the same firm.

The control group was made by 13 almost healthy faces without any somatic pathology. Static processing of results of research was carried out by means of “Statistica” program. For each selection average values (M), a standard error of an average (m) were calculated. The critical significance value at check of statistical hypotheses in this research was accepted peer 0.05.

Results and discussion

The diagnosis of VKH syndrome was made on the basis of a complex of eye and extraocular symptoms, specific for this disease. Extra eye implications of a disease were fixed in 68.3% of patients, neurologic symptoms in a prodromal stage in the form of headaches in combination with a sleepiness and retardation were present at 23.9% of patients.

Expression and ratio of symptoms of a forward and back uveitis in survey samples of patients varied, a lesion of both eyes were symmetric. In 54.8% of cases appreciable changes both back, and forward department of eyes became perceptible. In 19.8% of patients in the period of a debut of a disease the neuroretinitis symptoms prevailed, and the iridocyclitis was mild or moderately severe. Thus, to the extremity of the period of observation at all patients the uveitis proceeded as a pan-uveitis typical for this disease.

![Figure 1. Indicators of T-system of immunity of peripheral blood at patients](image-url)
Immunoreactivity research at patients with a syndrome of VKH showed that at surveyed persons deficiency of T-lymphocytes was defined. As a result of this research depression of the average level of the T-general lymphocytes (CD3+) in a peripheral blood groups of patients is defined. So, the relative maintenance of CD3+ in group of patients made 57.2% that was on 16.6% lower in comparison with control group (p<0.05). The average relative maintenance of T-helpers was on 23.1% lower in comparison with control group (p<0.05).

The maintenance of T-cytotoxic (CD8+) in groups of patients authentically didn't differ from indicators of control group.

It is known that uveitis of any etiology associate with infiltration of mediums of an eye by inflammatory and immunocompetent cells and development of the local immune answer provoked by a starting factor (an infection, autoantigens, intoxication, etc.). Disturbance of a hemato-ophthalmic barrier of a sore eye is accompanied by an exit in circulation of textile-specific antigens, emergence of autoantibodies. An important role is played thus by a systemic hyperproduction of the cytokines possessing ability to cause changes at the level of a vascular endothelium of a hemato-ophthalmic barrier, increasing its permeability, activating molecules of cellular adhesion (Yermakova, 2003; Panchenko, 1998; Jap and Chee, 2011; Yun, Ahjoku, Cheng-Rong, and Charles, 2011). The strengthened synthesis of molecules of intercellular adhesion under the influence of IL-1 promotes emergence in the centers of an inflammation of hemiatreaktant and synthesis by hepatocytes of mediators of an inflammation, in particular S-reactive protein and a component of system of a complement.

As it seen from the presented results of research (Figure 2), at early stages of an endogenous uveitis we observe reliable body height of level of S-reactive protein - by 12.4 times in comparison with control group. It is necessary to specify that the maximum values of S-reactive protein at damage of tissues it becomes perceptible in the first 5 days.

Apparently from the presented results of research, at patients with a syndrome of VKH rising of the CIC of the small and large sizes is noted. Thus, in surveyed patients the circulating immune complexes of the large size increases in average by 2.9 times (P<0.05). In this situation small immune complexes can get through a hemato-ophthalmic barrier and cause changes at the level of a vascular endothelium, increasing its permeability, activate molecules of cellular adhesion. Autoantigens, infectious toxins which in turn, are one of the reasons of lifting of concentration of antibodies of a class M and G at VKH syndrome can be the reason of rising of level of pro-inflammatory cytokines in a blood.

![FIGURE 1. INDICATORS OF T-SYSTEM OF IMMUNITY OF PERIPHERAL BLOOD AT PATIENTS](image)
The augmentation of level of the CIC and antibodies various classes promotes activation of system of a complement that activates a chemotaxis of neutrophils and a phagocytosis of cells.

FIGURE 2. MARKERS OF INFLAMMATION AND HUMORAL FACTORS OF IMMUNITY AT PATIENTS

Thus, the uveitis at VKH syndrome is characterized by the changes of cellular immunity which were more expressed at an excavation and complication of inflammatory process. The significant role in a uveitis pathogenesis at a syndrome of VKH is played by autoimmune process that proves accumulation in blood serum of excess concentration of circulating immune complexes and immunoglobulins of classes G and M. Studying of immune mechanisms of a uveitis at a syndrome of VKH opens new opportunities for well-timed diagnostics and pathogenetically focused therapy of this disease.
References


