CHANGES INTERFERON STATUS IN CORONARY HEART DISEASE

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ABSTRACT — Currently, coronary heart disease (CHD) is the leading cause of death in developed countries (up to 57% of all diseases) [L.A.Bokeriya, 2006]. In the present study analyzed literature data on studying immune spectrum of blood (in particular, interferons IFN-α, IFN-β, IFN-ω, IFN-τ and soluders) for ischemic heart disease. Investigation of violations of the immune status opens new pathogenetic mechanisms of ischemic heart disease, which require a more detailed study.

KEYWORDS — immune status, interferons, coronary heart disease

Currently, coronary heart disease is the leading cause of death in developed countries (up to 57% of all diseases). [1] Ischemia and myocardial damage alters protein structure myocardium, which leads to their antigenic properties and new formation of autoantibodies antikardialnyh [3]. At various periods of myocardial infarction the emergence and growth of circulating immune complexes and fixed protivokardialnyh circulating autoantibodies have been seen, and change of the properties of T and B lymphocytes and their subpopulations. [3] Insufficient production of factors contributes to the progression of immune protection subepicardial and subendocardial ischemia in Q-myocardial infarction [Hanferyan RA, Orange PP, 2009].

At present, the authors of medical publications are more often considered an immunological component in various pathological conditions and diseases, given the inextricable link of the nervous, endocrine and immune systems. There was technically possible on the one hand, and the urgent need on the other hand, for the discovery of new mechanisms of pathology at the cellular and molecular level in order to find new methods and approaches to the treatment of diseases.

Interferons (IFN) are key regulators not only protective, but also of many physiological processes in the body. IFN I type regulates hematopoietic processes, immune response, tumors, responses to infection. IFN produced and acts locally autocrine and paracrine manner. The first type has four subtypes of IFN: IFN-α, IFN-β, IFN-ω, IFN-τ. The receptor consists of two subunits, IFNAR1 and IFNAR2. IFNAR1 is species-specific — human, bovine, sheep, chicken, mouse. A soluble form of human (hu) IFNAR2 was first detected in the urine. This identification led to the cloning of its own DNA and two forms of hu hu IFNAR2b and IFNAR12e . All three forms are associated IFN I type only form IFNAR12e involved in signal path. Functions hu IFNAR2α (extracellular soluble form), and hu IFNAR2b have only a short intracellular dominant. A soluble form can often bind ligands, block or reduce the maximum opportunity to compete with other cytokines, membrane- stabilizing components for general ligand. Another function of the soluble receptor ligand is protection from destruction or separation. Soluble receptors may also be converted into sensitive ligands resistant. Soluble

receptors can act as agonists or as antagonists. The role of inflammation in the soluble receptor agonists or antagonists, concentrated ligand -related proteins, cytokines require active learning. Solyudery are ekstrotsellyulyarnymi dominant transmembrane receptors, attaching molecules in biological fluids. Cellular release of soluble receptors is regulated by two mechanisms: first, production and secretion of only the extracellular dominants (interleukin 4 , epidermal growth factor and IFNAR2): Second, proteolytic specificity to cell surface receptor (IL-1, interleukin-2 , TNF-α).

Currently actively studied due IFN-α and-β receptors, and the importance of their strength. Interferons I (IFNs) determine antiviral, antiproliferative, immunomodulatory response through communications with the receptors which are transmembrane proteins of IFNAR1 and IFNAR2 [9].

Signalling IFN-α and IFN-β implies involvement of the different receptor zones . The authors used reflectometry interference spectroscopy to study the kinetics and chemical properties of the interaction between IFNs and ekstrotsellyulyarnymi receptor, which is dominated by IFNAR1 and IFNAR2. The result revealed that the relationship between IFN-α and IFN-β receptor , which is dominated IFNAR2 stronger, and the relationship to the receptor , which is dominated IFNAR1, less stable . The results showed that IFN first binds to IFNAR2, and then gradually interact with IFNAR1, and this second stage is more significant for IFN-β, than IFN-α, which may explain the different activity IFNs [9]. Obviously, the concentration of these components and a surface receptor depends genetic stabilization.

In the study of the mechanism of action of IFN-α in the treatment of chronic myelogenous leukemia patients with leukemia cell installed immediately in IFNAR2 expression unlike control group. In contrast, the expression of cell surface IFNAR1 was lower than IFNAR2, and correlated with the level before treatment and clinical outcomes [7]. The authors examined Publication interferon receptor comprising IFNAR1 and IFNAR2, IFN I type virus and their antiproliferative activity [2, 3].

Conducted studies have demonstrated that binding of IFN-α2 with IFNAR2 is a N-terminal dominant and increase immobility receptor may play an important role in intracellular signal cascade stage interferon. The study turned knowledge about components IFN I receptor type interaction force with ligands and their role in the transmission of different signals.

Now the question remains little known changes of immune status in coronary heart disease. It is known that in ischemic heart disease, myocardial infarction increased concentration of circulating immune complexes, JgG, and reduced JgM, decreases the level of T-cells, B-cells is increased . Phospholipid syndrome in the study of coronary heart disease little work. The development of these diseases associated with overproduction of an extremely wide range oganospetsificheskih autoantibodies reactive with DNA and other nuclear antigens , cytoplasmic and membrane components [2]. However, patients who died of myocardial infarction in postmortem copper on the intima of the aorta and the coronary vessels were found circulating immune complexes and antibody class IgM and IgG antibodies to their own cardiomyocytes [9, 10, 11]. This suggests the formation of autoimmune mechanism as one of the variants of the anti-phospholipid syndrome [10, 11].

Many authors believe that the cytokine system in ischemic heart disease, myocardial infarction, has been actively involved in the implementation of the immune response in aterosklerotromboticheskih coronary events [1]. In acute myocardial infarction found to have high serum concentrations of interleukin-6.8, correlated with high levels of troponin and creatine kinase [4,9].

Analysis of published data shows that the commonly used serological and biochemical markers for the first time detected in the later stages of the disease. While the study of more subtle mechanisms of autoimmunity opens broad prospects of early diagnosis. Patients with poliendokrinologicheskoy pathology in 100% were recorded antiinterferonovyh high titers of antibodies in the early stages of the disease, which allows to think that these antibodies may be used as a diagnostic marker in patients with metabolic syndrome , diabetes mellitus, coronary heart disease. Antiinterferonovye antibodies pushing for the development of other autoantibodies with various endocrine clinical features. This raises the question of the role of these antibodies in the manifestation of the disease. When poliendokrinologicheskom syndrome observed defects γ-interferon and interleukin-12 [11]. Conducted studies have identified new lines disorders of immune response in patients with poliendokrinologicheskim syndrome. Suggested noted an important role of type 1 interferons as well as its role in the regulation of self-tolerance.

In the literature there are individual information about the early changes in the immune status — serum levels of interferon and antibodies to it in acute Q-myocardial infarction, however, there is a description of the increase in activity only later γ-interferon [6, 9, 10]. Changes in the activity of the earliest violation of interferon status, — α-interferon, myocardial infarction have been conducted.

Thus, the study of immune status opens new pathogenetic mechanisms of ischemic heart disease,

which require a more detailed study. At this stage, the data conducted worldwide research raises more questions than from quick advice. They play a key role in the autoreactive antiinterferonovye antibody response of T and B cells in reducing T-cell attack antibodies in other tissues and organs (such as heart) in these disorders? Whether there was an increase in production of anti IFN antibodies on the progression of coronary heart disease? This encourages further study of the role of type 1 interferons, their receptors IFNAR1 and IFNAR2 and their antibodies in the interferometer new immunity in patients with ischemic heart disease.

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