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ROLE OF CELLULAR IMMUNITY IN CHRONIC HEART FAILURE WITH ISCHEMIC ETIOLOGY

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Abstract:
Currently, the importance of the role of inflammation in the pathophysiology of chronic heart failure (CHF) has been determined. It is reliably known that an increased level of circulating proinflammatory cytokines in patients with ischemic CHF correlates with the severity and prognosis of the disease. Monocytes play a key role in the inflammatory cascade and are the main source of both pro- and anti-inflammatory cytokines. An imbalance of physiological inflammation during myocardial damage and repair can lead to the formation of pathological chronic inflammation.
This article discusses the role of monocytes and inflammation in CHF and its decompensation, and describes the types of cytokines and their involvement in inflammation. In addition, an analysis of the results of studies of drugs aimed at modulating the immune response in CHF is presented.

Keywords: acute decompensation of chronic heart failure, macrophages, cytokines, innate immunity, adaptive immunity.

Introduction

According to epidemiological studies, chronic heart failure, chronic ischemic heart disease is one of the nosological forms of, and remains one of the pressing health problems in many countries around the world. Despite advances in the study of pathogenesis, early diagnosis and treatment options, chronic heart failure remains one of the most severe and prognostically unfavorable diseases of the cardiovascular system.

The currently dominant neurogormonal theory did not fully justify the expectations placed on it. This theory is based on disturbances in the activity of sympathoadrenal and renin-angiotezin-aldosterone systems. Despite the positive effects of the neuromodulators used in the clinic, chronic heart failure continues to develop, which is due to the impossibility of completely blocking the "interested" neurogumoral systems. Obviously, in addition to neurogormonal systems, other pathogenetic mechanisms are involved in the pathogenesis of chronic heart failure. Depending on this case, in recent

years, the attention of researchers and clinicians has become increasingly focused on the immunological aspects of the pathogenesis of chronic heart failure. A similar trend can be observed not only in relation to this pathology, but also in completely different diseases. This led to the formation of a new medical and biological discipline - neuroimmunoendocrinology, which studies the interaction of the body's interconnected systems - the nervous, immune and endocrine systems. The study of these indicators made it possible to take a new approach to the problem of predicting complications and results of the pathological process. This determines the relevance of our study, which is devoted to the study of the pathogenesis of chronic heart failure.

Thus, the available information is scarce and contradictory. In this regard, it is interesting to study the correlation of the sympathoadrenal system and the immune status of patients with chronic heart failure, which appears against the background of chronic ischemic heart disease.

The purpose of the study

Study of the role of cellular immunity in patients with chronic heart failure against the background of ischemic heart disease.

Materials and methods of research

55 people participated in the study, according to the criteria for inclusion in the study. Of these, the main group of patients with coronary atherosclerosis (CHD) consisted of 40 people. The control group is represented by 15 practically healthy individuals of comparable age. The theoretical stage consisted in reviewing the available literature data on key links in the pathogenesis of coronary heart disease due to atherosclerosis, changes in endothelial properties, hemostasis, and quality of life analysis.

The degree of study of the dynamics of these markers was clarified, depending on the method of myocardial revascularization at various times after surgery and clinical and immunological predictors of PS in the long term. Based on the analysis of the available ideas, the relevance of the topic was formulated and the need for a more detailed study of the role of the immune system in patients with coronary heart disease, the influence of immune processes on the outcome of revascularization was proved for the possible determination of significant prognostic markers. Next, the planning of the empirical stage of the study aimed at confirming the scientific hypothesis was carried out. Its design has been compiled.

The study included patients with coronary artery disease (taking into account exclusion criteria) who were recommended for coronary artery stenting or bypass surgery. Based on the conducted pilot study, the sample size for each group was calculated.

The results of the study

Patients of all study groups were comparable in age (years) (coronary heart disease-62.9±0.5, CABG-61.6±0.7, SCA-64.1±0.8, control-59.6±1.5). By gender, the control

and general group of coronary heart disease, as well as the groups of CABG and SKA did not differ. The duration of coronary heart disease in the general group was 7.2 years, CABG - 7.9 years, and SKA - 6.3 years. According to the ratio of angina pectoris of tension of different functional classes, the prevalence of II-III FC was noted: 62.8% - coronary heart disease, 67.6% - CABG, 58.5% - SKA, fewer patients had IV FC. Diabetes mellitus did not exceed 26% of cases in all study groups. There were no differences in the presence of comorbid pathology when comparing the groups with each other, except for the presence of postinfarction cardiosclerosis (PICS), which was more common (p=0.0008) in the CABG group (64.9%) compared with the SKA group (45.5%).

When conducting a coronary angiographic examination, in patients with coronary heart disease, the most involved in atherosclerosis were permanent residence, PKA and OV. To a lesser extent, DV, VTK, ZMZHV and the trunk of the LKA were involved. When comparing the percentage of coronary artery lesions in both groups of CABG and SKA (Figure 2A), a greater lesion of the trunk of LCA, permanent residence, OV, DV in the first group was revealed. The quantitative ratio of coronary artery lesions in the IHD group demonstrates the prevalence of multifocal (37%) and tricavascular (27%) lesions of the coronary bed, followed by a bicavascular (25%) lesion and to a lesser extent one coronary artery was involved in atherosclerosis (11%).

In the CABG group, multifocal coronary lesion dominated, in the SKA group, the single-vessel and double-vessel types of coronary artery lesion, the value of the three-vessel lesion was comparable between the groups.

During echocardioscopy in patients with coronary heart disease, CABG and SCA, the values of the size of the left atrium, end-systolic and end-diastolic, were in the acceptable range. The thickness of the interventricular septum and the posterior wall of the left ventricle, in the groups of coronary heart disease (12.5± 0.4; 11.8±0.1) and CABG (13,3±0,4; 11,3±0,1), it was significantly higher ($p<0.05$) than in the control group (10,29±0,9; 10,57±0,1). In the SKA group, these indicators (11.7±0.4; 11.1±0.1) were comparable with the control ones. The ejection fraction (EF) and shortening fraction (FU) in all groups did not differ from the control values. The presence of hypokinesis zones was detected in 47.5% of cases in the CHD group, and this indicator was higher ($p<0.05$) in the CABG group (57.6%) compared with the SKA group (38.4%).

The analysis of the subpopulation composition of T lymphocytes did not reveal significant differences from the control values. The absence of a change in the IRI is also natural. At the same time, an increase in the cytotoxic potential of CD8+ lymphocytes was recorded, which was expressed in an increase in the number of Granzyme-containing cells (CD8+Gr+) by almost 2 times. An increase in the pool of circulating CD3+CD4+lymphocytes expressing the early activation marker (CD25+) should be noted. Attention is drawn to a decrease in the relative number of CD4+CD25+Foxp3+lymphocytes, indicating a dysregulation of the immune response,

an increase in the number of CD4+CD154+ lymphocytes determining T-Cell cooperation.

Analysis of the parameters of innate immunity in patients of the general group of coronary heart disease compared with control values revealed an increased content of CD16+ cells, a significant increase in their cytolytic activity, estimated by the number of CD16+ lymphocytes containing intracellular Granzyme B (CD16+Gr+). In the group of patients with coronary heart disease, the expression of Toll-like receptors on monocytes (CD282+, CD284+, CD289+) was increased, which play an important role in recognizing not only bacterial foreign agents, but also molecular patterns associated with damage to their own tissues. It should be particularly noted that the expression of TLR9 in patients with coronary heart disease is increased several times in relation to the control. The relative content of monocytes carrying HLA DR+ and participating in the presentation of antigens is significantly lower than in the control.

Thus, in patients with coronary heart disease, in comparison with the control, changes in the indicators of adaptive immunity were revealed, consisting in an increase in the number of memory T-lymphocytes and a decrease in naive T-lymphocytes, increased early activation and expression of intercellular interaction coreceptors on both T and B lymphocytes. At the same time, there was a decrease in the processes of late activation and a decrease in the activity of apoptosis processes. Activation of the cytotoxic potential of T-effectors is recorded in dysregulatory processes due to a decrease in the content of CD4+CD25+Foxp3+ lymphocytes. The humoral link of patients with coronary heart disease is distinguished by an increase in the relative number of circulating B cells, as well as the content of serum immunoglobulins of classes A, M and G, and the level of CEC. Significant changes in indicators reflecting the work of the innate immune system were revealed. An increase in the number and functional activity of CD16+ cells was noted. An increase in the number of monocytes carrying toll-like receptors was revealed. At the same time, a decrease in the number of monocytes providing antigen presentation processes through HLA DR. was recorded. Changes in the neutrophilic link of innate immunity are ambiguous: on the one hand, an increase in the spontaneous production of reactive oxygen species was revealed while inhibiting the potential for further increase in oxygen-producing activity.

Conclusions

1. Activation of immunocompetent cells, inhibition of T-lymphocyte apoptosis and immunosuppression were revealed in patients with coronary artery disease caused by atherosclerosis. In innate immunity, there was an increase in the expression of TLR2,4,9, an increase in the cytotoxicity of CD16+ lymphocytes, microbicidal activity of neutrophils, which contributes to the pro-inflammatory orientation of the immune response, aggravation of endothelial dysfunction and procoagulant potential of blood plasma, and a decrease in quality of life.

2. Patients with a more severe clinical and angiographic manifestation of coronary heart disease are distinguished by the predominant helper and cytotoxic activity of T lymphocytes, increased processes of intercellular cooperation and the production of autoantibodies in the adaptive link of the immune response, as well as more significant expression by CD289 monocytes and reduced microbicidal potential of neutrophils, increased endothelial dysfunction and plasma coagulation.
3. In the early stages after coronary artery bypass grafting, increased expression of CD282 and CD289, inhibition of T-lymphocyte apoptosis, activation of T-B cell cooperation, increased microbicidal activity of neutrophils and cytokine production of Th1 profile significantly increase the risk of recurrent events in the long term.

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