Diagnostic significance of IL-8 and IL-17 in various forms of interstitial lung disease

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Abstract: Interstitial Lung Disease (ILD) refers to a group of disorders characterized by progressive scarring (fibrosis) of the lung tissue. This scarring affects the interstitium, a network of tissue and space around the air sacs of the lungs. ILD can lead to significant morbidity and mortality due to the impairment of gas exchange and resultant respiratory insufficiency.

Keywords: interstitial lung diseases (ILD), cytokines, immunopathogenesis

Introduction. Interstitial lung diseases (ILDs) constitute a large group of disorders of various etiologies characterized by inflammatory damage to the alveolar walls (alveolitis) and the surrounding interstitial tissue. Currently, this group includes more than 130 diseases; however, infectious lung diseases of known etiology and malignant tumors (e.g., lymphangitic carcinomatosis), which can present with similar clinical symptoms, are not considered interstitial lung diseases [2,4,5]. ILDs are rightly regarded as immunopathological diseases, with allergic reactions of the 3rd and 4th types playing a leading role in their development [1,6,7].

Cytokines released as a result of immune complex damage, especially TNF-alpha (tumor necrosis factor), induce the expression of adhesive molecules on the cell membranes of leukocytes and endothelial cells, significantly increasing the subsequent migration of lymphocytes and monocytes to the inflammation site. A distinctive feature of delayed-type reactions is the activation of macrophages by gamma-interferon secreted by activated CD4+ lymphocytes. Ongoing antigenic stimulation sustains the development of delayed-type reactions, leading to the formation of granulomas and the activation of fibroblasts by growth factors.

Among the majority of known cytokines, cytokines interleukin-8 and -12 are of great importance, having an effect on the active movement of various types of leukocytes and other cells, as well as regulating cellular immunity in various inflammatory processes.

Aim and work. To study diagnostic values of cytokines secreted by lymphocytes in peripheral blood serum, in particular, to determine the production of interleukin (IL-8 and IL-17) by immunocompotent cells in patients with interstitial lung disease.

Material and methods. Sixty IBL patients with different course of the disease, who were hospitalised in the pulmonology department of Samarkand City Medical Association No.1, were examined. Verification of the diagnosis was carried out according to the WHO international classification (ICD-10, heading J84,9). All ILD patients were divided into 3 groups depending on the stage: Group 1 - acute (20), Group 2 - subacute (20), Group 3 - chronic (20) stage of the disease. All clinical and biochemical, laboratory examinations were performed by standardised methods. Determination of IL-8 and IL-17 levels in blood serum was performed by enzyme-linked immunosorbent assay using ELISA test systems: "ELISA-IL-8" and "ELISA-IL-17" (CJSC "Vector-Best", Russia). The control group consisted of 20 practically healthy individuals. The obtained data were subjected to statistical processing on a personal computer using programmes developed in EXCEL package using a library of statistical functions.

Research results. To clarify the immunological content of IL-8 in patients with exogenous allergic alveolitis examined by us it was shown that its level in the general group of examined patients is 33.2±1.8 pg/ml (Fig. 1) and significantly exceeds the values typical for practically healthy individuals (16.5±1.6 pg/ml, $p<0.01$).

When comparing the studied parameters in groups of patients with different course of the disease, it was revealed that the highest IL-8 level is registered among patients with acute course of ILD. In this group the IL-8 content is 38.1±2.91 pg/ml, which is more than 3 times higher than in the control group. On the contrary, IL-8 level was relatively low in chronic exogenous allergic alveolitis, having intermediate values in patients with subacute ILD.

Thus, when analysing the results obtained by us, it was found that in patients in subacute stage of ILD the level of IL-17 is 83.9±3.51 pg/ml, significantly exceeding the indicators of the group of practically healthy individuals (59.8±6.7 pg/ml, $p<0.01$). As it turned out, IL-17 level fluctuated significantly in the groups of patients with different stages of ILD compared by us. The highest level was in patients with chronic stage of ILD (124.6±9.0 pg/ml), significantly differing from the parameters of the healthy group (59.8 ± 6.7 pg/ml; $p<0.01$) and patients with acute course of ILD (105.6±10.2 pg/ml; $p<0.01$). Also in patients with subacute ILD the level of IL-17 was more than twice higher than in the control group ($p<0.02$).

Consequently, the obtained results indicate that all studied clinical variants of ILD are characterised by an increase in IL-8 content in the blood serum of patients, however, the prevalence of humoral allergic mechanisms in the pathogenesis of the

disease is accompanied by the highest level of this proinflammatory cytokine, significantly different in acute ILD (38.1±2.39 vs. 16.5±1.6 pg/ml, $p<0.05$).

The study of IL-17 serum content in the patients examined by us revealed the following peculiarities of this index depending on the phase of ILD.

Thus, the highest level of the studied parameter is noted in ILD patients in the chronic stage, which distinguishes this group among the general group of studied ILD patients, and also distinguishes it from the two compared groups with acute and subacute stages of the disease.

Conclusions: The results of the study of IL-8 and IL-17 production levels showed that ILD during the acute course is accompanied by the most pronounced changes in the pro-inflammatory cytokine IL-8, which provides active movement of various types of immune cells to the focus of inflammation, and the period of subacute and chronic allergic inflammation was accompanied by pronounced changes in the production of cytokines regulating cellular immune response in particular IL-17 in patients with ILD. Consequently, the obtained data indicate that ILD patients have multidirectional changes in cytokine production depending on the stage of the disease, which have an important clinical-diagnostic and therapeutic significance.

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