

STUDY OF THE MAIN SERUM CYTOKINES IN PATIENTS WITH LIVER ECHINOCOCCOSIS

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Annotation: *we examined 53 patients with liver echinococcosis aged 17-70 years who were hospitalized at the Bukhara Regional Multidisciplinary Medical Center in 2017-2021. The control group consisted of 30 donors aged 18 to 30 years (18 men and 12 women). Clinical examination and specific immunological examination were performed before surgery, on the 1st, 3rd, 5th days. In 53 patients with liver echinococcosis, the levels of IL-1 beta , IL-4 and IL-6 in peripheral blood serum were determined. Echinococcosis of the liver is accompanied by immunosuppression, which is expressed in the suppression of the production of IL-1 beta and an increase in the anti-inflammatory interleukin IL-6, which in turn leads to tension in the humoral and cellular parts of the immune system. Serum concentration of IL-6 is a reliable diagnostic and prognostic criterion for the prognosis of this disease.*

Key words: *liver echinococcosis, cytokine, IL-6, IL-1, immunology .*

Relevance. It is known that echinococcosis most often (60-80%) affects the liver [1, 2, 3, 8] and the only method of treating patients with liver echinococcosis is surgery [4, 5, 6, 7, 9]. Currently, despite the progress made in liver surgery, the treatment of liver echinococcosis still presents certain difficulties.

Target. Study of the levels of some serum cytokines in liver echinococcosis and their changes after echinococcectomy .

Materials and methods. We examined 53 patients with liver echinococcosis aged 17-70 years who were hospitalized at the Bukhara Regional Multidisciplinary Medical Center in 2017-2021. The control group consisted of 30 donors aged 18 to 30 years (18 men and 12 women). Clinical examination and specific immunological examination were performed before surgery, on the 1st, 3rd, 5th days. In 53 patients with liver echinococcosis, the levels of IL-1 beta , IL-4 and IL-6 in peripheral blood serum were determined. Patients were taken fasting whole blood in the amount of 5 ml from peripheral veins, followed by its centrifugation and plasma separation. The study of cytokines was carried out using ELISA kits manufactured by Vector-Best, Russia. Statistical analysis

was carried out using the Excel package of statistical computer programs of the Office package. XP and using manuals on medical and biological statistics. To assess the degree of statistically significant differences between the qualitative data for a multi-field table, the criterion χ^2 was used with a confidence level of probability $P < 0.05$. Differences between the indicators were considered significant at $P < 0.05$.

Results and discussion. As a result of the study of patients with liver echinococcosis, it was found that the concentration of IL-1 beta in the peripheral blood serum of patients was significantly suppressed relative to the control group. In the control group, this indicator was 9.95 ± 1.84 pg /ml, while in the group of patients with liver echinococcosis it was 1.70 ± 0.55 pg /ml ($P < 0.05$). The serum concentration of IL-1 beta in the group of patients was suppressed by 5.9 times, which indicates a pronounced imbalance and immunodeficiency of nonspecific defense factors in patients with liver echinococcosis. It is known that IL-1 beta is a key pro- inflammatory cytokine that plays an important role in the formation of the cytokine cascade in the body. Proinflammatory cytokines, including IL-1, control cellular interactions during inflammation. They regulate cell migration to the focus of inflammation, their activation and cell apoptosis. It has been established that inflammation is a physiological, universal response of the body to the introduction of an infecting agent, antigen, and tissue damage. Induction of the production of cytokine molecules can be caused by trauma, toxins, and infection. The course and intensity of the inflammatory response is also controlled by anti -inflammatory cytokines (IL-6), which suppress the secretion of pro - inflammatory cytokines. IL-1 is involved in almost all stages of the immune response. It activates antigen -presenting cells and CD4 + T-lymphocytes, affects the differentiation of T- and B-lymphocytes and other immunocompetent cells. IL-1 activates cytotoxic T-lymphocytes and EKK, participates in the regulation of the production of other cytokines, granulocyte-macrophage colony stimulating factor (GM-CSF) and other cytokines.

The main producers of IL-1 are monocytes and macrophages. IL-1 is also formed by B-lymphocytes, white process epidermocytes (Langerhans cells), glial, endothelial and synovial cells, fibroblasts, epithelium of the skin and thymus, and others. The biological effects of IL-1 can be conventionally divided into immunological, inflammatory , hematopoietic, and intersystemic. IL-1 stimulates myelopoiesis and early stages of erythropoiesis. Serum IL-6 in liver echinococcosis was significantly higher ($P < 0.05$) compared to control values. Thus, in the group of patients, the serum concentration of IL-6 was 9.45 ± 2.64 pg /ml, while in the control group of healthy individuals it was 3.42 ± 0.28 pg /ml. It follows that IL-6 in the peripheral blood serum of patients with liver echinococcosis was increased by 2.8 times relative to the value of the control group. According to the literature, it is known that IL-6 is an intermediate cytokine that plays the role of both pro- and anti-inflammatory cytokine. In this situation, given that echinococcosis is a chronic infectious disease, the

production of IL-6 is due to the long-term presence of echinococcosis in the body, i.e. we can say that the cell type of the immune response has shifted to the humoral one, which is due to a significant production of IL-6, which has pronounced anti-inflammatory properties and promotes the transfer of the cellular immune response to the humoral one. IL-6 producing cells are extremely numerous, they are fibroblasts, monocytes/macrophages, lymphocytes, hepatocytes, etc. According to the literature, bacterial products, polyelectrolytes, mitogens, as well as IL-1, TNF- α can be inducers of IL-6 production, interferons, etc. The biological effects of IL-6 are similar to those of IL-1. First of all, it is participation in the implementation of inflammatory and immune reactions and hematopoiesis. It is described that IL-6 promotes both exacerbation of chronic and chronicity of acute inflammatory processes. It has antibacterial, antiparasitic and antiviral effects. Being released somewhat later than IL-1 and TNF- α , IL-6 suppresses their formation (they, on the contrary, stimulate its production) and therefore belongs to the cytokines that complete the development of the inflammatory reaction. Therefore, IL-6 is a polyfunctional cytokine produced by macrophages and liver cells. According to the spectrum of biological action, it is involved in the development of inflammation, immune reactions, in the regulation of hematopoiesis, serves as a growth factor for plasma cells, and participates in intersystem interactions.

In the interpretation of cytokines, in order to understand their role in the pathogenesis of the pathological process, one resorts to the relationship between pro-inflammatory and anti-inflammatory cytokines. Thus, the ratio index of IL-1 beta/IL-6 is a diagnostic and prognostic criterion for infectious diseases. Normally, this ratio is 2.9. In the group of patients with liver echinococcosis, the ratio index of IL-1 beta/IL-6 was 0.2. Our data indicate a sharp shift towards the production of the anti-inflammatory cytokine IL-6. The condition of patients with liver echinococcosis was accompanied by a significant suppression of the production of IL-1 beta against the background of a significant production of IL-6, which caused a pronounced immunodeficiency of the cellular link of immunity in patients with liver echinococcosis against the background of activation of humoral immunity.

We have studied the cytokine profile of patients with liver echinococcosis immediately after surgery. The level of IL-1 beta in the peripheral blood serum immediately after the operation slightly increased, but also remained significantly reduced relative to the control group. There were no significant differences between the two groups of patients before and after surgery. Before the operation, the concentration of IL-1 beta was 1.70 ± 0.55 pg/ml, and after the operation it was 1.98 ± 0.43 pg/ml. Interest was aroused by the analysis of IL-6 immediately after surgery, where the value of IL-6 was significantly increased and amounted to 44.26 ± 18.2 pg/ml (before the operation it was 9.45 ± 2.43 pg/ml). The production of IL-6 sharply increased immediately after the surgery by 4.7 times. The ratio index or rather immunodeficiency was even lower and

amounted to 0.05. Naturally, the study of IL-6 immediately after the operation showed a significant increase in IL-6 relative to the value of the control group. We have established a relationship between the size of echinococcal cysts and the concentration of IL-6 in peripheral blood serum. Thus, the concentration of IL-6 in the blood serum was proportional to the size of echinococcal cysts in the liver. Our data are consistent with literature data, where the authors point to the relationship between cyst sizes and serum cytokines, in particular IL-6 and IL-1 beta .

Conclusions. 1. Echinococcosis of the liver is accompanied by immunosuppression, which is expressed in the suppression of the production of IL-1 beta and an increase in the anti-inflammatory interleukin IL-6, which in turn leads to tension in the humoral and cellular parts of the immune system.

2. The serum concentration of IL-6 is a reliable diagnostic and prognostic criterion for the prognosis of this disease.

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