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EVALUATION OF SUB-POPULATION COMPOSITION OF LYMPHOCYTES IN CHRONIC TOXIC LIVER DISEASE AND ANEMIA OF CHRONIC DISEASE ON THE BACKGROUND OF TRANSMITTED INFILTRATE PULMONARY TUBERCULOSIS

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ABSTRACT

The article presents the results of the estimation of the subpopulation composition of lymphocytes in 66 patients with chronic toxic liver damage and anemia of a chronic disease on the background of the transferred infiltrative pulmonary tuberculosis. The use of a combination of sirepar and sodium nucleate in the treatment of such patients contributes to the elimination of the clinical phenomena of the combined pathology, and along with the improvement or complete normalization of the clinical indices in the patients examined, normalization of the cellular immunity parameters was noted, which gives grounds for recommendations on the use of the proposed combination of drugs in the complex treatment.

Keywords: lymphocytes, cellular immunity, tuberculosis infection, chronic hepatitis, anemia.

Introduction. Among infectious diseases, tuberculosis continues to be one of the leading causes of morbidity and mortality among adults throughout the world. Approximately 2 billion people of the world's population are infected with M. Tuberculosis [12]. Every year, almost 10 million people become infected with an active form of tuberculosis and 2 million people die from it [14]. Every 10 seconds from tuberculosis in the world one person dies. So, in the territory of Lugansk region in recent years, due to a number of problems: forced migration, the formation of post-traumatic stress disorder and a decrease in the standard of living of the population, there is an increase in the incidence of tuberculosis. According to statistical data in 2015, the incidence was 58.9 per 100 thousand people, the mortality rate is 12.3 per 100 thousand population, in 2016 these figures were 68.2 and 15.3, in 2017 70.4 and 15.8 per 100.000 of the population, respectively, which exceeds the epidemic threshold.

The need for continued use of antituberculosis drugs led to an increase in the proportion of adverse reactions [11]. The development of adverse reactions to antituberculosis drugs poses a threat to a full-fledged chicken chemotherapy [2, 10]. Interruptions in taking antituberculosis drugs lead to a decrease in the effectiveness of treatment, the formation of tuberculosis with drug resistance, and to an increase in the reservoir of tuberculosis infection [1, 3, 8].

One of the most common hematological disorders in patients with acute or chronic activation of the immune system due to various infectious diseases is anemic syndrome [4, 5]. According to modern ideas, anemia arising in similar situations is conventionally designated as anemia in chronic diseases (ACH). The frequency of ACH in acute and chronic infections varies from 18 to 95% [13]. AChs with long-term preservation of the inflammatory process, which is typical for tuberculosis infection, may present difficulties in terms of differential diagnosis with iron deficiency anemia and further treatment.

One of the pathogenetic links of the studied comorbid pathology is the binding of metabolites to hepatocyte proteins with the appearance of autoantigens circulating and fixed on the membranes of hepatocytes, the formation of immune complexes of autoantigen-autoantibodies, and the development of T cell-mediated immunological reactions.

Purpose of the study: evaluation of the subpopulation composition of lymphocytes in chronic toxic liver damage (CTLD) and anemia of a chronic disease against a background of transferred infiltrative pulmonary tuberculosis.

Materials and methods of research. Under our supervision, there were 66 patients with CTLD, with AChs on the background of tuberculosis of the lungs, age from 18 to 50 years. The criteria for inclusion in the study were: age from 18 to 50 years, hospital treatment, history of first diagnosed infiltrative pulmonary tuberculosis, chemotherapy under standard regimens using 4 drugs or more, informed consent for participation in the study, the presence of toxic liver damage caused by reception of antituberculous drugs. The criteria for exclusion were: age younger than 18 years and over 50 years, refusal from inpatient treatment, lack of informed consent, positive ELISA test for the presence of certain markers of viral hepatitis.

All observed patients were divided into two groups: the main group (34 patients) and the comparison group (32 patients), randomized by sex, age, and course of the disease. All patients received standard therapy of hepatitis, including hepatotropic therapy, drugs ursodeoxycholic acid, essential phospholipids, a mixture of amino acids. Patients from the main group were additionally received in a combination of sireppar therapy of 3 ml IV drip in 100 ml of 0.9% fiz. solution and sodium nucleate for 2 capsules (200 mg) 4 times a day for 2 weeks.

The diagnosis of toxic hepatitis was established expertly, taking into account the history, the results of clinical and laboratory (biochemical) research, characterizing the functional state of the liver and gallbladder, as well as data from sonographic examination of the abdominal cavity. To confirm anemia of a chronic disease, hemoglobin (Hb), hematocrit (Ht), reticulocyte count, serum iron level (Fe), total iron binding capacity of serum (TICS) were evaluated.

To achieve the goal of the study, an additional immunological study was performed to analyze the state of the cellular immune system. At the same time, the content of T- (CD3 +) and B-lymphocyte (CD22 +) populations, T helper / inductor subsets (CD4 +) and T-suppressor / killer (CD8 +) populations was studied in the peripheral blood using a cytotoxic test using monoclonal antibodies (MBAT). Commercial MCAT classes CD3 +, CD4 +, CD8 +, CD22 + NIC of "MedBioSpectr" (RF - Moscow) were used in the work. The immunoregulatory index

CD4 / CD8, which was treated as the ratio of lymphocytes with helper and suppressor activity (Th / Ts), was taken into account. Evaluation of immunological shifts of T-cell regulatory subpopulations was performed using the "immunological compass" method, taking into account the relationship between subpopulations of T-helpers and T-suppressors. Functional activity of T-lymphocytes was studied by the reaction of blast transformation of lymphocytes (RTBL) when it was formulated with a micromethod using phytohemagglutinin (PHA) as a nonspecific mitogen.

Statistical processing of the results was carried out according to methods common in experimental medicine using the package of licensed programs Microsoft Exel. The reliability of the differences in the groups was determined by the Student's t-criterion using the Microsoft Exel 5.0 and MedStat software packages [7].

Results and discussion. The clinical picture of CTLD and AChs on the background of the transferred infiltrative pulmonary tuberculosis is characterized by the presence of varying degrees of asthenic, astheno-neurotic, moderate cytolytic syndromes, anemia, hepatomegaly, in some patients – cholestatic syndrome, and characteristic changes on the chest radiograph (resorption of infiltrative focal changes in the affected lobes of the lungs, scarring of cavities of decay and compaction of foci).

In the ultrasound study, signs of moderate increase in the liver and an increase in its echogenicity were found in all patients, no signs of obstruction of the biliary tract. In laboratory studies, a tendency to anemia was found in the blood (a decrease in the level of red blood cells and hemoglobin, hematocrit (Ht) was reduced, the number of reticulocytes in the blood was normal or slightly elevated, the serum iron level was normal or moderately lower, the OJSS was normal or decreased, moderate leukocytosis, moderate increase in ESR, hyperbilirubinemia with a predominant increase in the conjugated fraction, a moderate increase in the activity of alanine aminotransferase, in some patients - an increase in the activity of alkaline phosphatase, gammaglutamiltranspeptidase, hypercholesterolemia.

Prior to the start of treatment in both groups, we observed similar changes in clinical immunity parameters characterized by T-lymphopenia, a decrease in the number of T-helper / inducers circulating in the blood (CD4 +) and an imbalance in the subpopulation composition of T cells with a decrease in the immunoregulatory CD4 / CD8 index relative to the norm that speaks about the formation in patients with CKTP and AChs on the background of the transferred pulmonary tuberculosis more often with respect to the suppressor variant of immunodeficiency (with the predominant decrease in the number of cells with helper activity Yu). In connection with general T-lymphopenia, the absolute number of lymphocytes with the CD8 + phenotype also moderately decreased, however, to a slightly lesser extent than the number of lymphocytes with the CD4 + phenotype (table).

Thus, the immunoregulatory index of CD4 / CD8 in all of the examined patients with CTLD and AChs was significantly lower than the norm (P <0.001) in the presence of pulmonary tuberculosis. The number of B cells (CD22 +) in most cases did not change significantly in relative value, whereas the absolute number of B-lymphocytes in patients was significantly reduced (Table). At the same time, the functional activity of T-lymphocytes in the examined patients for this combined diagnosis was significantly reduced: in the main group, an average of 1.82 times the norm (P□0.01) and in the comparison group 1.74 times (P □0.01).

Thus, before the beginning of the treatment, the examined patients of both groups had quite significant disorders from the cell link of immunity. They consisted in the presence of T-lymphopenia, an imbalance in the subpopulation composition of T lymphocytes with a predominant decrease in the number of T helper / inducers (CD4 +) circulating in the peripheral blood and a decrease in the immunoregulatory index of CD4 / CD8. The number of lymphocytes with the CD8 + phenotype (T suppressor / killer) and CD22 + (B-lymphocytes) did not decrease in relative amounts, however, due to general lymphopenia, the absolute number of CD8 + and CD22 + lymphocytes decreased moderately. At the same time, there was a significant decrease in the functional activity of T-lymphocytes according to RBTL data.

In a second study of the cellular response of the immune response after completion of the treatment, we found that in the main group of patients (who received a combination of sirep and sodium nucleate), the amount of CD3 + cells (total population of T-lymphocytes) and T-helper / inducers CD4 +) almost completely normalized, in connection with which the immunoregulatory index CD4 / CD8 rose to normal. It is significant that along with the normalization of the quantitative indices of the T-cell link of immunity, the restoration of the functional activity of T-lymphocytes was also noted in the examined patients, which is confirmed by the dynamics of RBTL with PHA. Indeed, in the patients of the main group (who received the combination of sirepah and sodium nucleate), the indicator of RBTL with PHA increased from 38.6 ± 3.0% to 68.2 ± 2.4%, that is, 1.76 times the baseline and reaches lower limit of the norm (table). Thus, under the influence of a combination of sirepar and sodium nucleate preparations in patients with CTLD and AChs on the background

Dynamics of cellular immunity indices in patients with CKTP and AChs on the background of the transferred pulmonary tuberculosis during treatmen(M±m)

Immunological parameter	Norm	Group of patients	
		the main (n=34)	comparison (n=32)
CD3+. %	69.8±2.1	51.3±2.0** / 67.9±0.2	50.9±1.8** / 56.3±0.9*
г/л	1.32±0.04	0.87±0.01*** / 1.25±0.04	0.85±0.03*** / 0.95±0.04**
CD4+. %	45.6±1.5	30.3±1.9** / 43.6±2.0	30.9±1.8** / 35.8±2.1*
г/л	0.87±0.03	0.46±0.01*** / 0.80±1.3	0.5±0.02*** / 0.60±1.4**
CD8+. %	22.3±0.9	18.5±0.1 / 21.5±2.5	19.0±0.2 / 21.3±2.1
г/л	0.42±0.02	0.29±1.1* / 0.38±0.01	0.3±1.0* / 0.33±0.02*
CD4/CD8	2.04±0.03	1.58±0.02*** / 2.1±0.03	1.6±0.02*** / 1.81±0.03**
CD22+. %	21.6±1.1	19.7±0.2 / 21.2±1.3	20.1±0.3 / 20.9±1.4
г/л	0.41±0.02	0.31±0.01* / 0.37±0.02	0.3±0.03* / 0.35±0.02
RTBL with PHA. %	69.5±2.3	38.6±3.0** / 68.2±2.4	39.1±2.7** / 50.9±2.5*

Note: in the numerator - indicators before the start of treatment, in the denominator - after its completion; the probability of a difference in the indicators relative to the norm: * - for P<0,05, ** - P<0,01, *** - P<0,001.

of transferred infiltrative pulmonary tuberculosis, normalization of both quantitative and functional indices of the T-cell link of the immune response is noted. Concerning the number of CD8 + and CD22 + lymphocytes in patients of the main group, these indicators also normalized (table).

In the comparison group, we also noted a positive dynamics of the studied indices of the cellular immunity, but it is much less pronounced. Therefore, after the completion of treatment in the comparison group patients, there are shifts between the majority of the immunological parameters studied, both in relation to the main group and the corresponding norm indicators (table). Thus, a significant difference in the number of T-cells (CD3 +) was established between the groups of patients both in relative terms (an average of 11.6 ± 0.7%, P <0.05), and in calculating the absolute number (in 1.3 times, P <0.05). The relative number of CD4 + lymphocytes in the comparison group after completion of treatment was 7.2 ± 0.5% lower than in the main group (P <0.05), and the absolute number of CD4 + cells was 1.3 times (P < 0.05). The immunoregulatory index of CD4 / CD8 after the completion of the course of treatment in the main group was 1.16 times higher than in the comparison group (P <0.05), the indicator of RBTL with PHA was 1.33 times higher (P <0.05) .

Thus, the obtained data indicate that the use of a combination of sireppara and sodium nucleate helps to restore the indices of immunological homeostasis in patients with CKTP and AChs on the background of the transferred pulmonary tuberculosis, namely, it ensures the elimination of T-lymphopenia, the normalization of the relation between the helper and suppressor subpopulations of T cells, an increase in the indicator of RBLT from the PHA.

It is significant that in the clinical plan, the use of sirepar and sodium nucleate in the treatment of drugs, accompanied by an improvement in the well-being and general condition of the patients, primarily a reduction in general weakness, malaise, increased capacity for work and appetite, and improved mood, disappeared in the right hypochondrium, the sub-skin and sclera. In the comparison group, we also noted a positive dynamics of clinical indicators, but less pronounced. When analyzing biochemical parameters, it was found that the activity of serum aminotransferases practically normalized in patients of the main group (96% of patients).

Thus, the obtained data testify that the use of a combination of sirepar and sodium nucleate preparations in the complex of treatment of patients with CTLD and AChs with pathology of lung tuberculosis is pathogenetically sound and clinically effective, since this combination of drugs contributes to both elimination of clinical and biochemical manifestations of the disease and normalization of indices of immunological homeostasis, namely the state of the cellular link of immunity. There were no any side effects from the use of the proposed combination of drugs, including allergic reactions.

Conclusions. 1. The clinical picture of CTLD and AChP in the presence of infiltrative pulmonary tuberculosis is characterized by the presence of varying degrees of asthenic, asthenic-neurotic, mild cytolytic syndromes, anemia, hepatomegaly, in some patients - cholestatic, as well as characteristic changes in the chest radiograph

2. Immunological examination revealed violations of the cellular immunity, characterized by T-lymphopenia, an imbalance in the subpopulation composition of T-lymphocytes, mainly by reducing the number of circulating lymphocytes circulating in the peripheral blood, having a CD4 + (T helper / inducer) phenotype and an immunoregulatory CD4 index / CD8, a significant decrease in the functional activity of T cells according to the data of RBTL with PHA. In general, the obtained data indicate the formation of a secondary immunodeficiency state, mainly on a relatively suppressor version.

3. The use in the treatment of patients with CTLD and AChs on the background of the transferred pulmonary tuberculosis, a combination of preparations of sirepar and sodium nucleate contributes to the elimination of the clinical phenomena of the combined pathology, and along with the improvement or complete normalization of clinical parameters in the patients examined, there was an improvement in biochemical parameters characterizing the functional state liver.

4. In patients who received a combination of sirepar and sodium nucleate, the normalization of the cellular immunity parameters was noted, which gives grounds for recommendations on the use of the proposed combination of drugs in complex treatment.

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CYTOLOGICAL ANALYSIS OF CERVIX INFLAMMATORY DISEASES IN DIFFERENT AGE GROUPS ON THE EXAMPLE OF THE SAKHA (YAKUTIA) REPUBLIC

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ABSTRACT

Cytological analysis of cervix inflammatory diseases was conducted on women aged 18 to 88. The results of the analysis showed a high incidence of disease in the age groups 18-29. In the middle age group (30-44 and 45-59 years), balancing of genital infections is noted and the first effects of infection with viral infections appear (dysplasias of varying severity and background changes in the epithelium). In women in the older age group, mainly inflammatory processes (atrophic colpitis) were observed, which is associated with the intense influence of sex hormones. Generally, long-term preservation of viral HPV is associated with high-oncogenic risk types of HPV infection (mainly HPV 16). Remote causes of viral infection were found rarely (2.9%) on menopause, but it has the important prognostic value, which can predict the risk of cervical pathology development. Inflammation processes (senile vaginitis) are found in the old age group of women (20,9%), which is due to the intensive influence of sex hormones (estrogens). At this period the lack of estrogen harms the main protective properties of the stratified squamous epithelium. As a result, the number of lactobacilli is decreased or completely disappeared by the cause of conditionally pathogenic and pathogenic flora overgrowth.

Thus, infectious-inflammatory diseases of the female genital organs caused by various pathogens, sexually transmitted diseases, or nonspecific microflora, represent a serious medical and social problem.

Keywords: oncocytology, diagnostics, inflammation.

Relevance. Pelvic inflammatory diseases (PID) establish itself as a leading position in the structure of gynecological disorders, also become the most common cause of women's reproductive system disability. Thereby, it creates a major health, social and economic problems worldwide [2, 7, 10, 11, 13, 15].

The starting moment for the progression of acute inflammatory diseases is the invasion of microorganisms. Cervix is an important protective barrier on the way for plaque formation in the internal genital organs. Almost all microorganisms those present in the vagina, except for lactobacillus and bifidobacteria, can be involved in the development of the inflammatory process [4]. However, in most cases, PID is caused by sexually transmitted infections [8, 12]. The immune system takes an important part in the pathogenesis of female genital organs inflammation. Inflammation and immune process are inextricably linked, and currently, inflammatory and immune responses are considered as a complete whole [9]. Notice that at the beginning of the pathological process only one infectious agent activates the inflammatory response, changes local immune system functioning. Thereby it prepares the breeding ground for further contamination with opportunistic pathogens [8, 14].

There are different factors in cervix inflammatory process: bacterial imbalance; thinning of stratified squamous epithelium in postmenopausal years along with the inflammatory process (senile vaginitis); various physical and chemical effects; earlier diseases that harm the immunity system; infections [1].

Modern PID is a problem of sexually active women. Recently most researchers find out that social factors take the main part in the genesis of the PID progression, such as early sexual debut, high sex frequency, high number of sexual partners, sexual activity during menstruation, using of drugs [6, 16]. Many scientists consider that genital inflammatory process is the onset of majority gynecological diseases. According to V. N. Serov et al, chronic inflammatory process in the genital organs responsible for the formation of such pathology as endometriosis, uterine fibroid, hyperplastic processes, infertility of various origins, neoplastic diseases