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Cellular Immune Response in Experimental Modeling of Complicated and Uncomplicated Hydatidosis Echinococcosis of the Liver

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ABSTRACT

Background. The incidence of echinococcosis of internal organs, due to the peculiarities of the pathomorphological manifestations of the disease, in the form of the organisation of specific cysts prone to dissemination, is considered very costly for the social sphere. Given that this disease most often affects people of working age, the pathology is also reflected in an increase in the number of disabilities, and the absence of treatment, in an increase in mortality.

Material and methods. The basis of the experimental material was made up of rabbits of the Chinchilla breed. The expression of CD-differentiated and activation antigens assessed the quantitative determination of cellular immunity. The following markers of immunocompetent cells were determined: $CD4^+CD28^+$, $CD8^+CD28^+$, $CD4^+CD25^+$. CD receptor expression was performed in a rosette formation reaction using LT series monoclonal antibodies manufactured by Sorbent LLC (Russia).

Results. Absolute and significant elevation of $CD4^+CD28^+$ was noted at all stages of modelling of hydatidosis echinococcosis of the liver ($p<0.05$). An increase in the number of $CD4^+CD25^+$ was noted in the late stages of the modelling of the pathological process. At the same time, against this background, there was a decrease in the number of $CD8^+CD28^+$, which indicates differentiated changes in the mononuclear cells of peripheral blood themselves.

Conclusion. Reproduction of the experimental model of hydatidosis echinococcosis of the liver leads to differentiated expression of lymphocyte subpopulations, transforming the body's defense response into a kind of immune response, which was characterized by the activity of T-cells to organize the process and form a protective layer. However, this response of the organism under the influence of a secondary, non-specific bacterial infection changed its nature of the immune trace, which can be traced in the following analysis.

Keywords: Hydatidosis echinococcosis of the liver, cellular immunity, peripheral blood mononuclear cells

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INTRODUCTION

Echinococcosis of the liver is a severe parasitic disease caused by a tapeworm belonging to the genus Echinococcus (E. granulosus). The disease is most common in regions where animal husbandry is popular. The Central Asian region is located in one of the zones characteristic of the endemic pathology of echinococcosis of the liver. In recent years, however, more and more information has been published on the spread of the disease in the regions, in particular in Europe. in which echinococcosis of the liver was previously considered sporadic cases [1, 2, 7].

According to the World Health Organization, the diagnosis and detection of hydatidosis echinococcosis of the liver should be considered an advanced form of the disease. However, in half of the cases, due to the obliteration of the clinical picture, the development of complications of the disease, in particular, purulent-septic ones, is more dangerous [3, 4, 10, 11].

Humans are accidental intermediate hosts of the parasite, causing the disease to take on a hydatidosis. Such damage can occur not only in the liver, but also in the lungs, spleen, and heart. The process of parasite infection of internal organs can proceed for decades without obvious clinical symptoms, and in this process, the parasite's evasion and regulation mechanisms play a crucial role in the human host's immune response. Echinococcus larvae appear to have evolved effective immune evasion mechanisms that promote asymptomatic incubation and long-term host-parasite coexistence. Larvae may persist for decades with progressive tissue invasive tumour-like cyst growth, but some patients with hydatidosis echinococcosis may present with self-healing disease.

This diversity suggests the presence of immunological mechanisms that can control the course of echinococcosis of internal organs. A characteristic feature of certain resistance to echinococcosis of the liver is the occurrence of cytokines of the Th_1 type, while increased production of cytokines IL-10 and Th_2 is associated with the progressive growth of parasite larvae [6].

Only 10–30% of seropositive cases of echinococcosis develop a clinical picture of the disease, suggesting that effective immune responses could destroy the larvae when penetrating the intestinal wall at an early stage of infection [8].

Patients with a strong Th_1 immune response are more likely to be able to limit or regress larval growth by forming periparasitic granulomas with macrophages and T-cells, as well as lesions or fibrosis and necrosis to encapsulate the parasite [3].

Successful evasion of the parasite's immune response results in a tolerant Th_2 immune response, which is unable to prevent the growth of echinococcus larvae [8].

The spectrum of the disease depends on acquired deviation of Th_1-associated immunity, and spontaneous secretion of IL-10 by peripheral mononuclear blood cells has been identified as an immunological sign of patients with advanced forms of hepatic echinococcosis involved in maintaining parasite tolerance and persistence [8].

The reactivity of peripheral blood cells to tape parasite antigens persists for many years in patients after complete resection of parasitic lesions, suggesting that the parasite's residual tissues will continue to stimulate cellular responses [9].

The tapeworm parasite can expand the regulatory T-cell response and promote a largely Th_2-shifted response, which ensures the long-term survival, proliferation, and maturation of the parasites [5].

However, all of the above is only an assumption based on the results of the study of the pathogenesis of other parasitic diseases. At the same time, the disclosure of the possibility of stimulating the immunological response of the body to the invasion of the echinococcal parasite would, in our opinion, make it possible to develop methods for predicting and preventing severe complicated forms of the disease, and, accordingly, to improve the results of treatment of patients with hydatidosis echinococcosis of the liver.

MATERIAL AND METHODS OF RESEARCH

The basis of the experimental material was Chinchilla rabbits weighing 1.5-2 kilograms, of both sexes, without the appearance of the disease, which were on a standard laboratory diet in the central research laboratory of the Bukhara State Medical Institute. The preliminary protocol for experimental studies was approved, after review and discussion, by the Bioethics Committee under the Ministry of Health of the Republic of Uzbekistan.

The planned experimental studies, which included sampling, biopsies and autopsies, were based on the principle of the conditions specified in the Council of Europe Convention for the Protection of Animals of 1986.

Experimental studies were prolonged, which was due to a long period of modeling of the pathological process and repeated sampling of blood samples from the same animal in the dynamics of the development of the disease. After taking blood samples, the animals were addi-

tionally given a volume of drinking fluid to prevent their dehydration.

The animals were divided into the following series of experiments:

Control series. It consisted of 10 intact animals that had not been exposed to any external influences other than blood sampling.

Basic series. This series was divided into 3 components, which determined the chronology of the modelling of the pathological process. It consisted of 10 animals, which as needed (death, incorrect manipulation, lack of reproducibility of the model, etc.). was supplemented by animals.

Comparative series. This series included at least 10 rabbits and consisted of two parts of the same animals with a transformation of the pathological process.

Blood samples to assess the immunological state of the body in animals were obtained by puncture of the central vein of the ear.

The expression of CD-differentiated and activation antigens assessed the quantitative determination of cellular immunity. The following markers of immunocompetent cells were determined: $CD4^+CD28^+$, $CD8^+CD28^+$, $CD4^+CD25^+$. CD receptor expression was performed in a rosette formation reaction using LT series monoclonal antibodies manufactured by Sorbent LLC (Russia).

The results of the studies were processed using the generally accepted method of variational statistics. A software package for biomedical research was used. The significance of the differences was determined using the Student test. Calculate EXCEL spreadsheets using built-in variational statistics. The differences were considered significant at $p<0.05$. The principles of evidence-based medicine were used in the organization and conduct of the research. The results of the research were expressed in units of the International System of Units.

RESULTS

To dynamically compare the data, at the first stage of experimental studies, we carried out an analysis of the grouped assessment of cellular immunity indicators characteristic of changes in parasitic diseases.

The total number of cells studied in animals with the starting intact position, i.e. the control group on day zero of the study, was 46.31±11.24 T-cells.

More than half (59.43%) of these cells were $CD4^+CD28^+$ T-cells and $CD8^+CD28^+$ T-cells (32.09%), accounting for a total of 91.51%. The rest of the cells were $CD4^+CD25^+$ T-cells (only 8.49%).

The comparative analysis of the content of the studied T-cells in peripheral blood in intact animals after 3 days of follow-up increased by an average of only 0.49±0.12 cells compared to the previous period. Increases were noted among $CD4^+CD28^+$ T-cells (by 0.21%) and $CD8^+CD28^+$ T-cells (by 0.20%). Against this background, a decrease in $CD4^+CD25^+$ count of 0.41% was revealed. The changes were not significant ($p>0.05$) and did not have any fundamental character in the occurring physiological parameters.

Evidence for our reasoning can be presented by these changes in the ratio of the cellular composition of T-cells in intact animals on day 7 of observation. The total level of the studied cells increased both compared to day zero and the previous study period (by 0.83% and 0.34%, respectively). At the same time, against the background of an increase in the specific gravity of T-cells, there is a decrease in the content of $CD4^+CD28^+$ and $CD8^+CD28^+$ T-cells.

The identical nature of T-cell changes at 14-day follow-up, namely, the specific gravity of $CD8^+CD28^+$ and $CD4^+CD25^+$ T-cells decreases. $CD4^+CD28^+$ cells remain elevated, reaching their maximum value throughout the entire observation period.

In subsequent follow-up periods, the level of the studied T-cells decreased. On average, the intact animals had 47.05±6.53 T cells. At the same time, the largest middle half were $CD4^+CD28^+$ T-cells (59.40%). To a lesser extent, $CD8^+CD28^+$ (32.41%) and $CD4^+CD25^+$ (8.19%) T-cells were represented.

In the animals in the comparison group, the population of studied T-cells averaged 41.86%.

The highest level, as well as in intact animals, was observed among $CD4^+CD28^+$ T-cells (66.06%). The level of $CD8^+CD28^+$ T-cells was reduced by 2.88-fold ($p<0.05$). The mean ratio of $CD4^+CD28^+/CD4^+CD25^+$ was a 6.02-fold decrease.

In the separate analysis between the comparative models with and without purulent-septic complication, we also revealed a difference in the ratio of the studied blood T-cells.

In animals with an aseptic process, the decrease in the content of $CD8^+CD28^+$ T-cells compared to $CD4^+CD28^+$ was 3.4-fold, and compared to $CD4^+CD25^+$ even more – 6.56-fold.

At the same time, in animals with a purulent-septic process, this ratio decreased by 2.38 and 5.43 times, respectively.

In the dynamics of reproduction of the experimental model of hydatidosis echinococcosis of the liver, the ratio of blood T-cells was ambiguous (Table 1).

Table 1

The Nature of Changes in the Studied T-Cells on the 20-Day Simulation of Hydatid Echinococcosis of the Liver Uncomplicated by a Purulent-Septic Process

SERIES OF EXPERIMENTS	T-CELLS (%)		
	CD4+CD28+	CD8+CD28+	CD4+CD25+
Control	27,49±1,12	15,11±1,66	3,77±0,42
Comparative	27,55±2,32	12,32±0,93	4,16±0,89
Basic	46,93±3,91*/**	15,16±1,28**	7,98±0,39*/**

*p<0.05 is a significant value to the control series of experiments
**p<0.05 is a significant value to the comparative series of experiments

As shown in Table 1, we noted significant values for all parameters in the animals of the main group both in comparison with the control and in comparison with the comparison groups (p<0.05).

The total amount of T-cells studied among the animals of the control group was 46.37%. At the same time, in the animals of the comparison group, it decreased to 44.03%, and in the animals on the 20th day of modelling the uncomplicated form of hydatidosis echinococcal cysts of the liver, there was an increase in the total number of studied T-cells by 1.5 times compared to the control group and by 1.6 times compared to the comparative group of experiments.

Throughout the study, $CD4^+CD28^+$ T-cells were the overall leader (63.54% on average), while $CD4^+CD25^+$ T-cells had the lowest number (9.91% on average).

Dynamic growth of the studied T-cells was noted to $CD4^+CD28^+$ (59.28% to 66.98%) and to $CD4^+CD25^+$ (from 8.13% to 11.39%). As for the dynamics of $CD8^+CD28^+$ T-cells, it should be noted that there was a relative decline (from 32.59% to 21.64%) in the proportion of participation in immune processes.

On day 40 of the simulation of hydatidosis echinococcosis of the liver without purulent-septic complications, changes in the number of studied T-cells were tendentious compared to the previous period of experiments (Table 2).

The total number of T-cells studied increased both in comparison with the control series of experiments (by 2.1 times) and to the comparative series of experiments (by 2.2 times). This significantly exceeded the changes compared to the previous period of the pathological period.

Table 2

The Nature of the Changes in the Studied T-Cells on the 40-Day Simulation of Hydatid Echinococcosis of the Liver Uncomplicated by the Purulent-Septic Process

SERIES OF EXPERIMENTS	T-CELLS (%)		
	CD4+CD28+	CD8+CD28+	CD4+CD25+
Control	28,18±1,55	15,72±1,41	3,95±0,35
Comparative	27,93±2,61	11,98±1,02	5,22±0,13*
Basic	54,85±4,17*/**	16,73±1,42**	27,94±1,15*/**

*p<0.05 is a significant value to the control series of experiments
**p<0.05 is a significant value to the comparative series of experiments

The peak percentages of $CD4^+CD28^+$ T-cell levels were in the animals of the comparison group (61.89%).

To $CD8^+CD28^+$, the leading value can be noted in the animals of the control group (32.85%). In the dynamics of the development of the pathological process, this indicator had a dynamics of decrease in general by 1.95 times.

As for the dynamics of changes in $CD4^+CD25^+$ T-cells, we can unequivocally note their gradual growth between intact animals and rabbits of the comparison group (1.4 times), and a leap in growth in the main series of experiments, both to the control series and to the comparative series (3.4 and 2.4 times, respectively; p<0.05).

On the 80th day of hydatidosis echinococcal liver cyst modelling, the total value of the studied T-cells was differentiated both to the control (2.12-fold) and comparative groups (2.24-fold). Although the total difference between the intact animals and the group with a false operation (comparative) was insignificant (p>0.05), nevertheless, their total value was still lower than in the animals of the main group (Table 3).

The average content of T-cells in peripheral blood in all animals studied at that time was equal to 64.68%. $CD4^+$ and $CD28^+$ T-cells prevailed (57.62%). The mean $CD8^+CD28^+$ T-cell count was 23.48% and the $CD4^+CD25^+$ T-cell count was 18.99%.

The basic $CD4^+CD25^+$ T-cell count in the control and comparison groups was 9.23%, while the increase in these cells in animals with hydatidosis echinococcosis was 3.01-fold higher (p<0.05).

Table 3

The Nature of Changes in the Studied T-Cells on the 80-Day Simulation of Hydatidosis Echinococcosis of the Liver Uncomplicated by a Purulent-Septic Process

SERIES OF EXPERIMENTS	T-CELLS (%)		
	CD4+CD28+	CD8+CD28+	CD4+CD25+
Control	27,98±3,11	15,81±1,12	3,99±0,61
Comparative	28,02±3,83	12,55±2,14*	4,56±0,36
Basic	55,82±5,42*/**	17,21±2,64*/**	28,11±2,32*/**

*p<0.05 is a significant value to the control series of experiments

**p<0.05 is a significant value to the comparative series of experiments

The reverse dynamics of the percentage of T-cells was noted to $CD8^+CD28^+$, the decrease of which was critical in animals with an experimental model of the pathological process by 1.94-fold (p<0.05). Meanwhile, in absolute abundance, there is a wave-like change in the number of cells studied.

The overall picture of the dynamics of changes in the number of studied T-cells showed significant shifts to $CD8^+$, $CD28^+$ and $CD4^+$, $CD25^+$.

Thus, an absolute and significant increase in $CD4^+CD28^+$ was noted at all stages of the modelling of hydatidosis echinococcosis of the liver (p<0.05). An increase in the number of $CD4^+CD25^+$ was noted in the late stages of the modelling of the pathological process. At the same time, against this background, there was a decrease in the number of $CD8^+CD28^+$, which indicates differentiated changes in the mononuclear cells of peripheral blood themselves.

A comparative study of the dynamics of changes in the content of T-cells in the process of modelling hydatidosis echinococcosis of the liver, complicated by a purulent-septic process, showed an ambiguous picture (Table 4).

The average total number of T cells studied in all animals was 72.33%. The peak level was observed in animals with an experimental model of hydatidosis echinococcosis of the liver, not complicated by a purulent-septic process.

As can be seen from the table, on the 3rd day of modelling hydatidosis echinococcosis of the liver, complicated by the purulent-septic process, there is an increase in T-cell populations of $CD8^+CD28^+$, against the background of a decrease in other studied parameters. However, it is interesting to note the comparative level of change, which is characterized by high differential values relative to intact animals. In other words, the addition of the purulent-septic process shifted the balance of the significance of the bacterial infection over the parasitic one.

Table 4

The Nature of Changes in the Studied T-Cells on the 3-Day Simulation of Hydatidosis Echinococcosis of the Liver Complicated by a Purulent-Septic Process

SERIES OF EXPERIMENTS	T-CELLS (%)		
	CD4+CD28+	CD8+CD28+	CD4+CD25+
Control	27,91±4,16	15,11±1,55	3,78±0,23
Comparative	26,99±4,12	11,93±3,16*	5,12±0,17
Basic	53,49±4,12*/**	17,96±3,11*/**	25,87±1,87*/**

*p<0.05 is a significant value for the control series of experiments

**p<0.05 is a significant value to the comparative series of experiments

Evidence of the above reasoning can be found in the data of T-cell values in animals with an experimental model of hydatidosis echinococcosis of the liver, complicated by a purulent-septic process for subsequent periods of experiments (Table 5).

Table 5

Nature of changes in the studied T-cells on the 7-day simulation of hydatidosis echinococcosis of the liver, complicated by a purulent-septic process

SERIES OF EXPERIMENTS	T-CELLS (%)		
	CD4+CD28+	CD8+CD28+	CD4+CD25+
Control	28,01±2,24	15,14±1,72	3,99±0,12
Comparative	27,34±3,18	11,58±3,88*	5,07±0,23
Basic	52,17±5,62*/**	18,32±2,15*/**	24,62±1,51*/**

*p<0.05 is a significant value about the control series of experiments

**p<0.05 is a significant value about the comparative series of experiments

The mean percentage of T-cells was between $CD8^+CD28^+$ and $CD4^+CD25^+$. This balance was as close as possible in animals with a complicated form of the disease, while in animals with an uncomplicated form, the digital interval was significantly higher (p<0.05).

In modelling the purulent-septic complication of hydatidosis echinococcosis of the liver against the background of a decrease in the specific gravity of $CD4^+CD28^+/CD4^+CD25^+$, an increase in the number of $CD8^+CD28^+$ T-cells (by 2.24%) was noted.

On the 14th day of modelling hydatidosis echinococcosis of the liver, complicated by a purulent-septic process, the trend of changes was maintained, manifesting itself identically compared to the previous period of experiments (Table 6).

Table 6

The Nature of Changes in the Studied T-Cells on the 14-Day Simulation of Hydatidosis Echinococcosis of the Liver Complicated by a Purulent-Septic Process

SERIES OF EXPERIMENTS	T-CELLS (%)		
	CD4+CD28+	CD8+CD28+	CD4+CD25+
Control	28,56±2,16	14,99±2,12	3,56±0,51
Comparative	28,14±3,12	11,13±2,43*	5,01±0,61
Basic	48,16±6,42*/**	18,91±2,35*/**	23,91±1,42*/**

*p<0.05 is a significant value for the control series of experiments

**p<0.05 is a significant value about the comparative series of experiments

The balance of the percentage of $CD4^+CD28^+$ T-cells in the control and comparison groups varied between 60.62% and 63.55%. In the simulation of hydatidosis echinococcosis of the liver, this indicator decreased, continuing its pattern of change in the future with the addition of purulent infection. The balance of the percentage levels of these cells ranged between 52.93% and 55.19%.

At the same time, the balance of the percentage of $CD8^+CD28^+$ T-cells in the control and comparison groups varied between 31.82% and 25.14%. In the simulation of hydatidosis echinococcosis of the liver, this indicator decreased, but the nature of the change in the future with the addition of purulent infection acquired the opposite direction. The balance of the percentage levels of these cells ranged between 17.02% and 20.78%.

Ultimately, the balance of $CD4^+CD25^+$ Tcell percentages in control and comparison animals varied between 7.56% and 11.31%. In the simulation of hydatidosis echinococcosis of the liver, this indicator increased to 27.79%, but with the addition of purulent infection, a decrease in the percentage of T-cells to 26.28% was revealed.

At this level, the general dynamics of T-cell changes in animals with an experimental model of hydatidosis echinococcosis of the liver, complicated by a purulent-septic process, had an identical picture to the previous variant of the pathological process.

The pronounced difference in the percentage level of $CD4^+CD25^+$ and $CD8^+CD28^+$ T-cells, which occurred in animals with hydatidosis echinococcosis of the liver in the case of the addition of a bacterial infection on the 7th-14th day of the disease, progressively decreases. This, in turn, indicates the dependence of the sensitivity of cellular immune dependence not only on parasitic infection, but also on bacterial infection.

When analyzing the dynamics of changes in cellular immunity among intact animals, it was not possible to identify a particular pattern in the correlation between the indicators. The maximum positive correlation was found for $CD4^+CD25^+$ and $CD8^+CD28^+$ (R=0.503). $CD4^+CD28^+$ and $CD8^+CD28^+$ (R=0.242) had a very weak direct correlation. $CD4^+CD25^+$ and $CD4^+CD28^+$ (R=0.242) had a low inverse relationship. All this testified to the low error in the statistical data and the identical nature of changes in intact animals during the 80-day period of dynamic housing in the standard regime.

In the spurious modeling of hydatidosis echinococcosis of the liver, an increase in the correlation in the opposite direction (R=-0.869) was noted among the $CD8^+CD28^+$ and $CD4^+CD28^+$ parameters.

The ratio of $CD4^+CD25^+$ to the rest of the studied T-cells was ambiguous, namely, if in the case of $CD4^+CD28^+$ it was characterized by a weak direct correlation (R=0.456), then in relation to $CD4^+CD25^+$ it was already an inverse correlation (R=-0.487). Apparently, these changes were associated with the peculiarity of the immunological reaction of the organism to the reproduction of a false model of the pathological process of the same name.

When a bacterial infection was introduced in the case of reproduction of a false model with a purulent-septic complication, the correlation of the studied indicators changed, and in some cases in a radical direction. For example, the inverse correlation between CD8+CD28+ and $CD4^+CD28^+$ (R=-0.919) continued to grow. $CD4^+CD25^+$ and $CD4^+CD28^+$ (R=-0.989) are inversely correlated and are approaching their maximum value. This characterizes the body's immune response to the arrival of a non-specific bacterial infection. A proof of our judgment can be found in the value of the correlation between $CD4^+CD25^+$ and $CD8^+CD28^+$ (R=0.871), which goes from a low inverse correlation to a high direct relationship.

Thus, the modelling of two variants of false pathological processes, differing only in the impact of a non-specific bacterial infection, leads to a radical change in the correlation dependence both about intact animals and to animals without the introduction of an infectious principle. The body's immune response to a trivial infection activates cellular immunity throughout the study.

When modelling hydatidosis echinococcosis of the liver without purulent-septic complications, the correlation value of all indicators acquires an absolute direct dependence. Under conditions of chronic inflammation, T-cells acquire an expressive character in dynamics, strengthening their immune response.

The high correlation significance of cellular immunity was determined by the high direct relationship between all studied populations of T-cells.

Maximum significance (R=0.996) was noted between $CD4^+CD25^+$ and $CD4^+CD28^+$ changes. The correlation between the dynamics of $CD8^+CD28^+$ and $CD4^+CD28^+$ was almost at the same level (R=0.992).

And the ratio of $CD4^+CD25^+$ and $CD8^+CD28^+$ indicators was distinguished by a relatively low, but again direct correlation. Their correlation value was R=0.976.

Thus, the reproduction of the experimental model of hydatidosis echinococcosis of the liver leads to differentiated expression of lymphocyte subpopulations, transforming the body's protective response into a kind of immune response, which was characterized by the activity of T-cells to organize the process and form a protective layer. However, this response of the organism under the influence of a secondary, non-specific bacterial infection changed its nature of the immune trace, which can be traced in the following analysis.

In all the studied cases, the correlation value was reflected by a high significance, characterizing the identity of the trend of immunological processes in the population of T-lymphocytes. Inverse correlations prevailed. $CD8^+CD28^+$ and $CD4^+CD28^+$ (R=-0.990) and $CD4^+CD25^+$ and $CD8^+CD28^+$ (R=-0.956) had the highest level.

Meanwhile, the correlation between $CD4^+CD25^+$ and $CD4^+CD28^+$ was characterized by a direct relationship (R=0.904). It should be noted that in the simulation of hydatidosis echinococcosis of the liver, which was not complicated by a purulent-septic process, the correlation of this parameter was identical.

Thus, the aggravation of the pathological process in the form of the addition of a purulent-septic complication of hydatidosis echinococcosis of the liver led to the development of both parallel and reverse processes in the expression of T-lymphocytes, enhancing the immunological response against the background of high sensitization of the body. This, in turn, leads to the restructuring of the immunological reaction of the macroorganism and contributes to the emergence of a load on the entire cell population of T-lymphocytes under study.

DISCUSSION

A specific immune cellular response, as usual, initiates an association of the body's extracellular defence mechanisms. It is this relationship that is determined by the functional capacity of the receptor molecules of the immune response.

The characteristic phenotypic features of leukocytes, namely their differentiation and the creation of conditions for their activation, are the surface molecules of white blood cells under normal conditions [9].

As you know, echinococcosis of the liver develops for a long time. The disease can be asymptomatic in the event of the death of the parasite and the development of calcification, as a result of regression of daughter cells. This can be considered an immunocompetent process that can be used to diagnose the progression or regression of echinococcosis of the liver.

Based on the multivariate analysis, we proved that in the conditions of progression of hydatidosis echinococcosis of the liver, the dominant role is played by the dominance of T-cells of the immune response, in particular, the Th_2 response of the body [8].

According to the results of experimental studies, in the dynamics of the development of hydatidosis echinococcosis of the liver, an increase in $CD4^+CD28^+$ and $CD4^+CD25^+$ was noted. A weakening T-cell response and expansion of regulatory T cells was observed by us about $CD8^+CD28^+$. The addition of the purulent-septic process leads to the stimulation of these cells and their growth in the blood. Such changes may have been due to the lack of a stage of transformation of the parasite into a daughter cell, which is possible that in a clinical setting, they would have been initially suppressive. Nevertheless, it is the balance of the developing T-cell response against the background of the spread of parasitic infection that can determine the outcome of the disease itself. The long-term course of the disease was characterized by the expression of receptors associated with a decrease in induced T-cell responses.

Because $CD25^+$ is induced on both Th_1 and Th_2 helper cells and is also present in other effector cell populations, e.g., activated B cells, dendritic cells, and monocytes, detailed studies should include high or low levels of $CD25^+$ expression along with intracellular cytokine profiling to confirm these findings.

Baseline $CD25^+$ receptor expression on $CD4^+$ cells was increased in peripheral blood mononuclear cells in animals with echinococcosis. The progression of the ex-

perimental model further increased $CD25^+$ expression in T-cells.

However, a likely explanation for the higher $CD25^+$ frequency is more "activated" $CD4^+$ cells – as seen for $CD28^+$ [7].

The higher number of activated $CD4^+CD28^+$ T-cells in animals with hydatidosis echinococcosis suggests that activated $CD4^+$ cells may be present around and inside periparasitic granulomas.

CONCLUSION

Reproduction of the experimental model of hydatidosis echinococcosis of the liver leads to differential expression of subpopulations of T-lymphocytes, transforming the body's protective response into a kind of immune response, which was characterized by the activity of T-cells to organize the process and form a protective layer. However, this response of the organism under the influence of a secondary, non-specific bacterial infection changed the nature of the immune trace. Translation of the body's immunological response to the Th_1 cell type of response should be a priority in the correction of the disorders that occur.

Conflict of Interest – None

Funding – None

Ethical Issues – The planned experimental research was based on the principle of the conditions specified in the Council of Europe Convention for the Protection of Animals of 1986.

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JIGARNING ASORATLANGAN VA ASORATLANMAGAN GIDATIDOZ ECHINOKKOZINI EKSPERIMENTAL MODELLASHTIRISHDA XUJAYRAVIY IMMUN REAKTSIYASI

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ABSTRAKT

Dolzarbligi. Kasallikning patomorfologik ko'rinishlarining o'ziga xos xususiyatlari tufayli ichki organlarning echinokokokkozi kasalligi tarqalishiga moyil bo'lgan o'ziga xos kistalarni tashkil etish shaklida ijtimoiy soha uchun juda qimmat hisoblanadi. Ushbu kasallik ko'pincha ish yoshidagi odamlarga ta'sir qilishini hisobga olsak, nogironlik sonining ko'payishida, davolanishning yo'qligida, o'limning ko'payishida ham namoyon bo'ladi.

Material va usullar. Eksperimental materialning asosi Chinchilla zotining quyonlaridan iborat edi. Xujayraviy immunitetini miqdoriy aniqlash CD-differentsiatsiyalangan va faollashtirish ifodasi bilan baholandi. Immunitetning quyidagi xujayralari aniqlandi: $CD4+CD28^+$, $CD8^+CD28^+$, $CD4^+CD25^+$. CD retseptor ifodasi Sorbent MChJ (Rossiya) tomonidan ishlab chiqarilgan LT seriyali monoklonal antikorlar yordamida rozet shakllanishi reaktsiyasida amalga oshirildi.

Natijalar. $CD4^+CD28^+$ ning mutlaq va sezilarli ko'tarilishi jigarning gidatidoz echinokkozini modellashtirishning barcha bosqichlarida qayd etildi ($p<0,05$). Patologik jarayonni modellashtirishning so'nggi bosqichlarida $CD4^+CD25^+$ sonining ko'payishi qayd etildi. Shu bilan birga, bu fonga nisbatan $CD8^+CD28^+$ soni kamaygan bo'lib, bu periferik qonning mononuklear hujayralaridagi farqlangan o'zgarishlarni o'zlari ko'rsatadi.

Xulosa. Jigarning gidratidoz echinokokkozi eksperimental modelining chaqirishda limfotsit subpopulatsiyalarining differentsial ifodalanishiga olib keladi, bu esa organizmning himoya reaktsiyasini immun reaktsiyasiga aylantiradi, bu jarayonni tashkil etish va himoya qatlamini hosil qilish uchun T-hujayralarning faoliyati bilan tavsiflanadi. Biroq, ikkilamchi, aniq bo'lmagan bakterial infeksiya ta'sirida organizmning bu javobi immun izining mohiyatini o'zgartirdi. Quyidagi tahlilda izdan chiqishi mumkin.

Tayanch iboralar: Jigarning gidatidoz echinokokkozi, hujayra immuniteti, periferik qon mononuklear hujayralari

КЛЕТОЧНЫЙ ИММУННЫЙ ОТВЕТ ПРИ ЭКСПЕРИМЕНТАЛЬНОМ ОСЛОЖНЕННОМ И НЕ ОСЛОЖНЕННОМ ГИДАТИДОЗНОМ ЭХИНОКОККОЗЕ ПЕЧЕНИ

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АБСТРАКТ

Актуальность. Заболеваемость эхинококкозом внутренних органов, в силу особенностей патоморфологических проявлений заболевания, в виде организации специфических кист, склонных к диссеминации, считается весьма затратным для социальной сферы. Учитывая, что наиболее часто данное заболевание поражает лица трудоспособного возраста.

Материал и методы. Основу экспериментального материала составили кролики породы Шиншилла. Количественное определение показателей клеточного иммунитета оценивали по экспрессии антигенов CD-дифференцированных и активационных. Определяли следующие маркеры иммунокомпетентных клеток: $CD4^+CD28^+$, $CD8^+CD28^+$, $CD4^+CD25^+$. Экспрессию рецепторов CD проводили в реакции розеткообразования.

Результаты. Абсолютное и достоверное повышение $CD4^+CD28^+$ отмечено во все сроки моделирования гидатидозного эхинококкоза печени ($p<0,05$). Рост количества $CD4^+CD25^+$ был отмечен в поздние сроки моделирования патологического процесса. В то же время на этом фоне имело место снижения количества $CD8^+CD28^+$, что свидетельствует о дифференцированных изменениях.

Заключение. Воспроизведение экспериментальной модели гидатидозного эхинококкоза печени приводит к дифференцированной экспрессии субпопуляций лимфоцитов, преобразуя защитную реакцию организма в своеобразный иммунный ответ, который характеризовался активностью Т-клеток для организации процесса и формирования защитного слоя. Однако данная ответная реакция организма под действием вторичной, неспецифической бактериальной инфекции изменяла свой характер.

Ключевые слова: Гидатидозный эхинококкоз печени, клеточный иммунитет, мононуклеарные клетки периферической крови