КЛІНІЧНА МЕДИЦИНА

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DYNAMICS OF INDICATORS IN THE CELL-MEDIATED AND HUMORAL LINKS OF THE IMMUNE SYSTEM IN PATIENTS WITH THYROID CANCER*

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This work is a fragment of research projects of Kharkiv Medical Academy of Postgraduate Education: "Cellular-molecular mechanisms of inflammation associated with chronic diseases", the state registration number 015U001186, and "Pathochemical mechani sms of action of radioiodine on the organism and principles of their early diagnosis and correction", state registration number 0117U000589.

This paper studied cell-mediated and humoral immunity in patients with thyroid cancer (TC) in terms of evaluation of specific and non-specific immunological resistance of the organism. Non-specific immunological resistance of the body was studied on the basis of determining the phagocytic activity of neutrophils, indices of white and red blood cells. Analysis of the study allows us to judge that under the conditions of oncopathology of the thyroid gland, there is a suppression of the cellular link of the immune system (macrophages, monocytes, histiocytes, T-lymphocytes, dendritic cells) and intercellular mediator interactions that are associated with a decrease in the activity of humoral immune system, which was confirmed by a significant drop in the level of B-lymphocytes and immunoglobulins (JgG, Jg M, JgA). The results of the research revealed the inhibition of non-specific resistance of the body in patients with thyroid cancer, depending on the cellular structure of the tumor, which was characterized by a decrease in phagocytic activity of neutrophils. These changes took place against the background of the development of endogenous intoxication, pathogenic links of erythropoesis and methemoglobinemia.

Keywords: cell-mediated and humoral immunity, immunological resistance, thyroid cancer

В роботі вивчали клітинний і гуморальний імунітет у хворих на рак щитоподібної залози за показниками оцінки специфічної і неспецифічної імунологічної резистентності організму. Неспецифічна імунологічна резистентність організму була вивчена на основі визначення фагоцитарної активності нейтрофілів, показників білої та червоної крові. Аналіз дослідження дозволяє судити про те, що в умовах онкопатології щитовидної залози відбувається пригнічення клітинної ланки імунної системи (макрофаги, моноцити, гістіоцити, Т-лімфоцити, дендритні клітини) та міжклітинних медіаторних взаємодій, які пов'язані зі зниженням активності гуморальної імунної системи, що підтверджувалося значним зниженням рівня В-лімфоцитів та імуноглобулінів (JgG, JgM, JgA). Результати досліджень виявили пригнічення неспецифічної резистентності організму у хворих на рак щитоподібної залози в залежності від клітинної будови пухлини, які характеризувалися зниженням фагоцитарної активності нейтрофілів. Ці зміни відбувались на тлі розвитку ендогенної інтоксикації, патогенетичної ланки еритропоезу і метгемоглобінемії.

Ключові слова: клітинний і гуморальний імунітет, імунологічна резистентність, рак щитоподібної залози

It is known that the physiologic function of the immune system is the protection of the body from bacteria, viruses, fungi, parasitic infections and substances bearing signs of genetically-foreign information [1, 2, 3, 4]. These processes provide support for the cellular composition of the lymphoid organs and the change in the immunocompetence of lymphocytes, according to the antigens that enter the body [5, 6, 7].

The aim of the research was to study the nonspecific and specific immunological resistance in patients with thyroid cancer.

Materials and methods

We observed 94 patients who were diagnosed with thyroid cancer. We used the classification of the tumor cell structure applied to assess the aggressiveness and rate of growth [8, 9]. According to this classification, patients were divided into 3 groups: group I included 41 patients with papillary adenocarcinoma; group II – 32 patients with follicular adenocarcinoma; group III consisted of 21 patients, diagnosed with low-differentiated thyroid cancer. The comparison group consisted of 27 patients without pathology of the thyroid gland and without a history of oncological disease. The thyroid gland cancer diagnosis was verified according to histological analysis.

The research program envisaged the study of cellular and humoral immunity in patients with thyroid cancer (thyroid gland cancer) according to indicators of evaluation of specific and non-specific immunological resistance of the organism. Non-specific immunological resistance

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of the organism was studied on the basis of the determination of phagocytic activity of neutrophils, indices of white and red blood.

In all examined patients, the total number of red blood cells, leukocytes, hemoglobin content, methemoglobin, and phagocytic activity of neutrophils were determined. All studies were conducted on the first or second day of hospitalization, after which patients received immunomodulatory antioxidant, anti-toxic therapy, for a period of three weeks.

Natural non-specific immunobiological resistance of the body of patients with thyroid gland was studied using the activity of phagocytic cells [10, 11].

The study of general population of T lymphocytes (CD3+), the subpopulation of T lymphocytes – T-helpers (CD4), T-suppressor (CD8) and B-lymphocyte (CD19) in serum was carried out using monoclonal antibodies CD3+, CD4, CD8, CD19, TNF-α by immunofluorescence method on the immune enzyme analyzer STAT-FAX303, USA.

The content of immunoglobulins A, M, G (IgA, IgM, IgG) and total immunoglobulin E (IgE) in blood serum was investigated using Sigma Inc. USA. Immune enzyme test systems and the content of allergen specific IgE were tested using immune enzyme test systems of "Sigma Inc." USA.

Statistical analysis of the results was carried out using a computer software package for processing statistical information Statistica 6.1 (StatSoft,Inc., USA).

Results and discussion

The study of the dynamics of white and red blood parameters in patients with TC showed a significant decrease in the content of erythrocytes in the group I with papillary adenocarcinoma by 7.1%, in the II group with follicular adenocarcinoma – by 23% and in patients with low-differentiation of thyroid cancer by – 30.5%. The obtained results had a direct correlation with the decrease in hemoglobin in all studied groups. There is a significant increase in the level of methemoglobin, depending on the cellular structure of the tumor, which is the pathogenic link of inhibition of erythropoesis in thyroid cancer, and this may be due to increased autointoxication, changes in the structure of macromolecules and violations of tissue respiration. As a result of our research, we established reliable ($p<0.05$) reduction of leukocytes in group II, which finds its confirmation in the hypothesis that non-nuclear cells (erythrocytes), in which significantly reduced reparative and restorative syntheses, are sensitive in the conditions of development of oncopathology.

As a result of the study in all groups of patients there was a significant ($p\leq0.05$) decrease in phagocyte count, absorption index and digestive index of microbes. The absorption and staphylococcal digestion of one active neutrophil were reduced, and there was a direct correlation with the cellular structure of the tumor.

The obtained results of the study indicate that in case of thyroid cancer, there is inhibition of the cellular immunity level, the severity of which is associated with autointoxication of the body and histological characteristics of the tumor (Fig. 1).

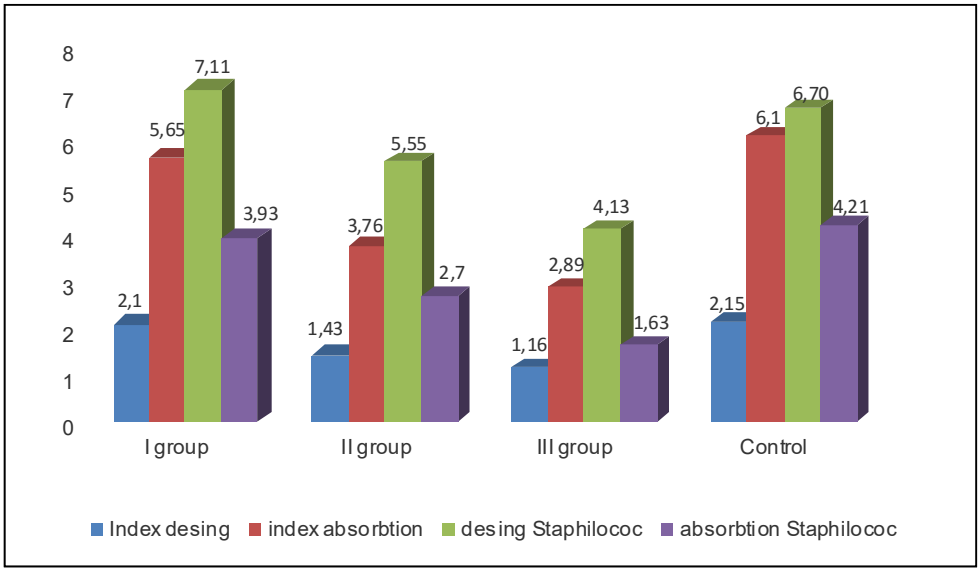

Fig. 1. Phagocytic activity of neutrophils of patients with thyroid cancer.

At the next stage, we examined the nonspecific and specific immunological resistance in patients with thyroid cancer, depending on the type of tumor (Table 1).

The data obtained in Table 1 show that the study of the status of cellular and humoral immunity did not reveal any significant changes in papillary adenocarcinoma of changes in T-lymphocytes (CD 3+), T-helpers (CD4), T-suppressor (CD8), B-lymphocytes (CD19) and immunoglobulins – JgG, JgM. However, a significant ($p\leq0.05$) difference was found in the reduction of natural killers (CD16). A correlation between CD16 and TNF-α, JgA, which increased by 15.5% and 12.8% respectively, was also established.

Table 1

Indicators of cell-mediated and humoral immunity in patients with thyroid cancer depending on the type of tumor

Indexes (pkg/ml)	Patients with thyroid cancer			Comparison group (n=27)
	papillary adenocarcinoma (n=41)	follicular adenocarcinoma (n=32)	low-differentiation cancer (n=21)	
T- lymphocytes (CD3+)	888.1±29.9	772.5±41.8*	558.1±25.5*	928.4±26.3
T- helpers (CD4)	311.5±16.2	230.3±12.5*	170.4±8.7*	330.20±12.6
T- suppressor (CD8)	284.4±19.0	254.1±9.1*	161.2±7.7*	295.6±18.2
T- killers (CD16)	238.6±13.7*	179.6±8.6*	134.5±7.1*	275.3±14.3
B-lymphocytes (CD19)	226.8±14.5	187.5±10.2*	160.5±6.5	232.6±19.8
TNF-α	277.3±15.7*	237.5±12.5*	186.7±16.8*	354.2±21.7
JgM	53.5±3.2	45.2±2.5*	37.3±1.5*	54.3±4.5
JgG	44.6±4.0	37.1±2.6*	26.5±2.2*	46.7±3.4
JgA	43.8±3.1*	61.5±5.0*	27.3±1.9*	37.9±2.8

*Note: * probability is reliable P<0.05*

In patients with papillary adenocarcinoma, a significant (p≤0.05) decrease in the levels of the studied parameters, secretory immunoglobulin JgA, which increased to 43.8 ± 3.1 pkg /ml was observed as opposed to the data of the comparison group of patients.

Significant inhibition of cellular and humoral immunity was observed in follicular adenocarcinoma in II group, thus, the total number of T-lymphocytes was reduced by 1.7 times, T-helper cells, T-suppressors, T-killers more than 2 times, B-lymphocytes – by 1.5 times. The tumor necrosis factor (TNF-α) was reduced by 2.5 times in the serum of patients with this stage, and immunoglobulins (JgG, JgM, JgA) more than by 1.5 times.

Analysis of the study in the dynamics of these indicators allows us to judge that under the conditions of oncopathy of the thyroid gland, there is a suppression of the cellular link of the immune system (macrophages, monocytes, histiocytes, T-lymphocytes, dendritic cells) and intercellular mediator interactions that are associated with a decrease in the activity of the humoral immune system, which was confirmed by a significant drop in the level of B-lymphocytes and immunoglobulins (JgG, JgM, JgA).

Conclusions. Thus, the results of the research revealed the inhibition of non-specific resistance of the body in patients with thyroid cancer, depending on the cellular structure of the tumor, which was characterized by a decrease in phagocytic activity of neutrophils. These changes took place against the background of the development of endogenous intoxication, pathogenetic links of erythropoesis and methemoglobinemia. The dynamics of these indicators was closely related to the formation of immunological insufficiency of the cellular and humoral link of the immune system, which requires antioxidant, antitoxic and immunological correction in the implementation of pathogenetic therapy for patients with thyroid cancer.

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