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IMMUNE STATUS IN PATIENTS WITH DERMATOLOGICAL MANIFESTATIONS AFTER CORONAVIRUS INFECTION

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INTRODUCTION

Despite a lot of research being carried out in the field of studying changes in the immunity of COVID-19, this still remains a studied problem. The only question that we would like to find out is whether there is a probable effect of immunological changes on the features of the course of dermatological manifestations after coronavirus infection. To solve this problem, we studied the state of humoral immunity, immunoreactivity and cytokine activity of the patient's body.

MATERIALS AND METHODS

To study the features of the course of dermatological manifestations in patients, we identified and studied skin manifestations after a coronavirus infection. After the start of the pandemic, we identified, described and followed up 108 patients, after suffering from COVID-19 infection, in whom skin changes were observed.

Some of the patients, for 1 to 20 years, previously suffered from various skin diseases, and were under dispensary supervision, the rest came to us with complaints of skin changes after infection (Table 1).

Table 1: Characteristics of patients included in the study depending on primary or secondary skin pathology.

№	Dermatological changes before COVID-19	Number of patients
1.	Psoriasis	15
2.	Vitiligo	12
3.	Other skin pathologies	20
4.	Previously intact skin	61
	Total	108

As we can see from the data in the table, initially, the vast majority of our patients with dermatological pathology suffered from vitiligo and psoriasis. The rest of the dermatological patients were previously diagnosed with neurodermatitis, eczema, pemphigus, shingles, atopic dermatitis, dyschromia, allergic dermatitis, infiltrative trichophytosis, rosacea, erythroderma, pityriasis versicolor, acne, toxicoderma, allopectival erythritis, excreta.

After infection with a coronavirus infection, the appearance of changes in the skin was noted at different periods of the disease (Table 2).

Table 2: Distribution of patients infected with COVID-19, depending on the timing of the appearance of skin changes.

№	Onset of skin manifestations of infection	Number of patients
1.	Before clinical manifestation of COVID-19	11 (10,2%)
2.	At the time of clinical manifestation of COVID-19	68 (62,9%)
3.	After recovering from COVID-19	29 (26,9%)
	Total	108

In 11 (10.2%) patients, 2-7 (3.1 ± 1.1 days) days before the appearance of other signs of coronavirus infection (fever, cough, shortness of breath, etc.), various skin changes appeared. In the vast majority of cases (62.9%), the skin manifestations of COVID-19 coincided with the clinical manifestation of the disease. In some patients (26.9%), after clinical recovery in the period from 1 to 11 days (3.6 ± 1.8 days), various skin changes appeared. As the study of the new coronavirus infection, it became known that the sex and age of patients has an important prognostic value. (Table 3).

Table 3: Distribution of patients included in the study depending on gender and age.

№	Age of patients	Number of patients		Total
		male	female	
1.	until 20	2	-	2
2.	21-30	5	1	6
3.	31-40	13	6	19
4.	41-50	18	9	27
5.	51-60	16	13	29
6.	Older 60	18	7	25
	Total	72	36	108

As can be seen from the data presented in the table, the most frequent cases of the disease were men over the age of 40 (58.5 ± 8.7). Frequent illness in men is associated with the biological characteristics of the male body. The average age of all patients was 54.2 ± 12.3.

As you know, the organisms of men and women react differently to a stress agent. If in women stress (an infection) causes an increase in cellular immunity, a decrease in metabolism, a decrease in pulse rate and a decrease in tidal volume, in men with suppression of cellular immunity, increased erythropoiesis, thrombocytopoiesis, an increase in tidal volume, an increase in pulse rate. Thus, under severe stress, the male body prepares for heavy physical exertion and possible blood loss (reaction of the "warrior"), the female body prepares for a long siege and passive survival.

It was important for us the appearance of new elements of the rash on the skin, their intensity, localization, degree of spread, depending on the severity of the course of the coronavirus infection. In this connection, we carried out a correlation between the severity of the course of the infection and the skin manifestations after the previous illness. For this, the patients included in the study were ranked, depending on the severity of the course of coronavirus infection and gender, into five groups (Table 4).

Table 4: Distribution of patients included in the study depending on the severity of the course of coronavirus infection.

№	The severity of the infection	Number of patients		Total
		male	female	
1.	Extremely heavy	3	-	3
2.	Heavy	18	3	21
3.	Medium severity	26	49	75
4.	Light flow	15	29	44
5.	Only cutaneous manifestations	10	9	19
	Total	72	36	108

A severe and extremely severe course was more often observed in men, since high levels of male testosterone are a prognostically unfavorable sign. In this category of patients, the disease was accompanied by severe respiratory distress syndrome, in 1 patient with oliguria. In 19 patients, the disease manifested itself with skin manifestations and the presence of coronavirus infection was established during the examination process based on PCR and ELISA studies. In 44 patients, the disease was mild with a subfebrile rise in temperature and signs of a mild cold.

As is already known, coronavirus infection causes a "cytokine storm", which is characterized by abrupt changes in both basic immune agents (cellular and humoral) and accompanied by a pathological excess of interleukins. An immunological component is involved in the development of a large group of skin diseases, the role of which is not fully understood. This group includes various forms of vasculitis, lichen planus, scleroderma, dermatomyositis, etc.

Adrenaline and norepinephrine exert a pressor effect on the vessels, which affects the state of tissue metabolism. Excitation of various adrenergic receptors due to impaired production of catecholamines as a result of viral damage, disrupting certain structures of the autonomic nervous system, can also lead to skin changes. An important role in the skin manifestations of the infection is also played by the violation of hemostasis

observed after the transferred COVID-19 infection. Deep immunoallergic processes can cause damage to the vessels of the skin, as a result of which hemorrhagic and hemorrhagic ulcerative rashes appear.

The depth of changes in physiological systems is indirectly evidenced by the duration of the disease (recovery). We studied the duration of the clinical course of coronavirus infection (Table 5).

Table 5: Distribution of patients included in the study depending on the severity of the course of coronavirus infection.

№	The severity of the infection	Number of patients	ays
1.	Extremely heavy	3	36,4
2.	Heavy	21	33,3
3.	Medium severity	75	31,4
4.	Light flow	44	29,5
5.	Only cutaneous manifestations	19	33,1

When studying the underlying disease, we took into account not only the nosological form of the disease, but also the area of the lesion and the severity of the disease. The variety of skin diseases, in fact, is due to various combinations of morphological elements of the rash, their specific shape, color, consistency, etc. To determine the degree of risk of coronavirus infection, we studied the skin manifestations of this pathology (Table 6).

Table 6: Distribution of patients included in the study depending on dermatological manifestations during and after coronavirus infection.

№	Dermatological manifestation of infection	Number of cases
1.	Chills (covid fingers)	33 (30,6%)
2.	Papulosquamous eruptions	21 (19,4%)
3.	Hives	13 (12,03%)
4.	Papulo-vesicular eruptions	14 (12,9%)
5.	Herpetic eruptions	17 (15,7%)

RESULTS

We analyzed fractions of immunoglobulins, which are of great practical importance in the diagnosis, treatment and prognosis of cutaneous manifestations after coronavirus infection. As you know, immunoglobulins are produced in response to the intake of foreign agents into the body, such as various antigens - bacteria, viruses, fungi, parasites or various organic substances. We conducted a study of the serum concentrations of the main immunoglobulins IgG, IgA, IgM. Since, one of the indicators of insufficient humoral immunity is a decrease in the level of serum immunoglobulins Ig M, IgG, Ig A.

Table 7: The state of humoral immunity factors in patients with dermatological manifestations of coronavirus infection.

Immunological parameters	Patient with COVID-19	Norma
Ig G	24±3,1	7 - 16 г/л
Ig A	4,1±2,3	0,7 - 4,0 г/л
Ig M	2,6±0,3	0,4 - 2,3 г/л
Ig E	0,27±0,09	0,075-0,3 г/л

Immunoglobulins are represented by 5 types of antibodies (IgA, IgG, IgM, IgE, IgD), which differ from each other in terms of molecular structure and functions. Immunoglobulin Ig G is the main factor in secondary immunity and is the only type of antibody involved in neutralizing toxins. Serum half-life is 23 days. Patients with skin manifestations after suffering a coronavirus infection were admitted to us on average 18 days after the disease. Despite this, Ig G was 50% higher than the upper limit of the norm, which indicates the continuing symptoms of intoxication in these patients.

Ig A provides local antimicrobial protection in various parts of the mucosa. The Ig A index in patients with dermatological manifestations of COVID-19 was 102.5% of the upper limit of normal. Ig M (macroglobulin) - is produced by activated B - cells during the primary immune response to incoming antigens (viruses, bacteria, fungi, etc.). The accumulation of Ig M in the body is a sign of a recent infection or immunization. In our patients, on average 20 days after the onset of the disease, the Ig M index was 13%.

Ig E (reagins or homocytotropic antibodies) - when the Ig E fragments are specifically overlapped by the corresponding antigen, due to the degranulation of cells and the release of specific mediators, an anaphylactic reaction develops. Although the average Ig E in patients

was within the normal range, in most patients with urticaria, the indicator was 20% higher than the upper limit of the normal and reached 0.36 g / l.

Until now, the role of immunoglobulin Ig D has not been fully understood, it is assumed that this immunoglobulin provides immunotolerance. We also studied the immunoreactivity of the body of patients with dermatological manifestations after coronavirus infection. To do this, we studied such indicators as: E-ROK (T-l); M-ROCK (V-l); CD4 + (T-x); CD8 + (T-c); EKK –CD16; CD38; CD95; CD25 (Table 4.10).

Table 8: Indicators of the body's immunoreactivity in patients with dermatological manifestations after coronavirus infection.

Indicators	Patient COVID-19	Norma
E-ROCK	27,4±1,4%	34,6 ±1,92 %
M-ROCK	22,5±0,9%	5-20
CD_4+ (T-x)	24,8±1,5%	40-69
CD_8+ (T-c)	6,0±0,7%	5-20
EKK –CD_{16}	18,6 ±1,1%	18,2±0,8%.
CD_{38}	21,8 ±1,6%	22,0 ±0,9%
CD_{95}	18,7±1,3	20,6 ±0,5%
CD_{25}	18,6 ±0,92%	22,4 ±1,2%

Note: E-ROCK: Erythrocyte - rosette-forming cells, M-ROCK monocyte- rosette-forming cells.

According to most studies, during coronavirus infection, T cell is suppressed and B cell immunity is activated. In our observation, the number of T lymphocytes averaged 27.4%, which was 22.2% lower than normal, and indicated the suppression of T lymphocytes under the influence of coronavirus infection. On the contrary, the number of B lymphocytes increased by 15% from the upper limit of the norm, which indicated the stressful nature of this infection and the disease caused by it.

We cannot answer the question whether these changes are characteristic only for patients with dermatological manifestations after coronavirus infection or are they a general reaction to this virus. We believe that clarification of this issue should be the task of a separate scientific study.

The suppression of T - cell immunity in these patients mainly occurs due to the suppression of T - helpers CD4 + by 35% of the lower limit of the norm.

The main function of T-helpers is to activate an adaptive immune response to an infectious agent. Activate T-killers, B-lymphocytes, monocytes, NK-cells, promotes the release of cytokines. 22 subtype T helpers are involved in the immune response in inflammatory skin diseases. At the same time, the indicators of T - suppressors CD8 + remained within the normal range. Considering that the main function of T - suppressors is to suppress autoimmune reactions, we can assume that the cutaneous manifestations of coronavirus infection are not an autoimmune reaction of the body in response to viral invasion and inflammation.

The main function of NKC (natural killer cells) - CD16 is the destruction (killing) of foreign agents entering the body. The number of these cells indirectly indicates the possible number of antigens (viruses, bacteria, fungi, tumor cells, etc.). In patients with skin manifestations after coronavirus infection, this indicator was 3.6% higher than the upper limit of normal.

CD38 is a compliment receptor. Upon entering the body, the complement is activated, through a cascade of biochemical changes forms a proteolytic enzyme, which is involved in the destruction of pathogens. In the absence of pathogens, the complement is at rest, i.e. the complement system is activated and becomes functionally active on the cell surface of pathogens or foreign bodies. In patients under our supervision, this indicator corresponded to the physiological norm, which indicates the absence of secondary bacterial infection of patients with dermatological changes.

CD95 is a trigger for programmed cell death. In our patients, this indicator turned out to be below normal. When apoptosis is passive (programmed cell death), cells damaged by the pathological process are preserved and remain capable of cloning. It can be assumed that skin cells are damaged under the influence of a viral infection. Damaged cells do not die, and under the influence of yet unknown reasons, it progresses and forms an accumulation of pathological epithelium, thereby forming this or that skin disease.

CD25 is part of the cytokine interleukin - 2 (IL-2). IL-2 co-promotes CD4 + leads to the activation and differentiation of a clone of cytotoxic lymphocytes attacking the cell containing the antigen.

The main function of cytokines is the regulation of intercellular and intersystem interactions. Cytokines in the body are responsible for lifespan and stimulation or suppression of cell growth. Also, cytokines determine differentiation, functional activity and apoptosis, ensure the coherence of the immune, endocrine and nervous systems in a healthy state and a state of pathology.

With coronavirus infection, about 15% of patients have a so-called "cytokine storm". With this reaction, the level of cytokines in the body increases sharply, as a result of which the immune system begins to attack the cells and tissues of its own body. This leads to the destruction of normal tissues and organs, which can be the cause of the death of the body.

Table 9: Analysis of cytokine values in the body of patients with dermatological manifestations after coronavirus infection.

Indicators	Patient with COVID 19	Norma
IL - 1	1,8±0,04	1,61±0,05
IL – 2	9,6±0,72	9,13±0,67
IL– 6	1,0±0,18	0,94±0,13
TNF	5,5±1,18	5,30±1,29

As we can see from the data in the table, the cytokine indicators in patients with dermatological manifestations after coronavirus infection are moderately increased. Each cytokine has its own functional properties.

IL - 1 is the main proinflammatory cytokine. IL - 1 induces the induction of adherent cells. It mediates the immune response to foreign substances, including viruses. As a trigger of the acute phase, it determines prodromal reactions, causes drowsiness, and stimulates stress reactions. In our patients, IL-1 was 10% higher than the upper limit of the norm, which caused the lethargy and anxiety encountered in most patients.

IL - 2, as mentioned above, together with CD4 + leads to the activation and differentiation of a clone of cytotoxic lymphocytes attacking the cell containing the antigen. An increase in this cytokine by 34.7% of the upper limit of the norm indicated a continuing inflammatory response of the body to the invading infection.

IL-6 provides differentiation of B - cells and induces a response in the acute phase of an infectious disease. It has a pro-inflammatory effect and is an endogenous pyrogen and is responsible for the production of antibodies. In patients with dermatological manifestations after coronavirus infection, this cytokine was 10.3% higher from the upper limit of the norm, which caused a temperature reaction and other general reactions of the patient's body.

TNF (tumor necrosis factor) - this cytokine is responsible for many reactions of the body infected with a viral infection of the patient, including: stimulates cytotoxicity, production of endogenous oxidants, induction of apoptosis, cachexia, collagenase, procoagulants, platelet activating factor, fibrinogenesis, etc. factor in patients with coronavirus infection was 1.4% higher than the upper limit of the norm.

CONCLUSION

In conclusion, it should be noted that the host immune response is a critical factor in the development of COVID-19, and analysis of this response can provide a clearer picture of how the host response affects the severity of the disease in some people, while most infected people show symptoms. only mild or no symptoms at all.

Thus, studying the host immune response in acute and convalescent people will provide a molecular understanding of the mechanisms by which we can provide protection and long-term immune memory, and will also allow the development of preventive and therapeutic measures to overcome future outbreaks of similar coronavirus infection.

REFERENCES

1. Blanco-Melo, D, Nilsson-Payant, EB, Liu, CW, Uhl, S, Hoagland, D, Møller, R, et al. Imbalance host response to SARS-CoV-2 drives development of COVID-19. Cell., 2020.
2. Lu, R, Zhao, X, Li, J, Niu, P, Yang, B, Wu, H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet, 2020.
3. Lim, YX, Ng, YL, Tam, JP, and Liu, DX. Human coronaviruses: a review of virus−host interactions. Diseases, 2016.
4. Liu, J, Li, S, Liu, J, Liang, B, Wang, X, Wang, H, et al. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. EBio Medicine, 2020.
5. Li, T, Qiu, Z, Han, Y, Wang, Z, Fan, H, Lu, W, et al. Rapid loss of both CD4+ and CD8+ T lymphocyte subsets during the acute phase of severe acute respiratory syndrome. Chinese Med J., 2003.