General Representations about Immunopatological State

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Abstract:
Many components of immunopathology, which include various types of immune deficiency, and their clinical manifestations, are considered. Deficiencies of cellular and humoral immunity, clinical manifestations of combined immune deficiency, phagocytic link, complement system are specifically discussed. The mechanisms and competition of types of immunity - antibacterial and viral, antifungal, antiparasitic and antihelmintic, anti-cancer, are considered in detail. The immunopathology of the COVID-19 SARS-CoV-2 infection is discussed. The problem of pathological stimulation of the immune system, specifically allergy and autoimmune lesions, as well as various mechanisms of modification of immune responses is discussed.
Key words: *immune deficiency, types of immunity, coronavirus infection-19, allergies, autoimmune pathology*

Introduction

The immune system, like any other, has a limit to its capabilities in providing immune surveillance, control of multicellularity and preservation of morphological constants. It should be noted that the mechanisms of immune reactivity provide optimal health preservation and prevention of health disorders only in non-extreme conditions (1). In extreme situations, the effectiveness of radical elimination of violations of the antigenic composition of the internal environment of the body may be incomplete, slow, requiring specific immunotropic treatment (2).

Types of immune deficiency

Excessive exogenous or endogenous antigenic aggression, as well as congenital pathology, can cause the development of structural and functional lesions of the immune system - immunopathology.
It can manifest itself in: (1) induction of primary and secondary immune deficiency up to tolerance or immune paralysis; (2) activation of reactivity, the extreme manifestations of which are autoimmune and allergic diseases; (3) the development of lymphoproliferative and neoplastic processes, which are a combination of excessive stimulation of the proliferation of lymphoid and non-lymphoid cells in combination with immunosuppression; (4) the formation of immune refractoriness to antigenic aggression, which is a form of immunopathology and at the same time a kind of defense mechanism. Based on these provisions, the development of a targeted effect on the immune system is of exceptional importance, primarily in extreme situations.
Pokrovsky et al (1) identified several types of immunopathological disorders in infectious and some other processes.

Acute immune deficiency

It develops in acute infectious diseases with generalization of the pathological process and the penetration of the causative agent into the blood. This situation develops under a number of conditions: (1) the presence of an initial congenital or acquired immunodeficiency, (2) excessive antigenic aggression and failure of the eliminating function of the immune system, (3) defects in the prompt response of protective reactions to the antigen, (4) temporary paralysis of the immune system by specific components of the pathogen, (5) impaired chemotaxis and bactericidal ability of phagocytes, lymphopenia, neutrophilia, (6) a decrease in the content of regulatory subpopulations of T cells, (7) hyperimmunoglobulinemia for all or individual classes of immune proteins, (8) inhibition of the synthesis of IL-2 (factor growth and differentiation of T- and NK-cells), (9) activation of the formation of pro-inflammatory cytokines (IL-6, IL-8, as well as prostaglandins).

Subacute immune deficiency

Its clinical equivalent is the stage of convalescence after acute infectious diseases. The ability of the pathogen to phenotypically change the host's immune response is one of the significant factors that determine its pathogenicity. Proceeding from this, any interaction with a foreign antigen does not pass without leaving a trace, since it causes the formation of immune memory - the basis of resistance to repeated contacts with the pathogen. In the stage of convalescence, a period of restoration of functional and structural damage to the immune system begins, the completeness and completeness of which determines the quality of recovery or the possibility of chronicity of the pathological process.

Chronic immune deficiency

An acute infectious process in most cases ends with recovery. However, in some patients, this process may be incomplete and underlie the subsequent chronicity of the disease. Chronization after an infectious process is not only the preservation of inflammation at the site of the primary focus, but also the emergence of secondary processes in other localizations, due to the induction of immune deficiency in the patient.

Clinical manifestations of damage to individual links of immunity

Clinical manifestations of cellular immunity deficiencies

T-immunodeficiencies can be isolated and combined. They are expressed in hypoplasia and aplasia, thymomegaly, a decrease in the formation of hormones by the thyroid gland and are accompanied by a quantitative or functional deficiency of regulatory cell subpopulations [T-helpers, T-cytotoxic/suppressors, T-counter-suppressors, T-killers, defects of other cytotoxic cells] (3, 4).

Pathology is accompanied by the development of infections with intracellular parasitism of the pathogen (tuberculosis, leprosy, brucellosis, viral infections, mycoses), as well as diseases caused by protozoa. In this case, infectious lesions caused by extracellular bacteria can proceed without complications. ***Skin lesions*** in T-immunodeficiency are manifested by herpes, psoriasis, lesions of the ***mucous eyes*** - catarrhal, membranous, ulcerative conjunctivitis, ***mucous membranes of the oral cavity*** - fungi, viral aphthous and ulcerative stomatitis. ***Bronchitis*** is characterized by a persistent course, cough without purulent sputum, mucosal atrophy. On the part of the ***gastrointestinal tract***, it is possible to develop enteritis and enterocolitis, Crohn's disease, candidiasis, giardiasis, and subsequently malignant neoplasms.

Clinical manifestations of deficiencies of humoral immunity

Immunoglobulins play a leading role in the "destruction" of bacteria and other infectious agents, contribute to the implementation of the opsonizing effect. A general deficiency of immunoglobulins is manifested by recurrent and chronic bacterial infections, including those caused by non-virulent pathogens. As a rule, the ***respiratory organs*** (bronchiectasis, pulmonary fibrosis), the ***gastrointestinal tract*** (diarrhea, malabsorption), the ***paranasal sinuses***, and the ***meninges*** are mainly affected. Infections proceed with severe intoxication, often complicated by septicemia. With acquired hypoimmunoglobulinemia, for example, with the loss of serum proteins in nephritis, inadequacy of their formation in myelomatosis, lymphatic leukemia, antiviral immunity suffers little, but the risk of developing allergization increases significantly. Deficiency of immunoglobulins can also occur in the form of total hypo-immunoglobulinemia or in the form of variants with a decrease in the level of one class or subclass of specific proteins or production of antibodies against a specific pathogen.

IgM deficiency

Patients have an increased risk of developing severe meningococcal meningitis with septicemia, repeated respiratory infections, bronchiectasis.

IgG deficiency

As a rule, there is a deficiency of one or more IgG subclasses. Clinically characterized by the development of respiratory infections, allergic diseases. With a deficiency of the IgG4 subclass, the pathology may be asymptomatic. IgG deficiency is often combined with IgA deficiency.

IgA deficiency

Often it is asymptomatic, since it is "blocked" by the formation of immune globulins of other classes. In some cases, the deficiency of these proteins can be clinically manifested by frequent respiratory infections and purulent bacterial processes on the skin and mucous membranes of the conjunctiva and oral cavity, febrile convulsions, atopy in the form of asthmatic bronchitis, bronchial asthma, diffuse neurodermatitis and food allergies. In the described conditions, mixed forms of infections with purulent-bacterial, viral, fungal agents can develop against the background of polyvalent allergies, dysbiosis, diffuse connective tissue diseases.

Clinical manifestations of combined immunodeficiencies (CIDs)

They are characterized by a combination of the clinic of humoral and cellular deficiency and other immune disorders. Such combinations most often cause death in the first year of a child's life. In such children, combinations of pneumonia with infections of the gastrointestinal tract and skin caused by bacteria, viruses, fungi are typical. Malignant neoplasms often develop. Infections are difficult, poorly responsive to therapeutic effects. It should be recognized that along with the classical forms of CID, there are more worn out light variants with a better prognosis for life and more amenable to therapeutic measures (5, 6).

Clinical manifestations of deficiency of the phagocytic link of immunity

Phagocytosis defects develop due to a decrease in the number of phagocytes, which manifests itself in the form of neutropenia syndrome or due to defects, which are divided into defects in the motor function of cells (chemotaxis) and killing defects.

Chemotaxis defect

It includes the syndrome of "lazy leukocytes", clinically manifested in children in the form of severe repeated infections, especially in the form of microabscesses. It is a combined defect of spontaneous migration and chemotaxis of phagocytes, accompanied by severe neutropenia.

Clinical manifestations of deficiencies of components of the complement system

They are characterized by recurrent or chronic bacterial infections of the respiratory system, urinary tract, enterocolitis, otitis media, meningitis, purulent lesions of the skin and subcutaneous tissue. Diseases proceed with massive intoxication, a tendency to septicemia. In some patients with defects in the complement system, infectious diseases occur without leukocytosis. Others may have decreased antiviral protection.

Mechanisms and competition of types of immunity and immune responses (7) There are phenomena of competition between certain types of immunity against various pathogens and between protective reactions induced by one pathological process.

Antibacterial immunity

If bacteria are found extracellularly, then their elimination proceeds in the following ways → bacterium + antibodies + complement → immune lysis. Antibodies promote opsonization of bacteria and thus stimulate phagocytosis. If bacteria are found intracellularly, then elimination occurs either due to cellular mechanisms (T cells, NK), or due to the formation of an infectious granuloma. If the organism is not weakened, then in the granuloma the microorganism either dies or remains in an unviable state for a long time. Otherwise, when the granuloma disintegrates, the microbe is disseminated throughout the body. To this should be added the development of immediate-type hypersensitivity (ITH) and delayed-type hypersensitivity (DTH) in patients, which, under certain conditions, "compete" with antibacterial immunity.

Antiviral immunity

Viral infections spreading hematogenously (poliomyelitis, measles, mumps, chickenpox) can be eliminated by humoral mechanisms, and these diseases are usually characterized by a long incubation period. Pathogens that multiply directly at the site of introduction [in situ], for example, influenza, have a short incubation period, which can be dangerous due to a certain inertia in the development of immune reactions and a severe course of the disease. Influenza viruses, parainfluenza, adenoviruses, coronaviruses are highly variable,

therefore, the concentration of specific antibodies against them is always insufficient in mucous secretions. Antibodies are produced against the extracellular virus, which combine with the virus, and the "virus + antibody" complex is captured by the macrophage. In the course of its penetration into the cell, in the course of its vital activity, the virus changes the antigenic structure of the cell membrane, against which T-killers are produced, and antibody-dependent cytotoxicity. Moreover, a granuloma may even form.

In severe viral infections (HIV/AIDS), a complex mechanism of immunopathology is formed, in which a number of important processes occur: (1) T-lymphocyte deficiency due to the CD4 subpopulation, (2) inhibition of the function of T-cells, especially helpers, (3) functional activity of B-lymphocytes with stimulation of spontaneous formation of immune globulins and "final" hyperimmunoglobulinemia, (4) decrease in the ability of B-cells to respond with the formation of immunoglobulins to "new" antigens, (5) accumulation of aggressive circulating immune complexes (CIC) in the blood, (6) inhibition of the cytotoxic activity of natural killer cells and cell-mediated cytotoxicity, (7) dysfunction of monocytic cells, specifically chemotaxis, cytotoxicity, IL-1 synthesis, (8) intensification of the formation of "abnormal" α-interferon, antilymphocytic antibodies, suppressor factors, β_2 -microglobulin, (9) a drop in serum thymosin levels, the number of natural killer cells, proliferative response to mitogens, (10) suppression of skin reactions to tuberculin, diphtheria and other antigens.

Another mechanism of complex immunopathology, which should be considered in more detail, is the coronavirus infection, which hit the world at the end of 2019, which has acquired alarming global dimensions and continues to spread rapidly (8). It is caused by a new strain of the coronavirus SARS-CoV-2, which causes the disease under the international name coronavirus disease-19 (CoViD-19) and has the ability to persist for a long time in the host's body. According to the Johns Hopkins University, more than 13 million people in more than 188 countries have already been infected with SARS-CoV-2 in the world, of which 584,000 have died. The virus differs in a number of features from other respiratory viruses. Mutates with a frequency of 1 mutation per week, replicates in the upper respiratory tract without a pronounced clinical picture, has the longest genome, and can multiply approximately 100 times in 48 hours. The disease is caused by a new virus and people do not have acquired immunity to it, therefore, people of all ages are susceptible to infection. Symptoms develop on average 5-6 days after infection, and the incubation period is 1-14 days. The asymptomatic course is up to 2 weeks with the release of the virus. The carrier of the virus becomes contagious two and a few days before the onset of symptoms, and the peak infectivity reaches a little less than a day before the onset of symptoms. This does not mean that after symptoms, COVID-19 loses its contagiousness, since about 44% of infections occur with "pre-symptomatic" transmission of the virus. The probability of infection by direct contact with the carrier of the virus is from 5 to 10%, but do not forget that the virus can live on different surfaces for a long time.

Coronavirus infection COVID-19 is a potentially severe acute respiratory infection caused by the SARS-CoV-2 coronavirus. It is a dangerous disease that can occur in the form of an acute respiratory viral infection of mild course and a severe form, the specific complications of which may include viral pneumonia, leading to acute respiratory distress syndrome or respiratory failure with the risk of death. Against the background of infection, it is possible to develop sepsis and septic (infectious-toxic) shock.

Information on immunopathology in coronavirus infection is of great interest, although at present this issue is completely insufficiently studied, since a short time of observation has passed. According to the literature, a carrier of coronavirus without symptoms does not develop immunity to infection, but with severe symptoms, it can infect three more people. The question of the possible reinfection of those who have recovered is currently open. However, there are reports that healthy people before contracting a coronavirus infection, after of a past illness with a clear clinical picture, a stable immunity to the virus may be developed (assumption) for 1-3 years. Moreover, the presence of persistent immunity makes it possible to successfully use their blood plasma containing specific IgG and IgM antibodies for specific immunotherapy of others infected, although there is also negative information on this issue. However, it can be assumed that the same practice substantiates the effectiveness of the use of human donor immunoglobulins for the treatment of patients with coronavirus infection. Recall that they contain up to 108 types of anamnestic antibodies, which include anti-

bodies from carriers or those who have recovered from an infection caused by other types of coronaviruses, or persons immunized with cross antigens.

There are reports that SARS-CoV-2 does not induce increased levels of type I, II or III interferons in infected tissues of human lungs, but causes the development of strong inflammatory processes, increases the levels of IL-2, IL-7, IL-10, GCSF, TNFα, which may indicate the development of secondary hemophagocytic lymphohistiocytosis. Coronavirus does not change the content of procalcitonin, which increases only in the case of a secondary bacterial infection. Patients have increased ferritin, C-reactive protein; lactate and D-dimer (especially if fatal), alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase (8). In severe cases of infection, deep lymphopenia and neutrophilia are noted. However, the often described eosinopenia is not associated with the severity of the disease. It is important to note that the severity of the disease in the absence of sepsis is determined based on the saturation of arterial blood with oxygen, the respiratory rate, and the detection of the RNA virus in the patient's blood.

*The **relationship between antibacterial and antiviral immunity***

The defeat of the epithelial layer by infectious agents promotes the penetration of viruses into the internal environment of cells and the launch of an antiviral immune response. In this case, the damaged surface of the epithelium is colonized by bacteria that easily penetrate into the internal environment of the body, which in turn induces a humoral immune response. The simultaneous need for the deployment of cellular (viruses) and humoral (bacteria) immune responses causes competition for cytokines, for a plastic pool of low molecular weight ribonucleotides, interleukins-2 and other components, and in certain cases causes a weakening of both defense mechanisms. Therefore, in the treatment of patients with such an initial or formed in the process of a pathological process mixed infection, additional use of immunotropic agents is necessary.

Antifungal immunity

It is close to antibacterial, but has its own characteristics, since mushrooms contain many polysaccharides, and mushrooms, in addition, can exist in the form of spores and vegetative forms. Nonspecific factors of innate immunity determine the "alternative" pathway of activation of the complement system, and fungal cells can also become the object of the action of natural killers. A humoral way of elimination of the forming complex "mushroom + antibodies + complement" with the outcome in its lysis is also possible. As you know, in fungal diseases, immunoglobulins E are produced, which are involved in the development of immediate allergic reactions, which can compete with the "general" immunity. It is essential that as a result of frequent and prolonged stimulation of T-suppressors/inductors, anergy can occur, which manifests itself in the absence or formation of a very "weak" immune response.

Antiparasitic immunity

It should be borne in mind that many parasites have several stages of development, a diverse antigenic composition, according to which specific antibodies are formed in the body. When the stage of development changes, parasite “leaves” for some time from the action of antibodies, which complicates the formation of an immune response. Cellular mechanisms, including the formation of granulomas, play an important role in protecting the body from parasites. To this should be added the ability of pathogens to induce allergies, to cause depletion of the T-suppressor immune link, destruction of various tissues with the release of autoantigens, which together provoke the development of autoimmune and autoallergic reactions that compete with anti-parasitic immunity.

Anthelminthic immunity

Helminths are endowed with a powerful immunotropic effect, which is based on the following mechanisms: (1) during the life cycle, parasites form a wide repertoire of antigens that deplete the immune system, and due to antigenic mimicry with the host's antigens, which reduce the effectiveness of the “recognition” of the alien, (2) induce the synthesis of IgE with the development of a topic, immunocomplex and cellular allergic reactions (types I, III, IV), (3) form infiltrates of eosinophils, basophils and mast cells at the site of introduction, which implement the effector path of defense.

Anti-cancer immunity

It is provided with natural (natural) killer cells NK/EK-cells, cytotoxic monocytes, reinforced with macrophages, granulocytes, mast cells, specific cytotoxic lymphocytes, antibody-dependent killers, cytotoxic antibodies, immune interferon, etc.

Anticancer immunity is a complex multicomponent event in the body, which is caused by a variety of biological processes and factors. There are many of them: (1) immune tolerance, consisting in the "insensitivity" of the immune system to tumor antigens, (2) immune enhancement, in which preexisting antibodies against cancer antigens mask them and protect them from killer T-cell attacks, (3) immune selection when tumor cells with a high density of antigens are quickly destroyed, and with a low density they survive, (4) the formation of immunodeficiencies, (5) the weak immunogenicity of tumor antigens, (6) the ability of tumor cells to induce the formation of polyclonal antigens that deplete the immune system, (7) high frequency mutations, especially in rapidly metastatic tumors, hindering the formation of adequate mechanisms for the elimination of neoplasms, (8) impermeability of the membranes of malignant cells for cytotoxic agents, (9) synthesis of tumor cells of suppressor factors-blockers of NK and T-killer receptors, LAK cells, reinforced macrophages, recognizing tumor markers, (10) insufficient amount in the host organism on the activator of immune reactions IL-2, (11) depletion of the blood
serum of patients with a pool of low molecular weight nucleic acids with the ability to enhance antitumor immunity, neutralize tumor toxins that provide plastic function, (12) the formation of chorionic gonadotropin, which is a natural immunosuppressive hormone of pregnancy, (13) increased synthesis of prostaglandins (PGE-2), actively suppressing immune responses, (14) there are undoubted observations in which it was shown that often anti-tumor defense cells not only do not “see” cancer cells, but also help them develop, (15) there is a problem of “dormant” tumor cells, which for a long time can be in a lethargic state, however, under the influence of reasons unknown today, they awaken and cause the formation of neoplasms. Apparently, close to this observation is the well-described phenomenon of self-healing from the most severe oncological diseases without any treatment. One might think that when we understand the essence of these problems, their deciphering will open up new tremendous horizons in cancer treatment.

In malignant neoplasms, a number of phenomena are realized that block antitumor immunity. (1) "The phenomenon of slippage", when defense mechanisms are triggered when an average number of malignant cells from 10 to 1000 enters or appears in the body. Smaller and larger numbers of them are difficult to recognize. (2) "Phenomenon of blocking", when cytotoxic antibodies are produced against cancer cells, which, in the absence of complement, do not kill the malignant cell, but shield it from the action of other effective protective factors. (3) "Phenomenon of tumor growth stimulation" due to suppression of B-suppressor function. (4) "Phenomenon of parity", that is, a stable ratio between the number of malignant cells and T-killers, which must destroy it. With a decrease in tumor mass, the number of killer cells also decreases. (5) "Phenomenon of variation in tumor types" induced by one carcinogen, but in different individuals. (6) Stimulation of cellular inhibitory mechanisms involving T- and B-suppressors, macrophage suppressors and other cell types. (7) The appearance in tumor carriers of inhibitors of "immune checkpoints" - PD1 receptors on the membrane of cytotoxic T-lymphocytes, which protect the body from autoimmune aggression and damage to its own tissues. The activation of these receptors by a soluble ligand for PD1 due to its overexpression in tumor cells and shedding into the extracellular environment protects them from the immune system by triggering apoptosis of T-lymphocytes and excluding these cells from the antitumor defense. (8) The presence in tumors of a large number of non-tumor cells (fibroblasts, T-lymphocytes, macrophages, NK cells, etc.), which significantly complicate the effectiveness of antitumor treatment.

Pathological stimulation of the immune system (9)

Allergies and autoimmune lesions

They are closely related biological phenomena, since they are realized by extremely strong, uncontrolled, autoaggressive reactions, which develop against the background of a decrease in the suppressive activity of

the organism and genetic predisposition. Moreover, the induction of these pathological processes has its own characteristics.

Development of allergic reactions

They are provoked by many factors and influences. These include: (1) low immunogenic antigens in large doses or repeatedly entering the body with a weakened immune system, (2) modification of autologous tissues with medications, radiation, burns, pathological process, (3) excessive stimulation of immune responses, (4) small size of haptens, their denaturation with formaldehyde, other solvents, (5) tissue denaturation with additional release of autoantigens, (6) development of chronic pathology of any genesis, (7) violation of the regulations for the use of drugs.

Auxiliary factors that provoke allergies

They are: (1) the intake of excess histamine in the body with food (cheese, chocolate, potatoes), (2) the appearance in the body of librators of its own histamine from the corresponding cells (fish), (3) disruption of the enzymatic inactivation of histamine in the body, (4) intestinal diseases with disorders of absorption processes, creating conditions for the penetration of large molecular compounds into the body, (5) insufficiency of the hepato-biliary system with disorders of histamine degradation in liver cirrhosis, cholecystitis, cholangitis, etc., (6) dysbacteriosis, in which the formation of histamine-like substances by the microflora is possible, (7) activation of the complement system, which causes the formation of intermediate products (C3a, C2b, C4a, C5a, etc.) that can cause the release of mediators from mast cells, basophils, neutrophils and platelets.

Autoimmune disorders

They are another variant of active aggression, which is determined by: (1) the appearance in the bloodstream of barrier antigens of the eye, gonads, and the brain, with which the immune system normally did not contact, (2) antigenic mimicry due to microbial antigens that have common determinants with normal host antigens, (3) mutation and modification of autoantigens, (4) release of hidden autoantigens as a result of the activity of autoreactive T and B cells, (5) the presence of "superantigens" formed by toxic proteins of cocci and retroviruses, (6) the formation in patients of a genetically programmed weakness of the immune response to a specific hypertension (immunodeficiency), (7) the ability of autoantibodies under certain conditions to "blind" lymphocytes by blocking recognition receptors, (8) induction by viruses and other agents of changes in the activity of autoantigens\ oncogenes, regulators of the production of cytokines and their receptors, (9) the formation of autoantibodies of the IgM class in the fetus to many components auto cells that are not eliminated from the body accumulate with age and in adults cause autoimmune diseases, (10) the formation of toxic immune complexes due to the death of hepatocytes in persistent viral infections, for example, hepatitis A, (11) the modification of autoantigens by pathogens or their toxins as a result of an acute rheumatic attack, (12) the integration of viral RNA into the cell genome, (13) the use of drugs provocateurs of autoimmune disorders (dopegita, apressin, sulfonamides, pyrazolone and its derivatives).

The ratio of immunodeficiencies and allergies

In reality, the simultaneous formation of immunodeficiencies and allergies often occurs. It should be borne in mind that IH (immediate hypersensitivity) provides protection against “large” and extratissue pathogens, and DTH (delayed-type hypersensitivity) through immune inflammation from phagocyte-resistant agents.

As shown by special studies on patients with atopic dermatitis or true eczema, manifestations of hypersensitivity were predominant over immune deficiency. A definite role in this phenomenon is played by biogenic amines, which, by binding to the receptors of immunocompetent cells, regulate the function of lymphocytes through the metabolic system. At the same time, there is a direct relationship between the concentration of histamine in the blood and the level of zero undifferentiated lymphocytes, immune globulins of class E, and the reverse relationship with the content of cytotoxic T-lymphocytes CD8+, corticosteroids, and monoamine oxidase activity. It is essential that specific mechanisms are formed for each type of immunopathology. For example, in atopic dermatitis, suppression of lymphocyte function was predominant, in the reaction of LBTR (lymphocyte blast transformation reaction) on PHA (phytohemagglutinin) - the formation of the en-

zyme lysozyme and an increased number of B cells, which was combined with the accumulation of streptococcus enzymes ASLO (antistreptolysin O), ASH (antistreptohyaluronidase) and eosinophils (10).

Allergy modifying effect on immune status

In the acute period of purulent soft tissue infection (PSTI) and PSTI with allergic dermatitis (PSTI + AD), 54.2 and 70.8% of hemato-immune parameters were significantly changed relative to the normative values. In qualitative terms, PSTI showed the presence of an inflammatory reaction in terms of hematological parameters, T- deficiency, an imbalance of the humoral link of immunity, an increased risk of the formation of auto-aggressive reactions by the CIC (circulating immune complexes), inhibition of the absorption capacity of phagocytes. The reference indicators were the accumulation of T-cytotoxic cells and pro-inflammatory interleukin-8 against the background of B-lymphocyte deficiency. In patients with PSTI + AD, suppression of cellular and phagocytic reactions, imbalance of B cells, IgG, increased risk of induction of auto-aggressive and toxic reactions against the background of accumulation of proinflammatory cytokines and cells with an apoptosis receptor was formed (11).

Modifying effect of autoimmune pathology on immuno-laboratory status

In patients with chronic autoimmune thyroiditis with bronchial asthma (CAIT + BA), suppression of the T-link of immunity in T-cells, regulatory subpopulations, and an imbalance of phagocytosis was observed. Humoral reactions were unchanged, traditional endocrine parameters of the thyroid gland - antibodies against thyroidin (TAb), microsomal fraction of thyrocytes (MFT) and antithyroid-stimulating globulin (ATSG) increased. Of the biochemical parameters, cholesterol (CH), atherogenic index, malondialdehyde, α_2-fraction increased, but suppressed high density lipoproteins (HDL), albumin, α_1-fraction (12). At the same time, patients with chronic autoimmune thyroiditis (CAIT) showed a significant decrease in the level of T-cells, T-cytotoxic lymphocytes, thyroxine, IgG, TAb, MFT, ATSG were found. The dynamics of indicators of lipid and protein metabolism turned out to be insignificantly changed. With one BA, a decrease in the number of T cells, T-cytotoxic lymphocytes, phagocytic index and phagocytic number, activation of neutrophil metabolism, monotony of endocrine parameters, imbalance in cholesterol (CH), HDL, and α_1-protein fraction levels are shown. Thus, with the simultaneous formation of allergy and immune deficiency in patients, the former has an advantage over the latter, and in the case of complications of diseases by hypersensitivity or auto-aggression, modification and aggravation of immune disorders is observed.

Mechanisms for modifying immune responses

The natural algorithm for the development of immune responses always includes alternative mechanisms (specificity and nonspecificity, stimulation and suppression, unity and variability, regionality and systemicity, disintegration and integration), the ratio of which determines the final vector of variability of immune homeostasis. It should be borne in mind that immune deficiency can be the cause of infectious complications or inhibition of autoaggressive processes, and stimulation is a way to eliminate tolerance or induce hypersensitivity (10,11, 13).

Specificity and non-specificity of the immune response

Immune responses are always specific, but at the same time subject to non-specific regulation. The latter factors include thymic factors myelopeptides, interleukins, interferons (α, β, γ), products of catabolic destruction of immunoglobulins ($F(ab)_2$ and Fc-fragments), endogenous hormones cortisol, mineralocorticoids, etc.

Stimulation and suppression of the immune response

In the process of the algorithm of pathological processes in patients with various diseases, alternative reactions of immune markers develop. In patients with multiple sclerosis in the acute stage, 74% of the immune indicators are significantly increased, and in 30% they are suppressed. In the stage of stabilization, this dynamics becomes parity "50 to 50%". In other clinical nosoforms of hypertension of stages 1, 2 and 3, hypertensive crisis, acute hypertensive encephalopathy, transient ischemic attack, hemorrhagic and ischemic strokes, the number of increased tests is 25-56%, and reduced 6-19%.

Unity and variability of the immune response

The evidence of the functional unity and variability of the regulatory systems of the body (central nervous, endocrine and immune) is the phenomenon of anaphylactic shock, induced by the reaction of the immune system to an allergen, which causes the release of biogenic amines, changes in the endocrine status and behavioral reactions of the nervous system.

The unifying factor of the unified functioning of the immune and nervous systems is the implementation of specific reactions and the formation of memory, i.e. variations in the response to repeated action of the factor, presented in all structures of the body simultaneously with the ability to change their functions.

Regionality and consistency of the immune response

Regional immunity provides protection for the integuments and organs of the body, directly communicating with the external environment. It is part of the general, it is determined by normal microflora, mechanical barriers, circulating humoral and cellular factors, secretory immune globulins, γ-interferon, etc. Systemic immunity implies a functional connection of the immune system with an imbalance of primary and secondary products of free radical lipid oxidation and proteins, activation of enzymatic and non-enzymatic mechanisms of the antioxidant system against the background of accumulation of pro-inflammatory cytokines (14).

Disintegration and integration of the immune response

With pathological and physiological destruction (degradation) of various foreign and own cells and tissues, endogenous biologically active substances are released: R-proteins, transfer factor, endotoxins, nucleic acids, which initially contribute to the induction of immunopathology, and later cause its elimination due to the integration of immune functions.

Thus, reaching the limit of competence of the immune system contributes to the formation of pathological conditions, which include various deficits and pathological activation, typical changes in the links of immunity, competition of protective reactions, perversion of the nature of clinical and laboratory disorders, etc. These processes are based on the alternative of the immune response, consisting in non-specificity and specificity, stimulation and suppression, regionality and consistency, unity and variability, disintegration and integration.

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