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IMMUNOLOGICAL FEATURES OF HELICOBACTER PYLORI ASSOCIATED GASTROINTESTINAL FOOD ALLERGY IN CHILDREN

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ABSTRACT
The authors conducted a study on the study of immune parameters in children with gastrointestinal allergies. An immunological cellular imbalance was established for Hp-associated gastrointestinal Allergy in children. The observed immunological imbalance in gastroenterology can occur against the background of food, microbial and parasitic sensitization, in most cases leads to a heavier course of diseases and, of course, requires not only timely diagnosis, but also adequate complex therapy.

KEYWORDS: Children, gastrointestinal allergy, Helicobacter pylori, food allergy, immunology.

INTRODUCTION

FA is an immunologically mediated clinical manifestation of hypersensitivity of a sensitized organism that occurs after the food antigen enters the digestive tract.[3] However, it was found that with age, tolerance to food allergens is often formed. For example, by the age of 3, 70-90% of children form a susceptibility to cow's milk proteins[4], by the age of 5, 80% of children become tolerant of chicken egg protein and 40% of children - to peanuts.[5,6,7]

The problem of food Allergy (FA) is extremely relevant all over the world, just over 200 million people have some form of food allergy, most of whom are young children.[1] The frequency of FA in children of the first three years of life is 6-8%, by adolescence the frequency decreases to 2-4%, by adult - up to 1%.[2] An adequate immunological response to food allergens is provided by food (oral) tolerance - specific immunological areactivity to an allergen that the body previously came into contact with during the enteral route of administration. Oral tolerance is produced as a result of a complex immunoregulatory strategy used by the gut and associated lymphoid tissues to make the peripheral immune system non-reactive to nonpathogenic proteins, primarily non-food proteins. Thus, this is a necessary mechanism that maintains a state of active areactivity on autoantigens and food antigens, while immune responses against pathogens continue to be implemented. From this point of view, allergic sensitization can be considered as a lack of immunological tolerance.[8]

Depending on the type of development of the immunopathological reaction, there are differences in the time of appearance, as well as the nature of clinical symptoms. Clinical manifestations of FA are polymorphic, these may be symptoms of the skin, respiratory system, and gastrointestinal tract (GIT). At the same time, up to 95% of food allergies are associated with skin manifestations, 10-12% of children realize respiratory manifestations of FA, gastrointestinal forms are most typical for young children 60-70%, in older age they are somewhat less common — up to 10%, it is noted that the share of combined forms of FA increases with age.[9] In young children, manifestations of FA can be isolated gastrointestinal symptoms — persistent regurgitation, colic, and defecation disorders. These children receive treatment for functional disorders of the gastrointestinal tract for a long time and often without effect.[10]

Currently, more and more often there are works that study the relationship of Helicobacter infection with the development of atopic dermatitis, food allergy, chronic recurrent urticaria, and bronchial asthma.[11] The gastrointestinal mucosa belongs to the local factors that protect the immune system. In the process of its damage, which occurs during the invasion of Helicobacter pylori (Hp), its barrier properties are violated and the passage of antigens through the mucosa increases. Besides in addition, Hp has low immunogenicity, which causes long-term interaction of the microorganism with the immune system of the mucosa with subsequent persistence of infection. This arises from the fact, that Hp is able to resist phagocytosis and persist intracellularly. It can increase apoptosis not only of epithelial cells, but also of macrophages and T-lymphocytes, which reduces the effectiveness of immune defense mechanisms. When

Helicobacter infection reduces the production of sIgA as a result Hp's ability to break down sIgA disulfide bonds, which also contributes to the reduction of the barrier properties of the mucosa and penetrationsance of the pathogen and other antigens. Since Hp has a direct damaging effect on the gastric mucosa, it provides permeability to food antigens and contributes to development of food allergy.[12] Not only IgE antibodies, but also specific IgG can participate in the implementation of intestinal hypersensitivity to food. The most frequently indicated growth of specific antibodies to various foods, as well as the development of dietary principles for patients with gastrointestinal allergies.[13,14] Difficulties and errors in the diagnosis of gastrointestinal FA are related to the fact that gastrointestinal reactions to food are often delayed and occur in a nonIgE mediated type.[15,16]

Purpose of the study: To study the parameters of immunity in children with gastrointestinal food allergy depending on the infection of Helicobacter pylori.

MATERIALS AND METHODS

In order to study the effect of concomitant pathology on the course and prognosis of FA, 63 sick children under 18 years of age with gastrointestinal allergies were examined, who were on inpatient examination and treatment at the Bukhara regional children's multidisciplinary medical center (BRCMMC). Patients were divided into 2 groups: 32-with gastrointestinal allergy, 31-with gastrointestinal allergy without Hp. All patients were examined for general, biochemical and enzyme immunological analysis (ELISA) of blood, and immunological methods of research were performed. Among the surveyed children, boys -24 (38.1%), girls-39 (61.9%), aged from 3 to 10 years. The analysis of morbidity and hospitalization at the place of residence showed that children living in the city are more often hospitalized -39 (61.9%). Children with gastrointestinal allergies were performed to study the state of immunity, immunological parameters of the blood.

DISCUSSION

CD3+, CD4 + of lymphocytes in relation to the threshold values of the control group in both observation groups. CD3 + CD4 + lymphocytes in gastrointestinal allergy regardless of the Hp association ($p<0.05$) (table. 1).

Table 1: Indicators of T-cell immunity in sick children with gastrointestinal allergies depending on Hp infection.

Blood parameters	Control group (n=30)	Hp associated gastrointestinal allergy (n=32)	Hp unassociated gastrointestinal allergy (n=31)
CD3, %	52,0 ± 1,0	38,3± 2,3*	44,27±0,41**
CD3+, abs	780 ± 27	675 ± 23*	1325,6± 90,03**
CD4, %	32,4± 0,5	29,4±0,9*	22,3±0,61**
CD4+, abs	521 ± 21	435 ± 32*	658,63± 44,78**
CD8, %	21,0 ±0,8	17,8±1,5	19,4±0,99
CD8+, abs	372 ± 13	238± 12*	567,17± 45,46**
CD16+, %	16,4±1,0	18,4±0,8	15,2±0,95
CD16+, abs	182 ± 9,0	198 ± 7,0	178±3,0

Note: * - differences relative to control group data are significant
(* - P<0.05, * * - P<0.01, *** - P<0.001)

In relation to absolute concentration, there was a significant opposite change: a decrease in gastrointestinal allergy associated with Hp to 675.0 ± 23.0 ml and 435 ± 32 ml, respectively, against control-780, 0 ± 27.0 ($P<0.05$) and an increase in CD3 + lymphocytes by 1.7 times (to 1325.6±90.03 ml) and CD4 + lymphocytes by 1.3 times (to 658.63± 44.78 ml) in gastrointestinal allergy without Hp association ($P<0.05$).

T-cell immunity in children with Hp-associated gastrointestinal allergy is characterized by a decrease in both the relative and absolute number of CD3+ and CD4+ lymphocytes, as well as the relative number of CD8 + lymphocytes against the background of an unreliable increase in killer (CD16+) activity. CD3 + lymphocytes are known to participate in delayed-type allergic reactions.[17] The decrease in the concentration of CD3+ and CD4+ lymphocytes observed in studies indicates the presence of infections and secondary immunodeficiency. In immunological blood tests in children with gastrointestinal allergy without Hp infection, a significant increase in the absolute values of CD3+, CD4+, CD8+ lymphocytes was found with a tendency to decrease CD16 + lymphocytes.

An increase in the absolute concentration of CD3+, CD4+, CD8+ lymphocytes indicates an acute phase of Allergy and stimulation of the immune system in response to an allergen (antigen), which confirms the formation of hyperreactive syndromes. For CD8 + lymphocytes, a decrease in the relative number of CD8 + lymphocytes was found, regardless of Hp infection. T-cell insufficiency is characteristic of many chronic autoimmune diseases of the gastrointestinal tract,

including primary biliary cirrhosis, primary sclerosing cholangitis, ulcerative colitis, Crohn's disease, pernicious anemia, and others.[16,17]

In our studies, the established deficiency of CD8 + T cells in Hp-associated gastrointestinal allergy is reliable in terms of their absolute concentrations-238± 12.0 ml versus control-372 ± 13.0 ml (P<0.05), which confirms the presence and/or formation of chronic gastrointestinal diseases by violating the control of CD8+ T-cell infections, resulting in a high risk of forming an autoimmune mechanism. During the immune response, B-lymphocytes differentiate into plasma cells that secrete antibodies. The B-system is represented in our studies by the content of CD20 + lymphocytes and the level of IgG, IgA, IgM and IgE antibodies (table.2).

B-lymphocytes can develop an adequate immune response only with the help of Thelpers. It was found that in the group of patients with gastrointestinal allergy associated with Hp, the level of B-lymphocytes was significantly higher - 28.8± 1.2 mg % of the control values-25.4 ±0.8 mg% (P < 0.05). Also, there was a significant increase in the relative and absolute levels of CD23 + cells -12.2± 0.8 mg% and 165 ±5.0 ml against the control - 9.4 ± 0.3 mg% and 145 ± 3.0 ml, respectively.

Table 2: B-cell immunity for gastrointestinal allergies in children.

Blood parameters	Control group (n=30)	Hp associated gastrointestinal allergy (n=32)	Hp unassociated gastrointestinal allergy (n=31)
CD20+, B-lymphocytes, %	25,4 ±0,8	28,8± 1,2*	18,17±0,99**
CD20+, B-lymphocytes (mkl)	438 ± 12	441 ±32	539,97± 53,15
CD23+ %	9,4 ± 0,3	12,2± 0,8*	19,47±0,77***
CD23+ mkl	145 ± 3,0	165 ±5,0*	334± 6,0***
Ig A (г/л)	3,1 ±0,5	8,8 ±1,2*	1,36±0,17*
Ig M (г/л)	2,2 ±0,5	3,5±0,8	1,91±0,19
Ig G (г/л)	14,8 ± 1,0	21,5±1,0*	9,54±0,43*
Ig E (нг/мл)	22,0 ± 1,2	25,0±1,1	88,67±4,84***

Note: * - differences relative to control group data are significant
(* - P<0.05, * * - P<0.01, *** - P<0.001)

In patients with gastrointestinal allergy without Hp infection, there was a significant decrease in the relative level of CD20 + lymphocytes-18.17±0.99 mg% versus control-25.4±0.8 mg% (P<0.05) and an increase in CD23 + lymphocytes19.47±0.77 mg% versus control - 9.4 ± 0.3 mg% (P<0.001).

There is evidence that B cells are a component of the humoral response in adaptive immunity and secrete antibodies and function as antigen-presenting cells. Having a proinflammatory phenotype, they have a high proliferative ability.[18] CD23 is known to be a low-affinity receptor for IgE and plays a transport role in regulating antibody feedback. Allergens entering the bloodstream are captured by antigen-specific IgE antibodies. The resulting IgE immune complexes bind to CD23 molecules on B cells. Studies have shown that elevated levels of soluble CD23 cause recruitment of unsensitized B cells when presenting antigenic peptides to allergen-specific B cells, hence increasing the production of allergen-specific IgE. In turn, IgE is known to enhance the cellular expression of CD23 and FcEpsilon RI (high-affinity IgE receptor).[19] Taking into account the above, it follows that an increase in CD23 + lymphocytes confirms the acute phase of the allergic process. In the study, patients with gastrointestinal allergy without association with Hp showed a significant 4-fold increase in IgE-88.67±4.84 ng / ml in relation to the control indicators - 22.0 ± 1.2 ng/ml (P<0.001).

An integral indicator of the functional activity of B-lymphocytes is the content of immunoglobulins of the main classes (G, A, M). Analysis of the blood test results of patients with gastrointestinal allergy associated with Hp showed a significant increase in the concentration of Ig A-8.8 ± 1.2 g / l versus 3.1 ± 0.5 g / l in the control and IgG-21.5±1.0 g / l versus 14.8 ± 1.0 g / l (P < 0.05). Comparative characteristics of the content of immunoglobulins in the blood of patients with gastrointestinal allergy without association with Hp revealed opposite shifts in the studied immunoglobulins. There was a significant decrease in the concentration of IgA to 1.36±0.17 g / l and IgG to 9.54±0.43 g / l (P<0.05) compared to the data of the control group. As for IgM, its concentration had an unreliable tendency to increase relative to the control for gastrointestinal allergy associated with Hp and Vice versa, for gastrointestinal allergy without association with Hp, it tended to decrease against the background of a significant increase in the level of IgE-88.67±4.84 ng / ml against-22.0 ± 1.2 ng / ml in the control.

CONCLUSIONS

The data obtained indicate that gastrointestinal allergy associated with Hp proceeds by the mechanism of an

allergic reaction of a delayed type. This is characterized by the formation of a secondary immunodeficiency state and infection against the background of a hyporeactive syndrome with an increase in the process of antibody formation. CD8+ lymphocyte deficiency contributes to the formation of chronic gastrointestinal diseases with an autoimmune mechanism. The marked significant increase in the level of CD23 + lymphocytes indicates an allergic sensitization of the body in chronic gastrointestinal diseases. The gastrointestinal form of allergy without Hp infection is accompanied by activation of the T - and B-cell system, which is accompanied by hyperreactive syndrome and increased synthesis of CD23 + lymphocytes in response to allergens, thereby increasing the synthesis of allergen-specific IgE.

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