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Article / Review

CLINICAL AND IMMUNOLOGICAL ASPECTS OF BRONCHIAL ASTHMA WITH ATOPIC DERMATITIS IN CHILDREN

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Abstract. This article presents the results of a clinical and immunological examination of 68 children with allergic bronchial asthma and 22 children with atopic dermatitis. **The purpose of the work** is to determine the concentrations of IgA, IgM, IgG to identify clinical and immunological features in the blood serum of children with allergic asthma and AD and to identify clinical and immunological features in groups of these patients. **Methods.** At the allergy department of the VDOCH, 68 children with allergic asthma and 22 children with AD aged from 4 to 14 years (of which 53 boys and 37 girls) were examined. All children were examined clinically and laboratory (complete blood count, general urine test, biochemical blood test, nasal swab for eosinophils, stool test for helminth eggs, scraping for enterobiasis), and a carefully collected medical history. **Results and conclusions:** Taking into account the number of acute respiratory infections in the history, we identified significant differences in these groups of patients (p = 0.017). The concentrations of IgA, IgM, IgG in the blood serum of the examined patients were determined using an enzyme-linked immunosorbent assay (ELISA). We found that 33.8% of children with asthma and 36.4% of children with atopic dermatitis have low IgA levels. We also determined low IgG concentrations in more than half of the examined patients both in the group with bronchial asthma and in the group with atopic dermatitis (58.8% and 59.1%, respectively), which, in combination with low levels of other immunoglobulins, can be regarded as transient immunodeficiency in children.

Key words. immunoglobulin, bronchial asthma, atopic dermatitis

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Relevance. The article presents the results of clinical and immunological examination of 52 children with allergic bronchial asthma (BA) and 14 children with atopic dermatitis (AD). Significant differences in the number of acute respiratory infections in the anamnesis were obtained in the groups (p=0.017). The concentrations of IgA, IgM, and IgG in the blood serum of the examined patients were determined by the method of solid-phase enzyme immunoassay (ELISA). It was found that 34.8% of children with AD and 29.4% of children with AD have reduced IgA levels. And more than half of the examined patients in both groups showed reduced IgG concentrations (68.8% and 49.1%, respectively), which, together with low levels of other immunoglobulins, can be regarded as transient immunodeficiency states in children. In recent years, there has been a steady increase in the proportion of allergies in the pathology of childhood. Especially obvious is the increase in the prevalence of such diseases among children as bronchial asthma (BA), atopic dermatitis (AD), allergic rhinitis (AR), and pollinosis[1,2]. Asthma is still an urgent problem in clinical pediatrics, as it is the leader among allergic diseases, as well as one of the most common allergopathologies in children[3]. In different countries of the world, the incidence of AD is recorded with a frequency from 1 to 18%[4,5]. So, in the United States, this disease it occurs among the child population with a frequency of 6.0-7.5%, which is about 5 million children[5]. In France, the incidence of AD among children over the age of ten exceeded 10%[6,7]. In Uzbekistan, the incidence of AD in the population is about 0.5%[5,7]. Asthma is a chronic respiratory disease that is based on local inflammation, as well as a concomitant increase in bronchial hyperreactivity. In the clinical picture of the disease, repeated episodes of shortness of breath, wheezing, chest tightness and coughing are noted, especially at night or in the early morning. These clinical manifestations of the disease are usually associated with widespread bronchial obstruction, which changes in its severity and is often reversible either spontaneously or under the influence of treatment[7,8]. Blood pressure in modern conditions is also a serious medical and social problem, which is due to its high prevalence among the child population, chronic recurrent course, and the appearance of severe forms of the. The frequency of AD detection among children in economically developed countries, especially in the group of primary school-age children, varies from 10 to 20%[2,9]. The manifestation of AD is considered a high risk factor for the further development of AD in children, which may be explained by the presence of a certain link between these two diseases. This fact is also evidenced by some epidemiological studies. For example, it

was found that AD is more often diagnosed in children whose families previously had cases of allergic asthma, and, conversely, with a rare detection of AD in the population, the manifestations of AD are relatively less common. Cases of allergic disease progression are known. For example, if children have a food allergy in the first year of life, and then clinical signs of AD appear and concomitant bronchial hyperreactivity is detected, the probability of progression of allergopathology and the development of AD is very high, which is due to the specificity of IgE - an antibody response[1,3,7]. Atopy plays a significant role in the pathogenesis of these and many other allergic diseases[9,10]. According to the definition of the European Society of Allergists and Clinical Immunologists atopy is considered an individual or family predisposition to hyperproduction IgE-antibodies in response to low doses of allergens, which as a result leads to the development of clinical manifestations of allergic disease[11]. Thus, numerous studies show a higher prevalence of AD among children whose parents had the same disease, compared to those children whose parents did not report the presence of certain allergic diseases, including AD[10]. However, there are claims that atopy, in particular as a risk factor for AD, occurs in no more than 40% of children, and environmental factors and immune disorders mediated by viral and bacterial infections have the greatest impact on the development of the disease. At the present stage, it is believed that the leading role in the pathogenesis of AD and AD belongs to IgE-mediated allergic reactions, a significant role in the development of which is played by the prevalence of Th2-cell response over Th1 with a violation in the system of cytokines that play an important role in the development of allergic diseases, including the activation, proliferation, and differentiation of immunoregulatory and effector cells[12,13]. However, the immune response to allergens is not limited to the formation of only IgE. It is also associated with other classes of immunoglobulins, which are of great importance and, together with other indicators, make it possible to assess the state of immunity in children. Therefore, the study of immune status indicators in children makes it possible to determine the activity of the disease, as well as the effectiveness of the treatment, and early diagnosis and timely initiation of adequate treatment are extremely important to prevent the formation of irreversible changes.

The purpose of the work is to determine the concentrations of IgA, IgM, IgG to identify clinical and immunological features in the blood serum of children with allergic asthma and AD and to identify clinical and immunological features in the groups of these patients.

Methods 68 children with allergic asthma and 22 children with AD aged from 4 to 14 years (including 53 boys and 37 girls) were examined on the basis of the allergological department of UZ «VDOKB». All children were examined clinically and in the laboratory (general blood test, general urinalysis, biochemical blood test, nasal smear for eosinophils, fecal analysis for helminth eggs, scraping for enterobiosis), and a medical history of the disease was carefully collected. Skin scarification tests (CSPs) with allergen kits produced by I. I. Mechnikov Biomed OJSC (Russia) were performed outside the exacerbation of the underlying disease. The concentrations were studied by solid-phase enzyme-linked immunosorbent assay (ELISA). in blood serum using reagent kits from the company ”VektorBest « (Novosibirsk, Russia). Concentrations estimated in g/l. Statistical processing of the obtained results was carried out using the application software package Statistica 6,0. Results and discussion Regardless of the general condition at the time of hospitalization, all children with AD complained of recurrent episodes of bronchial obstruction, clinically manifested by attacks of wheezing and coughing, and children with AD complained of recurrent skin rashes. In the group of children with BA, 50 children (73.5%) were in remission of the underlying disease, 9 patients (13.2%) were in incomplete remission or in the post - onset period, 8 children (11.8%) were in the state of acute BA. 58 children (85.3%) were previously diagnosed with mild asthma 9 patients (13.2%) had moderate BA and 1 (1.5%) had severe BA. 31 (45.6%) examined patients were found to have concomitant diseases, including allergic year-round rhinitis-12 children, atopic dermatitis-9 children, GER with non-erosive esophagitis-5 children, vasomotor rhinitis-3 patients, exogenous-constitutional obesity, enuresis, adenoids, chronic urticaria, giardiasis-1 case each. The first clinical manifestations of AD were observed at the age of 3.54±0.60 years (according to the anamnesis of 50 examined children). Hereditary developmental burden allergic diseases were detected in 28 (41.2%) of 68 examined individuals. The incidence of asthma among parents was noted in 10 cases, allergic rhinitis occurred in 6 cases, allergic dermatitis and drug allergy occurred in 5 cases, pollinosis occurred in 3 cases, and Quincke’s edema was detected in 1 case. The average

duration of breast-feeding was 4.26±1.03 months. 7 children (10.3%) were on artificial feeding from birth. 33 children (48.5%) were breastfed up to 3 months of life, and 16 children were breastfed from 4 to 6 months of life (23.5%), and only 12 children (17.7%) received breast milk for more than 6 months. Early transfer of children to artificial feeding contributed to the occurrence of food allergies in the first year of life in most of the examined patients. Clinically, food allergies were manifested by skin rashes and were observed in 55.9% of the examined children (38 out of 68 children with asthma). So, among 33 children who received breast milk before 3 months of life, 23 (69.7%) had food allergies after being transferred to artificial feeding. This confirms the fact that there is a definite relationship between the duration of breastfeeding and the further development of allergic pathologies in children. Problems with the gastrointestinal tract in the form of a stool disorder in the first year of life occurred in 8 children. 21 patients (30.9%) indicated a previously detected drug allergy. The incidence of childhood infections was detected in 37 children (54.4%). Chickenpox was the most common childhood infection, with a history of 33 children (48.5%), 1 child with rubella, 2 children with rubella and chickenpox, 1 child with rubella and measles,and 1 child with mumps. 17 children (25%) out of 68 with asthma had previously diagnosed pneumonia. Acute respiratory infections (ARI) with a frequency of episodes more than 4 times a year, against the background of which the majority of patients had an exacerbation of asthma, were noted in the anamnesis in 37 children (54.4%), of which only 17 previously had childhood infections. CPR was performed on 54 children who were out of the main disease exacerbation. Sensitization to household allergens was detected in 34 children (63%). Positive reaction during CPR to allergens of mites of the genus Dermatophagoides pteronissynus It was detected in 27 children, for house dust allergens-in 23 children, for library dust-in 18 patients, for feather pillows - in 3 children. 4 children had positive CP to epidermal allergens (reactions to horse dandruff allergen-2 children, to dog hair-3 children, to cat hair-1 child, to sheep wool-2 children). Eosinophils were detected in nasal smears in 37 children, and in 18 patients above 5%. According to the results of an ELISA study of blood sera of children with asthma (Table. 1) average concentration IgA was 1.10 ± 0.16 g / l, IgM 1.07 ± 0.15 g / l, IgG 6.81 ± 1.00 g / l. 40% of children were found to have low blood pressure. IgG in relation to the accepted age norms (the average level was 4.20 ± 0.42 g / l). 23 children have the following level IgAnd in the blood serum was also lower than the values corresponding to the accepted age norms (the average level was 0.48 ± 0.07 g / l). Within the age limit IgA had 43 children (1.35 ± 0.16 g / l), IgM – 42 children (1.08 ± 0.11 g / l), IgG – 26 children (9.71 ± 0.85 g / l). Advanced level IgM in the blood serum of 8 children with AD (2.10 ± 0.68 g/l). In the group of children with AD, 9 children (40.9%) were in a state of exacerbation of this allergopathology, 8 patients (36.4%) had a subacute course of the disease, and 5 children (22.7%) were in remission. Concomitant diseases were identified in 10 (45.5%) of the examined patients, including GER with non-erosive esophagitis-5 children (50%), asthma, recurrent obstructive bronchitis, ichthyosis, giardiasis, vasomotor rhinitis – 1 child each. In 13 examined patients (59.1%) with AD, the initial clinical manifestations of the disease were observed they were noted already in the first year of life. Hereditary burden of developing an allergic disease was determined in 12 (54.6%) of the 22 surveyed individuals. The incidence of allergic dermatitis among parents was noted in 6 cases, in 3 cases there was allergic asthma, in 1 case drug and insect allergies, chronic urticaria were detected. The average duration of breastfeeding in the group of children with AD was 4.77±2.60 months. 6 children (27.3%) were on artificial feeding from birth. Breastfed up to and including 3 months of life was 7 children (31.8%), from 4 to 6 months of life-4 children (18.2%), and only 5 children (22.7%) received breast milk for more than 6 months. The manifestation of food allergy in the first year of life was observed in 17 (77.3%) of the examined patients. Problems with the gastrointestinal tract in the form of a stool disorder in the first year of life occurred in 3 children (13.6%). Previously detected drug allergy was indicated by 6 patients with AD (27.3%). The incidence of childhood infections was detected in 10 children (45.5%), and all cases accounted for chickenpox. 3 children (13.6%) had previously diagnosed pneumonia. ORI with frequency episodes more than 4 times a year were recorded in the anamnesis of only 3 children with AD (13.6%), and according to this indicator, the groups of children with AD and AD differed significantly (p=0.017). CPR was performed on 9 children who were out of exacerbation of the underlying disease. Sensitization to household allergens was detected in only 2 children (9.1%). Positive skin tests were found for library dust, allergens of mites of the genus Dermatophagoi despteronissynus and feather pillows. In the acute and subacute periods

of AD, children (n=13) underwent the Shelley test, which was considered positive if the percentage of basophil degranulation was more than 25. Thus, a positive Shelley test was registered in 6 children to house dust (46.2%), in 5 - to feather pillows (38.5%), in 3 - to chicken (23.1%), in 2 - to buckwheat (15.4%), in 1 child - to pork, egg, cow's milk and millet (7.7%). According to the results of an ELISA study of blood sera of children with AD (Table. 2) the average concentration of IdA was 0.92 ± 0.23 g/l, IgM 1.22 ± 0.33 g/L, IgG 6.56 ± 1.23 g/l. It was found that 13 children (4.72 ± 0.72 g/l) had a reduced level of IgG in relation to the accepted age norms. In 8 patients, the serum IgA level was also lower than the corresponding values. according to the accepted age norms, and amounted to 0.54 ± 0.22 g/l. Within the age norm, 14 children had IgA (1.14 ± 0.29 g/l), 15 children had IgM (0.80 ± 0.16 g/L), and 9 patients had IgG (9.22 ± 1.64 g/L). Elevated serum IgM levels were observed in 6 children with BP (2.29 ± 0.42 g / l). In the course of the study, it was determined that fluctuations in serum immunoglobulin levels relative to generally accepted age norms occur in both groups of children examined ($p>0.05$). In the group of children with asthma, 58.8% of patients have a low level of IgG in the blood serum, and 33.8% have relatively low concentrations of IgA. In the group of children with AD, these results are 59.1% and 36.4%, respectively. The level of IgM in the group of children with AD is reduced in 22.1% of children, increased in 27.3%, while in AD there are only increases in 11.8% of cases.

Conclusion 1. Hereditary predisposition to allergic diseases occurs in 41% of the examined children with asthma and 54.5% of children with AD. Moreover, in the structure of allergopathologies among close relatives of the first group, asthma occurred in 35.7% of cases, and in the second group, allergic dermatitis was observed in 50% of cases in relatives. 2. Manifestation of food Allergy in the first year of life were observed in 55.9% of children with asthma and 77.3% of children with AD, due to the type and timing of feeding, considering the fact that in the group of BA 10.3% of the children were bottle-fed, 48.5% of children breastfed to 3 months and in the group of AD, these figures amounted to 27.3% and 31.8%, respectively. 3. 45.6% of the examined children with asthma have concomitant diseases, with allergic rhinitis accounting for 38.7% year – round, atopic dermatitis-29%, and GER with non-erosive esophagitis-16.1%. 4. In the group of children with AD, concomitant diseases are noted in 45.5% of patients, among whom GER with non-erosive esophagitis occurs in half of children (50%). 5.ARI with a frequency of episodes more than 4 times a year occurred in 37 out of 68 children with AD (54.4%), while only 3 out of 22 children (13.6%) had it in the group of children with AD. According to this indicator, the groups of children with asthma and blood pressure differed significantly ($p=0.017$). 6. According to the results of CP, 63% of all children with asthma examined during remission are sensitized to household allergens. The leading allergens were mites of the genus Dermatophagoidespteronissynus (79.4%), house dust (67.7%), (2021) 65 and library dust (52.9%). 7. In the group of children with AD, only 9.1% of patients were sensitized to household allergens by CPR, and a positive Shelley test was recorded in 46.2% of children to house dust, 38.5% to pillow dust, 23.1% to chicken, 15.4% to buckwheat, and 7.7% to pork, egg, cow's milk, and millet. 8. Relatively low serum IgA levels are observed as in children with AD, and in children with AD. IgA values determined below the generally accepted age norms are detected in 33.8% of patients with AD and 36.4% of children with AD. 9. More than half of the examined patients with AD and AD have reduced serum IgG concentrations (58.8% and 59.1%, respectively), which, together with low levels of other immunoglobulins, can be regarded as transient immunodeficiency states in children.

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