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FEATURES OF THE SPECTRUM OF SENSITIZATION DERMATORESPIRATORY MANIFESTATIONS OF ALLERGY IN CHILDREN OF KHAKASSIA

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The study examined the characteristics of the spectrum of sensitization to food and inhalant allergens in children of Khakassia with atopic dermatitis in combination with respiratory manifestations of allergies based on allergological history, objective examination data, and skin testing results (prick-test). It is defined, that risk factors for the development of dermatorespiratory syndrome in children with upper respiratory tract damage or multiple organ respiratory tract damage may include: long course of the atopic dermatitis, manifestation of atopic dermatitis in the 1st year of life, aggravated heredity, pruritus, seasonality of the disease, high concentration of total IgE in blood serum, the presence of sensitization to food and pollen allergens, multivalent sensitization to milk, egg, cereals. Our study showed that the children of Khakassia have features of the sensitization spectrum depending on the expansion of the “shock” organs of atopy from atopic dermatitis to dermatorespiratory syndrome.

Keywords: dermatorespiratory syndrome, atopic dermatitis, allergens, sensitization.

Introduction. Atopic dermatitis (AD) is a key factor in the start of the “atopic march”, which is characterized by the staged development of sensitization and the transformation of pathology from skin manifestations to damage to the respiratory tract. The combined clinical manifestations of allergic skin and respiratory tract damage are referred to in the literature as dermatorespiratory syndrome (DRS) [1, 7]. DRS is characterized by the expansion of the spectrum of sensitization to causally significant allergens with the development of polyvalent allergies, often to food and inhalant allergens [2, 4]. Moreover, the spectrum of sensitization to certain allergens has regional characteristics, which is associated with environmental and ethno-household characteristics of the region where patients live [3]. The steady increase in morbidity, the severe clinical course of pathology with the defeat of several "shock" organs and systems necessitates the study of clinical and immunological features of the systemic manifestations of allergies, with the aim of developing effective measures to prevent the progression of atopy.

Purpose of the research was to study the characteristics of the spectrum of sensitization to food and inhalant allergens in children of Khakassia with atopic dermatitis in combination with respiratory manifestations of allergies.

Materials and methods. A retrospective examination of children of Khakassia, patients with atopic dermatitis, who were under the supervision of an allergist-immunologist, was performed. We analyzed 63 case histories of 34 children aged 1.5 to 18 years. The following nosological groups were distinguished: group 1 — atopic dermatitis (n=20, average age - 5,0 ± 1,6 years), group 2 — atopic dermatitis in combination with allergic rhinitis (n=22, average age - 6,5 ± 1,1 years), group 3 - atopic dermatitis in combination with bronchial asthma (n=21, average age - 5,0 ± 0,9 years), in its pure form - in 28,6% (n=6), or in combination with allergic rhinitis - a single respiratory tract disease (one way, one disease) - in 71,4% (n=15).

All examined underwent determination of the concentration of total IgE in blood serum by enzyme-linked immunosorbent assay.

The study of the spectrum of sensitization to food and inhalant allergens was carried out on the basis of an allergological history, objective examination data, and skin test results (prick test) taking into account the size of the blistering reaction and the magnitude of hyperemia. For statistical analysis, the Statistica 6.0 application package was used with the non-parametric Mann-Whitney test; calculation of generalizing coefficients: median (Me) and mean error (m). Data on the concentration of total IgE in blood serum are presented as medians, 25 and 75 quartiles [Me, Q 25 - Q 75]. Comparison of qualitative characteristics in groups was carried out by the method of variational analysis using the exact Fisher test. Differences were considered statistically significant at $p < 0.05$.

Results and discussion. In all groups of patients, children's (manifestations of the disease from 2 to 12 years old) and teenage (over 12 years old) forms of atopic dermatitis dominated. The highest incidence of childhood atopic dermatitis was noted in group 3 - in 85,7% (n=18), and adolescent in the second group - in 36,4% (n=8). Infant form of atopic dermatitis (from birth to 2 years) was observed only in children of the 1st group - in 10% (n=2) cases. Consequently, the presence of childhood and adolescent forms of AD is a risk factor for the development of systemic manifestations of allergies with damage to both the upper and lower respiratory tract, which is consistent with the literature [8].

The manifestation of AD in most patients occurred in the first year of life: in the 1st group of patients in 68,4% (n=13/19), in the 2nd group - in 90% (n=18/20), in the 3rd group - in 100% (n=20/20) cases, $p_{1,3}$=0.006. Moreover, the debut of AD up to 6 months of age in group 1 was noted in 42% (n=9/19), group 2 - in 90% (n=18/20), group 3 - in 85% (n=17/20) cases, $p_{1,2}$ =0.004, $p_{1,3}$ =0.01.

Analysis of anamnestic data on the duration of breastfeeding showed that in the 2 group of patients breastfed up to

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1 month of age there were 28,5% (n=4) children, which is more compared with the indicators of other groups: 5,6% (n=1) in group 1 and 5,8% (n=1) in group 3. In addition, breastfeeding up to 1 year was less frequently observed in group 2 patients compared with groups 1 and 3: 14,2% (n=2) versus 27,8% (n=5) and 41,2% (n=7). Children who were breast-fed from birth in groups 1, 2, and 3 comprised 5,6% (n=1), 7.1% (n=1), and 5,8% (n=1), respectively.

The duration of the course of AD was statistically significantly longer in the groups of patients with dermatorespiratory manifestations (group 2 and 3) compared with the group of patients with AD with isolated skin lesions (group 1): 6,5±1,0 years and 5,0±1,0 years relative to 3,5±0,8 years, $p_{1,2}$=0.003, $p_{1,3}$=0.1, $p_{2,3}$=0.06. Burdened heredity was most often observed in patients of groups 2 and 3, mainly along the maternal side, in comparison with group 1: 82,3% (n=14/17) and 80% (n=12/15) relative to 52,6% (n=10/19). Complaints of skin itching: in group 1 in 63,1% (n=12/19), in the second group in 89,5% (n=17/19), in group 3 in 75% (n=15 / 20) cases, $p_{1,2}$=0.05. Therefore, the prolonged course of the AD contributes to the progression of the disease with the development of respiratory forms of atopy. There is evidence in the literature about the association of AD and the risk of developing respiratory allergies. Moreover, in 60% of children with severe course of AD, bronchial asthma develops [8].

The concentration of total IgE in serum was: in the 1st group - 48,5 IU / ml [27,5; 121,5], in the 2nd group - 53,0 IU/ml [41,0; 59,0], in the 3rd group - 189,0 IU/ml [37,0; 371,0], $p_{1,3}$=0.01, $p_{2,3}$=0,2. It should be emphasized that with the expansion of the shock territories of AD to DRS, the concentration of IgE in the blood serum increases, which is consistent with the literature [8].

Data on the characteristics of food allergies in children with dermatorespiratory syndrome are extremely few in the literature [1, 2]. When analyzing the spectrum of sensitization to food allergens, it was noted that in group 3, the sensitization to fish (cod, hake) was statistically significantly more often compared with groups 1 and 2: 75,0% (n=12/16) versus 22,2% (n=4/18) and 33.3% (n=7/21), respectively, $p_{1,3}$=0.002, $p_{2,3}$=0.01 (Table 1). It is noted that the presence of food allergies to fish in patients with AD over 14 years of age increases the risk of developing bronchial asthma [5], which is consistent with our data. Sensitization to cow's milk is more often defined in groups 1 and 2 in comparison with group 3: 70.0% (n=14/20) and 77,3% (n=17/22) relative to 47,6% (n=10/21), respectively, $p_{2,3}$=0.04.

There were no statistically significant differences in sensitization to other food allergens of animal origin between the examined groups. However, it was noted that in the group of patients with AD with multiple organ damage to the respiratory tract (group 3), sensitization to chicken meat was more often defined in comparison with 1 and 2groups: 57.1% (n=12/21) versus 30.3% (n=6/20) and 40.9% (n=9/22).

An analysis of the spectrum of sensitization to allergens of plant origin showed that in group 3, a sensitization to rice was statistically significantly more often compared with group 1: 52,4% (n=11) versus 15% (n=3), respectively, $p_{1,3}$=0.01. In group 3, the sensitization to beets and pears was statistically significantly more often compared with group 1: 55,6% (n=10/18) versus 15,4% (n=2/13), $p_{1,3}$=0.02 and 35,7% (n=5/14) relative to 0% (n=0/11), $p_{1,3}$=0.03, respectively.

There were no statistically significant differences in sensitization to other foodborne allergens of plant origin between the examined groups. However, it was noted that sensitization to cereals was more often determined in groups of patients with DRS in comparison with AD with isolated skin lesions, however, the data were not statistically significant. Buckwheat sensitization was determined in all groups, but most often in patients with DRS: in group 3 - in 38,1% (n=8) and in group 2 - 31,8% (n=7) cases, while in 1 group in 25% (n=5).

Bivalent sensitization to the main food allergens was statistically significantly more often observed in group 1 - 55.,0% (n=11/20), compared with groups 2 and 3 - 40,9% (n=9/22) and 20.0% (n=4/20), respectively, $p_{1,3}$ =0.02. Polyvalent sensitization to the main food allergens in group 1 was noted in 30.0% (n=6/20) cases, in group 2 - 45,5% (n=10/22), group 3 - 45,0% (n=9/20).

According to the literature, the incidence of sensitization to inhaled allergens in patients with AD is up to 89% [7]. According to the allergological history, seasonal exacerbations of the underlying disease (DRS or AD) were statistically significantly more often detected in groups 2 and 3 compared with group 1: 45,5% (n=10) and 42,9% (n=9) versus 5% (n=1),

Table 1

Features of the spectrum of sensitization to food allergens in patients f the selected groups, n (%)

Allergen	Group			
	1	2	3	p
Animal origin				
Cow's milk	14 (70)/20	17 (77.3)/22	10 (47.6)/21	2.3=0.04
Beef meat	8 (40)/20	9 (40.9)/22	8 (38.1)/21	–
Egg yolk	9 (47.4)/19	10 (47.6)/21	9 (45)/20	–
Chicken Egg Protein	9 (47.4)/19	6 (27.3)/22	6 (31.6)/19	–
Whole Chicken Egg	13 (65)/20	12 (54.5)/22	12 (57.1)/21	–
Chicken's meat	6 (30)/20	9 (40.9)/22	12 (57.1)/21	–
Fish	4(22.2)/18	7(33.3)/21	12(75.0)/16	1.3=0.002 2.3=0.01
Plant origin				
Cereals	11 (55)/20	17 (77.3)/22	13 (61.9)/21	–
Wheat Flour Protein	9 (45)/20	9 (40.9)/22	9 (45)/20	–
Rye flour protein	3 (17.6)/17	5 (23.8)/21	4 (20)/20	–
Barley grits	5 (27.8)/18	11 (50)/22	8 (40)/20	–
Oat groats	3 (17.6)/17	10 (54.5)/22	8 (40)/20	–
Rice	3 (15)/19	6 (27.3)/22	11 (52.4)/20	1.3=0.01
Buckwheat	5 (25)/19	7 (31.8)/22	8 (38.1)/20	–
Citrus	5 (31.2)/16	8 (50.0)/16	8 (57.1)/14	
Beet	2 (15.4)/13	9 (45)/20	10 (55.6)/18	1.3=0.02
Carrot	6 (42.9)/14	8 (38)/21	11 (61.1)/18	–
Cucumber	4 (30.8)/13	10 (52.6)/19	9 (50.0)/18	–
Tomato	5 (45.5)/11	10 (62.5)/16	6 (46.2)/13	–
Cabbage	4 (36.4)/11	6 (54.5)/11	8 (61.5)/13	–
Apple	2 (18.2)/11	5 (26.3)/19	4 (22.2)/18	–
Pear	0 (0)/11	3 (18.8)/16	5 (35.7)/14	1.3=0.03
Grape	2 (20)/10	9 (56.2)/16	6 (46.2)/13	–
Banana	4 (33.3)/12	4 (22.2)/18	7 (46.7)/15	–

Note: p-values are indicated only for p<0.05.

Table 2

Features of the spectrum of sensitization to inhalant allergens in patients of the selected groups, n (%)

Allergen	Group			
	1	2	3	p
Pollen				
Meadow grass	10 (50)/20	17 (77.2)/22	16 (76.2)/21	–
Trees	11 (55)/20	12 (54.5)/22	15 (71.4)/21	–
Weed grass	10 (50)/20	15(68.2)/22	17 (80.1)/21	1.3=0.04
Household				
Dermatophagoides pteronyssinus	3(25)/12	10(58.8)/17	7(43.8)/16	–
Dermatophagoides farinae	2(18.2)/11	9(60)/15	6 (50.0)/12	1.2=0.03
House dust	9(64.3)/14	12(66.7)/18	13(65.0)/20	–

respectively, $p_{1,2}$ =0.002, $p_{1,3}$ =0.004.

The analysis of the spectrum of sensitization to inhalant allergens in the selected groups showed that sensitization to pollen allergens was detected in 51,6% in group 1 (n=31/60), in 66,7% in group 2 (n=44/66), in group 3 - in 76,2% (n=48/63), $p_{1,3}$=0.005 (table 2).

Sensitization to weed pollen was statistically significantly more often defined in group 3 compared with group 1: 80.1% (n=17/21) versus 50% (n=10/20), respectively, $p_{1,3}$=0.04, which may indicate the role of these allergens in the development of allergic rhinitis and bronchial asthma in patients with DRS. There were no statistically significant differences in sensitization to other pollen allergens between the examined groups. However, sensitization to pollen of meadow grasses was more often observed in the group of patients with atopic dermatitis in combination with allergic rhinitis (group 2), which also suggests that these allergens play a role in upper respiratory tract damage in DRS.

Polyvalent sensitization to pollen of a mixture of meadow, weed grass and trees is defined in group 3. The high frequency of sensitization to plant pollen in DRS is probably a risk factor for multiple organ damage to the respiratory tract, as a barrier to the penetration of pollen allergens. The lowest frequency of sensitization to pollen allergens was observed in patients with AD (group 1). However, taking into account the fact that the clinical manifestations of seasonal AD in this category of patients are noted in only 5% (n=1/20) of cases, the frequency of sensitization to pollen allergens in group 1 is quite high - 51,6% (n=31/60) Sensitization to pollen allergens of patients with AD can be associated with cross-sensitivity to food products of plant origin based on the binding of specific IgE to homologous structures of the allergen [8].

In the study of sensitization to household allergens, the highest frequency of sensitization to house dust was observed in group 2 in comparison with group 1: 62,0% (n=31/50) versus 37,8% (n=14/37), $p_{1,2}$=0.02. Dermatophagoides farinae house dust mite sensitization was statistically significantly more often determined in the group of patients with DRS (group 2) compared with the group of patients with AD (group 1): 60% (n=9/15) and 18,2% (n=2/11), respectively, $p_{1,2}$=0.03. Dermatophagoides pteronyssinus house dust mite sensitization was also more common in group 2 compared with other groups, but did not reach statistical significance. In the group of patients with AD compared with the groups of patients with DRS, sensitization to house dust mites Dermatophagoides farinae and Dermatophagoides pteronyssinus was relatively low, while sensitization to house dust was detected in 64,3% (n=9/14) of cases, which, according to the literature, can be associated with damage to the epidermal barrier and percutaneous sensitization to aeroallergens in patients with AD [1,7,8].

Conclusion. As a result of the studies, it was found that dermatorespiratory syndrome is more often noted in childhood and adolescent AD. The childhood form of AD is a risk factor for the development of DRS with multiple organ damage to the respiratory tract (allergic rhinitis and bronchial asthma), and adolescent form of atopic dermatitis with allergic rhinitis.

Risk factors for the development of DRS in children with upper respiratory tract infections or multiple organ respiratory tract infections may include: prolonged course of AD, manifestation of AD in the 1st year of life, aggravated heredity, pruritus, seasonality of the disease, high concentration of total IgE in blood serum, presence sensitization to food and pollen allergens, multivalent sensitization to milk, egg, cereals.

Thus, our study allows us to determine the characteristics of sensitization with the indication of causally significant allergens, to find out their influence on the formation of the sensitization spectrum depending on the expansion of the “shock” organs of atopy from atopic dermatitis to dermatorespiratory syndrome in children of Khakassia.

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