

## POINT OF VIEW

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## ALLERGIC MECHANISMS AS NEW TRIGGERS FOR PSORIASIS DEVELOPMENT

**Introduction.** Psoriasis and atopic dermatitis combine signs of a systemic inflammatory process with damage not only in the skin, but also in other organs and systems with the formation of severe forms of the disease, the so-called "psoriatic disease" and "atopic march". The question of the causal relationship between allergy and psoriatic disease and the peculiarities of the spectrum of sensitization to allergens in psoriasis is relevant, and its study can lead to the discovery of new triggers for the development and progression of pathology.

**The purpose of the study:** to analyze the spectrum of sensitization to pollen, household, fungal and epidermal allergens in patients with psoriasis in order to identify new triggers of psoriatic disease.

**Materials and methods.** Patients with psoriasis (Group 1, n=41) aged 18 to 66 years were examined. Patients with atopic dermatitis (Group 2, n=20) were examined as a comparison group. The control group consisted of practically healthy people matched by sex and age (group 3, n=19). Specific allergological examination included collection of an allergic history, determination of the spectrum of sensitization by analyzing the concentration of total immunoglobulin E (IgE) and allergen-specific IgE to pollen, household, fungal and epidermal allergens by the method of enzyme-linked immunosorbent assay. The calculation and analysis of the obtained data was carried out using the Statistica 8.0 software package.

**Results and discussion.** In a comparative analysis of the spectrum of sensitization to pollen allergens between groups of patients, it was noted that in atopic dermatitis, sensitization to pollen from trees, meadow grasses and weeds was statistically significantly more frequent in comparison with psoriasis. In the group of patients with psoriasis, monovalent sensitization was statistically significantly more frequent in comparison with the group of patients with atopic dermatitis, in which, on the contrary, polyvalent sensitization was more often determined.

**Conclusion.** The data obtained in the course of this study confirm the concept that atopic mechanisms are characteristic of psoriasis, but to a lesser extent than for atopic dermatitis and are protective against the development of autoimmune mechanisms, which is consistent with literature data. Consequently, further study of psoriasis and allergies from the standpoint of comorbidity should be carried out in the direction of investigating both atopic and non-atopic mechanisms of triggering allergic reactions involved in the immunopathogenesis of psoriatic disease.

**Keywords:** psoriasis, atopic dermatitis, sensitization, allergens, immunoglobulin E, immunopathogenesis.

**Introduction.** Psoriasis (PS) and atopic dermatitis (AD) are chronic inflammatory skin diseases, in the pathogenesis of which the cells of the immune system play a key role [3,4,10]. PS and AD combine signs of a systemic inflammatory process with damage not only in the skin, but also in other organs and systems with the formation of severe forms of the disease, the so-called "psoriatic disease" and "atopic march" [1,2,7]. PS and AD are genetically determined diseases, the development and course of which is associated with the influence of numerous environmental factors: mechanical and physical effects, insolation, microorganisms, allergens and others [3,4,6]. Defects of the epidermal barrier in psoriasis and atopic dermatitis promote the penetration of various antigens through the epidermis with the development of sensitization and subsequent activation of al-

lergic mechanisms of skin damage [7,14].

It is worth noting that the link between autoimmune diseases and atopy is actively discussed in modern research. Previously, it was believed that diseases caused by mutual counter-regulation of immunopathological responses of Th1 and Th-2 types cannot occur simultaneously in the same person. However, in modern studies, data on the combination of psoriasis and atopy are increasingly found [10,12,15].

Atopic dermatitis is a classic example of atopy, in which the predominance of the Th2-type immune response is noted and the key role of IgE-mediated mechanisms has been proven [6]. Whereas psoriasis, in contrast to atopic dermatitis, is characterized by the formation of a Th1/Th17-type immune response [4]. For a long time it was believed that the presence of psoriasis in a patient is "protective" in relation to the development of allergies. Therefore, allergy can be one of the triggers of psoriasis. Evidence in favor of this hypothesis is provided by the results of studies indicating that a long course of inflammatory reactions in PS leads to an increase in the concentration of B-cells in psoriatic plaques with a deviation of the immune response from Th1 to Th2 type [9]. This opinion is supported by data on the confirmed role of Th17 and Th1 lymphocytes both in psoriasis and in some forms of AD [6]. There is evidence of an increase in the production of immunoglobulin E by B-lymphocytes under the action of IL-17a, a key

cytokine involved in the development of PS [11].

Thus, the fundamental scientific problem to be solved by this research is to study the role of atopic immunopathological mechanisms of allergic reactions in the development of psoriatic disease based on the analysis of the concentration of specific IgE to pollen, household, fungal, epidermal allergens. Comparative analysis of data from specific allergological examination of patients with psoriasis and atopic dermatitis is aimed at identifying new specific markers of psoriatic disease that can be used for a personalized approach to the diagnosis and treatment of psoriatic disease. **Purpose of the study:** to conduct a comparative analysis of the spectrum of sensitization to pollen, household, fungal and epidermal allergens of patients with psoriasis and atopic dermatitis in order to determine new specific markers of psoriatic disease.

**Materials and methods.** Patients with psoriasis were examined (Group 1, n=41). The age of patients varied from 18 to 66 years, the average age of patients with PS was  $40,0 \pm 2.1$  years. Patients with atopic dermatitis (Group 2, n=20) were examined as a comparison group, since AD is a classic example of atopic allergic disease. The average age of AD patients was  $30,5 \pm 2,7$  years. In both groups of patients, women were more common: in the group of patients with PS – 60,9% (n=25) of cases, in the group of patients with AD – in 60,0% (n=12). The control group

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consisted of practically healthy people matched by sex and age (group 3, n=19). All subjects signed informed consent to participate in the study. The survey protocol was approved by the local ethics committee. The severity of the clinical course of PS was assessed by calculating the PASI index (Psoriasis area and severity index). The average value of the PASI index in the group of patients with PS was 9,9 [5,8; 14,3].

Specific allergological examination included collection of an allergic history, determination of the spectrum of sensitization using the analysis of the concentration of total immunoglobulin E (IgE), eosinophilic cationic protein and allergen-specific IgE to pollen, household, fungal and epidermal allergens in the blood serum by the method of enzyme-linked immunosorbent assay by semi-assay Scientific Multiskan FC. Reagents were used to determine allergen-specific IgE to the following allergens: a mixture of meadow grasses (hedgehog, meadow fescue, perennial ryegrass, timothy grass, meadow bluegrass), a mixture of tree allergens (ash-leaved maple, gray alder, warty birch, hazel, oak, plane tree maple-leaved, willow, triangular poplar), a mixture of weeds (wormwood, plantain, white gauze, goldenrod, stinging nettle), a mixture of fungal allergens (*Penicillium notatum*, *Cladosporium herbarum*, *Aspergillus fumigates*, *Mucor racemosus*, *Alternaria alternata*), a mixture (house dust, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cockroach), a mixture of epidermal allergens (cat epithelium, dog epithelium, horse dander, cow dander). According to the manufacturer's instructions (AlkorBio, Russia), the concentration of IgE  $\geq 0.35$  kE/l indicated a positive reaction.

The calculation and analysis of the obtained data was carried out using the Statistica 8.0 software package. In the comparative analysis of qualitative characteristics, Fisher's exact test was used. Indicators were considered statistically significant at  $p < 0.05$ . The analysis of qualitative traits was carried out by assessing the relative frequency of the trait (prevalence) P and determining the average error in the proportion of m.

**Results and discussion.** Analysis of allergological anamnesis data showed that in 43,9% (n=18) of cases, PS patients previously noted episodes of food, insect and drug allergies, manifested by urticaria and dermatitis. Seasonal manifestations of allergy were observed in 9,8% (n=4) of patients with PS. A burdened hereditary allergic history (the presence of allergic reactions and / or diseases in close relatives) was revealed in 17,1% (n=7) of

patients with PS. A burdened hereditary history (the presence of psoriasis in close relatives) was noted in 39,0% (n=16) of cases. According to the allergological anamnesis, in the group of patients with atopic dermatitis in 95% (n=19) of cases there were episodes of food, insect and drug allergies, manifested by urticaria and dermatitis. Seasonal manifestations of allergy were observed in 60% (n=12) of patients with AD. A burdened hereditary allergic history (the presence of allergic reactions and / or diseases in close relatives) was detected in 55% (n=11) of cases. Therefore, in the present study, it was found that the incidence of aggravated allergic anamnesis in patients with PS is less than in patients with AD, but more often than in controls, which is consistent with the literature data [14].

The duration of symptoms of the disease in the group of patients with psoriasis was  $11,0 \pm 1,8$  years, the onset of psoriasis at the age of  $25,0 \pm 2,5$  years, the onset of articular syndrome was  $46,0 \pm 3,0$  years. The duration of the disease in the group of patients with atopic dermatitis was  $10,0 \pm 1,7$  years, the onset of the disease in childhood in the form of exudative-catarrhal diathesis, neurodermatitis with transformation into AD at the age of  $20,0 \pm 2,7$  years. In the group of AD patients, a combination of skin rashes and allergic rhinitis (dermato-respiratory syndrome) was observed in 100% (n=20)

cases. The average age of onset of allergic rhinitis was  $21,0 \pm 3,3$  years.

The concentration of total immunoglobulin E in the blood serum was statistically significantly higher in the group of patients with atopic dermatitis in comparison with the group of patients with psoriasis and the control group: 210,4 IU/ml [56,2; 1000,0] relative to 63,0 IU/ml [30,4; 133,8] and 45,1 IU/ml [23,4; 144,0], respectively,  $p_{1,2}=0,005$ ,  $p_{2,3}=0,001$ ,  $p_{1,3}=0,4$ . In the group of AD patients, a high level of total IgE was found in 60,0% (n=12) cases, in the group of PS patients - in 34,1% (n=14) cases. The concentration of eosinophilic cationic protein in the blood serum was statistically significantly higher in the group of patients with atopic dermatitis in comparison with the group of patients with psoriasis and the control group: 28,7 ng/ml [13,9; 37,1] relative to 8,6 ng/ml [4,8; 17,2] and 7,9 ng/ml [4,6; 27,1], respectively,  $p_{1,2}=0,005$ ,  $p_{2,3}=0,003$ ,  $p_{1,3}=0,8$ .

The features of the spectrum of sensitization of patients with psoriasis and atopic dermatitis have been determined. In the group of patients with psoriasis, sensitization to pollen, household, fungal and epidermal allergens was statistically significantly less frequent in comparison with the group of patients with AD: 36,6% of cases relative to 75,0% of cases,  $p_{1,2}=0,005$  (Table 1), which is consistent with the literature data [5].

When assessing the spectrum of sen-

**Comparative characteristics of the spectrum of sensitization to pollen, household, fungal and epidermal allergens in patients with psoriasis and atopic dermatitis, % (n)**

| Allergen                                               | 1st group<br>PS (n=41)    | 2nd group<br>AtD (n=20)   | p                                                     |
|--------------------------------------------------------|---------------------------|---------------------------|-------------------------------------------------------|
| The presence of sensitization to the studied allergens | 36.6% $\pm$ 7.5<br>(n=15) | 75.0% $\pm$ 9.9<br>(n=15) | $p_{1,2}=0.005$<br>$p_{1,3}=0.002$<br>$p_{2,3}<0.001$ |
| A mixture of meadow grasses                            | 7.3% $\pm$ 4.1*<br>(n=3)  | 35.0% $\pm$ 11.8<br>(n=7) | $p_{1,2}=0.006$<br>$p_{1,3}=0.2$<br>$p_{2,3}=0.003$   |
| A mixture of tree allergens                            | 9.8% $\pm$ 4.6<br>(n=4)   | 35.0% $\pm$ 11.8<br>(n=7) | $p_{1,2}=0.02$<br>$p_{1,3}=0.1$<br>$p_{2,3}=0.003$    |
| A mixture of weeds                                     | 4.9% $\pm$ 3.4*<br>(n=2)  | 40.0% $\pm$ 11.2<br>(n=8) | $p_{1,2}=0.0005$<br>$p_{1,3}=0.3$<br>$p_{2,3}=0.001$  |
| A mixture of allergens of house dust                   | 12.2% $\pm$ 5.1<br>(n=5)  | 45.0% $\pm$ 11.4<br>(n=9) | $p_{1,2}=0.004$<br>$p_{1,3}=0.1$<br>$p_{2,3}=0.0006$  |
| A mixture of fungal allergens                          | 4.9% $\pm$ 3.4*<br>(n=2)  | 15.0% $\pm$ 8.2*<br>(n=3) | $p_{1,2}=0.2$<br>$p_{1,3}=0.3$<br>$p_{2,3}=0.07$      |
| A mixture of epidermal allergens                       | 4.9% $\pm$ 3.4*<br>(n=2)  | 35.0% $\pm$ 11.8<br>(n=7) | $p_{1,2}=0.002$<br>$p_{1,3}=0.3$<br>$p_{2,3}=0.003$   |

Note. % (n) – relative and absolute number of sensitized patients. \* $p > 0.05$ . Sensitization to the studied allergens was not detected in the control group.

sensitization to household allergens of patients with PS, the highest frequency of occurrence of sensitization to a mixture of house dust allergens was found in comparison with other types of allergens. When studying pollen sensitization in PS patients, sensitization to a mixture of trees prevailed in comparison with other types of pollen allergens. The highest concentration of allergen-specific IgE in psoriasis is determined to house dust allergens. In the group of AD patients, the highest incidence of sensitization was revealed to weed pollen - 40% of cases. Sensitization to pollen from trees and meadow grasses was noted in 35% of cases. The presence of sensitization to epidermal allergens in AD patients was revealed in 35% of cases. The lowest incidence of allergen-specific IgE was found in the group of patients with AD to a mixture of mold allergens - in 15% (n=3) cases.

In the group of AD patients, sensitization to pollen, household fungal and epidermal allergens was found statistically significantly more often in comparison with the group of patients with psoriasis,  $p_{1,2}=0,005$ . In a comparative analysis of the spectrum of sensitization to pollen allergens between the groups of patients, it was noted that with AD, sensitization to pollen from trees, meadows and weeds was statistically significantly more frequent in comparison with psoriasis,  $p_{1,2}=0,02$ ,  $p_{1,2}=0,006$ ,  $p_{1,2}=0,0005$ , respectively. In addition, in the group of AD patients, sensitization to house dust and epidermal allergens was found statistically significantly more often in comparison with PS,  $p_{1,2}=0,004$ ,  $p_{1,2}=0,002$ . There were no intergroup differences in sensitization to mold allergens.

In the group of patients with PS, monovalent sensitization was statistically significantly more frequent in comparison with the group of patients with AD: 93,3% (n=14) and 26,7% (n=4), respectively,  $p_{1,2}<0,001$ . In turn, in the group of patients with AD, polyvalent sensitization to allergens was statistically significantly more frequent in comparison with the group of patients with PS: 53,3% (n=8) and 0%, respectively,  $p_{1,2}=0,0009$ . Data on the nature of sensitization in patients with PS are few and contradictory. Thus, an increase in the level of specific IgE to inhalation allergens has been reported in patients with PS in comparison with the group of healthy people and patients with psoriatic arthritis [10]. In another study, sensitization to allergens of birch pollen, timothy grass, rye, potatoes, and carrots was found in patients with PS [5]. There are data on the absence of statistically

significant differences in the concentration of specific IgE to household allergens (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*) in the blood serum in the groups of PS patients relative to the group of healthy people [9]. The literature data on the concentration of total IgE in patients with PS are contradictory. In some studies, an increased level of total IgE was found in comparison with the control [8,9,11,12]. In another study, on the contrary, there were no statistically significant differences in the concentration of total IgE in the groups of patients with PS and controls [15].

Our previous studies, based on skin testing, showed the features of the spectrum of sensitization to food, household, pollen, fungal allergens in patients with psoriasis. So, in the group of patients with psoriasis in more than 50% of cases, the prick-testing method revealed sensitization to pollen and fungal allergens.

**Conclusion.** Thus, in the study, new triggers of psoriasis were identified. The features of the spectrum of sensitization to pollen, household, fungal and epidermal allergens in patients with psoriasis have been established. The data obtained in the course of this study based on the study of the concentration of general and specific IgE on a lower frequency of occurrence (36.6%) of sensitization to pollen, household, fungal and epidermal allergens in PS may be associated with the fact that in psoriatic disease, participation of either reagents of a different class (IgG4), or other immunopathological mechanisms of triggering allergies (II, III, IV type according to the Gell & Coombs classification) are the basis. The results obtained in the course of this study confirm the concept that atopic mechanisms are characteristic of psoriasis, but to a lesser extent than for atopic dermatitis and are protective against the development of autoimmune mechanisms. Consequently, further study of psoriasis and allergies from the standpoint of comorbidity should be carried out in the direction of investigating both atopic and non-atopic mechanisms of triggering allergic reactions involved in the immunopathogenesis of psoriatic disease.

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