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## Food allergen sensitization patterns in psoriasis patients

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### ABSTRACT

**Background.** Psoriasis is a chronic relapsing systemic disease characterized by inflammation in the skin. Etiology of psoriasis remains elusive, since there are many factors triggering a pathological process in the skin. Data on the frequency of allergies in patients with psoriasis are extremely few and contain conflicting results in the literature, which determines the relevance of the study. Researchers described coexisting atopic dermatitis (AD) and psoriasis (PS), which does not exclude common causes and mechanisms leading to skin damage.

**Aim.** To study and conduct a comparative analysis of food allergen sensitization patterns in patients with psoriasis and atopic dermatitis.

**Materials and methods.** A prospective study included patients with psoriasis (group 1,  $n = 51$ ) and atopic dermatitis (group 2, comparison group,  $n = 20$ ) aged 18–57 years. A control group (group 3,  $n = 19$ ) encompassed apparently healthy sex- and age-matched individuals. Specific allergy testing included allergy history and determination of sensitization patterns by analyzing serum concentrations of total immunoglobulin E (IgE) and allergen-specific IgE (sIgE) to food allergens using ELISA test systems (Alkor-Bio, Russia) on the Thermo Scientific Multiskan FC microplate photometer. The calculation and analysis of the obtained data were carried out using the Statistica 8.0 software package.

**Results.** The concentration of total immunoglobulin E in the blood serum for PS patients was 57.9 [31.6; 135.1] IU / ml, for AD patients – 210.4 [56.2; 1,000.0] IU / ml, and for the control group – 45.1 [23.4; 144.0] IU / ml, respectively,  $p_{1,2} = 0.005$ ;  $p_{2,3} = 0.001$ ;  $p_{1,3} = 0.4$ . Food allergen sensitization was determined significantly more often in the group of AD patients compared to the group of PS patients: 95.0 ( $n = 19$ ) vs. 37.2% ( $n = 19$ ), respectively,  $p_{1,2} = 0.005$ . In the group of AD patients, sensitization to chicken eggs, tomatoes, and peanuts was found significantly more frequently than in the group of PS patients and in the control group. Sensitization to beef, buckwheat, and potatoes was significantly more common in the group of PS patients than in the controls.

**Conclusion.** Following the study of the serum concentration of allergen-specific IgE (sIgE) to food allergens, we revealed food allergen sensitization not only for AD patients, but also for PS patients. However, in our study, sensitization patterns to the studied allergens have their own characteristics depending on the specific disease.

**Keywords:** psoriasis, atopic dermatitis, food allergy, sensitization, allergen-specific IgE

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## Сенсибилизация к пищевым аллергенам больных псориазом

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### РЕЗЮМЕ

Псориаз – хроническое рецидивирующее системное заболевание, характеризующееся воспалительным процессом в эпидермисе. Вопрос об этиологии псориаза остается открытым, так как существует множество триггеров для запуска патологического процесса в коже. Данные о частоте возникновения аллергии у больных псориазом крайне немногочисленны и содержат противоречивые результаты в литературе, что определяет актуальность исследования. Известно о сочетании атопического дерматита и псориаза, что не исключает общности причин и механизмов, приводящих к поражению кожи.

**Цель.** Изучить и провести сравнительный анализ спектра сенсибилизации к пищевым аллергенам больных псориазом и атопическим дерматитом.

**Материалы и методы.** Проведено проспективное исследование больных псориазом (ПС, 1-я группа,  $n = 51$ ) и атопическим дерматитом (АД, 2-я группа, группа сравнения,  $n = 20$ ) в возрасте 18–57 лет. Контрольная группа (3-я группа,  $n = 19$ ) включала практически здоровых людей, сопоставимых по полу и возрасту с больными. Специфическое аллергологическое обследование включало сбор аллергологического анамнеза, установление спектра сенсибилизации путем определения концентрации общего иммуноглобулина Е (IgE) и аллерген-специфических IgE к пищевым аллергенам с использованием тест-систем (компания «Алкор-Био», Россия) методом иммуноферментного анализа на полуавтоматическом анализаторе Thermo Scientific Multiskan FC. Расчет и анализ полученных данных проводили с помощью пакета программ Statistica 8.0.

**Результаты и обсуждение.** Концентрация общего иммуноглобулина Е в сыворотке крови больных ПС составила 57,9 [31,6; 135,1] МЕ/мл, больных АД – 210,4 [56,2; 1000,0] МЕ/мл, в контрольной группе – 45,1 [23,4; 144,0] МЕ/мл соответственно,  $p_{1,2} = 0,005$ ;  $p_{2,3} = 0,001$ ;  $p_{1,3} = 0,4$ . Сенсибилизация к пищевым аллергенам статистически значимо чаще определялась в группе больных АД в сравнении с группой больных ПС: 95,0% ( $n = 19$ ) против 37,2% ( $n = 19$ ) соответственно,  $p_{1,2} = 0,005$ . В группе больных АД сенсибилизация к куриному яйцу, томатам и арахису выявлена статистически значимо чаще в сравнении с группой больных ПС и группой контроля. В группе больных ПС сенсибилизация к говядине, гречке и картофелю выявлена статистически значимо чаще в сравнении с контрольной группой.

**Заключение.** Таким образом, выявлена сенсибилизация на основе изучения концентрации аллерген-специфических IgE (sIgE) к пищевым аллергенам в сыворотке крови не только больных АД, но и больных ПС, причем спектр сенсибилизации к изучаемым аллергенам имеет свои особенности в зависимости от нозологии.

**Ключевые слова:** псориаз, атопический дерматит, пищевая аллергия, сенсибилизация, аллерген-специфические IgE

**Конфликт интересов.** Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

**Источник финансирования.** Авторы заявляют об отсутствии финансирования при проведении исследования.

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## INTRODUCTION

Despite multiple theories of psoriasis (PS), its etiology and pathogenesis remain elusive [1, 2]. Ineffectiveness of current curative and pathogen-specific therapies for PS makes its study relevant and determines the need to search for new approaches to the study of the disease, including its etiology and pathogenesis [3–5].

Psoriasis and atopic dermatitis (AD) are skin diseases both characterized by the simultaneous presence of systemic inflammation and skin damage. Canonically, PS is considered as a Th1 / Th17-mediated skin disease, while AD is characterized by a predominant type 2 immune response [1, 6]. Earlier, it was believed that the presence of AD excluded simultaneous development of PS in patients due to fundamentally different immune responses. Recently, researchers have described coexisting AD and PS [7–11]. Therefore, studying coexisting AD and PS may lead to discovery of new therapeutic targets and facilitate the development of strategies for personalized care [8–10].

AD is the earliest manifestation of allergic march characterized by progression of a systemic allergic reaction from eczema to allergic rhinitis and bronchial asthma [11]. In recent years, the term “psoriatic march” has been coined, which reflects the polysystemic nature of inflammation in PS [12].

Modern researchers have described that AD and PS are characterized by similar histologic changes in skin lesions. Thus, in patients with AD and PS, histology revealed neutrophil infiltration in foci of skin lesions [13, 14]. The hypothesis according to which chronic inflammation in PS contributes to an increase in the number of B lymphocytes in skin lesions followed by overproduction of total IgE in the blood serum and predominant Th2 response in these patients is of great interest [15]. The role of Th17- and Th22 lymphocytes in the pathogenesis of both AD and PS was discussed [14–18]. Studies on the concentration of specific IgE antibodies to various groups of allergens in PS are few, which determines the relevance of this research [19, 20].

According to some authors, patients with PS are characterized by an increase in specific IgE antibodies

to birch pollen, timothy, rye, potato, and carrot [19]. According to the dual allergen exposure hypothesis, food allergen sensitization may develop not only via oral exposure but also following allergen penetration through impaired skin barrier [19, 21]. This fact determines the relevance of studying food allergen sensitization in patients with coexisting PS and AD, while a comparative analysis of food allergen sensitization patterns can help identify new factors and mechanisms leading to skin damage.

The aim of the study was to investigate and conduct a comparative analysis of food allergen sensitization patterns in patients with PS and AD.

## MATERIALS AND METHODS

The study included patients with PS (group 1,  $n = 51$ ) and AD (group 2, comparison group,  $n = 20$ ) aged 18–57 years. The average age of patients in group 1 was  $40.0 \pm 1.8$  years, in group 2 –  $25.0 \pm 2.0$  years. In the gender profile of both groups, women prevailed: 52.9% ( $n = 27$ ) in group 1, 55% ( $n = 11$ ) in group 2. A control group (group 3,  $n = 19$ ) encompassed apparently healthy sex- and age-matched individuals. The severity and extent of PS were measured by the Psoriasis Area and Severity Index (PASI). The average PASI score in the PS group was 10.0 [6.0; 14.4].

All patients underwent specific allergy testing, including allergy history and determination of sensitization patterns by analyzing serum concentrations of total immunoglobulin E (IgE) and allergen-specific IgE (sIgE) to food allergens using ELISA test systems (Alkor-Bio, Russia) on the Thermo Scientific Multiskan FC microplate photometer. We used reagents for determining sIgE to the following food allergens: cow milk, beef, chicken egg (whole), chicken meat, gluten, wheat, oat, rice, buckwheat, potato, carrot, tomato, apple, peanut.

According to the manufacturer’s instruction (Alkor-Bio, Russia), the level of  $sIgE \geq 0.35$  kIU / l indicated a positive response. Sensitization to the studied allergens in the control group was not detected. The calculation and analysis of the obtained data were carried out using the Statistica 8.0 software package. Statistical processing of the results was performed by calculating the mean and the error of the mean

( $M \pm m$ ). The data were presented as the median and the interquartile range  $Me [Q_{25\%}; Q_{75\%}]$  and as the absolute and relative number of sensitized patients  $n$  (%). The differences were considered statistically significant at  $p < 0.05$ .

## RESULTS

In the group of PS patients, prior history of allergy (allergy and / or allergic diseases) was established in 41.2% ( $n = 21$ ) of cases, seasonal allergy – in 7.8% ( $n = 4$ ) of patients, family history of allergy (allergy and / or allergic diseases among close relatives) – in 27.5 % ( $n = 14$ ) of cases, and family history of PS – in 39.2% ( $n = 20$ ) of cases.

The average age at PS onset was  $24.0 \pm 2.1$  years, the total disease duration was  $11.0 \pm 1.6$  years. In 76.5% ( $n = 39$ ) of cases, skin rash was accompanied by intense itching. The main clinical manifestations of PS were a monomorphic rash with flat papules of various sizes and large pink and red plaques, characterized by hyperproliferation and aberrant differentiation of the epidermis. In PS patients, relapsing – remitting skin disease was observed in 56.7% ( $n = 29$ ) of cases, exacerbations in autumn and winter occurred in 33.3% ( $n = 17$ ) of cases, and exacerbations in spring and summer were noted in 9.8% ( $n = 5$ ) of cases, mainly in patients with coexisting pathology (seasonal allergic rhinoconjunctivitis).

According to allergy history, urticaria, allergic rhinitis, and insect and drug allergies were noted in 95% ( $n = 19$ ) of AD patients. Family history of allergy in AD patients was detected in 55% ( $n = 11$ ) of patients and seasonal allergic manifestations – in 60% ( $n = 12$ ) of cases. The following clinical manifestations of AD were detected: erythema, dry skin, excoriations, peeling. Itching was observed in 95% ( $n = 19$ ) of AD patients. Skin damage in most AD patients was as follows: limited – 60% ( $n = 12$ ) of cases, generalized – 30% ( $n = 6$ ) of patients, diffuse – 10% ( $n = 2$ ) of cases. Moderate AD was found in 90% ( $n = 18$ ) of cases, whereas a severe course of AD was recorded in 10% of patients.

The serum level of total IgE for PS patients was 57.9 [31.6; 135.1] IU / ml, for AD patients – 210.4 [56.2; 1,000.0] IU / ml, for the control group – 45.1 [23.4; 144.0] IU / ml, respectively,  $p_{1,2} = 0.005$ ;  $p_{2,3} = 0.001$ ;  $p_{1,3} = 0.4$ . Literature data on the concentration of total IgE in PS are conflicting. Increased serum levels of total IgE have been reported in some studies [15], whereas others did not demonstrate statistically significant differences in total IgE

concentrations between PS patients and controls [22]. Higher concentrations of total IgE were shown to be associated with the duration of skin lesion in PS and correlated with the severity of the clinical course of the disease [19].

Food allergen sensitization was detected significantly more often in the group of AD patients compared to the PS group: 95.0 ( $n = 19$ ) vs. 37.2% ( $n = 19$ ), respectively,  $p_{1,2} = 0.005$  (Table).

Table

Comparative characteristics of food allergy sensitization patterns in patients with psoriasis and atopic dermatitis, $n$ (%)			
Parameter	PS patients, $n = 51$	AD patients, $n = 20$	$p$
Cow milk	2 (10.5)	5 (26.3)	$p_{1,2} = 0.2$ $p_{1,3} = 0.1$ $p_{2,3} = 0.02$
Beef	5 (26.3)	2 (10.5)	$p_{1,2} = 0.2$ $p_{1,3} = 0.02$ $p_{2,3} = 0.1$
Chicken egg (whole)	0	4 (21.1)	$p_{1,2} = 0.04$ $p_{2,3} = 0.04$
Chicken meat	0	1 (5.3)	$p_{1,2} = 0.3$ $p_{2,3} = 0.3$
Gluten	0	1 (5.3)	$p_{1,2} = 0.3$ $p_{2,3} = 0.3$
Wheat	1 (5.3)	4 (21.1)	$p_{1,2} = 0.1$ $p_{1,3} = 0.3$ $p_{2,3} = 0.04$
Oat	3 (15.8)	7 (36.8)	$p_{1,2} = 0.1$ $p_{1,3} = 0.08$ $p_{2,3} = 0.004$
Rice	1 (5.3)	2 (10.5)	$p_{1,2} = 0.5$ $p_{1,3} = 0.3$ $p_{2,3} = 0.15$
Buckwheat	6 (31.6)	2 (10.5)	$p_{1,2} = 0.1$ $p_{1,3} = 0.01$ $p_{2,3} = 0.15$
Potato	4 (21.1)	0	$p_{1,2} = 0.04$ $p_{1,3} = 0.04$
Carrot	3 (15.8)	2 (10.5)	$p_{1,2} = 0.6$ $p_{1,3} = 0.07$ $p_{2,3} = 0.1$
Tomatoe	1 (5.3)	8 (42.1)	$p_{1,2} = 0.008$ $p_{1,3} = 0.3$ $p_{2,3} = 0.002$
Apple	3 (15.8)	6 (31.6)	$p_{1,2} = 0.3$ $p_{1,3} = 0.07$ $p_{2,3} = 0.008$
Peanut	2 (10.5)	12 (63.1)	$p_{1,2} < 0.001$ $p_{1,3} = 0.1$ $p_{2,3} < 0.001$

Note. In the control group, sensitization to the studied allergens was not detected.

Sensitization to chicken eggs, tomatoes, and peanuts was found significantly more frequently in the group of AD patients than in the group of PS patients. Chicken egg allergy is known to be one of the most common in the world [23]. According to the literature, chicken egg allergy is observed in one third of adult American population [23]. Consequently, high incidence of sensitization to chicken eggs in patients with AD identified in this study does not contradict the literature data [24]. Sensitization of AD patients to tomatoes and peanuts is likely associated with cross-reactivity with pollen allergens [25]. In the group of AD patients, the frequency of sensitization to cow milk protein, chicken eggs, wheat, oat, tomatoes, apples, and peanuts was significantly higher compared to the control group (Table).

An interesting aspect of the study is the presence of food allergen sensitization in patients with PS. The study showed that sensitization to beef, buckwheat, and potatoes in the group of PS patients was significantly more common than in the controls. According to the literature, sensitization to beef may be associated with cross-reactivity with cow milk proteins [26]. Literature data indicate the presence of antigenic determinants common for some foods and pollen allergens [27, 28]. Sensitization to potatoes and buckwheat in PS patients is most likely associated with cross-reactivity with pollen allergens, since this group of patients showed higher sensitization to birch pollen, sage pollen, timothy, and rye [19].

## DISCUSSION

Literature data on the influence of food allergens on the development and course of PS are scarce, which determines the need for further study of the role of food allergy in the etiology and pathogenesis of PS. In the present study, sensitization was determined by studying the level of sIgE to food allergens in the blood serum of not only patients with AD, but also patients with PS. The study revealed features of sensitization patterns to food allergens depending on the type of skin lesion. Thus, AD was characterized by a wider range of sensitization to food allergens compared to PS: chicken eggs, tomatoes, and peanuts. Since AD is a classic example of an IgE-mediated disease, high incidence of sensitization to food allergens in this category of patients should have been expected.

The study revealed high frequency of sensitization to food allergens in patients with PS. Sensitization to beef, potatoes, and buckwheat was more often detected, which may indicate the influence

of these allergens on the development of skin lesions in PS.

A steady increase in the incidence of allergies in all diseases is reported all over the world. Assessing the role of food allergies in PS development is of great interest. Recently, an increase in the incidence of coexisting AD and PS has been reported [8, 19]. The presence of food allergies can facilitate damage to digestive organs, leading to impairment of their barrier function, thus increasing the permeability and absorption of various allergens and endotoxins [28]. Moreover, the involvement of the gastrointestinal tract in the systemic allergic reactions to food allergy in PS patients is a characteristic sign of dermatologic manifestations of gastrointestinal diseases [29].

It is known that food allergen sensitization is marked by aggravation of allergy symptoms after consuming foods that are causal allergens [28]. This fact should be considered in clinical practice and requires prescription of an elimination diet for AD and PS patients with account of their individual sensitization patterns to food allergens.

## CONCLUSION

Skin lesions and chronic inflammation in PS and AD result in impaired epidermal barrier and, therefore, facilitate more intense penetration of various allergens through the skin, which contributes to extension of the sensitization range and progression of the pathology [30, 31]. Food allergen sensitization in patients with PS can be both a trigger of the disease and a risk factor for its development and progression.

The preliminary results of the study determine the need for prescribing a personalized elimination diet therapy and other methods of allergy diagnosis, such as skin prick test, elimination and provocation tests.

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