RESEARCH ARTICLE

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The sensitization spectrum to fungal allergens with atopic dermatitis and psoriasis in patients

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INTRODUCTION: The fungal allergy in the progress of atopic dermatitis (AD) and psoriasis (PS) are of special interest and determines the relevance in the study. The aim of the study to conduct a comparative analysis of the sensitization spectrum to fungal allergens in patients with atopic dermatitis and psoriasis.

MATERIALS AND METHODS: The study involved patients with AD (Group I, n = 53) and PS (Group II, n=53) and aged group (15-60) years old. Sensitization to fungal allergens was determined by skin prick testing using standardized fungal allergens: *Candida albicans, Alternaria alternata, Aspergillus fumigatus, Cladosporium herbarum, Penicillium notatum* (ThermoFisher Scientific, Dubai). The concentration of allergen-specific IgE to a mixture of fungal allergens: *Penicillium notatum, Cladosporium herbarum, Aspergillus fumigatus, Alternaria alternata* (ThermoFisher Scientific, Dubai) were determined by indirect immunofluorescent analysis on a ELISA analyzer. The IgE level test of positive was considered in IgE level ≥ 0.35 kU/l.

RESULTS: The highest frequency of sensitization to fungi of the genus *Cladosporium herbarum, Aspergillus fumigatus* and *Alternaria alternata* were established In the group of patients with PS. The frequency of sensitization to fungi was higher in the group of patients with PS than in the group of patients with AD. Sensitization to a mixture of fungus allergens, according to the concentration of allergen-specific IgE, it were observed in the group of patients through compared with the group of patients in PS was : 2.7% and AD was 7.5%. Therefore, fungal allergy may play an important role in the etiopathogenesis of AD and PS.

RECOMMENDATIONS: The study of the diagnosis and treatment of these pathologies, including a specific allergological examination of patients with AD and PS. To study of the genotyping of fungi causing human infection.

INTRODUCTION

Human skin is the largest barrier organ in body from area interacting with the environment and a habitat for many different symbiotic microorganisms [1]. Skin microbiome are the presence of bacteria, viruses, fungi and parasites, which can play an important role in the etiopathogenesis of dermatological diseases [2]. In turn, a congenital or acquired defect in the stratum corneum of the epidermis in AD and PS contributes to a change in the species diversity of the skin microbiome,

which leads to a violation of the barrier function of the skin and a chronic inflammatory process [3].

The resident skin microflora is protective against the growth of pathogenic microorganisms and influences of the strength and intensity in the immune response[4]. Consequently, the skin microbiome is consider important of function in the immune system by inducing T and B cells that control the functional activity of organs and systems [5].

In that previous studies are proved the protective role of fungi (commensals) in the development of inflammatory processes in the intestines and lungs, the participation of opportunistic fungi in skin homeostasis and the etiopathogenesis of dermatological diseases remains unclear [6]. The fungal is an important part of the microbiome in the skin and intestines infections, can act as allergens with the development of sensitization and the formation of allergic inflammation in patients with AD and PS[7].

In the fungal antigens (enzymes, toxins, cell wall components, cross-reacting proteins) have a high sensitizing ability with the activation of infectious-allergic mechanisms, with the participation of T-lymphocytes, proliferation and differentiation of epidermal cells[8]. There is evidence of association of altered fungal skin microbiome with PS [9]. The skin of patients with PS is characterized in active colonization by fungal flora, including Candida fungi[9]. Fungi that colonize of the skin promote the activation of Th17 lymphocytes[8]. In the fact that most of the circulating Th17 clones react in response to fungal antigens and, in particular, are specific for *Candida albicans*[10]. The potential role of *Candida albicans* in the development of PS is confirmed by a decrease in the activity of the inflammatory process in skin lesions during etiotropic therapy with systemic antimycotic drugs [11].

Exposure patients to fungal components, including spores (in and out)doors are a provoking factor in respiratory allergies (bronchial asthma and allergic rhinitis), as well as AD, with the formation of dermatorespiratory syndrome in some cases [12]. The microbiome of skin lesions in AD is characterized by a low species diversity of bacteria, a decrease in the number of proteobacteria, and an increased colonization by *Candida* and *Malassezia* fungi [13]. The pathogenesis of AD in fungal allergies can be associated with both IgE- and non-IgE-mediated mechanisms [10]. It has been shown that Th17-lymphocytes specific to fungi can cross-react to antigens expressed by various fungi, especially in inflammatory diseases of the respiratory tract [13].

The most important the fungal allergy in the development of skin lesions are of particular interest and determines the relevance of the study. PS and AD are systemic chronic inflammatory skin diseases [14]. The lack of effective etiotropic and pathogenetic methods for the treatment of PS requires were the new approaches and studies of its etiopathogenesis, including the standpoint of the cause-and-effect relationship between PS and fungal infections [11].

The vital role of the immune system in the development of immune-mediated pathologies from through skin damage in PS and AD, and also that comparative analysis of the sensitization spectrum to fungal allergens in patients with AD and PS and are consider of the important part in the aim of this study.

MATERIALS & METHODS

The study involved patients with AD (group I, n = 53) and PS (group II, n = 53), and the age groups from (18 to 66) years old . A specific allergic examination was carried out (collection of an allergic history, determination of sensitization to fungal allergens by skin prick testing, taking into account the size of the wheal reaction and the amount of hyperemia: a weakly positive reaction (2–5 cm), positive(6–9cm), strongly positive(10–13 cm), hyperergic(14-17cm). During prick tests, standardized fungal allergens were used: *Candida albicans, Alternaria alternata, Aspergillus fumigatus, Cladosporium herbarum, Penicillium notatum* (ThermoFisher Scientific, Dubai). A specific allergological examination was carried out by an immunologist. The indications of the skin testing were: a history of anaphylactic reactions, taking beta-blockers, severe exacerbation of an allergic disease, dermographic urticaria, taking antihistamines, antidepressants, systemic and local glucocorticosteroids within 14 days before the study. The concentration of allergen-specific

Table 1 . Characteristic of the spectrum of sensitization to fungal allergens in patients with AD/PS according to aged categories

P-VALUE	GROUP IV AD/PS	GROUP III AD/PS	GROUP II AD/PS	GROUP I AD/PS	FUNGUS INFECTION	
p < 0.01	25.05±2.5	27.6±5.45	50.1±4.5	55.2±10.9	M±SE	*Candida albicans*
	24/15	24/21	47/35	48/39	No. 53	
p < 0.01	34.1±6.8	20.33±1.5	68.1±9.8	66.7±3.5	M±SE	*Cladosporium herbarum*
	43/18	25/15	44/36	41/30	No. 53	
p < 0.05	30±3.12	41.8±2.5	50±3.1	49.9±2.2	M±SE	*Penicillium notatum*
	24/30	21/9	42/33	40/14	No. 53	
p < 0.05	32.9±1.4	23.07±1.7	42.8±1.4	46.03±1.5	M±SE	*Alternaria alternata*
	17/15	17/20	34/37	35/15	No. 53	
p < 0.05	13.4± 3.11	17.8±3.9	26.4± 6.5	35.8±2.2	M±SE	*Aspergillus fumigatus*
	20/12	2/14	39/24	34/4	No. 53	

Age Group I:(15-25), Group II:(26-35), Group III:(36-45), Group IV:(46-60)

IgE to a mixture of fungal allergens: *Penicillium notatum, Cladosporium herbarum, Aspergillus fumigatus, Mucor racemosus, Alternaria alternata* (Bioneer, Dubai). The test was considered positive of result at IgE levels ≥ 0.35 kU/l.

Statistical analysis

Statistical 21.0 software package was used for statistical analysis. t-test for qualitative features. The indicators were considered statistically significant at p < 0.05.

RESULTS

The total samples of the study was (106) patients, whereas divide in two groups were 53 cases of AD and 53 cases of PS, with aged categories form (15 - 60) years old (Table 1).

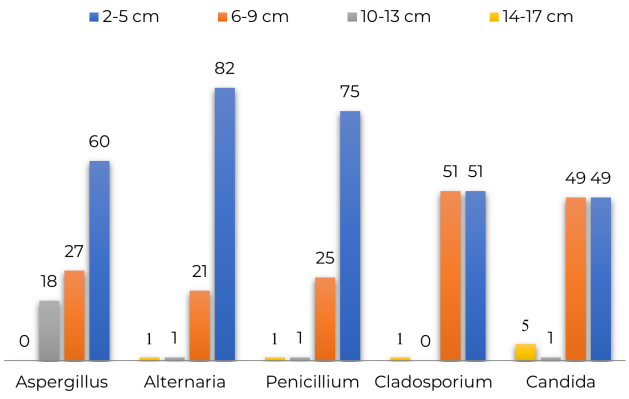

FIGURE 1. Sensitization level to fungi in AD patients

In the group of patients with AD, a positive reaction to the prick-test (6-9cm) was found more often to *Alternaria alternate* and *Penicillium notatum* in comparison with other types of fungal allergens (Fig. 1). A sharply positive reaction (10-13 cm) was more often observed in relation to *Aspergillus fumigatus, Alternaria alternate, Penicillium notatum* and *Candida albicans*. Hyperergic reaction (14-17 cm) in patients with AD was noted to *Candida albicans* and *Alternaria alternata*. While in the group of patients with PS, a positive reaction to the prick-test (6-9cm) was detected more often to *Penicillium notatum* in comparison with other types of fungal allergens (Fig. 2).

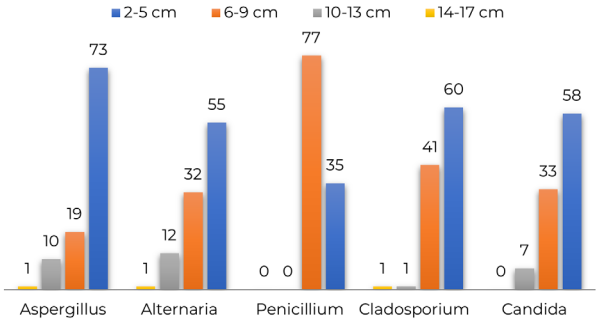

FIGURE 2. . Sensitization level to fungi in PS patients

A sharply positive reaction (10-13 cm) was determined for *Candida albicans, Alternaria alternata, Aspergillus fumigatus*. A hyperergic reaction (14-17 cm) in patients with PS was found only to *Alternaria alternate* and *Aspergillus fumigatus*.

The concentration of allergen-specific IgE to a mixture of fungal allergens with PA and PS were stud-

ied in groups of patients. A positive result was 7.5% ± 4.1 cases, and also with PS was 2.7% ± 1.8 cases. While a negative result with AD was 20% ± 1.9 cases, in the group of patients with PS was 39.6% ± 10.9 cases, The sensitization of the positive or negative results of allergen-specific IgE with AD and PS of patients and the significant difference (p-value <0.05) .

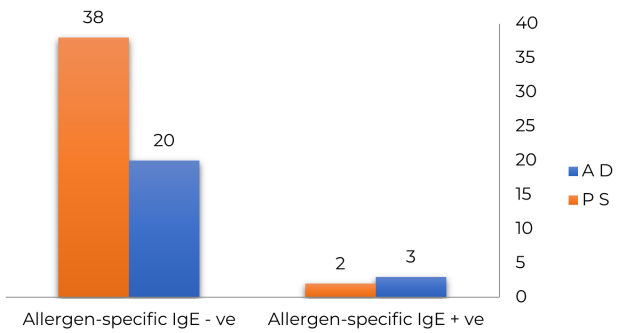

FIGURE 3. Relationships between Allergen-specific IgE with AD and PS

DISCUSSION

The sensitization spectrum to fungal allergens in patients with AD/PS and established certain features depending on the nosology were consider a comparative analysis. The frequency of occurrence of fungal sensitization in allergic diseases varies from 2 to 60% depending on the type of pathogen and geographical features of the region[15, 16].

It is known that fungal allergens can enter in the body by inhalation, food, and by contact on the skin [17]. The most important to increase of fungal allergens include spores, mycelium, as well as enzymes, toxins, cell wall components, and cross-reacting proteins [10]. The genus *Candida albicans, Alternaria alternata, Aspergillus fumigatus, Cladosporium herbarum*, and *Penicillium notatum* of fungal have a high sensitizing [18]. *Alternaria* and *Cladosporium* are found in large numbers in the environment, are mainly associated with the development of respiratory allergies (bronchial asthma and rhinitis), while the genus *Penicillium, Aspergillus* and *Candida* which live mainly in indoors, by leading to diseases and causing allergic of the skin lesions [10]. There is evidence of an increase by the incidence of sensitization to fungi *Candida* and *Cladosporium* in patients with AD, for which cross-reactivity has been proven [17]. *Candida albicans* is one of the most common commensal yeast fungi that is more often associated with various diseases [12]. It should be noted that eczematous skin inflammation can be caused both by IgE- and non-IgE-mediated mechanisms [16]. The study of fungal sensitization and classical antigen-presenting cells (dendritic cells), B-lymphocytes have play a certain role in antigen presentation, especially at low concentrations and skin inflammation[19]. It is known that in some patients with AD, sensitization to antigens causes autoreactivity to human proteins as a result of molecular mimicry, which leads to an increase in the inflammatory process in the skin [20]. Colonization of skin lesions by fungi in areas with a high density of sebaceous glands (eg, head, neck, upper chest, and back) can also complicate in the clinical course of AD [21].

The pathology of AD in some patients have a combined of the skin lesion and respiratory tract (dermatorespiratory syndrome) [19]. There are data in the study on the concentration of specific IgE to *Alternaria alternata* in patients with dermatorespiratory syndrome (combination of AD and bronchial asthma) [22]. It is known that *Alternaria alternata* is one of the most common fungi transmitted by airborne droplets(in and out)doors, and therefore it can cause an allergic reaction in sensitized people [10]. In addition, the play an important role in reducing the allergic reaction in patients by indoor growth control of *Alternaria alternata*.

In our study, the most significant fungal allergens were the genus *Alternaria alternata* and *Penicillium notatum*. A hyperergic reaction test in the group of patients with AD was noted *Candida albicans*. In previous study, it was found that in the group of patients with PS, sensitization to *Candida albicans, Alternaria alternata, Penicillium notatum,* according to the results of skin by prick testing, the results were observed more often than in the group of AD patients, however, the indicators in the study are consider of statistical significance in results [23]. In study, we found a high incidence of sensitization to *Cladosporium* and *Penicillium notatum* in the group of patients with PS, which may be due to the

fact that these types of fungi are commensals of the mucous membrane of the gastrointestinal and respiratory tracts, as well as the skin lesion [24].

In studying of the concentration of allergen-specific IgE to a mixture of fungal allergens in the group of patients with AD and PS. Sensitization to a mixture of fungus allergens according to the concentration of allergen-specific IgE was more often observed in the group of patients with AD than in the group of patients with PS. The AD is a classic example of a topic, IgE-mediated mechanisms have been identified in only 7.5% of cases. When studying the concentration of allergen-specific IgE to a mixture of fungal allergens in the group of patients with PS, positive reactions to the studied allergens were detected in 2.7% of cases.

CONCLUSION

AD and PS are the most common inflammatory skin diseases with a complex etiopathogenesis in which fungal allergy. The study of the diagnosis and treatment of these pathologies, including a specific allergological examination of patients with AD and PS. And also the relationship between specific-mediate-IgE with atopic dermatitis and Psoriasis.

RESUMO

Enkonduko: La funga alergio en la progreso de atopika dermatito (AD) kaj psoriasis (PS) estas de speciala intereso kaj determinas la gravecon en la studo. La celo de la studo fari komparan analizon de la sensiviga spektro al fungaj alergenoj en pacientoj kun atopika dermatito kaj psoriazo.

Materialoj kaj metodoj. La studo implikis pacientojn kun AD (Grupo I, n = 53) kaj PS (Grupo II, n = 53) kaj aĝa grupo (15-60) jaroj. Sensivigo al fungaj alergenoj estis determinita per haŭta piktestado uzante normigitajn fungajn alergenojn: *Candida albicans, Alternaria alternata, Aspergillus fumigatus, Cladosporium herbarum, Penicillium notatum* (ThermoFisher Scientific, Dubajo). La koncentriĝo de alergen-specifa IgE al miksaĵo de fungaj alergenoj: *Penicillium notatum, Cladosporium herbarum, Aspergillus fumigatus, Alternaria alternata* (ThermoFisher Scientific, Dubajo) estis determinita per nerekta imunofluoreska analizo sur ELISA analizilo. La IgE-nivela testo de pozitivo estis konsiderita en IgE-nivelo ≥ 0.35 kU/l.

Rezultoj: La plej alta ofteco de sentivigo al fungoj de la genro *Cladosporium herbarum, Aspergillus fumigatus* kaj *Alternaria alternata* estis establita en la grupo de pacientoj kun PS. La ofteco de sentivigo al fungoj estis pli alta en la grupo de pacientoj kun PS ol en la grupo de pacientoj kun AD. Sensivigo al miksaĵo de fungaj alergenoj, laŭ la koncentriĝo de alergen-specifaj IgE, ĝi estis observita en la grupo de pacientoj tra kompare kun la grupo de pacientoj en PS estis: 2.7% kaj AD estis 7.5%. Tial, funga alergio povas ludi gravan rolon en la etiopatogenezo de AD kaj PS.

Rekomendo: La studo de la diagnozo kaj traktado de ĉi tiuj patologioj, inkluzive de specifa alergologia ekzameno de pacientoj kun AD kaj PS. Por studi la genotipadon de fungoj kaŭzantaj homan infekton.

Conflict of Interest

The authors of this article declare that there is no conflict of interest.

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