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Fungal sensitization of the patients with bronchial asthma

Key words: *asthma, fungal sensitization, skin tests, immunoglobulin E, mold fungi.*

Role of the fungal allergies in humans is increasing due to the global warming and increasing CO_2 concentration in the atmosphere. It leads to the increased levels of the airborne fungal spores [20] with the size range from 2–3 μm (*Cladosporium, Aspergillus, Penicillium*) to 160 μm (*Helminthosporium*) and up to 500 μm (*Alternaria longissima*), average 2–10 μm [17] that determines their good permeability into the smaller airways. Concentration of the fungal spores in the air may exceed the concentration of the pollen in 100–1000 times depending on the humidity, temperature and wind, latitude, time of year (fall, winter) – although seasonal fluctuations are not so significant as for the pollen [23, 24].

Thirty per cent of patients with the allergic respiratory symptoms and 6 % of the total population have skin hypersensitivity to the microscopic fungi [15]. *Alternaria, Cladosporium, Aspergillus, Penicillium, Bipolaris (Helminthosporium), Epicoccum, Fusarium, Stemphylium, Botrytis, Curvularia* are the most common 10 allergenic fungi according to the skin testing.

Epidemiological studies in the US and Europe have shown that severe bronchial asthma in adults is associated with the increased fungal susceptibility (*Alternaria alternata, Cladosporium herbarum, Aspergillus fumigatus*) [21]. Children with the fungal exposure in the first 3 years of life have increased risk of developing asthma [13]. Sensitization to *Alternaria* at the age of 6 correlates with the development of asthma at age of 22 years (OR = 7,4) [31], and at the age from 6 to 11 years significantly increases the risk of asthma in the childhood [12]; 40 % of children with the asthma are sensitized to *Alternaria* in the US [9].

Large differences in the fungal allergy research results are likely due to the use of the various non-standardized fungal extracts obtained from fungal spores and/or mycelium with the various protein compositions [7, 15]. The additional difficulties appear due to the existence of the cross-reactivity – uneasy phenomenon that complicates the diagnosis of the fungal sensitization. Significant improvements have been achieved in the recent years due to the recombinant allergens and standardized extracts: the development of genetic engineering technologies has helped to define about 80 of the total known 150 fungal allergens in the last 20 years.

The main allergens, such as *A. fumigatus, A. Alternata, Coprinus comatus* and *Malassezia sympodialis* (Asp f 1, Alt a 1, Cop c 1, and Mala s1, respectively) are species-specific proteins which are not found in other genuses [5]. Alt 1 is defined as the predominant, species-specific antigen among the *A. alternata* 13 allergens – typical for this micromycete. An antigen Cla h 8 (NADP-dependent mannitol dehydrogenase) is the predominant component of the *C. herbarum* 14 allergens from the crude extract. Allergen Asp f 1 is considered a virulence factor contributing to colonization and infection of human tissues among the most important 40 IgE-binding components of *A. Fumigatus*. Asp f 1 is abundantly released after spore germination at the early stages of the fungal growth [15, 29].

Unlike the pollen, the fungal spores/conidia and mycelium cells may provoke the development not only of type I hypersensitivity reactions – allergies (in asthma, allergic rhinitis, sinusitis, hives, allergic bronchopulmonary mycosis, etc.) when the allergen is fixed to the IgE on the surface of mast cells and basophils, which are the direct sources of biologically active substances – but also type III hypersensitivity reactions (in allergic bronchopulmonary aspergillosis – ABPA, exogenous allergic alveolitis), when the circulating immune complexes with the complement are fixed on the vascular or bronchial wall with the involvement of immune cells that generate proinflammatory cytokines, and the development of the inflammatory response. As this takes

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place the neutrophils phagocytize the complexes, causing inflammation (vasculitis, bronchitis, etc.) [18, 29]. Type IV hypersensitivity reaction (T-cell mediated) is developed at ABPA, atopic dermatitis, and reaches its maximum in 24–72 hours after exposure to the antigen (in the case of the prior exposure), which leads to the formation of granulomas and infiltration [16].

However, the contact of respiratory system with fungus does not necessarily lead to the development of hypersensitivity reactions and depends not only on the human immune system status, but in particular, on the size of fungal elements that enter the airways. So, the small spores/conidia can be effectively phagocytosed and digested by neutrophils, alveolar macrophages and dendritic cells (innate immune response). When the fungal spores adhere to the bronchial mucosa and the germinating hyphae have significantly larger sizes – the immune cells are not able phagocytize them. The dendritic cells induce more efficient mechanisms of adaptive immunity then, and the nature of the reaction may vary depending on factors formed during the primary immune response to the fungal intrusion [19, 25].

After the alveolar macrophages and dendritic cells have contacted with fungus they migrate to lymph nodes and spleen, where they induce the local and peripheral activity of T-helper (Th) cells with starting protective Th1-response or inhibitory «allergic» Th2-response. When the dendritic cells secrete interleukin IL-12 T-helper type 1 response (Th1) is activated with an effective cleansing from fungal elements (without the development of hypersensitivity reactions). Spores and budding cells trigger such response mainly. The dendritic cells secrete IL-23 and IL-4 type 17 (Th17) and Th2 are induced respectively, in this case the fungal cleansing is accompanied by inflammation and allergies. Pseudohyphae and hyphae often generate such a response. The T-regulatory cells are getting mature under IL-10 secretion, they limit the inflammation area but with contribute to the long lasting fungal persistence in the body. In this case the fungi are able to inhibit the cellular response actively with the intracellular persistence in monocytes, macrophages and dendritic cells.

Thus, the fungal allergen is passing processing in the antigen-presenting cells (with the fragmentation to simplified peptides), and then it is presented to T-helper lymphocytes for destruction. The dendritic cells are the main modulators of the antifungal response by regulating the fungal phagocytosis through the various interleukins production.

When the Th2-response is forming the Th2-cytokines stimulate the IgE synthesis. This activates eosinophils [14, 19, 21, 28] which secrete IL-4, IL-5, IL-13 and determine the development of the Th2-dependent chronic allergic reaction with the airways remodeling (bronchial muscle proliferation, bronchial walls fibrosis) and clinical manifestations of asthma. Supposedly, the more intense Th2-response (in practice diagnosed via the total IgE serum level) causes more severe asthma form: from asthma associated with the fungal sensitization (AAFS) to severe asthma with the fungal sensitization (SAFS), then – to a seropositive allergic bronchopulmonary aspergillosis (ABPA-S) and further – to ABPA with the central bronchiectasis (ABPA-CB) [3, 4, 8, 32].

AAFS is diagnosed in patients with the mild or moderate form of asthma with the immediate positive skin test to any fungal allergen and elevated total or antiaspergillus IgE level (but not higher than 1000 IU/ml). For the severe asthma with the fungal sensibilization (SAFS) the skin test with fungal allergens is positive, total and specific IgE serum level is above 1000 IU/ml.

ABPA-S is considered an early stage of ABPA, with colonization/invasion of *Aspergillus* in the bronchi, but without the formed bronchiectases. The central bronchiectases are formed at ABPA-CB due to the prolonged local fungal exposure. There are the next additional criteria of ABPA: lung infiltrates on the CT scan, the presence of precipitating antibodies to *A. fumigatus*, eosinophilia, mucous plugs in the bronchi.

It is likely that the seropositive ABPA and ABPA with central the bronchiectasis are the results of the Th2-response accumulation, and the diagnosis can be determined by a positive immediate skin tests to *A. fumigatus* with the presence of total and / or specific IgE serum level above 1000 IU/ml [11, 27]. It is considered that ABPA can develop due to the bronchial colonization with *A. fumigatus*, which may relate to 0,7–3,5 % of patients with asthma and 7–9 % of patients with the cystic fibrosis [21].

It is determined that the most patients with ABPA and SAFS have sensitization to *Aspergillus spp., Penicillium spp., Candida spp., Cladosporium spp., Helminthosporium*, however it is not always possible to identify the cause of the allergies [3].

There is an evidence of the effectiveness of antifungal agents at SAFS and ABPA [6, 26], which confirms the possibility of the fungal invasion. The probable causes of the AAFS progression are illustrated on the *Figure*, which shows that the antifungal drugs can be effective for the fungal invasion, whereas the effectiveness of the allergen-specific immunotherapy (ASIT) is not excluded for type 1 hypersensitivity development, it is possible for all forms of the fungal infections in atopic patients, but more research is needed to confirm this statement.

The most of fungi are not able to colonize the bronchopulmonary system. The yeasts are normally colonizing the gut (*Candida spp.*) or damaging intestine, skin, nails (*Candida*, *Trichophyton spp.*). Theoretically in some cases the yeast allergens may reach the respiratory system hematogenically and cause a cascade of the immunological reactions leading to the asthma development in atopic patients or worsening its course. However, this assumption is questionable: it is difficult to confirm or refute it.

Overall, despite a century of experience in the fungal research, there are still many unresolved questions about the mechanisms of fungal influence on the asthma and other allergic diseases pathogenesis. Basic mechanisms of the allergenic fungal influence on the human body can be summarized as follows:

- fungi are one of the etiological factors, sensitizing the human body and contributing to the development of asthma and its exacerbations;
- additional fungal sensitization is aggravating asthma course;
- fungal sensitization reflects the cross-sensitization status of patients with asthma, being a random association.

The aim of our work was to study the clinical and allergologic features of bronchial asthma in patients with fungal sensitization and the role of mold infection of the respiratory tract in this.

Subjects and methods

Hundred patients with asthma in remission were examined, mean age is (46,4 ± 1,4) years old (range from 16 to 74 years), of which – 69 women (69 %), disease duration – (9,3 ± 0,9) years, the frequency of exacerbations – (3,0 ± 0,2) times/year. There were 6 patients (6 %) with the mild intermittent asthma, 30 patients (30 %) – with the mild persistent asthma, 48 people (48 %) – with the moderate persistent asthma, 16 people (16 %) – with the severe persistent asthma. The average forced expiratory volume in 1 second (FEV_1) was (79,1 ± 2,1) %; 71 patients (71 %) have been receiving inhaled corticosteroids for at least 1 month.

The patients were examined with the general clinical and functional methods, skin prick tests with the fungal allergens *Alternaria alternata, Aspergillus mxt, Botrytis cinerea, Chrisonilia sitophila, Cladosporium, Penicillum*, house dust allergen («Immunologist», Vinnitsa, Ukraine). Serum total IgE and antiaspergillus IgE level was quantitatively determined by ELISA (sandwich option) using test kits «HEMA» (Russia). Serum antiaspergillus IgE was investigated by a semiquantitative enzyme immunoassay using commercial test kits «Allergen» of NPO «Microgen» (Stavropol, Russia) in 37 patients. These immunological parameters were also determined in a group of 20 healthy blood donors.

Microbiological studies of sputum for the mold fungi were carried out with the sowing of spontaneous or induced sputum on Sabouraud medium.

The licensed statistical software included the package Microsoft Office Professional 2000 on a personal computer IBM Atlon in Excel. Student t-test, Wilcoxon test, c2 Pearson test, Pearson and Spearman correlation methods, Fisher's exact test were used [1]. Calculation of the criteria values and confidence intervals (CI) was done at a given significance level of p = 0,05. All results were expressed as n – number of examined patients in the group, the arithmetic mean value (M), the error of the arithmetic mean values (m), in the proportions and percentages indicating the CI.

The work was carried out at the expense of the state budget.

Results and discussion

There were immediate positive skin reactions to the mold allergens in 14 patients (14 %) with asthma, 9 of them (64,3 %) had positive immediate-type reactions to two or more fungal allergens, most likely – due to the presence of cross-allergy. These patients did not differ from the patients without the fungal sensitization in age and asthma severity.

The reason of the cross allergy is that some fungal antigens have a similar protein structure caused by the evolutionary affinity of the various fungi. This causes a cross-reactivity phenomenon when a specific IgE binds to another antigen having common B-cell epitopes encoded by a single mRNA [7, 22]. Phylogenetic relationships of the fungi determine their structure and reflect their ability to

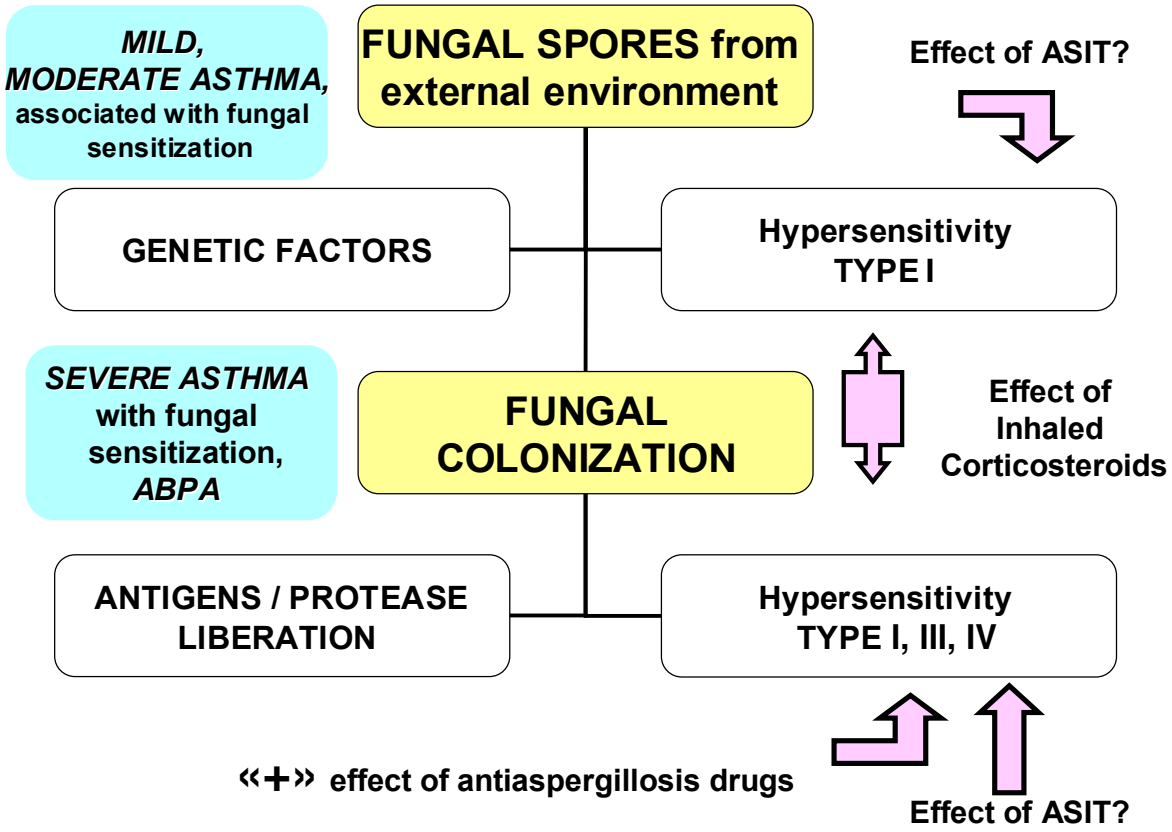

Figure. **Possible causes of the asthma progression with the fungal sensitization and methods of pathogenetic therapy**

Notes: ABPA – allergic bronchopulmonary aspergillosis; ASIT – allergen-specific immunotherapy.

induce IgE antibodies production (so-called allergic antibodies or reagin) in susceptible individuals [30]. It is observed when more than 50 % of the antigen proteins are identical [2]. In particular, antigens Pen c 3 and Asp f 3 are identical by 83 % and they cause the cross-reactions to *Penicillium* and *Aspergillus*. Pen 22 causes cross-reactions with *A. fumigatus* and *A. alternata* [15, 29]. Therefore the fungal allergens can be divided into the species-specific antigens and the cross-reactive allergens [7]. Most fungal allergens are the cross-reactive structures of the different protein families. Cross-reactivity was also identified for the glycoproteins *Malassezia furfur* (causes dandruff) and *Candida albicans* (these yeasts are the part of the normal human microflora), as well as *Cryptococcus spp.*, *Candida spp.* and *Trichosporon spp.* (causes nails diseases). And it should be considered when treating allergic diseases [15]. The cross-reactivity range is not fully defined yet, but it is described for almost 20 fungal allergens. More than the half of them (aldehyde dehydrogenase, alkaline serine protease, serine protease, enolase, GST and HSP70) have cross-reactivity with the non-fungi antigens, including human proteins (thioredoxin, cyclophilin, MnSOD, ribosomal protein P2). This can cause auto-reactivity and severe course of the chronic allergic diseases [29].

Sensitization to the house dust was determined at 9 of 14 people (64,3 %, CI = 35,1–87,2) with a positive skin sensitivity to the mold allergens, whereas a negative skin prick test to house dust was observed at 16 of 83 patients only (19,3 %, CI 11,4–29,4), p = 0,001. It can be explained by the house dust contamination with the fungal allergens or with the presence of the cross-allergy.

The patients with the skin sensitization to mold had a twice elevated total serum IgE level up to (477,7 ± 125,8) IU/ml (patients with negative skin prick test had (219,4 ± 39,1) IU/ml, p = 0,05, in the healthy group – (26,0 ± 4,5) IU/ml), indicating a direct relationship between the total IgE level with the mold skin sensitization. The severity of asthma in both groups did not differ significantly: FEV1 in patients with the skin mold sensitization was (82,1 ± 5,2) %, whereas in the group with the negative skin mold tests – (78,9 ± 2,5) %, p > 0,05. It confirmed the phenotype of AAFS at the majority of the examined patients with positive skin tests to mold allergens.

On the other hand, 16 people with severe asthma had serum total IgE level (202,6 ± 54,3) IU/ml (36–680 IU/ml), whereas all other patients with mild and moderate asthma – (252,5 ± 40,1) IU/ml (16–1250 U/ml), p > 0,05. Moreover, there were no patients with severe asthma (with SAFS and ABPA phenotype) among the 8 patients (8,0 %) with the high levels of serum IgE (980 IU/ml and above).

Increased specific antiaspergillus IgE serum level was detected at the majority of patients – in 22 cases out of 37 patients (59,5 %, CI = 42,1–75,2; p = 0,05), but only at 3 patients (13,6 % CI=2,9–34,9) with the positive skin mold tests. Therefore, in the most of cases the asthma patients could have had a hidden mold sensitization with the only increased specific serum IgE level, but it did not exclude the cross-reactivity.

Eight of the 22 patients (36,4 %, CI = 17,2–59,3) with the presence of the serum antiaspergillus Ig E have experienced negative occupational exposures of respiratory tract in their histories, whereas this ratio was significantly less in the group without serum antiaspergillus IgE – 1 of 15 patients (6,7 %, CI = 0,2–31,9), p < 0,05. This indicates a negative role of the occupational exposures in the event of fungal sensitization, probably due to the weakening of the protective properties of the respiratory tract. The respiratory function was not associated with the presence and the level of the serum antiaspergillus Ig E in this case.

The increased specific antiaspergillus IgE serum level directly correlated with sputum eosinophilia (r = 0,40; n = 37; p < 0,05) and negatively – with the number of lymphocytes in the lower respiratory tract (r = -0,44; n = 37; p < 0,01). This reflects the relationship of the fungal sensitization with the eosinophilic inflammation of the airways and increased Th2-response.

Only 3 patients (13,6 %, CI = 2,9–34,9) with the increased antiaspergillus IgE serum level had *Aspergillus* culture in the sputum, and only 1 patient had both positive skin mold test, serum specific antiaspergillus IgE and *Aspergillus* culture in the sputum. So, the mold fungi which infected the airways of some asthma patients could sensitize the patients, but not always caused a positive skin or reagin sensitivity.

Mold fungi were culturally identified at sputum of 14 patients (14 %), but it was not associated with any positive *Aspergillus* skin test (0 of 14 patients, CI = 0,0–19,3). While the skin *Aspergillus* test was positive among 6 of 86 patients without mold fungi at sputum (7,0 %, CI = 2,6 – 14,6), p > 0,05. It should be noted that the microbiological method can be not sensitive enough for the effective diagnosis of the fungal infection in airways [10].

We also found that molds at sputum of the asthma patients were associated with:

1. Total serum Ig E level rise to (441,8 ± 108,7) IU/ml (patients without molds had (217,5 ± 33,3) IU/ml, p = 0,05; blood donors – (26,0 ± 4,5) IU/ml) – indicating the allergic processes strengthening with the fungal presence;

2. Expectoration of the mucopurulent sputum was detected in 9 infected persons from 14 (64,3 %, CI = 35,1–87,2), whereas only 23 of the 86 (26,7 %, CI = 17,8–37,4) patients without a mold fungi infection expectorated mucopurulent sputum, p < 0,01. Other differences were not detected.

It is currently assumed that the SAFS is developed through the inhalation of the *A. fumigatus* fungal spores or another fungi from the environment, which may lead to the fungal colonization (sometimes – to invasion) of the respiratory tract at atopic asthmatics. Continuous or repeated contacts with the fungi support and reinforce the sensitization state, amplifying the inflammatory response at the respiratory tract, burdening the course of asthma, worsening asthma control and increasing the need for inhaled corticosteroids, sometimes – with the need to use their system forms [3].

The use of the inhaled corticosteroids (IC) in the basic treatment of asthma patients (n = 69) led to:

- reduction of percentage of patients with the positive skin mold tests to 10,1 % (CI = 4,2–19,8), or 7 patients, whereas this index was higher among the patients without IC – 28,6 % (CI = 13,2–48,7; p = 0,047), or 8 persons (n = 28);
- reduction of percentage of patients with the positive skin tests to house dust – to 15,9 % (CI = 8,2–26,7), or 11 patients,

versus 53,6 % (CI = 33,9–72,5), or 15 patients in the group of patients without IC, $p < 0,001$.

At the same time there were no significant differences in serum levels of total IgE and specific antiaspergillus IgE in these groups. Hence the use of inhaled corticosteroids caused the skin fungal sensitivity weakening because of the bronchial inflammation reduction. It may indirectly indicate the cause of the fungal sensitization – temporary/periodic inhalation of fungal spores/conidia from the air (of the environment or the interior) or cross-sensitization to another allergens (e.g. house dust). Permanent fungal infection (carriage, colonization, invasion of respiratory tract, skin, intestines) is unlikely in patients with asthma associated with the fungal sensitization.

Conclusions

1. Fourteen per cent of patients with asthma have positive immediate skin reactions to the mold allergens, which is associated with the increased levels of total serum IgE to (477,7 ± 125,8) IU/ml, $p = 0,05$; 64 % of them have positive reaction to two or more fungal allergens, and 64 % of them have the increased skin sensitivity to the house dust ($p < 0,05$) which may reflect a cross-allergy status, and the majority of patients with positive skin tests to mold allergens have phenotype of asthma associated with the fungal sensitization (AAFS).

2. Sixty per cent of patients have serum antiaspergillus IgE; it coincides with the results of skin tests only at 14 % of patients and coincides with the Aspergillus content in sputum in 14 % of cases only, this suggests either hidden / latent mold sensitization or a cross-allergy status; serum antiaspergillus IgE are detected in the most of patients with the occupational exposures of respiratory tract in the history (36 % patients), probably due to the weakening of the protective properties of the respiratory tract.

3. The serum antiaspergillus IgE level correlates with the sputum eosinophils number directly ($r = 0,40$; $p < 0,05$) and reflects the intensity of the allergic processes.

4. Mold fungi in the airways of 14 % of asthma patients do not determine a positive skin tests or reagin sensitivity, but they define the mucopurulent sputum expectoration at the 64 % of patients and elevated serum level of total IgE to (441,8 ± 108,7) IU/ml, which confirms the molds involvement into the allergic processes.

5. The use of the inhaled corticosteroids (IC) in the basic treatment of patients with asthma is associated with the weakening of the skin sensitivity to fungal allergens, which is detected at 10 % of patients who use IC (versus 29 % of patients who do not use IC, $p < 0,05$), and weakening of skin sensitivity to the house dust allergens (detected in 16 % of patients versus 54 % respectively, $p < 0,05$), reducing fungal sensitization.

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ФУНГАЛЬНА СЕНСИБІЛІЗАЦІЯ ПРИ БРОНХІАЛЬНІЙ АСТМІ

Ю. І. Фещенко, О. М. Рекалова, Ж. Б. Бегоулева, Л. В. Петренко

Резюме

Мета дослідження: *вивчення клініко-алергологічних особливостей перебігу бронхіальної астми (БА) у хворих з фунгальною сенсибілізацією з визначенням ролі інфікування дихальних шляхів хворих БА пліснявими мікроміцетами.*

Об'єкт дослідження*: 100 хворих на БА у фазі ремісії, середній вік – (46,4 ± 1,4) року, давність захворювання – (9,3 ± 0,9) року, частота загострень – (3,0 ± 0,2) разу на рік, $ОФВ_1$ – (79,1 ± 2,1) %.*

Методи дослідження*: загальне клініко-функціональне, шкірні проби (прік-тести) з фунгальними алергенами Alternaria alternata, Aspergillus mxt, Botrytis cinerea, Chrisonilia sitophila, Cladosporium, Penicillum, алергеном домашнього пилу, рівень загального і протиаспергільозного IgE в сироватці крові хворих, мікробіологічне дослідження мокротиння на цвілеві мікроміцети.*

Результати. *Позитивні результати прік-тестів з фунгальними алергенами отримано у 14 % хворих, що супроводжувалось у 64,3 % хворих підвищенням чутливості до домашнього пилу (p = 0,001) з підвищенням загального IgE до 478 МО/мл (p = 0,05). Підвищення специфічного IgE виявлено у 60 % хворих, що тільки в 14 % збігалося з результатами шкірних проб і в 14 % – з інфікуванням мікроміцетами, і частіше (у 36 % хворих, p < 0,05) визначалося за наявності негативних професійних факторів в анамнезі. Рівень протиаспергільозного IgE корелював з еозинофілією мокротиння (r = 0,40; p < 0,05). Цвілеві мікроміцети, які було виявлено у 14 % хворих, зумовлювали виділення слизово-гнійного мокротиння у 64 % хворих (p < 0,01) і підвищення рівня загального IgE до (441,8 ± 108,7) МО/мл (p = 0,05), але не були пов'язані з наявністю позитивної шкірної або реагінової чутливості (p > 0,05). Застосування інгаляційних глюкокортикоїдів супроводжувалося ослабленням шкірної чутливості (10 % пацієнтів проти 29 % хворих без препаратів; p < 0,05), і чутливості до алергенів домашнього пилу (16 % хворих проти 54 %; p < 0,05), зменшуючи прояви загальної та фунгальної сенсибілізації.*

Висновки. *Позитивні реакції негайного типу до шкірних фунгальних алергенів виявлено у 14 % хворих на БА (два і більше фунгальних алергенів – у 64 %), часто поєднувалися з підвищеною шкірною чутливістю до домашнього пилу та підвищенням рівня загального сироваткового IgE. Останні дві ознаки є характерними для хворих на БА, що асоційована з фунгальною сенсибілізацією, а отже можуть відображати перехресну алергізацію організму.*

Наявність сироваткових протиаспергільозних IgE (у 60 % хворих) тільки у чверті випадків збігається з результатами шкірних проб або вмістом аспергил у мокротинні, частіше визначається за наявності негативного професійного впливу в анамнезі (36 % хворих), ймовірно, у зв'язку з ослабленням захисних властивостей слизової оболонки респіраторного тракту, і свідчить або про прихований/латентний характер фунгальної сенсибілізації, або про перехресну алергізацію.

Рівень сироваткових протиаспергільозних IgE прямо корелює з вмістом еозинофілів у мокротинні та відображає напруженість алергічних процесів.

Цвілеві мікроміцети, що інфікують дихальні шляхи 14 % хворих на БА, в основному, не визначають виникнення позитивної шкірної або реагінової чутливості, але зумовлюють виділення слизово-гнійного мокротиння і сенсибілізують організм хворих, що сприяє підвищенню рівня сироваткового загального IgE та підтверджує їх участь в алергічних процесах.

Застосування інгаляційних глюкокортикоїдних препаратів при базисній терапії хворих на БА супроводжується послабленням шкірної чутливості до фунгальних алергенів і алергенів домашнього пилу та зменшує прояви сенсибілізації організму.

Ключові слова: *бронхіальна астма, фунгальна сенсибілізація, шкірні проби, імуноглобулін Е, цвілеві мікроміцети.*

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FUNGAL SENSITIZATION OF THE PATIENTS WITH BRONCHIAL ASTHMA

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Summary

The purpose of the study was to investigate the clinical and allergic features of bronchial asthma (BA) at patients with fungal sensitization and the role of mold infection of the respiratory tract infection in this.

Object of the study: *100 patients with asthma in remission were examined, mean age is (46,4 ± 1,4) years old, disease duration – (9,3 ± 0,9) years, the frequency of exacerbations – (3,0 ± 0,2) times/year, FEV1 – (79,1 ± 2,1) %.*

Methods: *clinical and functional investigation of patients, skin prick tests with mold allergens (Alternaria alternata, Aspergillus mxt, Botrytis cinerea, Chrisonilia sitophila, Cladosporium, Penicillum), house dust allergen, serum total IgE and antiaspergillus IgE level, microbiological investigation of sputum for mold fungi, statistical methods.*

Results. *There were positive results of skin prick tests with the mold allergens in 14 % of patients, and the increased sensitivity to the house dust in 64,3 % of them ($p = 0,001$), and the increased total IgE serum level to 478 IU/ml ($p = 0,05$). The increased specific IgE serum level was detected in 60 % of patients, and only at 14 % – with the positive skin mold tests and at 14 % – with the mold infection in the respiratory tract. The most of patients with the increased specific IgE level (36 %, $p < 0,05$) had the occupational exposures of respiratory tract in the history. The increased specific IgE serum level correlated with sputum eosinophilia ($r = 0,40$, $p < 0,05$). Mold fungi were culturally identified at sputum of 14 % of patients and accompanied with expectoration of mucopurulent sputum at the 64 % of patients ($p < 0,01$), and the increasing of the serum level of total IgE to (441,8 ± 108,7) IU/ml ($p = 0,05$), but were not associated with the presence of a positive skin or reaginic sensitivity ($p > 0,05$). The use of the inhaled corticosteroids led to the weakening of the mold skin sensitivity (at 10 % of patients who use IC versus 29 % of patients who do not use IC, $p < 0,05$), and the skin sensitivity to the house dust allergens (16 % of patients versus 54 %, $p < 0,05$), – reducing the manifestations of common and mold sensitization.*

Conclusions. *The positive immediate skin reactions to the mold allergens in 14 % of patients with asthma (to two or more mold allergens – 64 %), often – with the increased skin sensitivity to the house dust and the increased levels of total serum IgE are the typical features for the asthma patients with the fungal sensitization phenotype and may reflect a cross-allergy status;*

The presence of antiaspergillus IgE in the serum (60 % of patients) coincides with the results of the skin tests or the Aspergillus content in sputum of a quarter of cases only and matches to the occupational exposures of respiratory tract in the history of 36 % patients, probably due to the weakening of the protective properties of the respiratory tract – and suggests either the hidden/latent mold sensitization or a cross-allergy status.

The serum antiaspergillus IgE level correlates with the sputum eosinophils number directly and reflects the intensity of the allergic processes;

Mold fungi in the airways of 14 % of asthma patients mostly do not determine a positive skin tests or reagin sensitivity, but they define the mucopurulent sputum expectoration and elevated level of serum total IgE, which confirms the molds involvement into the allergic processes;

The inhaled corticosteroids is associated with the weakening of the skin sensitivity to the molds and to the house dust allergens in the basic treatment of asthma patients, reducing sensitization.

Key words: *asthma, fungal sensitization, skin tests, immunoglobulin E, mold fungi*

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