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Profile of sensibilisation to major and minor components of domestic allergens in patients with allergic rhinitis and helminthosis

Allergic rhinitis (AR) belongs to the group of the most widespread diseases in different parts of the world. Over the recent 10 to 15 years, the incidence of AR has risen by 20 % in Europe and has reached for 10 % to 40 % of the population, which constitutes nearly 47 million patients. The AR is traditionally subdivided into seasonal allergic rhinitis and perennial allergic rhinitis (PAR). For the PAR, it is typical to demonstrate such symptoms as nasal congestion, effuse, itching, and loss of sensory sensitivity during the whole year, with a possibility of temporal correlation of the exacerbation after a contact with an allergen (house dust, mushroom spores, animal hairs, etc.) [9, 12,18]. In this context, patients with PAR often reveal comorbid conditions including helminthoses.

The most widespread helminthes in humans are nematodes: enterobiasis, ascariasis, and toxocariasis [1,3,4,6,10].. In the event of invasion, parasitic antigens penetrate the mucous membrane of the gastrointestinal tract (GIT) where they are captured by macrophages or dendrite cells. The latter perform the antigenic presentation to the T-helpers, which differentiate predominantly into the Type 2 T-helpers. The latter activate the mast cells and cause their intensive mitosis by means of the production of IL-3 and IL-4 [2, 5, 7,8].. On the other hand, the Type 2 T-helpers give impact to the B-lymphocytes of solitary follicles (IL-4 and IL-5), thus causing them to produce the IgE. The synthesized specific IgE's cover the surface of the mast cells, thus playing the role of their receptors for antigenic recognition. The interaction of the soluble antigens of a helminth with the IgE of the mast cells brings about the degranulation of the latter, and that results in the freeing of histamine and chemotaxic factor of the eosinophils. The chemotaxic factor attracts eosinophils into the hotbed of a helminth, while the IL-5 Type 2 T-helpers essentially increase their cytotoxic potential [8, 11, 16]. By means of increasing vascular penetration, histamine ensures the required access for wandering cells. The arriving eosinophils attack the parasite cells, thus taking part in the antibody-dependent cell-mediated cytotoxicity (ADCC). The eosinophilic cationic protein (ECP) is one of the protectins, which is a part of cytoplasmic granules of eosinophils. As it penetrates the blood stream during the degranulation of eosinophils, the ECP reflects the degree of evidence of allergic manifestations in the case of helminthosis as well and also indicates the age of the process. Specific IgE not only ensures the ADCC, but also blocks the surface molecules of a helminth, thus disrupting its metabolic processes. However, in order to run these processes, it is necessary that a non-specific mechanism of anti-helminth protection runs efficiently. The latter comprises the activation of microphages and neutrophils in the mucous membrane of the gastrointestinal tract (GIT) in the course of phagocytosis of the components of a helminth and the production of IL-1β and FNO- , which intensify the intestinal motility and increase the secretion of mucus in goblet cells.

The said mechanisms facilitate speedy expulsion of a helminth damaged by the immune reaction. It should also be pointed out that helminthes increase the frequency of pseudoallergic and toxicoallergic reactions. Pseudoallergic agents are not capable of forming the sensibilisation, but they can cause the effect of direct degranulation of mast cells, basophiles, and other types of cells, and they can also cause the symptoms, which are similar to the pseudoallergic ones (pseudoallergy) [2, 7, 11,16]. The pathological flow of PAR with parasitosis at the background

may result from the formation of pseudoallergy or from a combination of true allergy to domestic allergens and toxicoallergic effect of helminth antigens.

In this regard, **the purpose of our research** was to study the profile of sensibilisation and to reveal the primary sensibilisation or cross reactivity in patients with PAR with concomitant helminthosis. To this end, we used the method, which is applied for the purposes of mapping the allergenic sensibilisation of patients at molecular level; the molecular allergological diagnostics [13, 14, 19].

Material and Methods

We were observing 112 patients (66 men and 46 women aged 18 to 50) with the PAR. The PAR was diagnosed in compliance with the Ministry of Public Health of the Ukraine order #432 dated July 3, 2006. All of the patients underwent the blood tests in order to detect the IgM and IgG class antibodies to helminthes (ascarids and toxocaras), and thus the patients were subdivided into two groups: Group 1 had 47 people with the PAR without helminthosis and Group 2 had 65 patients with the PAR and with helminthosis. All of the patients underwent skin tests (the prick tests) with domestic allergens and the detection of the number of eosinophils and the overall level of the IgE and the ECP in their blood. The immunological research was conducted with the Microplate Reader RT 2100C immunoenzyme analyzer manufactured by Rayto Electronics Inc. (China). The level of the IgE class specific antibodies to major and minor components of domestic allergens in blood serum was also detected in all of the patients with the aid of the ImmunoCAP immunofluorescent analyzer manufactured by Phadia (Sweden). For the purposes of statistical processing of the results, the T-test for Dependent Samples was used. The results with $p < 0.05$ were considered veracious.

Results and their Interpretation

As the result of the skin tests with different allergens, 47 patients with the PAR without concomitant helminthosis most often (65 % of cases) revealed sensibilisation to house dust mites and, more seldom, to mold fungi (12.7 %) and also to the epithelium of cats (6.3 % of cases). The sensibilisation profile differed essentially in 65 patients with the PAR with concomitant helminthosis. Same frequency of sensibilisation (55.3 % of cases) was observed as the reaction to house dust mites and, more seldom, to feline epithelium (6.1 %). However, the combined sensibilisation to domestic allergens was detected in a greater number of cases (38.4 % as compared to 12.7 % with $p<0.05$) while there was no sensibilisation to mold fungi at all. We have also studied the degree of the hypersensitivity to allergens in patients with the PAR and with/without helminthosis depending on the size of the papules during the prick tests, and that has been shown in Table 1 below. The data contained in this table witness that the presence of helminthosis facilitates a more frequent buildup of the positive (35.4 % versus 17.0 % of cases), expressly positive (47.7 % vs. 4.2 % of cases), and hyperergic results of a prick test with allergens ($p<0.05$, $p<0.01$).

As mentioned hereinabove, the number of blood eosinophils and the level of the general IgE and ECP as well as the level of the class IgE specific antibodies to major and minor components of domestic allergens were detected in the blood serum of the patients in the both groups at the second stage of the research by means of immunofluorescent analysis. The relevant data are shown in Table 2 below and hereinafter as well.

The above data show that the PAR patients with concomitant helminthosis revealed an increase in both relative and absolute numbers of eosinophils (by 56 % and by 16.6 %, respectively) and in the ECP level by 44.8 % as well as a 39.8 % increase in the general IgE level as compared to the control group of the PAR patients without concomitant helminthosis.

All of this may be indicative of the negative impact of helminthes on the flow of the PAR since the parasites produce metabolic, secretion, and excretion products in the course of their vital activity, and those products have allergenic properties. The excess of general IgE blocks the receptors of mast cells, which eventually leads to increased allergic reactions resulting from the instability of mastocytes. Helminthes increase the frequency of toxicoallergic reactions. The pseudoallergic agents are unable to produce sensibilisation, but they can cause the direct degranulation effect in mast cells and the symptoms similar to the allergic ones (pseudoallergy). Hence, the PAR may serve as a sign of a pseudoallergic pathology in case of helminthoses. In the group of the PAR patients with helminthosis, it has been revealed that there is a vast percentage of combined sensibilisation to domestic allergens as compared to the PAR patients without helminthosis, and that speaks for the production of polyclonal allergic antibodies of the IgE class with helminthosis at the background. In this respect, it is recommended for the PAR patients with the sensibilisation to domestic allergens that they undergo the examinations aimed at detecting a possible helminthosis.

	PAR patients without helminthosis (n = 47)		PAR patients with helminthosis (n = 65)	
Allergen skin test results	**Absolute number**	**%**	**Absolute number**	**%**
Weak positive (papule of 3 to 5 mm in size)	37	78.8	11	16.9
Positive (papule of 6 to 8 mm in size)	8	17.0	23	35.4
Expressly positive and hyperergic (papule of 8 to 10 mm and larger in size)	2	4.2	31	47.7

Table 1

Results of the prick test with domestic allergens in the PAR patients with and without concomitant helminthosis

	Table 2	
Results of the laboratory research of the PAR patients with and without concomitant helminthosis		
Laboratory parameter	PAR patients without helminthosis (n=47)	PAR patients withhelminthosis (n=65)
Eosinophils (%)	5.3±2.6	9.3±3.1•
Eosinophils (abs. No.)	0.1±0.04	0.6±0.3•
ECP lever (mcg/l)	9.1±3.5	20.3±5.1•
General IgE level (MV/ml)	98.8±39.9	248.2±18.2•

Note: • The veracious results between the PAR patients with helminthosis as compared to the PAR patients without helminthosis, with $p<0.05$.

As the result of the molecular diagnostics undertaken in a group of 31 people with the PAR without helminthosis and with the sensibilisation to house dust mites (Dermatofagoides pteronissimus et farine), the sensibilisation to the major components of the said allergen (Der p1, Der f1) was detected in 30 patients (96.7 % of cases) while the sensibilisation to its minor component (Der p10) was found in only one (1) patient. In this context, no combined sensibilisation to the major and minor components of the said allergen was detected. In a group of 36 patients with the PAR and helminthosis with the sensibilisation to house dust mites, the hypersensitivity to the major component of the allergen (Der p1, Der f1) was not detected in any of the patients while the sensibilisation to the minor component Der p10 was detected in 3 (8.3 %) patients and the sensibilisation to the major and minor components was found in 33 (91.6 %) patients. Hence, the profile of the sensibilisation to domestic allergens in the PAR patients *without* helminthosis included predominantly the major components of the dust mite allergens. When it came to the PAR patients *with* helminthosis, the said profile was dominated by a combination of the major and minor components of the dust mite allergens.

It is also necessary to point out that the group of patients with the sensibilisation to the allergens typical for mold fungi (Aspergillus fumigates, Alternaria alternate) was not large and included only 7 (6.2 %) patients. In the PAR group without helminthes, sensibilisation was detected to the major component (Asp f1,Alt a1) in 6.2 % of the patients. No sensibilisation to the minor components (Asp f6, Alt a6) and no combination of the major and minor components were detected. In the group of the PAR patients *with* helminthosis, no sensibilisation to mold allergens was detected and the sensibilisation to feline epithelium was also insignificant as it was found in 7 (6.2 %) of the patients out of the 112 people examined. Furthermore, out of the 47 PAR patients *without* helminthosis, only 3 (6.3 %) patients were sensible to the major component (Fel d1), and we detected no sensibilisation to the minor component (Fel d2) in them. However, as far as the PAR group *with* helminthosis is concerned, the sensibilisation to the minor component (Fel d2) was detected in 4 (6.1 %) patients. It is also to single out that the group of the PAR patients *with* helminthosis is dominated by a combination of major and minor components of domestic allergens of the dust mite, which may be indicative of the primary sensibilisation of the patients with the major protein Der p1 or Der f1, while the helminthosis facilitates the cross reactivity by means of the tropomyosin proteins, which amplify the clinical manifestations of the allergic rhinitis. The patients of the said categories are recommended to take the anti-helminth therapy, after which it is prescribed to run the specific allergoimmunotherapy with the major component of domestic allergens.

Conclusions

1. Patients with the perennial allergic rhinitis must be checked for helminthes.

2. The helminthosis, which accompanies the perennial allergic rhinitis, aggravates the flow of the major disease and facilitates the formation of a more manifest hypersensitivity to domestic allergens.

3. The management of patients with the perennial allergic rhinitis and a background helminthosis must comprise anti-helminth and specific allergoimmunotherapy with regard to the data about the sensibilisation to the major and minor components of domestic allergens.

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