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Research Paper

Allergy to Pet: Differential Approaches to Selection 0f Specific Allergotherapy Prescription With Due Account of Component Studie

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ABSTRACT
Introduction: *One of the topical problems is allergy to home pets, viz. to cat and dog that occurs among adults at the rate of 5-15%.*
Aim: *To choose an adequate therapy and to make the prognosis of its efficacy in patients with sensitization and clinical manifestations of allergy to cat and dog.*
Material and methods: *22 patients aged 16-36 have been studied. The diagnosis was verified on the basis of objective and subjective data, overall laboratory and instrumental tools, prick tests, general and specific IgE determination. The study of allergen components was made by immunofluorescence method ImmunoCAP.*
Results: *According to the results of skin prick tests sensitization to cat was traced in 81.8% persons, of whom monosensitization was traced in 27.8%, association of cat allergens with other types of allergens – in 72.2%, most frequently this being – cat+dog. Higher levels of general IgE were traced in 77.3% patients. Specific IgE only to cat was traced in 16.6% ones, while the rest 83.4% of patients had specific IgE to cat in the combination with different domestic allergens. Patients with major cat allergen Fel d 1 alone or in combination with minor allergen Fel d 2 were prescribed allergen immunotherapy with high/medium efficacy prognosis. People with panallergy were prescribed a stage-by-stage therapy. Patients with only minor allergens traced were not recommended to undergo allergen immunotherapy.*
Conclusion: *On the basis of allergen-component analysis allergen immunotherapy was recommended for 58.8% of patients only, and for 23.5% the content of allergen immunotherapy was modified.*

Keywords:- *allergy to home pets, allergen-component diagnostics, allergen immunotherapy.*

I. INTRODUCTION

According to literature data, sensitization to house pets (cat, dog) was traced in 30-57.3% of patients with bronchial asthma (BA), allergic rhinosynusitis or exema[1]. Incidence of allergy to cat among adults reaches 10-15%, to dog - 5-10%, and it has some regional peculiarities and annual growth tendency. Scientists connect this to different factors, primarily to "fashion" trend to have pets (from 30% to 80% families in Europe and the USA have pets) [2]. For persons with verified BA of importance is genetic propensity to the given type of allergy. In particular, there has been described the data that in 50% of children with BA there was a connection of allergy to cats in close relatives, most frequently along the father's line [3].

Thus, allergy to pets is one of the topical problems of today. On the whole, the results of scientific search in the given direction show that the issues of dependence of the level and duration of exposition to pet allergens remain open concerning specific sensitization development, the issues of preventive role of cross-over contacts with different pets (in particular, cat-dog) and other animals (cat-horse), cross-over reactions of allergens of cat and food allergens (syndrome swine-cat, allergy to oligosakharide alfa-gal), as well as literal diagnostics (in vivo/in vitro) of the given type of allergy for choosing effective approaches to treatment, etc.[4].

Today one of those problems may be solved thanks to the development of component (molecular-based) diagnostics (MD)[5]. Over the last 40 years researchers from different countries have pointed out and characterized quite a number of allergens classified by their capacity to evoke primary sensitivity (major ones) or explain cross-reactivity (mainly minor ones) to similar-structure proteins.

Thus, a wide range of molecular data on allergic components of dog/cat, on the one hand, enables to talk with great accuracy about cause-and-effect issues in determining clinical symptoms which is anamnestically

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related (or not related!) to those animals, and on the other hand – points to the need for highly-accurate approaches to diagnostics of that type of allergy to choose an effective therapy.

The goal of our research was to choose a correct approach to AIT and to assess the prognosis of its efficacy in patients with sensitization and clinical manifestations of allergy to cat and dog on the basis of allergy-component diagnostics

II. MATERIAL AND METHODS

We had pets under our observation 22 patients who addressed the Regional Centre of Clinical Immunology and Allergology during 2014-2015 with a suspicion of having allergy to pets. The patients were aged 16-36, of them there were 63.6% of women and 36.4% of men. The diagnosis was verified on the basis of the clinical picture of the diseases, anamnesis data, including allergic anamnesis. General laboratory tests and instrumental studies, cytological study of smears of an imprint from the mucous tunic of nose, prick tests with allergen extract (Diater, Spain), determination of general and specific IgE (sIgE) by enzyme multipled immunoassay using test systems "Euroimmun" following the producer firm's instructions were made for patients. To trace type-specific allergen components immunofluorescence method ImmunoCAP ("Phadia AB", Sweden) was used. Blood serum constituted the material of the study.

III. RESULTS

The patients' complaints were as follows: nasal obstruction and gasp (100%), rhinorrhea, watery eye, which was regularly accompanied by itch, frequent sneezing, in particular, while staying in closed premises. 31.8% pointed out cough that became of a paroxymal nature and was often accompanied by gasp in contacting with animals.

Analysis of the results of the general laboratory data has shown that in complete blood count of 31.8% of persons there has been traced absolute light eosinophilia, in 22.7% – absolute lymphocytosis, in biochemical values no special deviations have been traced.

Thus, the obtained preliminary results of subjective and objective data with high degree of probability pointed to formation of allergy to pets with patients and dictated the need to conduct further stages of allergy diagnostics.

The results of skin tests show that in all patients there was hyper skin reaction to different types of house allergens, in particular, with different degree of sensitization from "+" to "++++", and of them 9 (40.9%) patients - monosensitization, in 13 (59.1%) – polysensitization, (table 1) . Further analysis of the results showed that sensitization to cat was available in 18 (81.8%) of persons, of which - monosensitization was available in five (27.8%), association of cat allergens with other types of allergens – in 72.2%, most frequently these were cat+dog (33.3%).

The next stage of the study was determination of general and specific IgE-antibodies using ELISA methods, the results of which are also provided in table 1. On the basis of the results of studies it has been traced that in 17 (77.3%) of patients the general serum IgE was higher and was within 117 to 1,755 MO/ml, this pointing to real allergy development. On the basis of the studies of specific IgE (> 0.35 kU/l) sensitization to cat was traced in 18 (81.8%) persons, out of whom monosensitization was available in 3 (16.6%), while the other 83.4% patients had specific IgE to cat in combination with different allergens, including allergens of different animals (dog, guinea pig, horse, rabbit). As it should have been expected, the results of skin prick tests and specific IgE identification differed. Thus, patients were offered to undergo an allergen-component analysis. Since the aim of our work was to assess the prognosis of AIT efficacy in patients with sensitization and clinical manifestations of allergy to cat, we analyzed that group of patients – 18 persons, and the results are provided in

Table 1.

The results of prick tests, general and specific IgE (ELISA), n=22

N □ □ □ □ □ Patient No.	**Age, years**	**Gender**	**Prick tests**	**Helminths**	**Gen. Ig E (□ □ / ml)**	**sIgE □0,35 KU/l**						
						cat	**dog**	**mix. mite. p. D.f.**	**alternaria**	**horse**	**guinea pig**	**Rabbit**
1	32	M	Mixture cat +++ Mixture dog+ Mixture of mites ++	tox	314	32.1	0.75	1.9		-	0.75	

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2	18	M	Mixture cat +++ Mixture dog +	asc	215	19.5	1.76		-	0.36		0.42
3	30	F	Mixture of mites +++	giar	954	-	-	24.8		-	-	-
4	31	F	Mixture cat+++ Mixture dog++		56	15.8	13.2		-	-		
5	24	F	Mixture cat+++		89	41.6	-		-	-	2.1	
6	22	M	Mixture fungi+++		652		-	-	67.5		-	-
7	16	F	Mixture cat + Mixture fungi+++		117	0.36		-	39.6		-	-
8	17	F	Mixture cat+ Mixture dog+		110	1.2	1.93		-	-	-	-
9	20	F	Mixture cat ++++ Mixture dog++		1265	>100	22.1		-	-		
10	17	M	Mixture cat+ Mixture of mites++++	asc	412	1.1		>100	-	-	-	-
11	25	F	Mixture cat+ Mixture of mites+	giar	212	1.08		1.3		-	-	-
12	18	M	Mixture cat+++ Mixture fungi++ Mixture dog++ Mixture of mites+	giar	311	19.86	5.8	1.9	12.3	0.36	-	0.36
13	36	M	Mixture cat+ Mixture dog+		65	0.5	0.36		-	12.9		-
14	20	F	Mixture of mites++	giar+ asc	957			21.3		-	-	-
15	22	F	Mixture cat+++ Mixture dog+++ Mixture of mites++	giar+as c	453	65.2	31.5	12.9		-	-	-
16	25	F	Mixture cat ++++		56	47.5	1.45			-	1.01	
17	29	M	Mixture cat ++ Mixture dog+++ Mixture fungi++		265	3.25	19.7		0.36		-	-
18	30	F	Mixture dog+++		211		62.7		-	-	-	-
19	19	F	Mixture cat+++		201	54.2		-	-	-	-	-
20	18	F	Mixture cat+++ Mixture dog++		1755	41.0	1.13		-	-	-	-
21	33	F	Mixture cat++++		64	11.2		-	-	-	-	-
22	31	M	Mixture cat+++		301	45.5		-	-		-	-

Table 2

The results of allergen-component studies (Immuno CAP, sIgE □ 0,35KU/l), n=20

Patient No.	**rFel d 1**	**rFel d 2**	**rCan f 1**	**rCan f 2**	**rCan f 3**	**rDer p 1, rDer p 2**	**rDer p10**	**Alt a 1**	**Recommended**
	maj	**min**	**maj**	**min**	**min**	**maj**	**min**	**maj**	
1	20.3	-	5.1	-	-	-	0.75		SLIT cat → high ef. + anti-helminthic therapy
2	10.3	17.5	-	1.35	4.0	_	_	-	SLIT cat → medium ef.
3/4	11.5	3.6	-		3.75				SLIT cat → medium ef.
4/5	13.7	-	-	-					SLIT cat → high ef.
5/7	-	5.35	-	-				15.6	SLIT alternaria → high ef. to Alt a 1
6/**8**	2.0	_	26.5	-					AIT dog → high ef.
7/**9**	28.5	1.5	14.7	1.5	1.5				SLIT cat + AIT dog → medium ef.

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8/**10**	-	2.5	-	-		27.8	14.3		SLIT mite→ high ef.
9/**11**	22.5	_		-			1.6		SLIT cat → high ef. + anti-helminthic therapy
10/**12**	11.6	9.3	-	10.5	5.4		2.3		SLIT cat → medium ef. + anti-helminthic therapy
11/**13**	-	-	-	-	-	-	-	-	SLIT (-),**ISAC** necessary
12/**15**	1.3	6.3			1.64		0.96		observation + anti-helminthic therapy
13/**16**	-	2.4	-	-	1.5	-	-		SLIT (-)
14/**17**	0.9	3.5	-	1.7	2.0				SLIT (-)
15/**19**	23.9		-	-		-			SLIT cat → high ef.
16/**20**	1.3	8.5	33.5	-	-	-			AIT dog → high ef.
17/**21**	7.5	2.3							SLIT cat → medium ef.
18/**22**	30.7	-							SLIT cat → high ef.

To choose the treatment method and to predict its efficacy a detailed analysis of component diagnostics data was made, it enabling to divide the patients into the following groups:

1st group - patients 5, 11, 19, 22 – monosensitized to major cat allergen Fel d 1. Those patients were recommended to undergo sublingual allergen-specific immunotherapy (SLIT) "Mixture cat" (Diater, Spain)", with high efficacy prediction. As far as patient 11 is concerned, Fel d 1 was traced in association with Der p 10 (tropomyosin) – a minor allergen of house dust mites. It is known that tropomyosin is included in all the cells of all the representatives of the animal world. The degree of cross reactivity between tropomyosin of mites and other sources reaches 75-80%, while the highest cross-reactivity gets manifested with seafood, cockroaches and nematodes [6]. Since giardias were traced in that patient, obviously, they constitute the reason for the availability of the given component. That is why patient 11 was recommended to have an additional anti-parasitic treatment, keep to elimination diet excluding seafood, follow hygienic recommendations on domestic conditions and undergo regular monitoring of parasitic invasions, etc.

2nd group – patient 21 sensitized to major cat component Fel d 1 and minor serum albumin Fel d 2. The patient was recommended to undergo SLIT "Mixture cat" (Diater, Spain)", the efficacy of which is expected as medium.

3rd group – patients 2, 4, 12, 15, 17 sensitized to major cat allergen against minor cat and dog allergens. Those patients showed a cross-reaction between cat and dog serum albumins (Fel d 2, Can f 3). While patients 2, 4, 12 with high level of Fel d 1 were offered "Mixture cat" (Diater, Spain)" with medium efficacy prediction, patients 15 and 17 with low level of Fel d 1 were recommended to undergo an examination and an anti-helminthic therapy, as well as to avoid contact with the corresponding animals.

4th group – patients 1, 8 – with parallel sensitization to major cat allergens Fel d 1 and dog allergen Can f 1. Patient 1 was recommended "Mixture cat" (Diater, Spain)", since the level of Fel d 1 is much higher than Can f 1 (correspondingly, 20.3 KU/l, 5,1 KU/l) and additional anti-helminthic treatment with a range of hygienic instructions. Patient 8 with anamnestic data could not clearly determine the cause of allergic symptoms, but in childhood he used to have a dog. He was offered AIT to dog since there dominated concentration Can f 1 (26.5 KU/l against 2.0 KU/l - Fel d 1). The prognosis of specific therapy efficacy for the above animals was high for both patients.

5th group – patient 20 – with parallel sensitization to major cat and dog allergens in the background of minor serum cat albumin Fel d 2. From the data of anamnesis it is known that the patient had never had pets, had a complicated hereditary anamnesis, regular skin manifestations had been occurring since early childhood and they had been mistakenly associated with reaction to food. Since the age of 14 there, in addition, also appeared symptoms of rhinoconjunctivitis. The patient was recommended AIT to dog since the concentration of the given component was higher (33.5 KU/l against 1.3 KU/l - Fel d 1), he was also recommended to avoid contact with animals. The AIT efficacy prognosis was high. As far as sensitivity to cat and identified major allergen Fel d 1 is concerned, the option of stage-by-stage addition of "Mixture cat" (Diater, Spain)" should be considered in the conditions of occurrence of clinical symptoms in future.

6th group – patient 9 sensitized to major cat and dog allergens in the background of minor allergens of those animals Fel d 2, Can f 2, Can f 3. According to anamnesis, he had been keeping both animals in the territory around the house for a long period of time. The patient was recommended to undergo a stage-by-stage therapy with Mixturei to begin the treatment depending on the concentration of major allergen. Therapy efficacy prognosis was medium.

7th group – patients 7, 10 16 sensitized to minor car allergen Fel d 2 only: Patient 16 of the group had serum cat and dog albumins Fel d 2 and Can f 3. On the basis of a detailed collected anamnesis there was traced

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availability ofregular manifestations of allergic reaction in the form of oropharyngeal urticarial fever after pork consumption, and the more pork was consumed in combination with alcohol, the stronger the allergic reaction was. On the basis of the received data of anamnestic and specific allergological studies one may talk about availability of "pork-cat" syndrome with the patient. The patient was recommended to undergo ISAC examination for the sake of tracing additional allergen components, in particular, pork albumin Sus s and to keep to the corresponding diet. SLIT "Mixture cat" was not recommended to the patient since it would not be effective.

Patient 7 was not recommended SLIT "Mixture cat", since he was offered SLIT "Mixture of mold fungi" due to availability of major allergen of alternaria alternata Alt a 1 in him, and its efficacy would be high. As far as minor car allergen Fel d 2 is concerned, multi-component diagnostics ISAC could possibly help to find the main source of appearance of that marker of cross reactions.

Patient 10 sensitized to major and minor allergens of house dust mites was recommended to undergo SLIT "Mixture of house dust mites", the efficacy of which would be high in the conditions of treatment of available ascaridosis, keeping to hygienic recommendations in daily life and to a diet excluding seafood. Similarly to patient 7 – he was recommended to have an ISAC examination.

8th group – patient 13, in whom allergen-component analysis appeared to be negative. From a detailed anamnesis it became known that he had had allergic symptoms in contact with horse twice, and for the first time that was in the form of cough and rhinorrhea manifestations, but for the second time cough was accompanied by gasp. Obviously, there is a suspicion of availability of sensitization of that patient to Fel d 8, which has a high homology with minor allergens of horse Equ c 4 and Equ c 5. Correspondingly, to verify the diagnosis the patient was primarily recommended to undergo ISAC examination.patient was primarily recommended to undergo ISAC examination.

Thus, on the basis of the allergy-component analysis made SLIT to cat with high/medium efficacy prognosis was recommended only for 10 (58.8%) patients, while for 23.5% the content of allergen immunotherapy was modified.

IV. DISCUSSION

According to literature data, sensitization to house pets (cat, dog) was traced in 30-57.3% of patients with bronchial asthma (BA), allergic rhinosynusitis or exema [7]. Incidence of allergy to cat among adults reaches 10-15%, to dog - 5-10%, and it has some regional peculiarities and annual growth tendency. Scientists connect this to different factors, primarily to "fashion" trend to have pets (from 30% to 80% families in Europe and the USA have pets) [8]. For persons with verified BA of importance is genetic propensity to the given type of allergy. In particular, there has been described the data that in 50% of children with BA there was a connection of allergy to cats in close relatives, most frequently along the father's line [9].

Clinical symptoms of allergy to pets could be different: from a light form of rhinoconjunctivitis to severe manifestations of asthma [10]. Hypersensitivity reactions occur by immediate and slowed-down type, are most frequently IgE-mediated. As a rule, symptoms may appear 5 minutes after contact with cat/dog ad reach their peak 2-3 hours later. In conditions of inhalant allergen penetration with sensitized persons with atopic BA already after 20-30 minutes there may appear cough, gasp, bronchospasm [11]. Besides that, scientists have come to the conclusion that permanent exposition to allergens of pets starting with early age increases the risk of BA development. It has also been studied that polysensitization with more than three components of animal origin has a relation to the increase in the general morbidity and deterioration of human life quality [12]. And direct manifestations of clinical symptoms are not always related to direct contact with cat/dog and do not show any linear dependence of allergen concentration, for instance, the clothes of cat owners constitutes a means of transfer of major cat allergen Fel d 1 into any other environment [13]. Passive transfer of cat allergens is also possible via hair, shoes, as the result – cat allergens were traced in schools, pre-school institutions, in public transport, etc. A visual demonstration here was the study by Luczynska et al., which analyzed the level of Fel d 1 in the vivarium where there lived 12 cats [14]. It has been identified that concentration of this allergen reached on average 40 ng/m3. To compare, in residential building with a boiler a wide range of Fel d 1 concentration in the air was identified – from 0.7 to 468.5 ng/m3. It is of interest that cat allergens were available in houses without cats, though the levels of Fel d 1 in them were much lower (0.24-1.78 ng/m3) [15]. Thus, the majority of authors have come to the conclusion that even low levels of Fel d 1 in the air (ng amounts in m3) can cause allergic symptoms in patients sensitive to cats [16,17].

There is a common opinion that for allergy development of importance is gender, age, colour and species of pets, in particular, less allergenic are considered to be cats of "Sphynx", "Devon Rex", "Ashera", "Cornish Rex", "Bombay" species. However, there does not exist 100% evidence data showing that the above species of cats do not cause human sensitization, and the results of molecular-based studies into the fact that major cat allergen is available in dander, sebaceous glands secretion and urine of that animal, refute the idea

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[18]. Similarly, as after cat treatment with hypoallergenic hygienic detergents – the level of major allergen Fel d 1 already 24 later corresponds to the initial one. As far as dogs are concerned, the myth about hypoallergenic species "Labradoodle", "Poodle", "Spanish Waterdog", "Airedale terrier" is also subject to "dispelling" due to proven facts of availability of same high levels of major dog allergen Can f 1 in samples of fur of both ordinary and "hypoallergenic" species. However, as far as gender is concerned, in 2009 Swedish scientists managed to secret from the animal urine a new major allergen – Can f 5 – prostate kallikrein, hence – it is available with males only [19]. Antibodies to Can f 5 were traced in 70% of patients with dog allergy, and almost one third of persons were monosensitized by that allergen. Thus, Can f 5 constitutes an important supplement to the diagnostic panel of other well-known dog allergens. Of interest is the fact that homology between kallikrein of dog prostate and prostate-specific human allergen (PSA) makes up from 55 to 60%. It is quite possible that sensitization to Can f 5 increases the risk of development of allergic responses to man's sperm [20]. In particular, in the study by Basagana et al. it was identified that dog prostate kallikrein is capable of binding IgE in patients with sperm allergy. Thus, IgE-mediated reactions to this dog allergen can play a trigger role in some cases of spousal infertility [21].

V. CONCLUSION

Monosensitization to cat was traced in 29.4% persons, it being confirmed by availability of the molecule of major protein Fel d 1, or minor polyvalent allergy marker Fel d 2, or their integrity. In 70.6% of persons polysensitization was traced, mainly – association of different allergens of cat and dog. In 78.6% of patients with identified major cat allergen Fel d 1 allergic reaction was IgE-mediated. Patients with major cat allergen Fel d 1 identified only were recommended SLIT "Mixture cat". The efficacy of sublingual immunotherapy is high. Patients with identified major cat allergen and in the background of availability of minor allergens were recommended SLIT "Mixture cat" with medium efficacy prognosis. Patients with identified major cat and dog allergens were recommended a stage-by-stage specific therapy with Mixturei to begin treatment depending on the major allergen concentration. Immunotherapy efficacy is high. Patients with minor cat allergens were not recommended to undergo a specific therapy, instead they need to undergo ISAC examination for the sake of additional allergic components identification. In patient treatment it is important to use allergens standardized by activity, which are controlled for availability of major components, this enabling to achieve high efficacy of treatment.

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