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IMMUNITY AND SENSITIZATION TO MICROBE ALLERGENS IN PATIENTS WITH CHRONIC TONSILLITIS

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Foreign Technology Division
Wright-Patterson Air Force Base, Ohio

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А а	*А а*	A, a	Р р	*Р р*	R, r
Б б	*Б б*	B, b	С с	*С с*	S, s
В в	*В в*	V, v	Т т	*Т т*	T, t
Г г	*Г г*	G, g	У у	*У у*	U, u
Д д	*Д д*	D, d	Ф ф	*Ф ф*	F, f
Е е	*Е е*	Ye, ye; E, e*	Х х	*Х х*	Kh, kh
Ж ж	*Ж ж*	Zh, zh	Ц ц	*Ц ц*	Ts, ts
З з	*З з*	Z, z	Ч ч	*Ч ч*	Ch, ch
И и	*И и*	I, i	Ш ш	*Ш ш*	Sh, sh
Й й	*Й й*	Y, y	Щ щ	*Щ щ*	Shch, shch
К к	*К к*	K, k	Ъ ъ	*Ъ ъ*	"
Л л	*Л л*	L, l	Ы ы	*Ы ы*	Y, y
М м	*М м*	M, m	Ь ь	*Ь ь*	'
Н н	*Н н*	N, n	Э э	*Э э*	E, e
О о	*О о*	O, o	Ю ю	*Ю ю*	Yu, yu
П п	*П п*	P, p	Я я	*Я я*	Ya, ya

*ye initially, after vowels, and after ъ, ь; e elsewhere. When written as ё in Russian, transliterate as yë or ë. The use of diacritical marks is preferred, but such marks may be omitted when expediency dictates.

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RUSSIAN AND ENGLISH TRIGONOMETRIC FUNCTIONS

Russian	English
sin	sin
cos	cos
tg	tan
ctg	cot
sec	sec
cosec	csc
sh	sinh
ch	cosh
th	tanh
cth	coth
sch	sech
csch	csch
arc sin	$\sin^{-1}$
arc cos	$\cos^{-1}$
arc tg	$\tan^{-1}$
arc ctg	$\cot^{-1}$
arc sec	$\sec^{-1}$
arc cosec	$\csc^{-1}$
arc sh	$\sinh^{-1}$
arc ch	$\cosh^{-1}$
arc th	$\tanh^{-1}$
arc cth	$\coth^{-1}$
arc sch	sech^{-1}
arc csch	csch^{-1}
rot	curl
lg	log

IMMUNITY AND SENSITIZATION TO MICROBE ALLERGENS IN PATIENTS WITH CHRONIC TONSILLITIS

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According to the data of a number of studies with chronic tonsillitis patients, nonspecific immunity indices have dropped, specific immunity indices have risen, but to the allergization indices are inversely proportional to the level of immunity (A. M. Ryndina, 1962; T. V. Dratvina, and N. P. Konstantinova, 1964).

In the majority of works the nonspecific and specific immunity, and also the state of the allergy have been researched by studying the appropriate index. A more complete idea of the state of adaptive possibility of the organism and the interrelation of the separate sections can be obtained by studying immunity and allergy through a parallel series of tests, which is the object of this research.

Procedure

The study took in 107 patients 16-38 years of age, who had entered the clinic of the Kiev Scientific-Research Institute of

Otolaryngology for operative treatment. Females, 69; males, 38. Ages: 16-20, 40; above 20, 67. Duration of illness - from 1 year to 20 years. In all patients the anamnesis of the disease was studied, including the allergological. On the basis of clinical and anamnestic data decompensated tonsillitis was diagnosed in 53 cases, and subcompensated in 54 cases (according to the classification of L. A. Lukovskiy). The control group was one of 25 virtually healthy persons with no indication in anamnesis of the presence of pyoinflammatory diseases over the last 6 months.

On the strength of assumptions that individual immunity indices are able to change independently of one another, the problem of specific and nonspecific immunity, and also sensitization was studied by several parallel tests.

The specific immunity was studied by investigating in the blood serum titers of antistreptolysin-O, Streptococcus antihyaluronidase and agglutinin to corpuscular Staphylococcus antigen. In order to determine the level of nonspecific immunity, titers of the complement, heterophyllous agglutinin and lysozyme in the blood serum, protein fractions in the blood serum were determined by the method of paper electrophoresis. All of these tests are indicators of the natural resistance of the organism (Ye. D. Genis, L. S. Kogosova, 1951; L. G. Elkonin, 1963; N. A. Zhukovskaya, G. N. Likina, 1961; Yu. O. Spasokukotskiy, N. B. Yakhin, 1950).

Allergization was determined on the basis of skin samples with microbe allergens, blood eosinophils and eosinophils from the tissues of removed tonsils (50 cases), and for some of the subjects skin tests with histamine. In addition, the C-reactive protein in the blood serum was investigated in all patients. All these indices were studied by generally-accepted methods.

In the case of the skin samples threshold doses of "complex" (complete) allergens were investigated: Streptococcus viridans,

β-hemolytic Streptococcus, Staphylococcus albus and Staphylococcus aureus, Candida and coliform bacterium prepared in the microbiology laboratory of the Kiev Scientific-Research Institute of Otolaryngology (A. Ye. Vershigora, 1966).

Results

Allergological anamnesis and the corresponding allergic diseases were disclosed in nine cases. The results were analyzed by subdividing the patients into 3 groups depending upon the intensity of the skin reactions to the allergens. The first group included cases with negative skin reactions and cases with weakly-expressed reaction; the second group included patients with average degree (++) of reaction, and the third group included those with a sharply expressed skin reaction (+++ and ++++).

Distribution of the skin reactions in terms of frequency, intensity and nature is given in Table 1.

Table 1. Characteristics of skin reactions to microbe allergens.

Intensity of skin reactions	All patients	Skin reactions: +	Skin reactions: -	Number of allergens & nature of reactions: β-hemolytic Streptococcus	β-Streptococcus	Staphylococcus aureus	Staphylococcus albus	Candida	Coliform bacterium	Number of reactions simultaneously to allergens of a series of microbes: 1	2	3	4	5	6	Relation of reactions to 1-2 to reactions to 3 & more allergens
				Immediate/delayed												
Negative and (+)	36	18	[illegible]	[illegible]	[illegible]	1/8	[illegible]	[illegible]	11	12	[illegible]	[illegible]	1	2	2	1
++	31	31	[illegible]	[illegible]	2/10	3/5	[illegible]	[illegible]	[illegible]	[illegible]	12	[illegible]	[illegible]	[illegible]	1	1.1
+++ and ++++	22	22	[illegible]	[illegible]	2 1	2.7	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	1	3.1

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As we see from the data of Table 1, the reactions were basically of the delayed type. Frequently tests were positive to Streptococcus and Staphylococcus, less pronounced to allergens of Candida and coliform bacterium.

Interesting regularities are revealed in counting the positive reactions simultaneously to several allergens in the groups of patients depending upon the intensity of skin reactions. Thus, in the first group the number of reactions to 1-2 allergens in relation to the number of reactions to 3 and more allergens is 2:1, and in groups with skin reactions to (++) and to (+++), (++++) it is respectively 1:1.4 and 1:3.4.

Comparison of indices of specific and nonspecific immunity depending upon the intensity of the skin reactions to allergens is given in Table 2.

Table 2. Specific and nonspecific immunity indices depending upon degree of skin reaction intensity.

Intensity of skin reaction	Number of patients	Form of chronic tonsillitis: subcompensated	Form of chronic tonsillitis: decompensated	Titers of immunological indices: complement	Titers of immunological indices: lysozyme	Titers of immunological indices: heterophyllous agglutinins	Blood serum protein fractions: total protein	Blood serum protein fractions: albumins	Globulins: all	Globulins: α1	Globulins: α2	Globulins: β	Globulins: γ	A/G coefficient	Titers: AH	Titers: ASL-O	Titers: agglutinins to staphylococcus
Absence of reaction or weak reaction (+)	51	44	21	0.05	392	5.7	6.89	35.9	44.6	6.1	7.7	8.5	21.9	1.25	261	182	335
Average degree (++)	31	12	19	0.05	337	6.1	7.27	51.1	36.4	6.4	8.2	8.6	21.8	1.22	183	151	222
Sharp reaction (+++ and ++++)	22	9	13	0.05	453	6.2	6.99	56.9	42.6	5.9	8.1	8.9	18.2	1.3	380	251	129
Mean indices	107	—	—	0.05	301	5.7	7.1	53.7	41.2	6.1	8.1	8.7	20.4	1.26	260	194	265
Healthy subjects (control studies)																	
	24	—	—	0.06	257	5.6	7.1	63.4	36.5	7.2	8.6	9.1	21.6	1.16	143	157	156

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From Table 2 it follows that in the case of chronic tonsillitis patients changes in indices of nonspecific immunity are noted in comparison with results obtained from the healthy subjects - increase in complement and lysozyme titer. Thus, for subjects in the control group the complement titer was 0.06, and the lysozyme titer 257. For the chronic tonsillitis patients the average levels of these indices were 0.05 and 364 respectively. The titer of heterophyllous agglutinins is somewhat higher (1:5.7) in comparison with indices for subjects in the control group (1:5.6). The average ASL-O, AH* titers and titers of agglutinins to Staphylococcus in the control group were 167, 143 and 166; the mean values for the chronic tonsillitis patients were 194, 260 and 265 respectively. An increase in the ASL-O titers (500-625) was observed in 12 cases and an increase in the antihyaluronidase titers (550-825) was observed in 18 patients. Still higher ASL-O and AH titers were encountered three times more frequently in the group of cases with skin reactions to (+++) and (++++); however, the correlation between these two indices is usually not noted. The highest lysozyme titers (1:640) were observed for 1/3 of the patients with a weak (+) and average (++) degree of skin reactions, and for 3/4 with sharply expressed reactions (+++ and ++++).

High titers of agglutinins to Staphylococcus (1:640) were observed in 16 patients of the first group; in three patients of the second group and were not noted in patients of the third group. The test to C-reactive protein turned out to be positive in four patients of the first group. In all these cases the antistreptohyaluronidase and antistreptolysine titers were increased.

According to certain indices the increased titers were seen even in the control subjects: lysozyme in one case, antistreptolysine in two, agglutininizing antibodies to Staphylococcus in one. AH titers for cases in the control group did not exceed 1:250.

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*ASL-O = antistreptolysin-O, AH = antihyaluronidase.

According to these tests essential differences were noted between groups of patients with skin reactions to (+) and to (+++) - (++++) on one hand and between the third and control group of the other: lysozyme - 453, ν-globulin - 18.2, ASL-O - 281, AH - 380, agglutinins to Staphylococcus - 129 in the third group and 362, 20.4, 182, 261, 335 respectively in the first group. Thus, titers of circulating antibodies to Streptococcus were higher in the chronic tonsillitis patients the more intensive the skin reactions were. An inverse relationship was noted with respect to titers of antibodies to Staphylococcus antigen. These latter decreased with an increase in the skin reaction intensity (325, 222 and 129 in groups with skin reactions to +, ++, +++ and ++++).

Skin reactions to histamine were encountered with identical frequency in groups of patients with skin reactions to microbe allergens of (+) and (++) intensity. However, in the third group intensive skin reactions to histamine were not observed. Blood eosinophil within limits of 5-8% was observed in ten patients of groups 1 and 2. No eosinophil was observed in tissues of removed tonsils.

Discussion

According to the data of a number of researchers (P. P. Sukharov et al., 1963) with chronic tonsillitis weakly positive skin reactions to allergens of Streptococcus are observed in 20-30%, and positive reactions in 60-70% of the patients. With the use of complete microbe allergens in our studies positive skin tests were noted in 81.7% of those checked, and in 54% of tests to Streptococcus allergens. We accept that sensitization to Streptococcus is specific for tonsillitis, independently of the degree of reaction intensity, then in these studies it appeared in more than half of the patients. However, according to our previous data (in rhinosinusopathia patients) it was established that principally reactions to (+++) and (++++) are of diagnostic value. Such reactions to Streptococcus antigens occurred in 10% of the cases in our studies.

Analysis of results depending upon the intensity of the skin tests makes it possible to isolate the group of patients with skin reactions to (+++) and (++++), for which a more significant deviation from the norm of the series of indices of specific and nonspecific immunity was noted. Only in 10 of 22 cases of this group were skin reactions of intensity to (+++) and (++++) to Streptococcus allergen, the rest being to other allergens. Evidently, in chronic tonsillitis there is sensitization not only to Streptococcus, but also to other microbe allergens. However, the possibility is not excluded that reactions to other allergens have a parallel nature due to recent pyoinflammatory disease or carriage of homologous flora.

A higher level of sensitization to microbe allergens in patients of the third group is determined not only by the intensity of skin reaction, but also by the number of simultaneously positive reactions to several allergens. In these cases skin reactions to three and more allergens were encountered six times more frequently than in patients of the first group. In these patients decompensated tonsillitis was diagnosed somewhat more frequently than among cases with skin reaction to (+). However, clinical diagnosis of decompensated tonsillitis was established for almost one-half of the patients with skin reactions to (+), which testified to a nonconformity in part of the cases of clinical data to a change in the reactivity indicators. The most expressed deviations in specific and nonspecific immunity among cases with skin reactions to (+++) and (++++) testify to the diagnostic value of intensive skin reactions as an index to the degree of allergization, and as an index of changes in immunologic reactivity.

In the opinion of a number of researchers, the skin test with histamine (Khodjanov, 1964) can serve as an index to allergization. Our data will make it possible to treat skin reactions to histamine as a reflection of the degree of reactivity of the organism, and not sensitization, because severe reactions to histamine were not observed in patients of the third group with sharply expressed skin reactions to microbe allergens.

The results of these studies on nonspecific immunity do not agree with the data of a number of authors. Thus, I. A. Lopotko and O. Yu. Lakotkina (1963), Yu. A. Grinevich (1967) found in chronic tonsillitis patients a drop in the complement and properdin titer, and T. V. Golosova and coauthors (1965) found a drop in the lysozyme titer.

In our studies the complement and lysozyme titer was increased in all patients, while higher lysozyme titers showed up in the group of cases with more severe skin reactions; titers of heterophyllous agglutinins did not change significantly. To a certain degree this coincides with data of studies by O. K. Fedorova-Patyakina (1966), which established that the blood serum of chronic tonsillitis patients possesses more expressed opsoning properties in comparison with the blood serum of healthy persons. In these studies the phagocytotic index for the chronic tonsillitis patients was high.

The protein fraction indices differed from the data obtained by other authors. A certain drop in the total protein was observed, as well as an increase in albumins and a reduction of the α_1, α_2 and β-fractions of globulin for all patients. However, analysis of changes in the protein fractions depending upon the intensity of the skin reaction shows a drop in γ-globulin for patients with skin reactions to (+++) and (++++). In numerous experimental studies and clinical observations a parallel increase is noted in the sensitization of the organism with an increase in γ-globulin in the blood serum (A. G. Likhachev, 1963; V. N. Dzyak, Ye. F. Bogatskiy, 1961; E. G. Mel'nik, 1958; Ye. I. Ugreninova, V. I. Tyunina, 1959 et al.).

The result of these studies on specific immunity to antigens of Streptococcus agree with the conclusions of other authors (K. P. Sarylova and coauthors, 1961; Ye. F. Bogatskiy, 1964; A. A. Gorlina, 1963; T. V. Dratvina, N. P. Konstantinova, 1964), who considered that titers of circulating antibodies to Streptococcus in comparison with the control showed an insignificant increase for cases with

compensated tonsillitis and considerably increased in patients wit.. decompensated tonsillitis. In our studies more essential deviations of titers of circulating antibodies from the norm occurred in the group of patients with skin reactions to (+++) and (++++).

O. K. Fedorova-Patyakina observed an increase in titers of antibodies in the blood serum of chronic tonsillitis patients both to Streptococcus and to Staphylococcus. According to our data titers of antibodies to Staphylococcus antigen increased if the mean indices for the entire group of patients were taken. However, analysis depending upon the intensity of skin reaction shows that titers of antibodies to Streptococcus increase as the intensity of the skin reactions, and show a corresponding decrease to Staphylococcus. The interrelationships of titers of circulating antibodies to Streptococcus possibly are reflections of the allergization to Streptococcus, and indirectly confirm the Streptococcus etiology of chronic tonsillitis. The correlation of increased (to a small degree) titers of antistreptohyaluronidase and antistreptolysine with intensive skin tests in this case lets us assume that the increased AH and ASL-O titers serve as a reflection of both immunity and sensitization. The decrease in titers of agglutinins to Staphylococcus possibly is a result of adaption to the specific Streptococcus antigen. However, it can be assumed that in patients with skin reactions to (+++) and (++++) titers of antibodies to staphylotoxins will also be increased.

The difficulties develop during interpretation of lysozyme data. In the experimental studies of Ye. S. Fidel'man and L. O. Aver'yanova (1962) it was established that with the immunization of animals by cellular Streptococcus allergen the lysozyme titer fell; however, if endocarditis developed during the immunization, it increased as the degree of growth of leukocytosis. Based on this, the authors assumed that the inflammatory focus is the source of formation and entry of lysozyme into the blood. It is possible that with chronic tonsillitis the rise in lysozyme titers indicates the presence of inflammatory process, not detected by the test to C-reactive protein.

Conclusion

In chronic tonsillitis sensitization to antigens of Streptococcus is observed in a significant majority of cases. Of patients with sharply pronounced skin reactions to microbe allergens an increase is noted to a greater degree of specific and nonspecific immunity indices. These titers change not only with intensive reactions to Streptococcus allergens, but also with the same reactions to allergens of other microbes. Sensitization to microbe allergens, correlated with more expressed deviations of a series of immunity indices, showed up in 20% of the cases. In these cases we should evidently recognize the role of allergy in the pathogenesis of chronic tonsillitis. In nine of these patients tonsillitis was combined with rheumatism. In the remaining (13) there were possibly indications of the development of metatonsillar diseases.

An insignificant number of intensive immediate reactions to microbe allergens, absence of expressed eosinophils of the blood and tonsillar tissue and negative allergenic anamnesis in patients with skin reactions to (+++) and (++++) confirm the generally accepted opinion that allergization in chronic tonsillitis patient is a hypersensitivity of delayed type.

In chronic tonsillitis both the general immunological reactivity (nonspecific immunity) and the specific immunity to Streptococcus allergen increase. However, a complete correlation of the levels of individual factors of nonspecific immunity is not noted. Thus, γ-globulin of blood serum in cases with sharply-expressed sensitization to microbe allergens is reduced.

These data confirm the rationality of classification subdividing tonsillitis in two basic forms: simple tonsillitis and toxic-allergic. Skin reactions to microbe allergens to (+++) and (++++) and deviation from the norm of indicators of specific and nonspecific immunity in chronic tonsillitis patients evidently can indicate the toxic-allergic nature of disease.

Results

1. Skin reactions to threshold doses of complete microbe allergens show the degree of allergization in chronic tonsillitis patients.

2. A number of indicators of nonspecific immunity and indicators of specific immunity to Streptococcus in chronic tonsillitis patients increases and correlates with the degree of allergization of the patients as shown by skin tests.

3. In chronic tonsillitis the pathogenic value is not in the presence of sensitization to microbe allergens, but the degree of manifestation.

4. In order to obtain correct evaluation of changes in reactivity with chronic tonsillitis, analysis of corresponding data should be carried out in correlation with the degree of allergization to microbe antigens.

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