Asian Journal of Immunology

3(3): 34-40, 2020; Article no.AJI.55718

Results of Allergological and Immunological Research in Patients with Polipoid Rhinosinusitis

J. A. Djuraev[1*], U. S. Khasanov[1], U. N. Vohidov[2] and S. S. Sharipov[2]

[1]Tashkent Medical Academy, Uzbekistan.
[2]Tashkent State Dental Institute, Uzbekistan.

Authors' contributions

This work was carried out in collaboration among all authors. Authors JAD and USK designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author UNV managed the analyses of the study. Author SSS managed the literature searches. All authors read and approved the final manuscript.

Article Information

Editor(s):
(1) Dr. Wagner Loyola, Brazilian Agricultural Research Corporation, Brazil.
(2) Dr. Darko Nozic, University of Belgrade, Serbia.
Reviewers:
(1) Ekaterini Goudouris, Universidade Federal do Rio de Janeiro, Brazil.
(2) Gilbert Batieka Bonsaana, University for Development Studies, Ghana.
Complete Peer review History: http://www.sdiarticle4.com/review-history/55718

Original Research Article

Received 10 February 2020
Accepted 16 April 2020
Published 22 April 2020

ABSTRACT

An exceptional role in protecting against pathogenic effects of various pathogenic and opportunistic microorganisms is played by immunoglobulins of the main classes. As our studies showed, before treatment, the IgG content in patients did not differ significantly from the control. The average IgA level in patients of both groups before surgery was slightly reduced (P> 0.05). Given the important role of IgA in protecting the body and, above all, the mucous membranes from infection, it can be concluded that such a disturbance of the biosynthesis of this class of immunoglobulin may be one of the reasons for the decrease in immune reactivity and frequent infectious processes. A sharp increase in serum IgE levels (239 ± 19.1 IU/ml) was observed in patients with eosinophilic polyposis rhinosinusitis, which we associate with an increase in IL-4 content and increased allergization of the body. This relative difference between patients of the two groups proves the need for appropriate diagnosis and treatment of chronic polyposis of rhinosinusitis. The aim of our research work was study allergically and immunologically results in patients with polipoidrhinosinusitis.

**Corresponding author: E-mail: drdjuraev@mail.ru;*

Keywords: Nasal polyposis; osteomeatal complex; rhinosinusitis; nasal septum; allergen; immune system.

1. INTRODUCTION

The second half of the last century was marked by the transition of the center of gravity from otiatrics to rhinology. The reason for this is not only an increase in the load on the upper respiratory tract from the outside in the human environment, but also significant changes in the population, expressed in the accumulation of negative genetic deficiency and, above all, in the immune system. Particularly complex and unclear are the causes of nasal polyposis [1,2].

Today, many theories have been proposed for the etiology and pathogenesis of chronic polyposis rhinosinusitis (CID), unfortunately, many causative factors, as well as their relationship and role in the formation of nasal polyps, are not fully understood [3].

A number of theories of the etiology of nasal polyposis are known, and they are not mutually exclusive: bacterial and fungal infections, superantigenic stimulation of the immune system, the formation of biofilms, anatomical abnormalities of the osteomeatal complex, ciliary dysfunction, allergies, secondary immune-deficiency [4].

In this regard, some foreign authors, according to which diseases accompanied by the formation of nasal polyps are divided into 5 groups. The first group consists of systemic genetically caused diseases in the form of Kartagener syndrome and cystic fibrosis, the second group is chronic polypous-purulent rhinosinusitis (neutrophilic polyps), the third group is a local pathology in the osteomeatal complex with impaired mucociliary clearance in the paranasal sinuses and the formation of a productive process in thechoanal polyps, the fourth group is a chronic infectious-allergic rhinosinusitis with a final stage of development in the form of a chronic polypous allergy rhinosinusitis (eosinophilic polyps), the fifth group is the “asthmatic triad” as a pseudo-allergic disease caused by a metabolic disorder of arachidonic acid: aspirin-induced nasal polyps [5,6].

S. V. Ryazantsev et al. (2006) consider nasal polyposis and SNPs as a multifactorial etiological syndrome that occurs in individuals predisposed to a specific tissue reaction. According to this theory, the formation of nasal polyps is associated with an innate predisposition and exposure to environmental factors, such as mechanical, physical, chemical, biological factors (viruses, bacteria, fungi, allergens). In this case, a disturbance of the reactivity of the parasympathetic nervous system, immunity, mucociliary transport, mucosal hypersensitivity, defects in membranes and DNA in the nuclei of cells areconsidered a congenital predisposition [7,8]. The combination of these two factors includes pathogenetic mechanisms, that is, they lead to a disturbance of neuro-trophic innervation, mast cell degranulation, the release of biologically active substances, which in turn increase vascular permeability, followed by tissue edema and the formation of polyps.

According to another theory proposed by M. Yu. Korkmazov (2010), forpolypous sinusitis, microcirculation in the middle nasal passage changes in the form of vasomotor reactions, narrowing of the arterioles and a decrease in the number of functioning capillaries, which lead to the accumulation of metabolic products and retention of tissue fluid, which contributes to the development of edema [9,10].

N. N. Naumenko et al. (2005) suggest that forpolypousrhinosinusitis, a disturbance of the adaptive-trophic function of the autonomic nervous system is important, and contributes to the development of neurodystrophic changes in the nasal mucosa, leading to the formation of polyps.

V. S. Piskunov (2006) believes that a disturbance of the aerodynamics of the nose during deformities of the nasal septum leads to a slowly developing inflammatory process of the nasal mucosa, which manifests itself as the formation of a polyp in the absence of pathological changes in the paranasal sinuses.

In recent years, the role of metabolic disorders of arachidonic acid, which leads to "aspirin intolerance" [11,12], has been intensively studied in patients with CID. The classical clinical picture of the “aspirin” triad implies the presence of bronchial asthma in combination with eosinophilic rhinitis or CPRS, the manifestations of which sharply increase after taking non-steroidal anti-inflammatory drugs (NSAIDs) [13]. In this regard, the importance of leukotrienes in the development of allergic inflammation is very

significant. They increase vascular permeability, promote the mobilization and activation of pro-inflammatory cells in the airways, participate in the release of other pro-inflammatory agents, increase the secretory activity of the glands, can enhance the action of other allergy mediators, for example, histamine [14] and as a result "aspirin-induced" polyps [15] develop.

In addition, recently, many authors have been paying attention to the role of toll-NOD- receptors in the occurrence of nasal polyps and the genetic aspects of the development of CPRS [16,17]. Unfortunately, the results of these studies have not yet led to a complete disclosure of the pathogenesis of the polyposis process.

Thus, chronic polypousrhinosinusitis should be considered amultiple etiologies disease, in the development of which the influence of infectious factors and allergens plays the main role, which leads to the development of a chronic inflammatory process and allergization of the body, which affect different body systems, which aggravates the main pathology and leads to a decrease in the quality ofpatient's life, therefore this problem is urgent, and needs a solution which is urgent.

2. MATERIALS AND METHODS

In accordance with the purpose of the study and to achieve its objectives, clinical studies were conducted in 150 patients with chronic kidney disease who were examined and treated in the ENT department of the 3rd clinic of the Tashkent Medical Academy in 2018-2019.

All patients with chronic kidney disease underwent specific allergological examination, which included collecting an allergic history and staging skin tests with allergens. Allergological examination was carried out according to a special scheme developed by the Allergy Research Laboratory of the 2nd clinic of the Tashkent Medical Academy.

3. RESULTS AND DISCUSSION

For skin tests, allergens from timothy grass pollen, team hedgehog, fescue, ryegrass, bonfire, birch, wormwood, ragweed, corn, sunflower, ash, walnut, oak and dandelion were used (Table 1).

Table 1 shows that the reaction to each allergen was different. So, in 92 patients there was a positive reaction of varying degrees to histamine. However, no reaction was observed on fescue, ragweed, and hedgehog. In addition, a negative reaction to an allergen was recorded in 58 patients.

In 92 patients, a scarification test gave a positive result. This indicates the undoubted participation of the allergic factor in the development of polypousrhinosinusitis. These data correlated with blood test results. So, in a blood test in 92 (33.3%) patients, eosinophilia was noted.

Peripheral blood eosinophils were determined in a general blood test in all patients. In 92 patients with chronic polypousrhinosinusitis, the number of eosinophils was increased. In particular, eosinophilia was observed in 88 examined with a

Table 1. Allergy data in patients with CRS

Pollenallergen	Patients with CRS (n=150)	Results		
		+	++	+++
Dandelion	18	2	2	14
Fescue	-	-	-	-
Sunflower	16	-	3	13
Sagebrush	6	-	4	2
Ash	8	2	2	4
Bonfire	10	2	2	6
Birch	2	1	1	-
Ragweed	-	-	-	-
Corn	9	-	3	6
Oak	8	4	4	
Cocksfoot	-	-	-	-
Histamine	92	38	25	29
Neg.	58	-	-	-

positive result for the allergen, however, in the remaining 62 patients the number of eosinophils remained within the normal range (Table 2).

Peripheral blood eosinophilia indicates the continued role of allergies in the development of CRS. Allergic background was found in 58.67% of the examined patients.

Based on the results of the study, it should be noted that the presence of a positive allergic reaction in patients with eosinophilia suggests the appointment of topical CS for the purpose of pathogenetic treatment, as well as 2-3 generation antihistamines for the symptomatic treatment and removal of symptoms of the disease.

Studies of the immune status in CRS patients were carried out in the laboratory of immunocytokines of the Institute of Immunology of the Academy of Sciences of the Republic of Uzbekistan (head of laboratory, MD Ismailova A.A.). The determination of cellular, humoral immunity units was carried out using monoclonal antibodies by the method of indirect rosette formation, to determine the cytokines used test systems produced by Vector-Best of the Russian Federation, based on the sandwich method of enzyme-linked immunosorbent assay using horseradish peroxidase as an indicator enzyme. The results will be analyzed in the following sub-chapters.

Given the important pathogenetic role of immune system disorders in the mechanisms of CRS development, as well as unsatisfactory treatment results, allergization of the body, and the possibility of developing toxic and side effects, we studied the immune status of patients.

An immunological study of cellular and humoral immunity was performed in 79 (52.7%) patients who were hospitalized in the ENT department of the 3rd clinic of the Tashkent Medical Academy in 2012-2013. (Table 2).

As can be seen from Table 3, in patients there was a significant decrease in the content of T-lymphocytes (CD3 cells), which averaged 47.56 ± 6.57 and 46.84 ± 4.52, significantly differing from the control data (p <0, 05). The absolute value of CD3 cells was also below normal.

The level of immunoregulatory subpopulations of T-lymphocytes of T-helper cells (T4) and T-suppressors/cytotoxic cells (T8) was lower than the control values. For T-helpers, the CD4 cell count averaged 26.96 ± 2.58 and 26.19 ± 2.18, which was significantly lower than the control (p <0.05). In addition, there was a significant decrease in the number of T-helpers (P <0.05).

Both the absolute and relative contents of T-suppressors - cytotoxic cells (CD8) were also significantly lower than the control (P <0.05).

An equivalent decrease in the number of both T-helpers and T-suppressors caused significant changes in the immunoregulatory index. The ratio of CD4/CD8 lymphocytes was below the control. These data indicate impaired immunity as a result of a prolonged inflammatory process that caused secondary immunodeficiency in the body of patients with various forms of chronic polypousrhinosinusitis.

Thus, in patients with CRS, there were significant disturbances of the T-cell immunity indices, which is typical for chronic respiratory diseases. Indicators of the humoral immunity are presented in Table 4.

An exceptional role in protecting against pathogenic effects of various pathogenic and opportunistic microorganisms is played by immunoglobulins of the main classes. As our studies showed, before treatment, the IgG content in patients did not differ significantly from the control. The average IgA level in patients of both groups before surgery was slightly reduced (P> 0.05). Given the important role of IgA in protecting the body and, above all, the mucous membranes from infection, it can be concluded that such a disturbance of the biosynthesis of this class of immunoglobulin may be one of the reasons for the decrease in immune reactivity and frequent infectious processes.

Table 2. The content of eosinophils in peripheral blood in patients with CRS

Eosinophils in the peripheral blood	Patients with EPRS, (n=90),%	Patients with NPRS, (n=60),%	Control group, (n=20),%
	6,7±1,51*	2,1±1,09	2,2±1,07

Note: - Differences regarding the group up to 5 years are significant (* - P<0,05)*

Table 3. Indicators of cellular immunity in patients with CRS

Indicator	Patients with EPRS, (n = 48)	Patients with NPRS, (n=31)	Control group, (n=20)
Whitebloodcells, μl	6187,5±943,88	6035,5±1759,84	6295,0±737,33
Lymphocytes, %	30,7±9,33	29,7±4,19	29,4±4,15
Lymphocytes, μl	1717,0±440,38	1790,3±328,99	1945,0±225,89
CD3+, %	47,2±6,05	47,2±5,24	57,9±4,26
CD3+, μl	814,2±281,30	758,8±135,84	1009,1±214,33
CD4+, %	26,9±2,43**	26,5±2,28**	36,4±1,90
CD4+, μl	466,4±140,06*	443,0±92,37***	856,7±71,23
CD8+, %	19,6±4,60	20,4±3,30	22,6±1,90
CD8+, μl	330,4±125,28	339,4±45,45*	498,4±60,84
IRI	1,44±0,21	1,3±0,13**	1,75±0,10
CD16+, %	19,7±3,60	16,1±4,89	14,2±1,84
CD20+, %	22,3±2,00	21,6±2,71	21,9±2,02
CD20+, μl	383,7±121,50	366,0±91,66	412,4±95,94
CD23+, %	24,2±2,25	19,8±1,47	20,0±1,34
CD38+, %	31,6±7,02	31,4±6,80	20,9±5,35
CD95+, %	24,0±3,15	19,7±1,55	19,8±1,51

*Note: * - Differences relative to control group data are significant (*** - P<0,001)*

Table 4. Indicators of cellular immunity in patients with CRS

Indicator	Patients with EPRS, (n=48)	Patients with NPRS, (n=31)	Control group, (n=20)
IgG, mg%	1144,2±168,93	1184,3±99,74	1176,2±99,17
IgA, mg%	141,9±14,15	167,8±17,88***	128,4±16,94
IgM, mg%	118,3±18,22	120,3±15,22	121,7±15,16
CIC large, cu	17,8±6,03	19,8±5,09	11,8±3,14
CIC small, cu	28,1±9,17***	22,3±8,80	21,8±6,92

*Note: * - Differences relative to control group data are significant (*** - P<0,001)*

The IgM content showed a tendency to increase, but both the average values and its individual values did not differ significantly from the norm.

The disturbances identified by us were manifested:

- disturbance of the cellular component of immunity with insufficiency of immunoregulatory subpopulations of T-helpers and T-suppressors (CD4 and CD8 cells);
- inhibition of humoral immunity (IgA);
- a decrease in natural cytotoxicity (CD16 cells).

This allows us to consider patients with CRS as patients with prevailing secondary immunodeficiency, which requires appropriate treatment using immunomodulators.

An immunological study of cytokines and total IgE in serum was carried out in 79 (52.7%) patients who were hospitalized in the ENT department of the 3rd clinic of the Tashkent Medical Academy in 2012-2013 (Table 5).

As our study showed, elevated levels of IL-2 in serum were observed in patients of both groups, but especially in patients with chronic "neutrophilic" polypousrhinosinusitis. Such an increase in the level of cytokine indicates a disturbance of the immune state of the body, since IL-2 is responsible for the immune response.

At the same time, the content of IL-4, which is responsible for the allergization of the body, was also increased in patients of both groups, but more in patients with eosinophilic poly-pousrhinosinusitis.

The content of IL-8 increased (9.9 ± 3.72 pg/ml) in patients with “neutrophilic” polyposis rhinosinusitis, remaining within the normal range in patients with “eosinophilic” polyposis rhinosinusitis.

Table 5. The content of cytokines and their ratio with total IgE in serum in patients with CRS

Indicator	Patients with EPRS, (n=48)	Patients with NPRS, (n=31)	Control group, (n=20)
2-2, pg / ml	10,6±3,53	12,5±4,81	5,5±0,44
2-4, pg / ml	6,4±2,31	7,3±1,13	4,7±1,15
2-8, pg / ml	8,3±4,58	9,9±3,72	5,7±0,84
IgE,IU / ml	239±19,1***	43,0±30,26	14,6±8,57

*Note: * - Differences relative to control group data are significant (* - P<0,05, ** - P<0,01, *** - P<0,001)*

A sharp increase in serum IgE levels (239 ± 19.1 IU/ml) was observed in patients with eosinophilic polyposis rhinosinusitis, which we associate with an increase in IL-4 content and increased allergization of the body. This relative difference between patients in the two groups proves the need for appropriate diagnosis and treatment of CRS.

4. CONCLUSIONS

Thus, we did not find a clear deficit in the content of IgG and IgM. Only an increase in the level of IgA was observed, indicating the activation of the body's immune systems, which can serve as a factor in the development of a long inflammatory process, and in the subsequent relapse of the disease. Our data confirmed that multistep surgical intervention and inadequate conservative treatment adversely affect the immunological reactivity of CRS patients. In these patients, disturbances of immune homeostasis and a deficiency of cellular and humoral immunity are detected. A study of cellular and humoral immunity revealed that “eosinophilic” polyposis rhinosinusitis is characterized by an increase in the number of natural killers, allergization factor and apoptosis, IL-2, IL-4 and IgE, while “neutrophilic” polyposis rhinosinusitis indicates a significant increase in IgA and IL- 8, which indicates the presence of a long-lasting chronic inflammatory process.

CONSENT

As per international standard informed and written participant consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard written ethical permission has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Voxidov UN, Xasanov US, Dƶuraev ƵA, Sultonov DM, Soвirov ŞŞ .Estimation of data of specific allergic research in chronic polypoid-rhinosinusitis.2016;(9):374-376.
2. Xasanov US, Voxidov UN, Dƶuraev ƵA. The condition of lumbar sinus in chronic inflammatory diseases of the nasal and paranasal sinuses in patients with myocarditis. Europeanscience. 2018;9(41).
3. Xasanov US, Dƶuraev ƵA, Toşpulatov Ƶ. Peculiarities of diseases of the nose and paranasal sinuses in patients with myocarditis. Molodoyuchenyy. 2016;10: 547-550.
4. Abdukhahharovich DJ, Saidakramovich KU, Nuridinovich VU. The prevalence of chronic inflammatory diseases of the nose and paranasal sinuses in patients with myocarditis. European Science Review. 2018;5-6.
5. Bellavite P, Marzotto M, Chirumbolo S, Conforti A. Advances in homeopathy and immunology: A review of clinical research. FrontBiosci (ScholEd). 2011;3: 1363-1389.
6. Bousquet J, Heinzerling L, Bachert C, Papadopoulos NG, Bousquet PJ, Burney PG, Lodrup Carlsen KC. Practical guide to skin prick tests in allergy to aeroallergens. Allergy. 2012;67(1):18-24.
7. Bousquet PJ, Combescure C, Neukirch F, Klossek JM, Mechin H, Daures JP, Bousquet J. Visual analog scales can assess the severity of rhinitis graded according to ARIA guidelines. Allergy. 2007;62(4):367-372.
8. Chen YS, Langhammer T, Westhofen M, Lorenzen J. Relationship between matrix metalloproteinases MMP□2, MMP□9, tissue inhibitor of matrix metalloproteinases □1 and IL□5, IL□8 in nasal polyps. Allergy. 2007;62(1):66-72.
9. Compalati E, Passalacqua G, Bonini M, Canonica GW. The efficacy of sublingual immunotherapy for house dust mites

respiratory allergy: Results of a GA²LEN meta□analysis. Allergy.2009;64(11):1570-1579.
10. Dutta R, Dubal PM, Eloy JA. The connection between seasonal allergies, food allergies, and rhinosinusitis: What is the evidence?. Current Opinion in Otolaryngology & Head and Neck Surgery. 2015;23(1):2-7.
11. Jutel M, Akdis CA. Immunological mechanisms of allergen□specific immunotherapy. Allergy. 2011;66(6):725-732.
12. Kouzaki H, Matsumoto K, Kato T, Tojima I, Shimizu S, Shimizu T. Epithelial cell-derived cytokines contribute to the pathophysiology of eosinophilic chronic rhinosinusitis. Journal of Interfer on & Cytokine Research. 2016;36(3):169-179.
13. Radulovic S, Wilson D, Calderon M, Durham S. Systematic reviews of sublingual immunotherapy (SLIT). Allergy. 2011;66(6):740-752.
14. Vokhidov UN, Khasanov US, Vokhidov NK. The effectiveness of use macrolides in the treatment of chronic"Neutrophil" polypoid-rhinosinusitis. Folia Otorhinolaryngologiae et Pathologiae Respiratoriae. 2014;20 (2):79-79.
15. Yamamoto M, Okano M, Fujiwara T, Kariya S, Higaki T, Nagatsuka H, Nishizaki K. Expression and characterization of PGD2 receptors in chronic rhinosinusitis: modulation of DP and CRTH2 by PGD2. International Archive Sofallergy and Immunology. 2009;148(2):127-136.
16. Yao T, Kojima Y, Koyanagi A, Yokoi H, Saitoh T, Kawano K, Kusunoki T. Eotaxin-1,-2, and-3 immunoreactivity and protein concentration in the nasal polyps of eosinophilic chronic rhinosinusitis patients. Actaclinica Croatica. 2009;48(1): 96-96.
17. Yonamine GH, Contim D, Moschione APB, Castro MD, Jacob CMA, Carlos A. Olfactory Disfunctions in Patients with Chronic Rhinosinusitis; 2012.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/55718