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THE ROLE OF VEGF IN THE DEVELOPMENT OF CHRONIC POLYPOUS RHINOSINUSITIS

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Abstract

The purpose of this study was to investigate VEGF in immunohistochemistry of various forms of chronic polypoid rhinosinusitis. We studied 45 patients with chronic polypoid rhinosinusitis in 2013-2017 year, which were performed surgery followed by morphological and immunohistochemical studies of macropreparations. The study showed that polyps of patients with “neutrophilic” polypoid rhinosinusitis had greater activation of VEGF than in polyps of patients with “eosinophilic” polypoid rhinosinusitis

Keywords: chronic polypoid rhinosinusitis, morphological study, immunohistochemical study, VEGF.

Introduction

Chronic polypous rhinosinusitis (CPRS) is a chronic inflammatory disease of the nasal mucosa and paranasal sinuses, characterized by the formation and recurrent growth of polyps, consisting mainly of edematous tissue infiltrated with eosinophils and neutrophils [1, 3, 10, 14].

Many authors give the leading role in the development of CPRS to eosinophils infiltrating the polyp stroma [2, 13], without taking into account the type of histological structure and other variants of cellular infiltration of the stroma of the polypous mucous membrane. Depending on the infiltration of the stroma of the nasal mucosa by different types of cells, polyps are divided into “infectious” (neutrophilic) and “allergic” (eosinophilic). This circumstance is based on the predominance of eosinophils in allergic inflammation, and neutrophils in non-allergic inflammation [5, 9, 12, 15].

One of the most potent stimulators of eosinophil migration is vascular endothelial growth factor (VEGF). Vascular endothelial growth factor (VEGF) is a signaling protein produced by cells to stimulate vasculogenesis (the formation of an embryonic vascular system) and angiogenesis (the growth of new vessels in an existing vascular system). The production of VEGF proteins can be triggered in cells that do not receive enough oxygen. When a cell is deficient in oxygen, it produces one of the transcription factors, the hypoxia inducible factor (HIF). This factor (in addition to other functions - in particular, modulation of erythropoiesis, i.e., the process of formation of erythrocytes in the bone marrow) stimulates the release of VEGF proteins. The circulating VEGF protein then binds to the VEGF receptor on endothelial cells and activates the action of tyrosine kinase, triggering angiogenesis [7, 8, 11].

VEGF promotes mucosal edema and polyp growth, and its effect is approximately 50,000 times greater than that of histamine. Immunohistochemical study of the nasal mucosa showed that VEGF protein is produced by endotheliocytes of blood vessels. VEGF expression was also detected in epithelial cells of nasal polyps [6, 8].

VEGF, as an endothelial cell mitogen, is involved in the development of polyps. Immunohistochemical analysis of nasal polyps in children showed an increase in VEGF staining in the vascular endothelium and an increase in the mean number of blood vessels, which correlated with the size of nasal polyps [7, 15]. Others

also showed increased expression of VEGF and its receptor, localized in the endothelium, basement membranes, perivascular spaces, and polyp epithelium [4, 8, 13]. These studies show that the epithelium is an essential, but not the only, source of VEGF in polyp tissues [4, 12]. However, to date, there have been no studies on the role of VEGF as an epithelial mitogen in CPRS. Therefore, we hypothesized that VEGF is a central pathway through which the growth of airway epithelial cells is regulated.

Based on the above, **the purpose of this study** was to study VEGF in immunohistochemistry of various forms of chronic polypous rhinosinusitis.

Material and Research Methods

The material for this study was paraffin sections of surgical material removed during endoscopic surgery on the nose and paranasal sinuses of 45 patients aged 18-77 years who were inpatient treatment at the 3rd clinic of the Tashkent Medical Academy (32 men and 13 women) in 2013-2017 year. Morphological research was carried out in the laboratory of morphology of the 3rd clinic of the Tashkent Medical Academy, immunohistochemical research - in the laboratory of immunohistochemistry of the Russian Scientific Center for Radiology and Surgical Technologies (St. Petersburg, Russia). Both studies were carried out on paraffin sections of surgical material with a thickness of 3 μm. Morphological examination was carried out with staining for hematoxylin-eosin, followed by a 200-fold increase. With the help of morphometry, the forms of polypous rhinosinusitis were identified by determining the prevalence of infiltration by eosinophils or neutrophils. Immunohistochemical study with silver impregnation was performed using Gordon-Sweet staining to determine the reticular fibers of the stroma of nasal polyps. Immunohistochemical unmasking of antigens was carried out by heating the sections in citrate buffer (pH 6.0) or in Tris-EDTA buffer (pH 9.0) in a water bath for 30 minutes at 950C. Used primary polyclonal rabbit antibodies to VEGF ready to use (Dako). The sections were incubated with primary antibodies for 30 minutes at a temperature of + 20- + 220C in a humid chamber. Then, after a series of washes from unbound antibodies, the sections were incubated with an Envision (Dako) imaging system for 30 minutes at a temperature of + 20- + 220C. After a series of washes from the unbound imaging system, a chromogen - diaminobenzidine was applied to the sections for 5 min to show the result of the reaction. The results of the studies were evaluated at a magnification of 40*10 using a light microscope. Statistical processing of the research data was carried out using Microsoft Excel 2010 (Microsoft Corp., USA).

Research Results and Discussion

Morphological examination of the mucous membrane of polyps of patients with CPMS revealed desquamation of the ciliated epithelium down to the basal layer, the lamina propria was edematous, densely infiltrated with eosinophils and neutrophils, plasma, goblet cells, the vessels of the lamina propria were filled with blood.

The surface of the polyps was covered with ciliated epithelium, which in some areas was represented by a multi-row epithelium equipped with numerous cilia, and others by mucus-forming prismatic cells, mostly desquamated or underwent metaplasia.

With extensive (total) exudative-hyperplastic (polypous and polypous-purulent) processes in the maxillary sinus, changes in the mucous membrane are difficult to reversible. In these states of intervention in the area of the lateral wall of the nasal cavity, we recommend complementing the partial removal of the sinus mucosa. The unchanged mucous membrane is not removed.

Most likely, difficultly reversible destructive-dystrophic changes in the mucous membrane, developing over the years, affect all layers of the mucous membrane of the maxillary sinus, and not its individual areas. In

this regard, we believe that the mucous membrane with the phenomena of pronounced fibrosis of the basement membrane and the absence of ciliated epithelium, against the background of focal leukocytic infiltration and hyalinization of the vessels, absolutely does not fulfill its main functions. This creates the prerequisites for the development of recurrent inflammation in the maxillary sinus.

The revealed polymorphism of the structure of the ciliated epithelium, in addition to theoretical, is also of great practical importance. Currently, most endonasal operations are performed without taking into account the features of the morphological structure of the nasal mucosa. Quite often, in order to create a wide communication between the affected sinus and the nasal cavity, a large volume of functionally important areas of the ciliated epithelium is removed.

In the morphometry of the postoperative material, 33 drugs (73,3%) showed a predominance of eosinophilic infiltration of the stroma of the nasal mucosa and paranasal sinuses, 12 drugs (26,7%) showed a predominance of neutrophilic infiltration of the stroma of the nasal mucosa and paranasal sinuses (Fig. 1, 2). In this regard, the patients were divided into two groups: patients with chronic “eosinophilic” polypous rhinosinusitis and patients with chronic “neutrophilic” polypous rhinosinusitis.

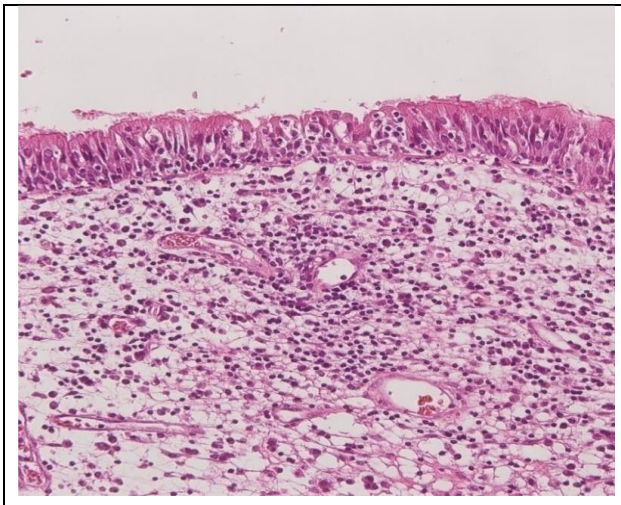


Figure 1. Magnification x200 times. Nasal polyp. Morphological examination determines the predominance of neutrophilic infiltration of the stroma of the nasal mucosa.

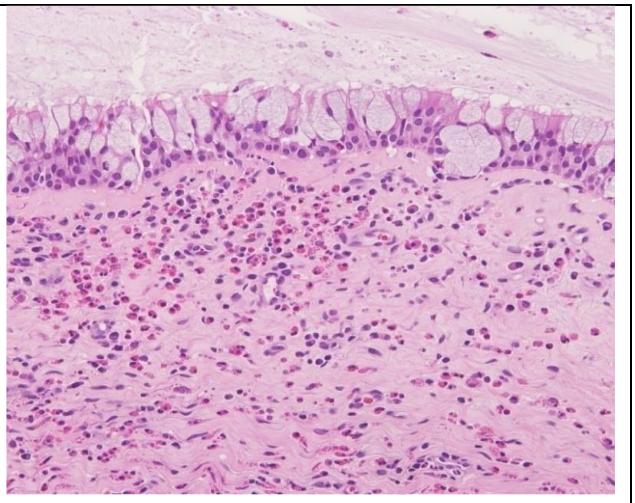


Figure 2. Magnification × 200 times. Nasal polyp. Morphological examination determines the predominance of eosinophilic infiltration of the stroma of the nasal mucosa.

Silver impregnation (Gordon-Sweet staining) of nasal polyp tissue was carried out to determine the nature of the structural organization of the stromal reticular fibers (Fig. 3, 4). With this type of staining, connective reticular fibers are well visualized.

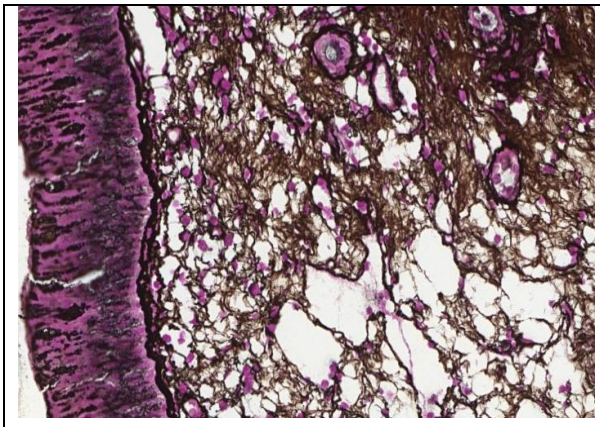


Figure 3. Staining of polyps according to Gordon, removed from patients with “eosinophilic” polypous rhinosinusitis. Magnification x200 times.

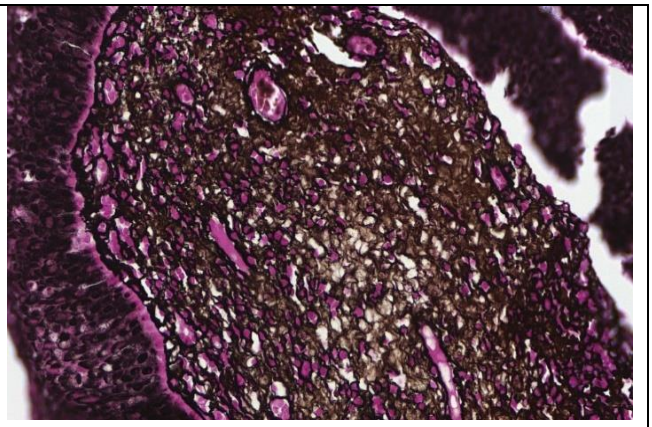
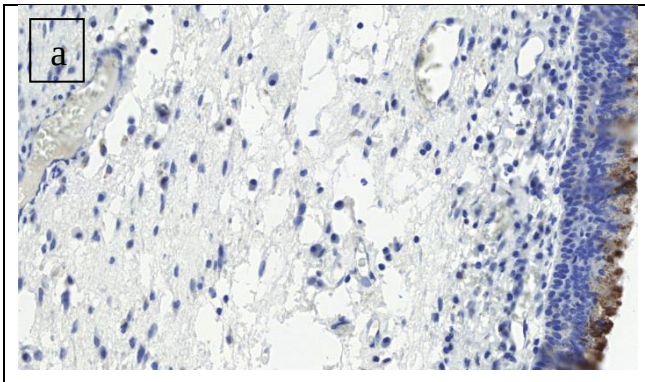
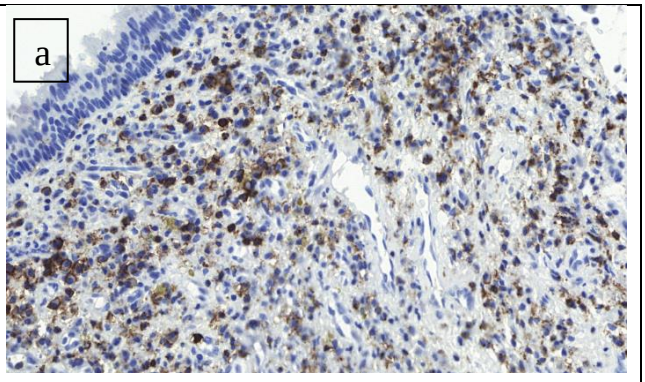


Figure 4. Staining of polyps according to Gordon, removed from patients with “neutrophilic” polypous rhinosinusitis. Magnification x200 times.

The reticular fibers, which, connecting with each other, create the framework of the stroma of the polyps, were destroyed and/or degraded, there is edema of the vascular endothelium. In the stroma of polyps of patients with “eosinophilic” polypous rhinosinusitis, strong expression of proteins was detected in all patients. With “eosinophilic” polypous rhinosinusitis, edema is noted, spreading in the form of several vacuoles. The edema consists of infiltrated tissue and fluid. Reticular fibers are destroyed and degraded, edema of the vascular endothelium is noted. With “neutrophilic” polypous rhinosinusitis, the reticular fibers are tightly interconnected. The stroma of “neutrophilic” polyps is distinguished by its density, high cellularity and good blood supply (Fig. 4). However, in some samples (16,1%), the expression of these proteins was weak, while in others (66,7%) the expression was high.

In the immunohistochemical study of macropreparations of both groups, the detection of the VEGF marker differed from each other. An immunohistochemical study of the macropreparation of “eosinophilic” polypous rhinosinusitis showed accumulation of the VEGF marker on the surface of the epithelium, but was not detected in the stroma itself. Immunohistochemical study of the macropreparation of “neutrophilic” polypous rhinosinusitis in the stroma of the polyp showed a diffuse expression of the VEGF marker, which was intense and occupied 1/3 of the stroma (Fig. 5-a, b, 6-a, b).





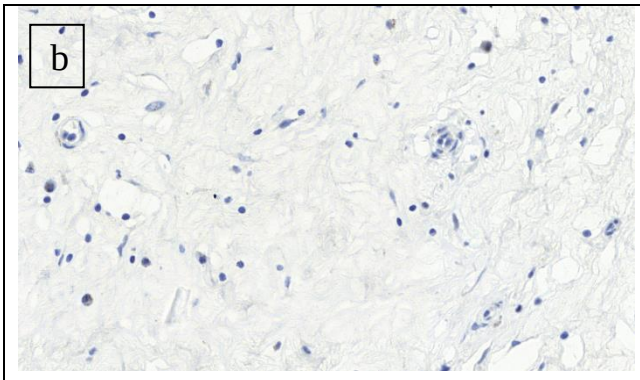


Figure 5 (a, b). Magnification x200 times. Immunohistochemical study of polyps removed from patients with “eosinophilic” polypous rhinosinusitis.

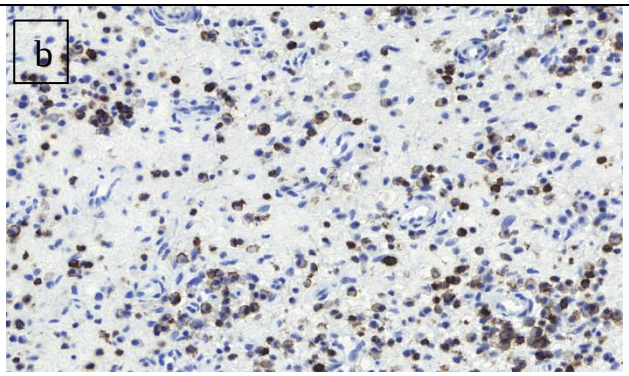


Figure 6 (a, b). Magnification x200 times. Immunohistochemical study of polyps removed from patients with “neutrophilic” polypous rhinosinusitis.

In a macro-preparation of “eosinophilic” polypous rhinosinusitis, edema of the stroma and several large blood vessels, inside which there are a large number of erythrocytes, is noted; however, the absence of VEGF expression indicates a good blood supply to the “eosinophilic” polyp tissue. This determines the allergic background of the disease, which proceeds with profuse mucous flow.

In contrast to this, large blood vessels are less often observed in the tissues of “neutrophilic” polyps. They have multiple capillaries, in most cases, their accumulation near the epithelium. In our opinion, a large amount of the VEGF marker in chronic “neutrophilic” polypous rhinosinusitis is caused by a lack of oxygen and blood vessels, which can subsequently contribute to the formation of new vasculature and fibrous tissue.

Conclusion

Thus, based on the research data, the following conclusions follow:

1. Identification of various forms of chronic polyposis rhinosinusitis is advisable to determine the course of the polyposis process with the subsequent choice of treatment tactics.

2. With “eosinophilic” polypous rhinosinusitis, there is a more pronounced inflammatory reaction in the form of edema and degradation of reticular fibers than with “neutrophilic” polypous rhinosinusitis.

3. Expression of the VEGF marker is more pronounced in “neutrophilic” polypous rhinosinusitis than in “eosinophilic” polypous rhinosinusitis, which indicates the possibility of early relapse.

REFERENCES

Bairashevskaia, A. V., Kytko, O. V., Vasilev, Y. L., & Kashtanov, A. D. (2020). Modern approaches to the treatment of chronic polypous rhinosinusitis. Research Results in Pharmacology, 6, 77.

Bezrukova, E. V., Vorobeychikov, E. V., Konusova, V. G., & Simbirtsev, A. S. (2020). Severity evaluation of bhronic polypous rhinosinusitis based on changes of IL-1β cytokine and IL-1ra concentrations in nasal secretions. Medical Immunology (Russia), 21(6), 1155-1162.

Cho, S. H., Hamilos, D. L., Han, D. H., & Laidlaw, T. M. (2020). Phenotypes of chronic rhinosinusitis. The Journal of Allergy and Clinical Immunology: In Practice, 8(5), 1505-1511.

Cho, S. W., Kim, D. W., Kim, J. W., Lee, C. H., & Rhee, C. S. (2017). Classification of chronic rhinosinusitis according to a nasal polyp and tissue eosinophilia: limitation of current classification system for Asian population. Asia Pacific Allergy, 7(3), 121-130.

Djuraev, J. A., Khasanov, U. S., & Vokhidov, U. N. (2018). The prevalence of chronic inflammatory diseases of the nose and paranasal sinuses in patients with myocarditis. European Science Review, (5-6), 147-149.

Djuraev, J. A., Khasanov, U. S., Botirov, A. J., & Shaumarov, A. Z. (2020). Results of an immunogistochemical study in patients with polipoid rhinosinusitis. European Journal of Molecular & Clinical Medicine, 7(2), 2526-2541.

Djuraev, J. A., Khasanov, U. S., Vohidov, U. N., & Sharipov, S. S. (2020). Results of Allergological and Immunological Research in Patients with Polipoid Rhinosinusitis. Asian Journal of Immunology, 34-40.

Pistochini, A., Rossi, F., Gallo, S., Pirrone, C., Preti, A., Gornati, R., ... & Castelnuovo, P. (2019). Multiple gene expression profiling suggests epithelial dysfunction in polypoid chronic rhinosinusitis. Acta Otorhinolaryngologica Italica, 39(3), 169.

Savlevich, E. L., Khaidukov, S. V., Kurbacheva, O. M., Bondareva, G. P., Shachnev, K. N., & Simbirtsev, A. S. (2017). Characteristics of cellular immune status in the patients with chronic rhinosinusitis with nasal polyps. Medical Immunology (Russia), 19(6), 731-738.

Savlevich, E. L., Khaidukov, S. V., Kurbacheva, O. M., Bondareva, G. P., Shachnev, K. N., & Simbirtsev, A. S. (2017). Characteristics of cellular immune status in the patients with chronic rhinosinusitis with nasal polyps. Medical Immunology (Russia), 19(6), 731-738.

Stupar, M., Špreng, Đ., & Perić, A. (2020). Application of questionnaires in the assessment of clinical severity of chronic rhinosinusitis. Vojnosanitetski pregled, 77(2), 182-188.

Vokhidov, U. N. (2015). State of reticular fibers in various forms of polypoid rhinosinusitis. European science review, (7-8), 39-40.

Vokhidov, U. N., & Akhundjanov, N. O. (2015). Features of mesenchymal formations of chronic polypoid rhinosinusitis. European Science Review, (11-12), 76-77.

Vokhidov, U. N., & Radjabov, R. R. (2020). Rinoendoscopic evaluation of chronic polypoid rhinosinusitis. International Engineering Journal For Research & Development, 5(4), 5-5.

Vokhidov, U. N., Khasanov, U. S., & Vokhidov, N. K. (2014). The effectiveness of use macrolides in the treatment of chronic “neutrophil” polypoid rhinosinusitis. Folia Otorhinolaryngologiae et Pathologiae Respiratoriae, 20(2), 79-79.