

# RESULTS OF AN IMMUNOGISTOCHEMICAL STUDY IN PATIENTS WITH POLIPOID RHINOSINUSITIS

Djuraev J.A., Khasanov U.S., Vohidov U.N., Botirov A.J., Shaumarov A.Z.  
*Tashkent Medical Academy Uzbekistan*

**Abstract:** *The marker of mesenchymal cells - vimentin with high and moderate expression is present in both epithelial and stromal cells with "eosinophilic" forms of polyps and only in the stroma in patients with "neutrophilic" polyps. The presence of high vimentin expression indicates a high activity of mesenchymal cells. In the prognostic plan, these changes indicate future relapses. Detection of the CD68 marker, its low and moderate expression can mean low participation of macrophages in the formation of nasal polyps of both forms. The presence of single stained cells in mesenchymal clusters indicates a low phagocytic activity. The high and moderate expression of CD45 in mesenchymal clusters located in "eosinophilic" polyps confirms our assumption that these mesenchymal clusters are a "growth zone" of formations. High and moderate expression of CD138 in mature epithelial cells in all tissue samples of both forms of polyps and the lack of expression of this marker in clusters of mesenchymal formations, as well as average expression in cells located in the stroma, may indicate the origin of the latter from active mesenchymal cells. With the "eosinophilic form" of polyps, moderate and high expression of CD34 is detected. These results confirm our assumption about the formation of a new vascular system in mesenchymal clusters. Near the epithelium and in the stroma, a well-developed vascular system is also observed. An increase in the number of vessels is a sign of recurrence, and an increase in the number of newly formed vessels is prognostically unfavorable and indicates the occurrence of relapse.*

**Keywords:** *polyp of the nose, cytokines, marker, expression, cell, stroma.*

## **Introduction.**

CPRS based on the materials of the International Consensus Conference on Nasal Polyps and Positional Documents on Rhinosinusitis and Nasal Polyps of the European Academy of Allergology and Clinical Immunology (EAACI) - Position Paper on Rhinosinusitis and Nasal Polyps (EP3OS, 2012) is defined as chronic productive Th-2-dependent eosinophilic inflammation, leading to remodeling of the nasal mucosa, its edema, followed by prolapse of the mucous membrane and the formation of nasal polyps. However, East Asian scientists believe that in most cases, chronic kidney disease develops against the background of Th-1-dependent inflammation, which leads to the formation of polyps in the nose and paranasal sinuses [1,4].

The key role of eosinophil migration regulated by cytokines is widely recognized [2]. The cytokine tissue profile of nasal polyps is a mixture of types Th1 and Th2 [3]. Cytokines in nasal polyps with increased concentration or expression of mRNA include Th1 cytokines, such as IL-1, INF- $\gamma$ , IL-12, TNF- $\alpha$ , and Th2 cytokines, such as IL-4, IL-5, IL-6, IL-13, and GM-CSF, IL-3, which are synthesized as Th1 and Th2 cells, and finally, TGF- $\beta$ , which is a powerful inducer of myofibroblasts [5,7]. Enhanced expression of IL-2 and IL-5 receptors is also reported [6]. With nasal polyps, adhesion molecules such as ICAM-1 (cell-to-cell

adhesion molecule-1), VCAM-1 (vascular adhesion molecule-1), and growth factors such as vascular permeability / vascular endothelial growth factor (VPF / VEGF) can be increased. ), which are the main inducers of capillary angiogenesis and permeability, keratinocyte growth factor (KGF), which is a fibroblast growth factor, stem cell factor (SCF), which serves as a cell growth mast and survival factor, profibrotic cytokines associated with collagen deposition on, such as IL-11 and IL-17, registered with CHC / NP (chronic hyperplastic sinusitis / nasal polyps) [8,10].

In a study by A. Peric et al. (2013) it can be seen that cytokines play an important role in the development of nasal polyps [11]. It has been suggested that atopy does not determine the presence of cytokines in the NP [12]. However, there are also reports of detecting differences between allergic and non-allergic nasal polyps. So, DL Hamilos (2011), when examining patients with nasal polyps or CHC / NP, found that allergies are characterized by higher levels of IL-4, IL-5 and IL-13, and non-allergic cases have higher levels of INF- $\gamma$ , GM-CSF and TNF- $\alpha$  [13]. In patients with atopic nasal polyps, a significant correlation was also found between IL-5 and tissue IgE concentration [14].

Eosinophilic infiltration, which is a key aspect of the pathogenesis of HPRS, depends on the physiological effects of a number of chemokines and adhesive molecules [15]. They include, first of all, IL-5, as well as eotaxin, RANTES, adhesion molecules of vascular endothelium - VCAM-1, vascular endothelial growth factor - VEGF, etc.

Chemokines (chemoattractant cytokines) affect monocytes, eosinophils, basophils, causing allergic and non-allergic inflammations, and their main sources are structural cells such as endothelial cells, epithelial cells and fibroblasts [16]. Th1 cytokines, such as TNF and IL-1, can also initiate chemokine production. In addition, there is evidence that with nasal polyps, not only Th1, but also Th2 cytokines can regulate chemokine production. It is believed that various chemokines, such as IL-8, RANTES and eotaxin, play an important role in the formation of nasal polyps. IL-8 is synthesized by macrophages, lymphocytes, neutrophils and structural elements. IL-8 is a chemoattractant for neutrophils and T-lymphocytes [17]. It can also inhibit IgE production and histamine release. According to J.B. Watelet et al. (2014), nasal neutrophilia correlates with the level of IL-8. V. Kirtsreesakul et al (2015) believes that an increase in IL-8 may be a sign of neutrophilic inflammation. In this regard, the study of the amount of IL-8 will indicate the state of neutrophilia in the stroma of polyps.

One of the most potent stimulators of eosinophil migration is vascular endothelial growth factor (VEGF) [18]. This vasodilating agent promotes edema of the mucous membrane and the growth of polyps; its effect is approximately 50 thousand times greater than that of histamine. An immunohistochemical study of the nasal mucosa showed that VEGF protein is produced by blood vessel endotheliocytes. VEGF expression was also detected in epithelial cells of nasal polyps [19].

S. Hu et al. (2014) demonstrated increased expression of VEGF in nasal polyps, confirming the potential role of VEGF in the development of chronic kidney disease. The authors used a culture of nasal epithelial cells from nasal polyps and showed active production of a huge amount of VEGF in response to hypoxia [20]. They suggested that this was the main reason for the formation of polyps in the middle nasal passage, where most of the paranasal sinuses open and where minimal swelling of the mucous membrane can lead to complete occlusion, the cause of hypoxia in the sinus [21].

Thus, an analysis of the literature showed that the key point in the pathogenesis of chronic kidney disease is immunological disorders, including Th1 and Th2 cytokines (IL-2, IL-4, IL-8), the study of which will provide the necessary data on the peculiarities of the course of the polyposis process.

### Material and research 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 2013-2019. All patients underwent clinical and functional studies of ENT organs, laboratory and instrumental studies, immunohistochemical studies.

### Results and discussions.

As noted in a morphological study when stained with hematoxylin and eosin, the stroma of nasal polyps was covered with a multilayer ciliated epithelium with clear contours of goblet cells, in some cases, the multilayer ciliated epithelium gradually turned into a flat epithelium with subsequent keratinization and desquamation.

In the stroma of the mucous membrane of "eosinophilic" polyps, edema, tissue loosening, apparent degradation and low cellularity are noted. With eosinophilic polyposis rhinosinusitis, edema spreads in the form of vacuoles (Fig. 1). Edema consists of infiltrated tissue and fluid.

The silver impregnation (staining according to Gordon-Sweet) of nasal polyp tissue was carried out to determine the nature of the structural organization of the stromal reticular fibers (Fig. 2). Reticular fibers, which, when connected together, create the framework of the stroma of polyps, were destroyed and degraded, edema of the vascular endothelium was noted. In the stroma of polyps of patients with "eosinophilic" polyposis rhinosinusitis, strong expression of proteins was detected in all patients (Table 1).

The stroma of "neutrophilic" polyps is characterized by density, high cellularity and good blood supply (Fig. 3). However, in some samples (16.1%) the expression of these proteins was weak, while in others (66.7%) the expression was high (Table 2).

Table 1: The frequency of occurrence of patients depending on the histological structure of polyps and the expression of proliferation and angiogenesis markers

Markers growth factors	The form, (n=79)					
	Eosinophilic, % (n =48)			Neutrophil, % (n = 31)		
	gene expression level in the cells			gene expression level in the cells		
	< 10% weak	>10% moderate	>50% high	< 10% weak	>10% moderate	>50% high
Ki – 67	39,6±7,1	20,8±5,9	20,8±5,9	0	0	16,1±6,7
	0	20,8±5,9	0	16,1±6,7	0	0
VEGF	20,8±5,9	0	39,6±7,1	0	16,1±6,7	16,1±6,7
	20,8±5,9	0	0	67,7±8,5	16,1±6,7	0
Vimentin	0	20,8±5,9	60,4±7,1	0	16,1±0,6	0
	0	20,8±5,9	60,4±7,1	0	0	83,9±6,7
Gordon	0	0	0	0	0	0
	0	0	100	16,1±6,7	0	67,7±8,5

Note: in the numerator - marker expression in the mucosa, in the denominator - in the stroma.

From the data of table 1 it is seen that the samples of all patients (100%) with "eosinophilic" forms of polyps and 83.8% with "neutrophilic" had expression of proteins detected by Gordon-Sweet color, this indicates a high activity of the formation of reticular fibers in the tissues.

When stained with hematoxylin and eosin, only lymphocyte accumulations are

detected, the application of the immunohistochemical method of investigation allows detecting the presence of cells carrying markers Ki-67, VEGF, Vimentin, CD68, CD45, CD138, CD34.

In an immunohistochemical study of “eosinophilic” polyps, the VEGF marker was studied (Fig. 4). The VEGF marker is a vascular endothelial and nitrooxysynthetase receptor growth factor. The family of VEGF proteins structurally close to each other together with the receptor play a role in the development and regulation of the activity of blood and lymph vessels. These proteins are expressed by endothelial cells, affect the development of a new vasculature and the survival of immature blood vessels, and are also a lymphangiogenic factor.

From table 1 it follows that the expression of this marker in the tissue of “eosinophilic” polyps was high in the mucous membrane in 39.6% of patients and weak in 20.8% of the samples, and in the stroma this marker was found only in 20.8% of patients and the expression of this gene was weak. The stromal vasculature in the remaining samples is well developed and consists of a large number of blood vessels of different sizes, inside which there are a large number of red blood cells. This fact indicates a good blood supply to the tissue of “eosinophilic” polyps, which determines the allergic background of the disease, which occurs with profuse mucus.

With “neutrophilic” polyps, the epithelium remained intact and the expression level of the VEGF marker in it was high and moderate in 32.2% of patients (Fig. 5). In the stroma of this form of the polyp, VEGF marker expression was observed in 83.8% of patients, and the expression level was weak and moderate (Table 3).

In patients of this group, the detection of VEGF expression in mesenchymal clusters indicates the formation of endothelial cells, which will subsequently participate in the formation of neoangiogenesis. In the absence of a developed vasculature, it is possible to form new vessels.

In the tissues of “neutrophilic” polyps, large blood vessels are less often detected. The stromal vasculature consists mainly of capillaries. In our opinion, weak and moderate expression of the VEGF marker in the stroma of “neutrophilic” polyps is caused by a lack of oxygen, and in some samples (in 16.2% of patients) due to the immaturity of blood vessels. The appearance of new blood vessels in polyp tissue can further contribute to the formation of fibrous tissue.

In the epithelium of more than 80% of nasal polyp samples with “eosinophilic” forms, a different level of expression of the Ki-67 proliferation marker is noted. In the stromal part of polyps, only 20.8% of the samples had moderate expression of this gene. In the epithelium of nasal polyps with chronic “neutrophilic” polyposis rhinosinusitis, weak and high expression of the Ki-67 antigen is noted in only 16.1% of the samples (Fig. 7, 8 and Table 1).

A positive reaction of the Ki-67 proliferation marker in polyp tissue indicates active deletion of cellular elements.

In the stroma of “neutrophilic” polyps, accumulation of plasma cells is observed, creating a ring called the “growth zone”. This sign indicates an unfavorable prognosis of the course of the disease (Fig. 9, 10). Mesenchymal stem cells - undifferentiated (immature) cells found in many species of multicellular organisms are able to self-renew, forming new stem cells, divide by mitosis and differentiate into specialized cells, that is, turn into cells of various organs and tissues. As can be seen from Figures 9 and 10 and Table 1, with both forms of nasal polyps, mesenchymal cells are present in large numbers in the epithelium itself, especially in the “eosinophilic” forms and in the stroma. Vimentin is a marker of mesenchymal cells, in endothelial and mesenchymal cells it is presented in the form of clusters (Fig. 10).

Thus, the marker of mesenchymal cells - vimentin with high and moderate expression is present in both epithelial and stromal cells with "eosinophilic" forms of polyps (from 20.8% to 60.4% of samples) and only in stroma in 83.9% of patients with "neutrophilic".

Figure 10 shows the formation of epithelial cells (stained blue) in a cluster of mesenchymal cells (stained brown). The presence of high vimentin expression in the stroma indicates a high activity of mesenchymal cells. In the prognostic plan, these changes indicate future relapses.

Also, the accumulation of mesenchymal cells in both forms of polyps is determined. These formations are the main growth zones of polyps, which are also called "growth zones". It was found that mesenchymal cells were directed from these formations towards the stroma, which may indicate the growth of the polyp. With "eosinophilic" polyps, these formations were noted most often in comparison with "neutrophilic" polyps. This may indicate that the reason for the frequent recurrence of "eosinophilic" polyps is associated with a large number of "growth zones".

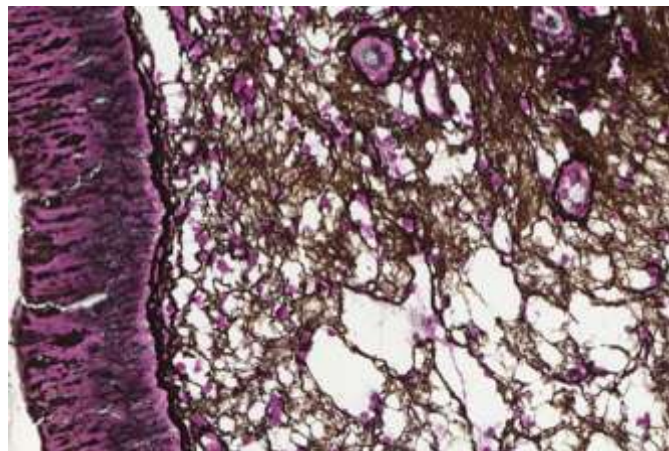


Fig. 1. Patient Ch., 69 years old, h/c No. 14850/754. D/s: Chronic polypous rhinosinusitis "eosinophilic" form. Edema, degradation and destruction of reticular fibers are noted. Immunohistochemical staining. SW OK. 10x, about 40x.

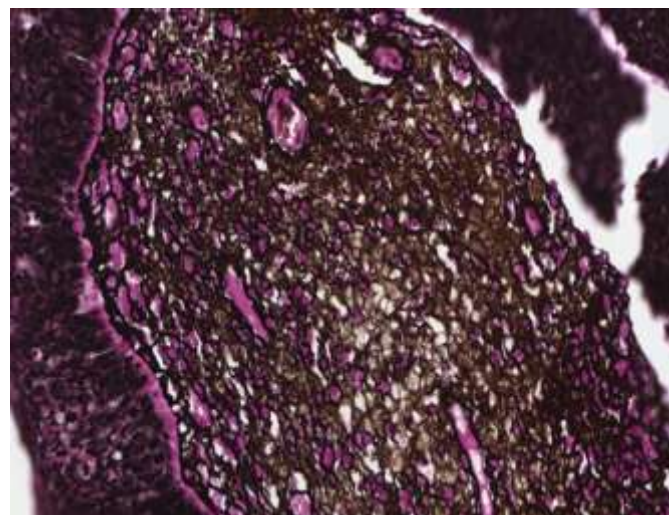


Fig. 2. Patient Z., 54 years old, h / c No. 7945/359. D / s: Polypous rhinosinusitis "neutrophilic" form. A dense connection of reticular fibers is noted. Immunohistochemical staining. SW OK. 10x, about 40x.

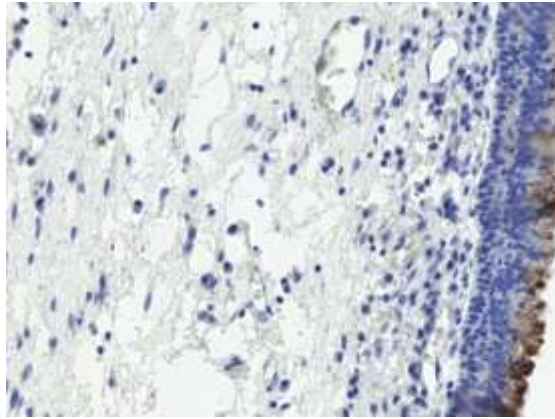


Fig. 3. Patient Ch., 69 years old, h / c No. 14850/754. D / s: Chronic polypous rhinosinusitis is an "eosinophilic" form. High expression of VEGF (+++). Immunohistochemical staining. SW OK. 10x, about 40x.

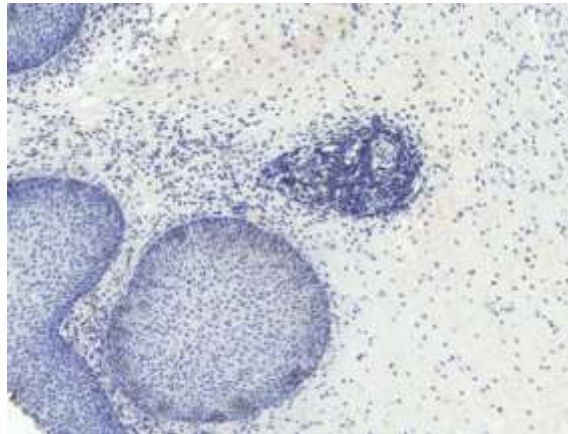


Fig. 4. Patient Z., 54 years old, h / c No. 7945/359. D / s: Polypous rhinosinusitis is a "neutrophilic" form. Moderate expression of VEGF (++) . Immunohistochemical staining. SW OK. 10x, about 20x.

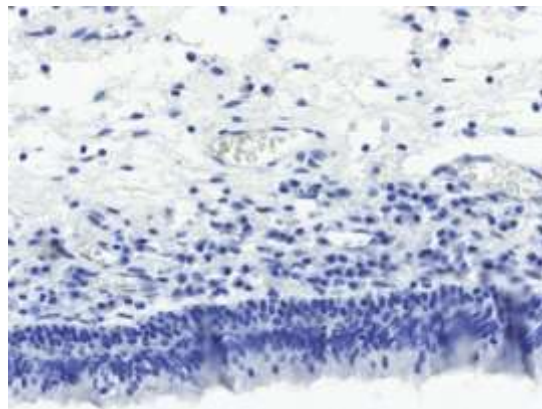


Fig. 5. Patient Ch., 69 years old, h / c No. 14850/754. D / s: Chronic polypous rhinosinusitis "neutrophilic" form. Low expression of Ki-67 (+). Immunohistochemical staining. SW OK. 10x, about 90x.



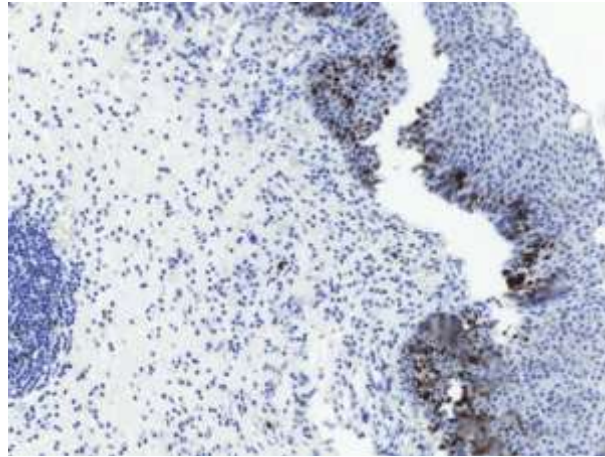


Fig. 6. Patient Z., 54 years old, h / c No. 7945/359. D / s: Polypous rhinosinusitis is an "eosinophilic" form. High expression of Ki-67 (+++). Immunohistochemical staining. SW OK. 10x, about 90x.

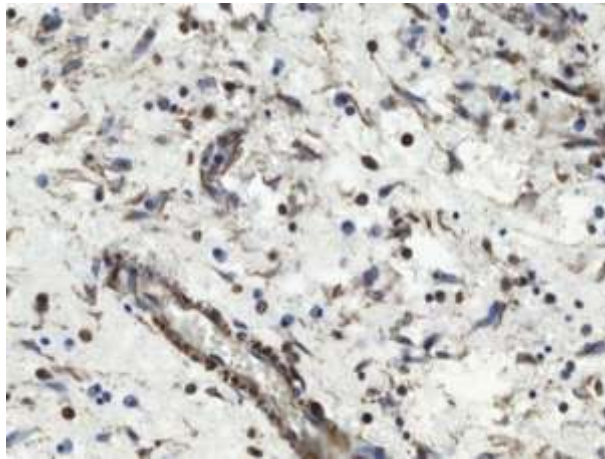


Fig. 7. Patient Ch., 69 years old, h / c No. 14850/754. D / s: Chronic polypous rhinosinusitis "eosinophilic" form. High expression of Vimentin (+++). Immunohistochemical staining. SW OK. 10x, about 40x.

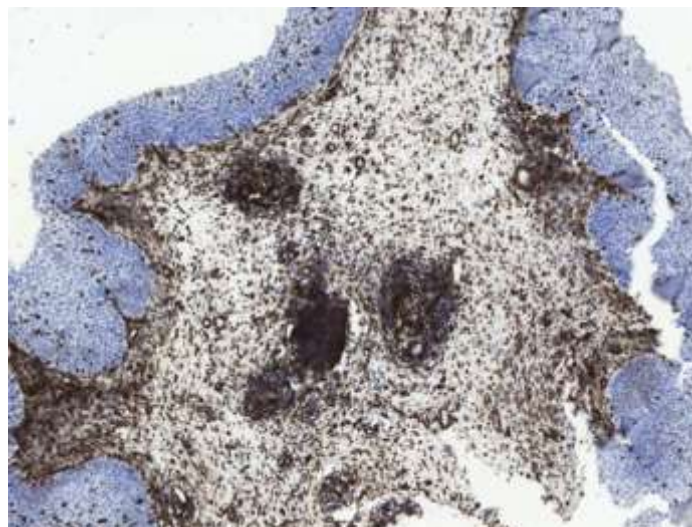


Fig. 8. Patient Z., 54 years old, h / c No. 7945/359. D / s: Polypous rhinosinusitis is a "neutrophilic" form. High expression of Vimentin (+++). Immunohistochemical staining. SW OK. 10x, about 20x.

In preparations with the identification of the marker CD68, its low and moderate expression is observed (Fig. 9.10 and Table 2), which may mean a low participation of macrophages in the formation of nasal polyps of both forms. The presence of single stained cells in mesenchymal clusters indicates low phagocytic activity.

Table 2: The frequency of occurrence of patients depending on the histological structure of polyps and the expression of differentiation clusters (CD)

Markers CD	The form, (n=79)					
	Eosinophilic, % (n=48)			Neutrophil, % (n= 31)		
	gene expression level in the cells			gene expression level in the cells		
	< 10% weak	>10% moderate	>50% high	< 10% weak	>10% moderate	>50% high
138	0	60,4±7,1	39,6±7,1	0	51,6±9,1	0
	0	60,4±7,1	39,6±7,1	0	0	51,6±9,1
34	0	0	39,6±7,1	16,1±6,7	0	16,1±6,7
	0	60,4±7,1	39,6±7,1	16,1±6,7	0	51,6±9,1
45	39,6±7,1	39,6±7,1	0	32,2±8,5	16,1±6,7	0
	0	39,6±7,1	60,4±7,1	16,1±6,7	16,1±6,7	16,1±6,7
68	0	81,2±5,7	0	51,6±9,1	0	0
	39,6±7,1	39,6±7,1	0	32,2±8,5	16,1±6,7	0

Note: in the numerator - marker expression in the mucosa, in the denominator - in the stroma.

Figures 11, 12 and Table 2 show the high and moderate expression of CD45 in mesenchymal clusters located in “eosinophilic” polyps (from 39.6% to 60.4% of samples), which confirms our assumption that these mesenchymal clusters are the “growth zone” of formations.

In “neutrophilic” forms, the number of samples with positive coloration of this marker was less (from 16.1% to 32.2%).

Figures 13,14 and Table 2 show the results of the detection of high and moderate expression of CD138 in mature epithelial cells in all tissue samples of both forms of polyps and the lack of expression of this marker in clusters of mesenchymal formations, as well as the average expression in cells located in the stroma Perhaps this indicates the origin of the last of the active mesenchymal cells.

Determining the number of vessels in one field of view is a prognostic sign of the rate of relapse, since an increase in the number of newly formed vessels with tumor growth is prognostically unfavorable and indicates the onset of relapse.

Figures 15,16 and Table 2 show that with the "eosinophilic form" of polyps, moderate and high expression of CD34 is detected (from 39.6% to 60.4% of samples). These results confirm our assumption about the formation of a new vascular system in mesenchymal clusters. Near the epithelium and in the stroma, a well-developed vascular system is also observed.

In the “neutrophilic” form of polyps, high expression of this marker was detected only in the stroma of polyps in 51.0% of patients. Weak expression of CD34 (16.7%) was detected in the mucosa and stroma.



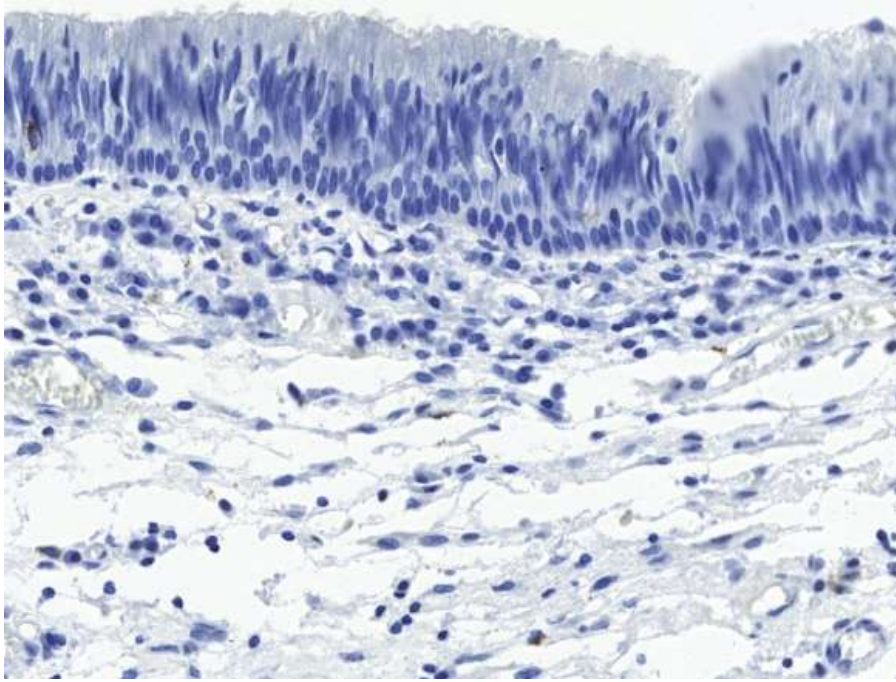


Fig. 9. Patient Ch., 69 years old, h / c No. 14850/754. D / s: Chronic polypous rhinosinusitis "eosinophilic" form. Low expression of CD68 (+). Immunohistochemical staining. SW OK. 10x, about 40x.

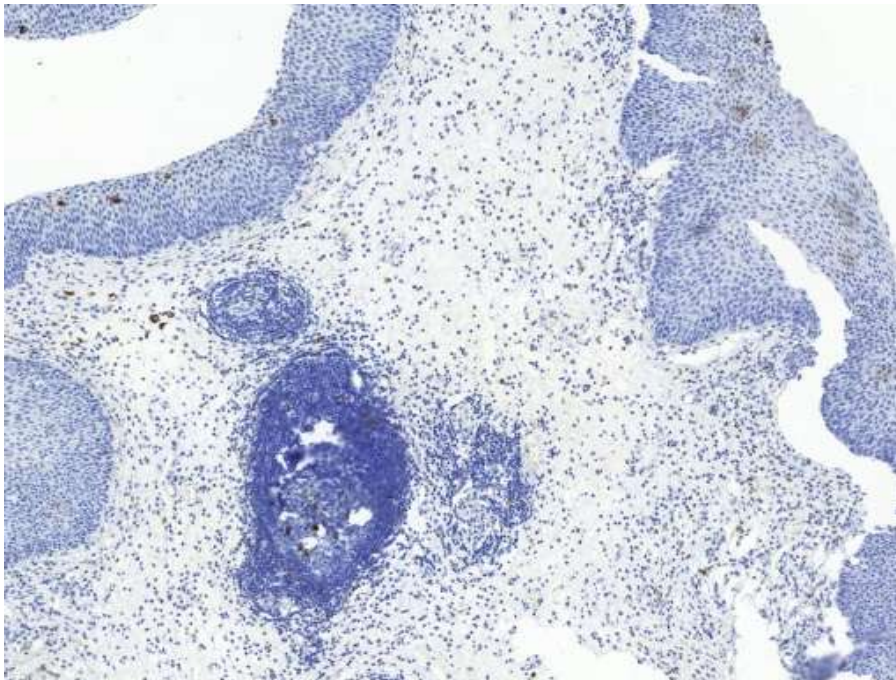


Fig. 10. Patient Z., 54 years old, h / c No. 7945/359. D / s: Polypous rhinosinusitis is a "neutrophilic" form. Low expression of CD68 (+). Immunohistochemical staining. SW OK. 10x, about 20x

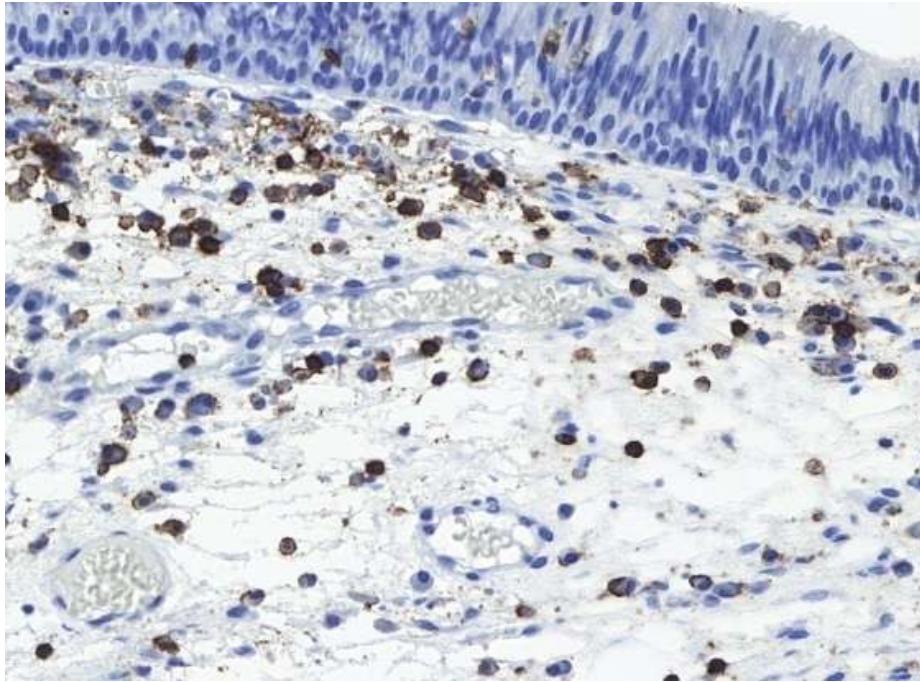


Fig. 11. Patient Ch., 69 years old, h / c No. 14850/754. D / s: Chronic polypous rhinosinusitis "eosinophilic" form. High expression of CD45 (+++). Immunohistochemical staining. SW OK. 10x, about 40x.

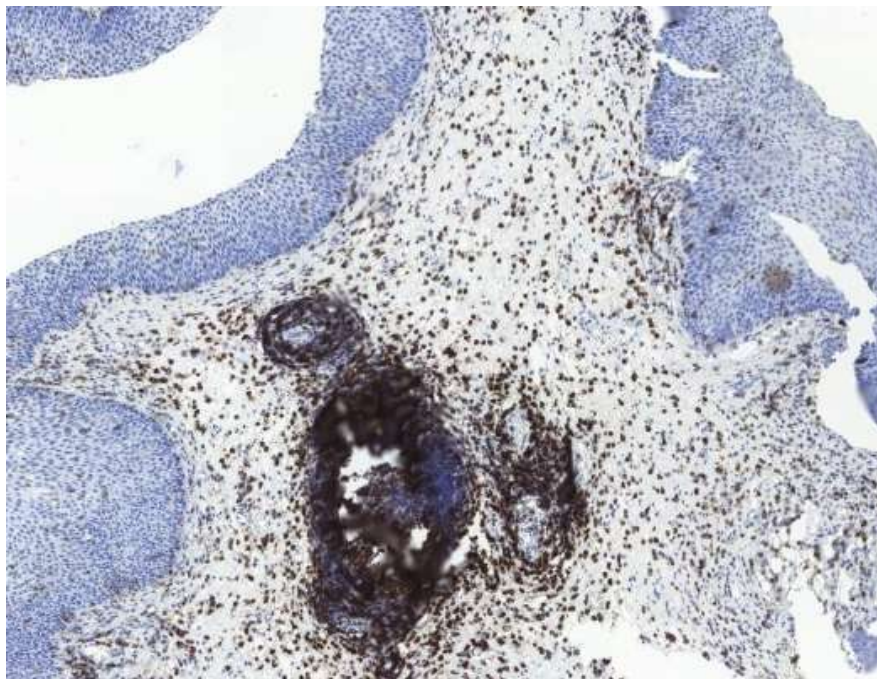


Fig. 12. Patient Z., 54 years old, h / c No. 7945/359. D / s: Polypous rhinosinusitis is a "neutrophilic" form. High expression of CD45 (+++). Immunohistochemical staining. SW OK. 10x, about 20x.



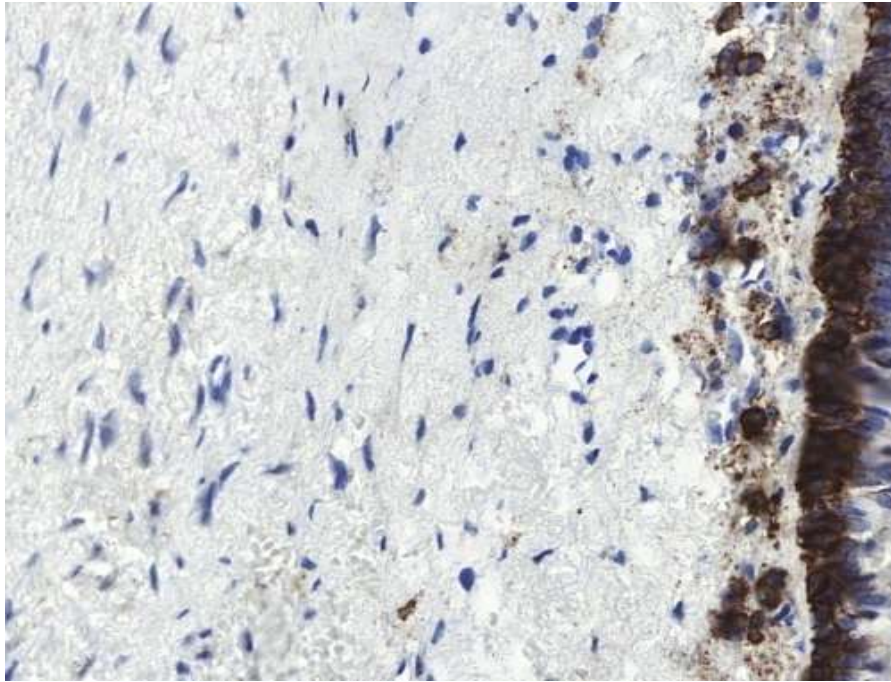


Fig. 13. Patient Ch., 69 years old, h / c No. 14850/754. D / s: Chronic polypous rhinosinusitis "eosinophilic" form. High expression of CD138 (+++). Immunohistochemical staining. SW OK. 10x, about 40x.

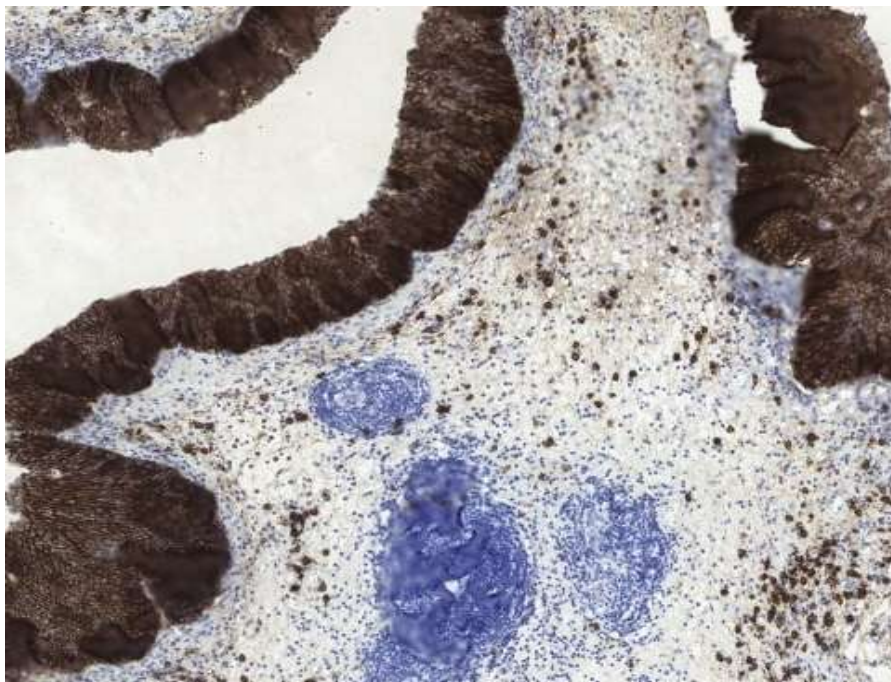


Fig. 14. Patient Z., 54 years old, h / c No. 7945/359. D / s: Polypous rhinosinusitis is a "neutrophilic" form. High expression of CD138 (+++). Immunohistochemical staining. SW OK. 10x, about 20x.

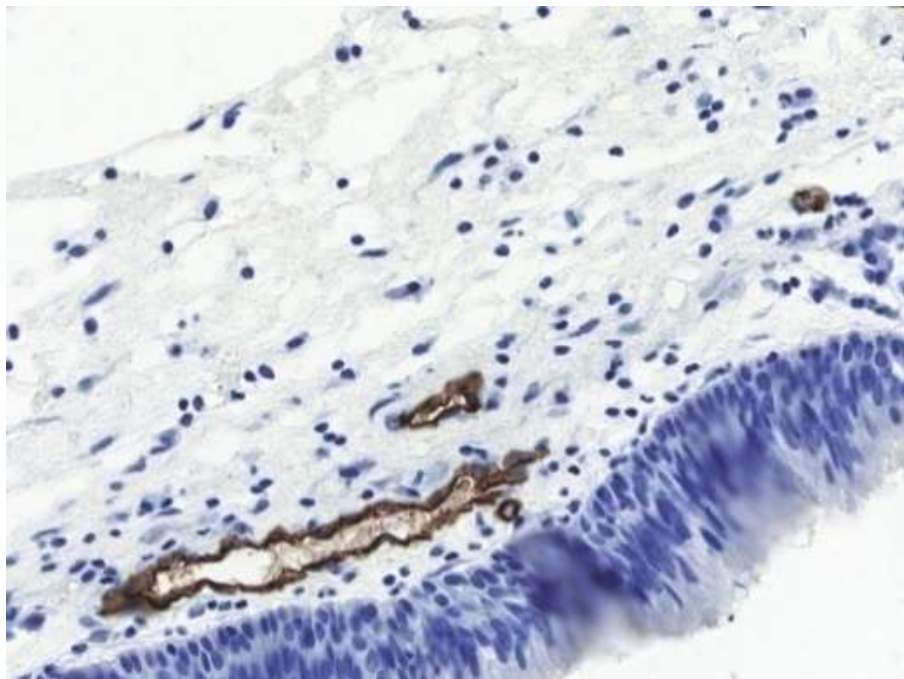


Fig. 15. Patient Ch., 69 years old, h / c No. 14850/754. D / s: Chronic polypous rhinosinusitis "eosinophilic" form. Moderate expression of CD34 (+++). Immunohistochemical staining. SW OK. 10x, about 40x.

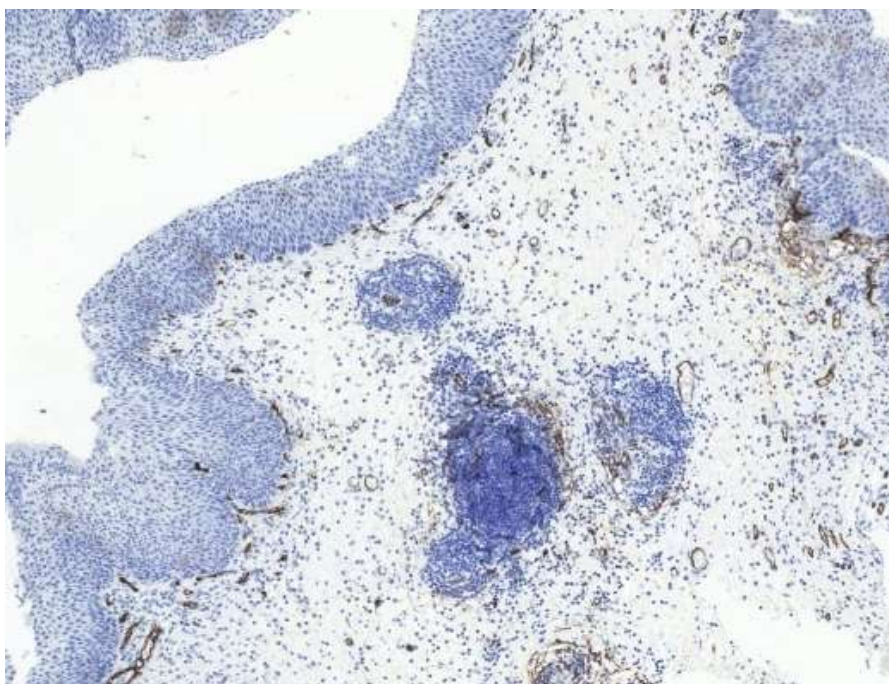


Fig.16. Patient Z., 54 years old, h / c No. 7945/359. D / s: Polypous rhinosinusitis is a "neutrophilic" form. High expression of CD34 (+++). Immunohistochemical staining. SW OK. 10x, about 20x.

Thus, both the mucous tissue and the stroma of the polyps differ in the form of chronic kidney disease, which implies different tactics of managing patients with this pathology. An immunohistochemical study revealed the formation of difficult reversible changes in the

nasal mucosa, leading to the loss of its functional activity and the creation of prerequisites for frequent relapses of chronic kidney disease.

Clinical example: Patient Ch., 69 years old, h / c No. 14850/754. He was hospitalized in the ENT department of diseases of the 3rd clinic of the Tashkent Medical Academy from 09.10.2019. until 10/14/2019. with a diagnosis of Chronic polypous rhinosinusitis. Complaints at admission: difficulty in nasal breathing, lack of smell, mucous discharge from the nose, sneezing, itching in the nose, headaches, general weakness.

From the anamnesis: considers himself ill for 9 years. Associates his illness with frequent colds and allergies. In the past 5 years, the patient was operated on 3 times by ENT doctors at the place of residence, a polypotomy was performed. In connection with the above complaints, the patient turned to the ENT clinic of the 3rd clinic of the Tashkent Medical Academy, where he was examined and hospitalized in the ENT department of diseases on 09.10.2019.

The general condition of the patient is relatively satisfactory. Consciousness is clear. Skin and visible mucous membranes of normal color. Peripheral nodes are not palpable. With auscultation of the lungs, vesicular breathing. Heart sounds are rhythmic, blood pressure 120/80 mm RT. Art. Pulse - 80 beats. per minute. The abdomen is soft, painless. The liver and spleen are not palpable. Stool and urination are normal.

Status localis: no facial deformity. With anterior rhinoscopy, hyperemia of the nasal mucosa and mucous discharge in both nasal cavities are noted. Transparent polypous formations are determined that completely obstruct both nasal cavities. Nasal septum in the midline.

Patient examination results: CT of the paranasal sinuses - CT signs of polypous dimming of both sides of the maxillary, ethmoid, frontal, major sinuses and nasal cavities.

By decision of the council 10.10.2019 operation performed: Bilateral polypotomy, maxillary rotor, frontotomy, ethmoidotomy and sphenoidotomy. Polyps were removed during surgery, but based on the principles of functional endoscopic sinus surgery, a polypous-modified mucous membrane of the nose and paranasal sinuses remained. Remote polyps were multiple with clear contours, soft consistency, smooth surface, and transparent.

The results of histological examination No. 5613-18: Fibrous polyp with cystic changes in the presence of chronic inflammation.

Morphometry results: polyp with a predominance of eosinophilic infiltration.

The results of an immunohistochemical study: Gordon-Sweet staining - edema, degradation and destruction of reticular fibers, VEGF - positive +++, high, Ki-67 - positive +++, high, Vimentin - positive +++, high, CD45 - positive +++, high, CD68 - positive +, low, CD34 - positive +++, high, CD138 - positive +++, high.

In the postoperative period for the purpose of prevention from 10/12/2013 to 10/22/2019. the patient underwent a course of antibiotic therapy. A short course of systemic corticosteroids was performed to treat the underlying disease. From 10/12/2019 until 12/30/2019 the patient was prescribed long-term use of fluticasone furoate insufflation, 1 dose in each half of the nose 1 time per day (daily dose 27.5 mcg).

During dynamic observation, recurrence of the polypous process was observed at a period of 18 months. The patient was again prescribed a short course of systemic corticosteroids and prolonged use of fluticasone furoate insufflation, 1 dose in each half of the nose 1 time per day for 6 months. The patient is under our supervision, the relapse of the polypous process for 3 years was not observed.

Clinical example: Patient Z., 54 years old, h / c No. 7945/359. He was hospitalized in the ENT department of diseases of the 3rd clinic of the Tashkent Medical Academy from 05.23.2019. on 05/27/2019 with a diagnosis of Polypous rhinosinusitis.



Complaints at admission: difficulty in nasal breathing, nasal discharge, headaches, general weakness.

From the anamnesis: considers himself ill for 3 years. Associates his illness with frequent colds. In the past 2 years, the patient was conservatively treated by ENT doctors at the place of residence, but did not receive satisfaction. In connection with the above complaints, the patient turned to the ENT clinic of the 3rd clinic of the Tashkent Medical Academy, where he was examined and hospitalized in the ENT department of diseases on 05.24.2019.

The general condition of the patient is relatively satisfactory. Consciousness is clear. Skin and visible mucous membranes of normal color. Peripheral nodes are not palpable. With auscultation of the lungs, vesicular breathing. Heart sounds are rhythmic, blood pressure 120/80 mm RT. Art. Pulse - 82 beats. per minute. The abdomen is soft, painless. The liver and spleen are not palpable. Stool and urination are normal.

Status localis: no facial deformity. With anterior rhinoscopy, the nasal mucosa is pale pink, purulent mucous discharge in both nasal cavities. A dense, fibrous polyposis formation in the right nasal cavity is determined, 1/3 of the obstructing nasal cavity. Nasal septum in the midline.

Patient examination results: CT of the paranasal sinuses - CT signs of polypous dimming of both the maxillary sinuses.

By decision of the council 05.24.2019 operation performed: bilateral maxillary sinusotomy. Polyps were removed during surgery, but based on the principles of functional endoscopic sinus surgery, a polypous-modified mucous membrane of the nose and paranasal sinuses remained. Remote polyps were single with clear contours, dense texture, smooth surface, pale.

The results of histological examination No. 1376-83: Chronic polyposis sinusitis, inflammatory polyp.

Morphometry results: polyp with a predominance of neutrophilic infiltration.

The results of immunohistochemical studies: Gordon-Sweet staining - a dense connection of reticular fibers is noted, VEGF is positive ++, moderate, Ki-67 is positive +, low, Vimentin is positive +++, high, CD45 is positive +++, high, CD68 - positive +, low, CD34 - positive +++, high, CD138 - positive +++, high.

In the postoperative period for the purpose of prevention from 05.24.2019. until June 4, 2019 the patient received a course of antibiotic therapy and insufflation of intranasal corticosteroid. For the treatment of the underlying disease from 06/04/2019. December 12, 2019 the patient was prescribed long-term use of low doses of macrolide roxithromycin 75 mg, 1 tablet 1 time per day inside after meals according to the scheme for 2 months.

The patient is under our supervision, with dynamic observation, the relapse of the polypous process for 3 years was not observed.

## **Conclusions.**

Summarizing this study, it follows that morphological and immunohistochemical studies revealed the formation of irreversible changes in the nasal mucosa, leading to the loss of its functional activity and creating the prerequisites for accelerated relapse. The revealed polymorphism of the structure of the ciliary epithelium is of great practical importance, since at present most endonasal operations are performed without taking into account the features of the morphological structure of the mucous membrane of the nasal cavity. Often, in order to create a wide message of the affected sinus with the nasal cavity, a large volume of functionally important sections of the ciliated epithelium is removed.

Given the results of morphological studies, we can say that the separation of polyps according to histological structure into "eosinophilic" and "neutrophilic" forms is justified, as

it is confirmed by the predominance of a particular cellular composition. From the obtained data it is seen that the samples of all patients (100%) with “eosinophilic” forms of polyps and most (83.8%) of “neutrophilic” had expression of proteins detected by Gordon-Sweet color, which indicates a high activity of reticular formation fibers in the tissues. The study of the expression of the VEGF marker in the tissue of “eosinophilic” and “neutrophilic” polyps was high only in some samples, and in the rest the expression of this gene was weak or moderate. However, the stromal vasculature in all samples was well developed and consisted of a large number of blood vessels of different sizes, inside which there were a large number of red blood cells. This fact indicates a good blood supply to the tissue of polyps of both forms.

The detection of VEGF expression in mesenchymal clusters indicates the formation of endothelial cells, which will subsequently participate in the formation of neoangiogenesis. In the absence of a developed vasculature, it is possible to form new vessels. The appearance of new blood vessels in the tissue of the  $\rightarrow$  polyp in the future can contribute to the formation of fibrous tissue. A positive reaction of the Ki-67 proliferation marker in polyp tissue indicates active deletion of cellular elements.

In both forms of nasal polyps, mesenchymal cells are present in large numbers in the epithelium itself, especially in the “eosinophilic” forms and in the stroma. Vimentin is a marker of mesenchymal cells, in endothelial and mesenchymal cells it is presented in the form of clusters.

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