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Research Article

IMMUNOHISTOCHEMICAL INDICATORS OF CHRONIC POLYPOUS RHINOSINUSITIS

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Dr. Prof. Ulugbek Khasanov
Dsc, Professor, Tashkent Medical Academy, Uzbekistan

ABSTRACT

A 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 of patients with "neutrophilic" polyps. The presence of high expression of vimentin indicates high activity of mesenchymal cells. In prognostic terms, these changes indicate future relapses. Identification of the CD68 marker; its low and moderate expression ¬may indicate a low participation of macrophages in the formation of nasal polyps of both forms. The presence of single stained cells in mesenchymal accumulations indicates low phagocytic activity. High and moderate expression of CD45 in - mesenchymal accumulations located in "eosinophilic" polyps confirms our assumption that these mesenchymal accumulations are the "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 absence of expression of this marker in clusters of mesenchymal formations, as well as average expression in cells located in the stroma, possibly indicate the origin of the latter from active mesenchymal cells. In 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 - accumulations. A well-developed vascular system is also observed near the epithelium and in the stroma. An increase in the number of vessels is ¬a sign of relapse, and an increase ¬in the number of newly formed vessels is prognostically ¬unfavourable and indicates the occurrence of a relapse.

KEYWORDS

Nasal polyp, cytokines, marker, expression, cell, stroma.

INTRODUCTION

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CPRS based on the materials of the International Consensus Conference on Nasal Polyps [5] and position papers on rhinosinusitis and nasal polyps of the European Academy of Allergy and Clinical Immunology (EAACI) – Position Paper on Rhinosinusitis and Nasal Polyps (EP3OS, 2007) [2] is defined as chronic productive Th -2-dependent eosinophilic inflammation, leading to remodeling of the nasal mucosa, its swelling, followed by prolapse of the mucous membrane and the formation of nasal polyps [1-4]. However, scientists in East Asia believe that in most cases, CPRS develops against the background of Th-1-dependent inflammation, which leads to the formation of polyps in the nose and paranasal sinuses [6].

The key role of eosinophil migration, regulated by cytokines, is widely accepted [10]. The cytokine profile of nasal polyp tissue is a mixture of Th1 and Th2 types [7-10]. Cytokines in nasal polyps with increased concentration or mRNA expression include Thl cytokines such as IL-1, INF-γ, IL-12, TNF-α, and Th2 cytokines such as IL-4, IL-5, IL-6, IL-13, and GM-CSF, IL-3, which are synthesized by both Thl and Th2 cells, and, finally, TGF-β, which is a powerful inducer of myofibroblasts [11]. Enhanced expression of IL-2 and IL-5 receptors has also been reported [12]. In nasal polyps, the following may be elevated: adhesion molecules such as ICAM-1 (intercellular adhesion molecule-1), VCAM-1 (vascular adhesion molecule-1), growth factors such as vascular permeability/vascular endothelial growth factor (VPF/VEGF)), which are major inducers of angiogenesis and capillary 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 such like IL-11 and IL-17, registered in CHC/NP (chronic hyperplastic sinusitis/nasal polyps) [13].

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 [14-17]. It has been suggested that atopy does not determine the presence of cytokines in the NP [18]. However, there are also reports of finding differences between allergic and non-allergic nasal polyps. Yes, DL Hamilos (2011), when examining patients with nasal polyps or CHC/NP, found that allergies were characterized by higher levels of IL-4, IL-5 and IL-13, and non-allergic cases had higher levels of INF-γ, GM-CSF and TNF-α [19]. In patients with atopic nasal polyps, a significant correlation was also found between IL-5 and IgE concentration in tissues [20].

Eosinophilic infiltration, a key aspect of the pathogenesis of CPRS, depends on the physiological effects of a number of chemokines and adhesion molecules [21]. These include, first of all, IL-5, as well as eotaxin, RANTES, vascular endothelial adhesion molecules - VCAM-1, vascular endothelial growth factor - VEGF, etc. [7].

Chemokines (chemoattractant cytokines) affect monocytes, eosinophils, basophils, causing allergic and non-allergic inflammation [3], and their main sources are structural cells, such as endothelial cells, epithelial cells and fibroblasts [2]. Th1 cytokines, such as TNF and IL-1, can also initiate chemokine production [1]. In addition, there is evidence that in nasal polyps, not only Thl, but also Th2 cytokines can regulate the production of chemokines [22-24]. Various chemokines such as IL-8 [25], RANTES [2] and eotaxin [8] are believed to 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 [26]. It may also inhibit IgE production and histamine release. According to J. B. _ Watelet et al. (2004) , nasal neutrophilia correlates with IL-8 levels [27]. V. _

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Kirtsreesakul et al (2005) believe that an increase in IL-8 levels may serve as a sign of neutrophilic inflammation [28]. In this regard, studying the amount of IL-8 will indicate the state of neutrophilia in the stroma of polyps.

One of the most powerful stimulators of eosinophil migration is vascular endothelial growth factor (VEGF) [29]. This vasodilator promotes swelling 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 endothelial cells of blood vessels. Expression of VEGF was also detected in epithelial cells of nasal polyps [30].

S. _ Hu et al. (2014) demonstrated increased expression of VEGF in nasal polyps, supporting a potential role for VEGF in the development of CPRS [31]. The authors used a culture of nasal epithelial cells from nasal polyps and showed the active production of huge amounts of VEGF in them in response to hypoxia [24]. They assumed that this was the main reason formation polyps in the middle meatus, where most of the nasal passages open paranasal sinuses and where is minimal swelling mucous membrane can lead to complete occlusion , the cause of hypoxia in the sinus [31].

Thus, an analysis of the literature has shown that the key point in the pathogenesis of CPRS is immunological disorders, including Thl and Th2 cytokines (IL-2, IL-4, IL-8), the study of which will provide the necessary data on the features of the course of the polyposis process.

METHODS

In accordance with the purpose of the study and to fulfill the assigned tasks, clinical studies were conducted in 150 patients with CPRS 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, and immunohistochemical studies.

RESULTS AND DISCUSSIONS

As noted during a morphological study when stained with heme- ¬toxylin and eosin, the stroma of nasal polyps was covered with stratified ¬ciliated epithelium with clear contours of goblet cells; in some cases, the stratified ciliated epithelium gradually transformed ¬into squamous epithelium, followed by keratinization and desquamation.

Tissue loosening, obvious degradation and low cellularity are noted . ¬With "eosinophilic" polypous rhinosinusitis, the edema spreads in the form of vacuoles (Fig. 1). The edema consists of infiltrated tissue and fluid.

Silver impregnation (Gordon-Sweet staining) of nasal polyp tissue was performed to determine the nature of the structural organization of the reticular fibers of the stroma (Fig. 2). The reticular fibers, which connect with each other and create the framework of the polyp stroma, have been destroyed and degraded, and swelling of the vascular endothelium is noted. In the stroma of polyps of patients with "eosinophilic" polypous rhinosinusitis, strong protein expression 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 other (66.7%) samples the expression was high (Table 2).

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Table 1

Frequency of occurrence of patients depending on the histological structure of polyps and the expression of markers of proliferation and angiogenesis

Markers growth factors	Form, (n=79)					
	Eosinophilic, % (n =48)			Neutrophilic, % (n =31)		
	gene expression level in cells			gene expression level in 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 in Table 1 it is clear that samples of all patients (100%) with "eosinophilic" forms of polyps and 83.8% with "neutrophilic ¬" forms had the expression of proteins detected by Gordon-Sweet staining, this indicates a high activity of formation of reticular fibers in tissues.

When stained with hematoxylin and eosin ¬, only lymphocytic accumulations are detected; the use of an immunohistochemical ¬research method makes it possible to detect 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 marker VEGF is a vascular endothelial growth factor and nitrooxysynthetase receptor. The VEGF family of

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proteins, which are structurally related to each other, together with the receptor, play a role in the development and regulation of the activity of blood and lymphatic vessels. These proteins are expressed by endothelial cells, influence the development of 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 of 39.6% of patients and weak in 20.8% of samples, and in the stroma this marker was found only in 20.8% of patients. Moreover, 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, within which there are a large number of red blood cells. This circumstance indicates a good blood supply to the tissue of "eosinophilic ¬" polyps, which determines the allergic background of the disease, which occurs with profuse mucus production.

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

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

In the tissues of "neutrophilic" polyps, you are less likely ¬to have large blood vessels. 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 ¬lip tissue may further contribute to the formation of fibrous tissue.

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

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

In the stroma of "neutrophilic" polyps, there is an accumulation of plasma ¬cells, creating a ring called the "growth zone". This ¬sign indicates an unfavorable prognosis for the course of the disease ¬(Fig. 9, 10) . Mesenchymal stem cells are undifferentiated (immature) cells found in many types of multicellular organisms that are capable of self-renewing, forming new stem cells, dividing through mitosis and differentiating into specialized cells, that is, turning into cells of various organs and tissues. As can be seen from Figures 9 and 10 and Table 1, in both forms of nasal polyps, mesenchymal cells are present in large numbers in the epithelium itself, especially in "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).

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

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

Also, the accumulation of mesenchymal cells in both forms of polyps is determined. These formations are the main growth areas 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 polyp growth. With "eosinophilic" polyps, these formations were observed most often compared to "neutrophilic" polyps. This may indicate that the reason for the frequent recurrence of "eosinophilic" polyps is associated with a large number of "zones" of growth.

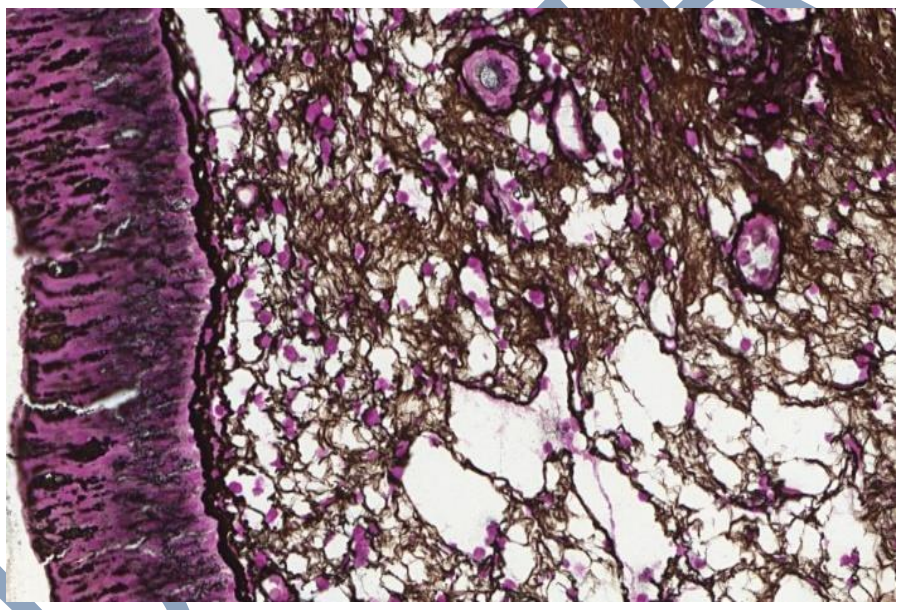

Fig . 1 . Patient Ch., 69 years old, case history No. 14850/754. D/s: Chronic polypous rhinosinusitis "eosinophilic" form . Swelling, degradation and destruction of reticular fibers are noted . Immunohistochemical staining.
Uv. OK. 10x, vol. 40x.

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2771-2265)
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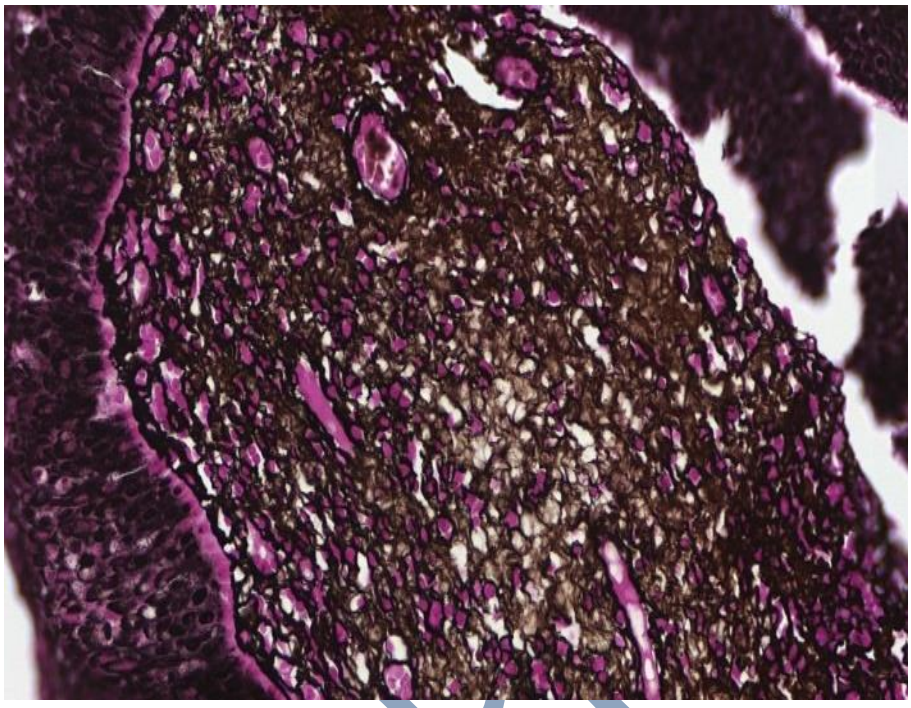
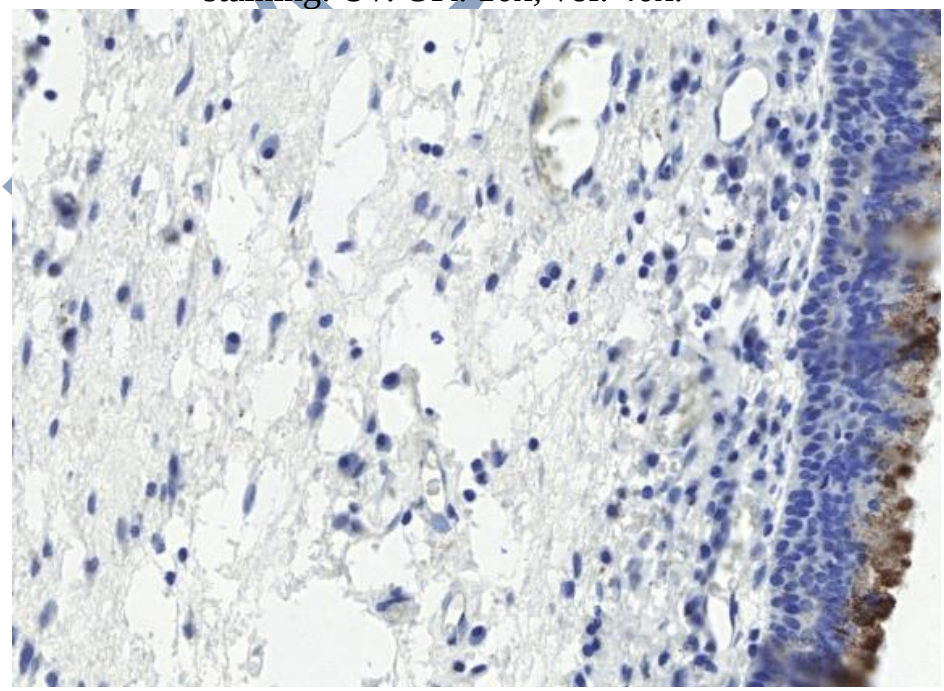


Rice. 2. Patient Z., 54 years old, case history No. 7945/359. D/s: Polypous rhinosinusitis " neutrophilic " form . There is a tight connection of reticular fibers . Immunohistochemical staining. Uv. OK. 10x, vol. 40x.



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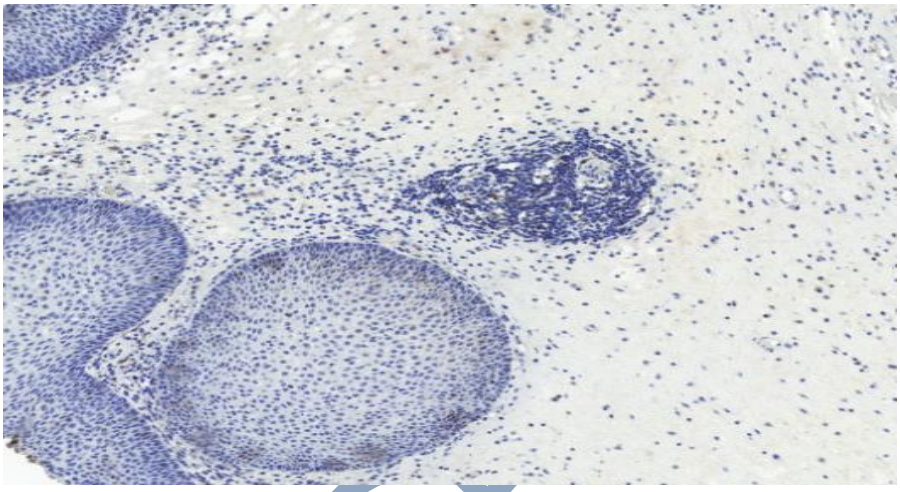
VOLUME 04 ISSUE 11 Pages: 34-53
SJIF IMPACT FACTOR (2021: 5.456), (2022: 5.681), (2023: 6.591)
OCLC –1242424495

Fig . 3. Patient Ch., 69 years old, case history No. 14850/754. D/s: Chronic polypous rhinosinusitis “eosinophilic ” form . High expression of VEGF (+++). Immunohistochemical staining. Uv. OK. 10x, vol. 40x.



Rice. 4 . Patient Z., 54 years old, case history No. 7945/359. D/s: Polypous rhinosinusitis "neutrophilic" form . Moderate VEGF expression (++). Immunohistochemical staining. Uv. OK. 10x, vol. 20x.

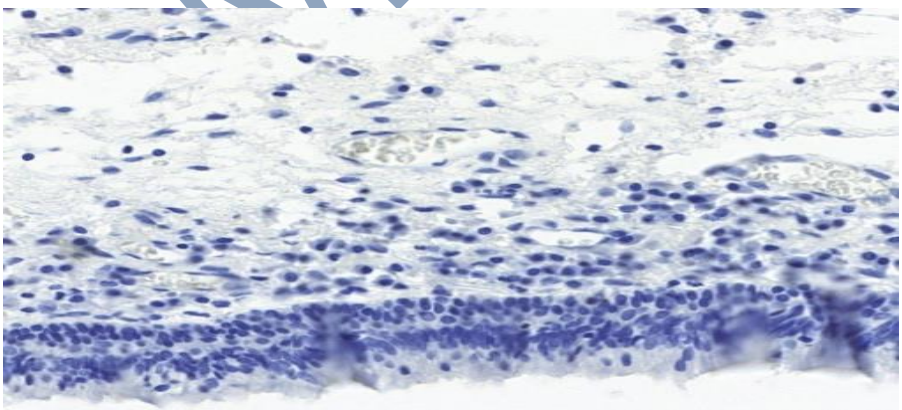


Fig . 5 . Patient Ch., 69 years old, case history No. 14850/754. D/s: Chronic polypous rhinosinusitis “neutrophilic” form . Low expression of Ki -67 (+). Immunohistochemical staining. Uv. OK. 10x, vol. 90s

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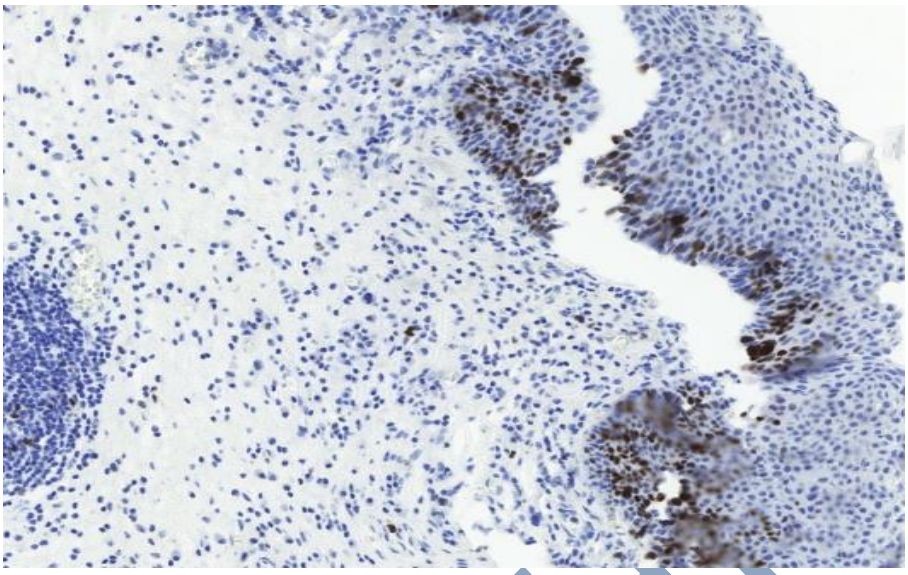
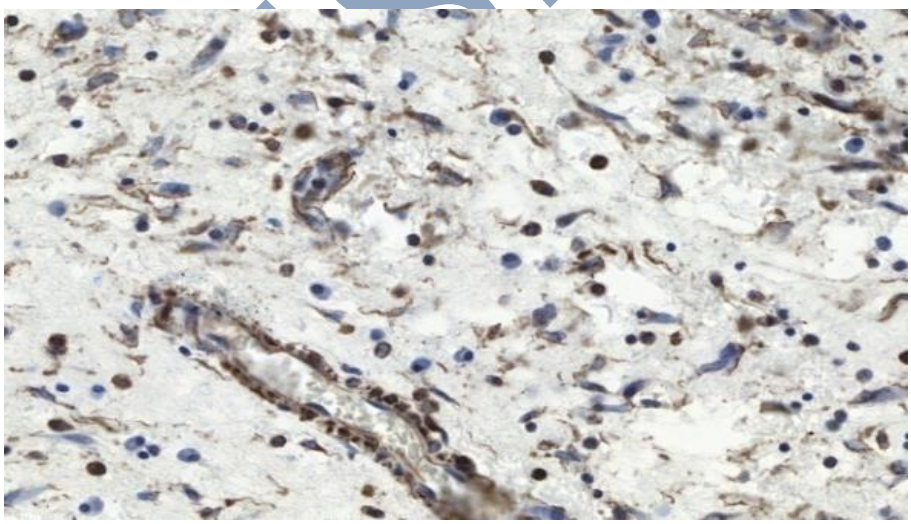
OCLC –1242424495



Rice. 6. Patient Z., 54 years old, case history No. 7945/359. D/s: Polypous rhinosinusitis "eosinophilic " form . High expression of Ki -67 (+++). Immunohistochemical staining. Uv. OK. 10x, vol. 90s



Rice. 7 . Patient Ch., 69 years old, case history No. 14850/754. D/s: Chronic polypous rhinosinusitis "eosinophilic " form . High expression of Vimentin (+++). Immunohistochemical staining. Uv. OK. 10x, vol. 40x.

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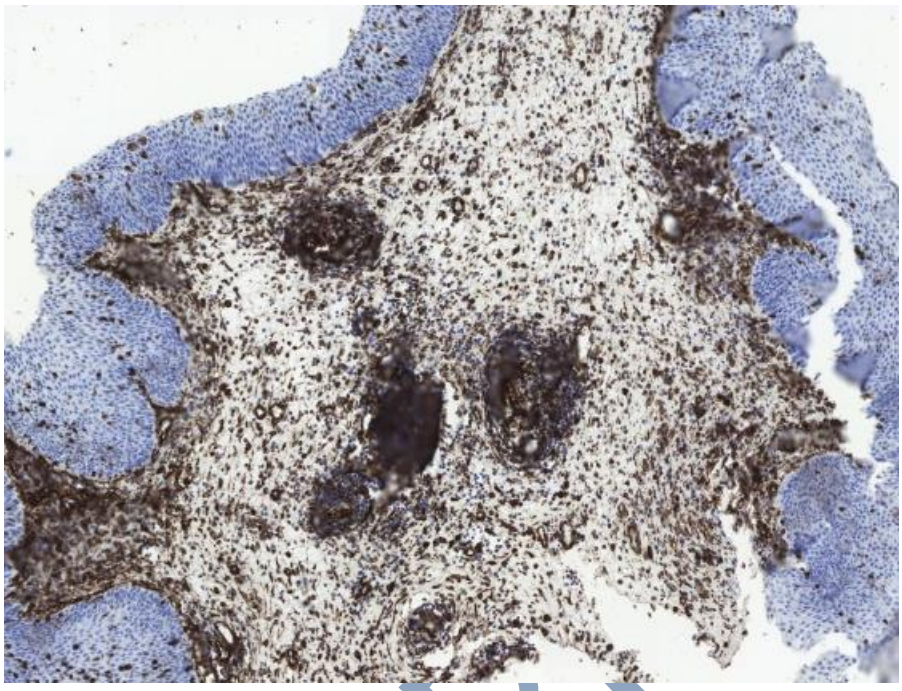
OCLC –1242424495



Rice. 8. Patient Z., 54 years old, case history No. 7945/359. D/s: Polypous rhinosinusitis "neutrophilic" form . High expression of Vimentin (+++). Immunohistochemical staining. Uv. OK. 10x, vol. 20x.

In preparations with the detection of the CD68 marker, 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 accumulations indicates low phagocytic activity.

table 2

Frequency of occurrence of patients depending on the histological structure of polyps and expression of clusters of differentiation (CD)

Markers CD	Shape, (n=79)					
	Eosinophilic, % (n =48)			Neutrophilic, % (n =31)		
	gene expression level in cells			gene expression level in cells		
	< 10%	>10%	> 50%	< 10%	>10%	> 50%

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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 high and moderate expression of CD45 in ¬mesenchymal accumulations located in "eosinophilic" polyps (from 39.6% to 60.4% of samples), which confirms our assumption that these mesenchymal accumulations are the "growth zone" of formations.

In "neutrophilic" forms, the number of samples with positive staining of this marker was smaller (from 16.1% to 32.2%).

Figures 13, 14 and Table 2 present the results of identifying high and moderate expression of CD138 in mature epithelial ¬cells in all tissue samples of both forms of polyps and the absence of expression of this marker in clusters of mesenchymal formations, as well as average expression in cells located in the stroma, perhaps this indicates the origin of the latter from active mesenchymal cells.

Determining the number of vessels in one field of view is ¬a prognostic sign of the rate of recurrence, since an increase in ¬the number of newly formed vessels during tumor growth is prognostically ¬unfavorable and indicates the imminent occurrence 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 ¬accumulations. A well-developed vascular system is also observed near the epithelium and in the stroma.

With 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

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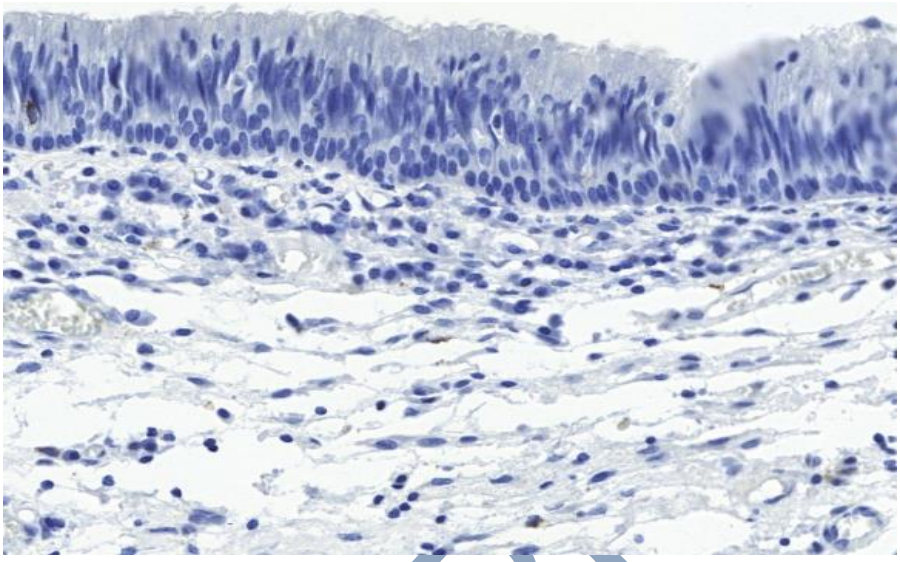
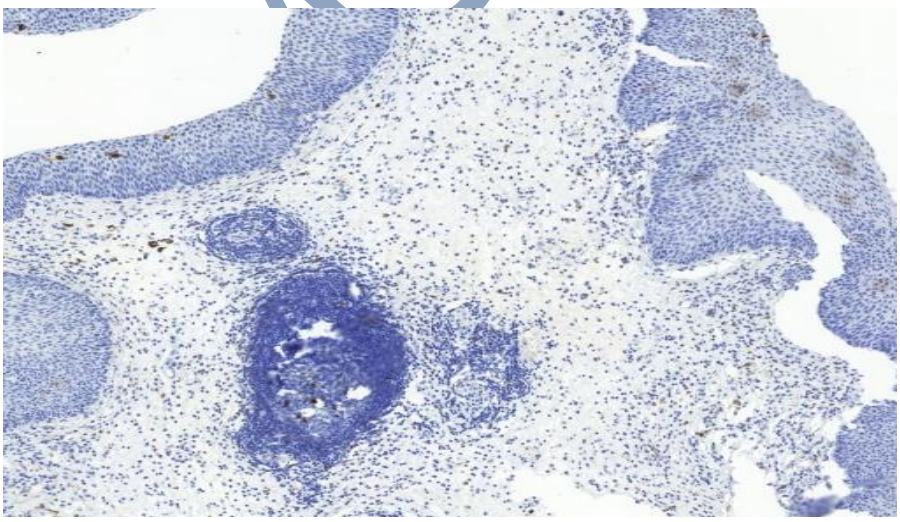
of CD34 (16.7%) was detected in both the mucosa and stroma.



Rice. 9 . Patient Ch., 69 years old, case history No. 14850/754. D/s: Chronic polypous rhinosinusitis "eosinophilic" form . Low expression of CD 68 (+). Immunohistochemical staining. Uv. OK. 10x, vol. 40x .



Rice. 10 . Patient Z., 54 years old, case history No. 7945/359. D/s: Polypous rhinosinusitis "neutrophilic" form . Low expression of CD 68 (+). Immunohistochemical staining. Uv. OK. 10x, vol. 20x

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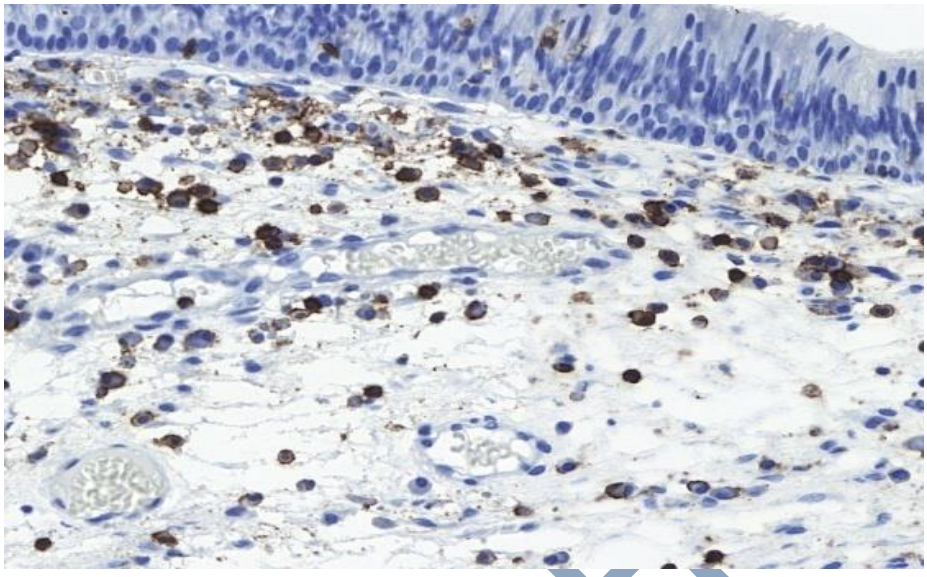
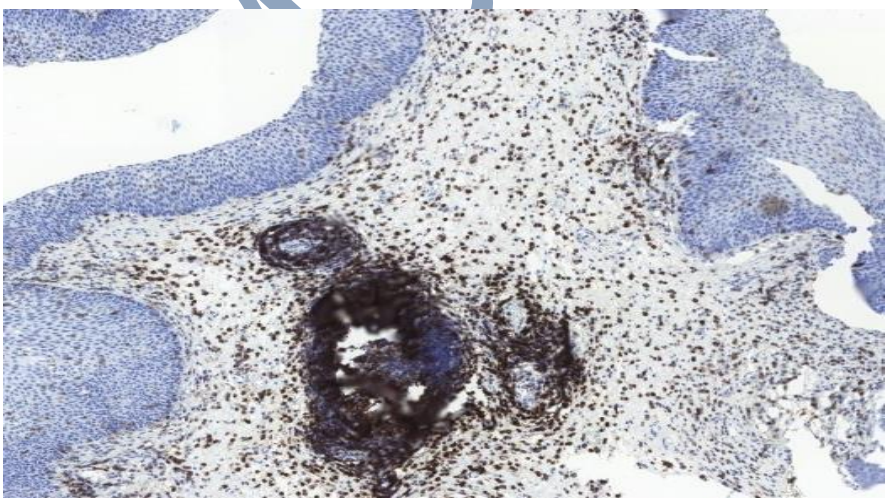
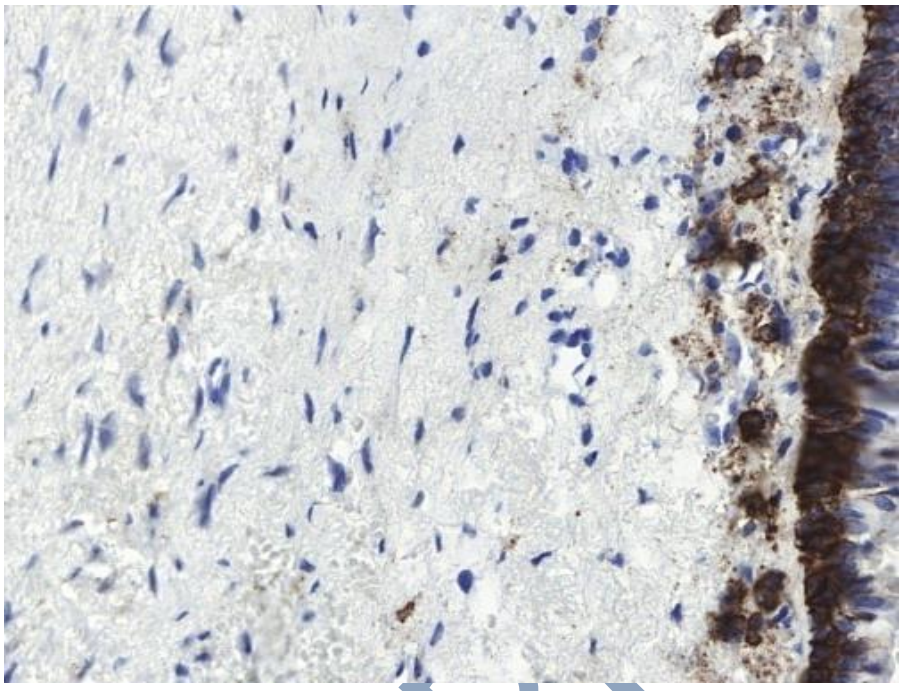


Rice. 11 . Patient Ch., 69 years old, case history No. 14850/754. D/s: Chronic polypous rhinosinusitis "eosinophilic" form . High expression of CD 45 (+++). Immunohistochemical staining. Uv. OK. 10x, vol. 40x.

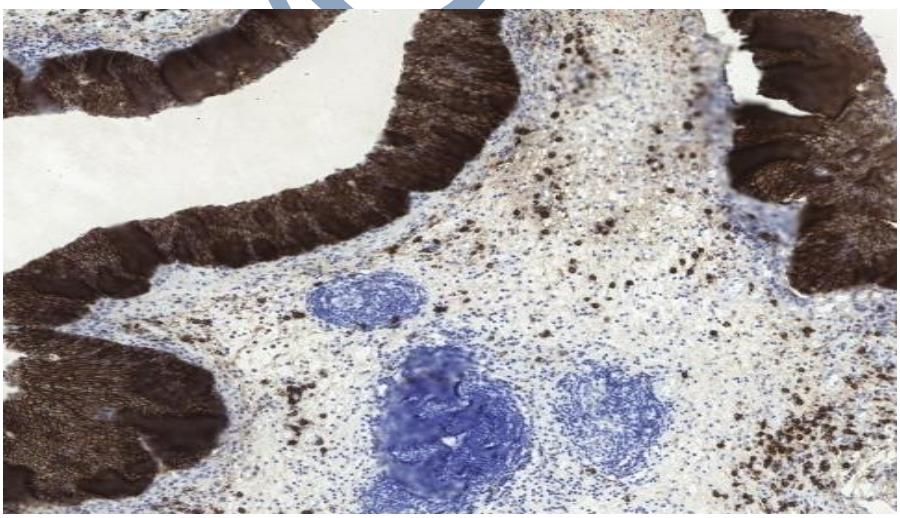


Rice. 12 . Patient Z., 54 years old, case history No. 7945/359. D/s: Polypous rhinosinusitis "neutrophilic" form . High expression of CD 45 (+++). Immunohistochemical staining. Uv. OK. 10x, vol. 20x.

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2771-2265)
VOLUME 04 ISSUE 11 Pages: 34-53
SJIF IMPACT FACTOR (2021: 5.456), (2022: 5.681), (2023: 6.591)
OCLC –1242424495

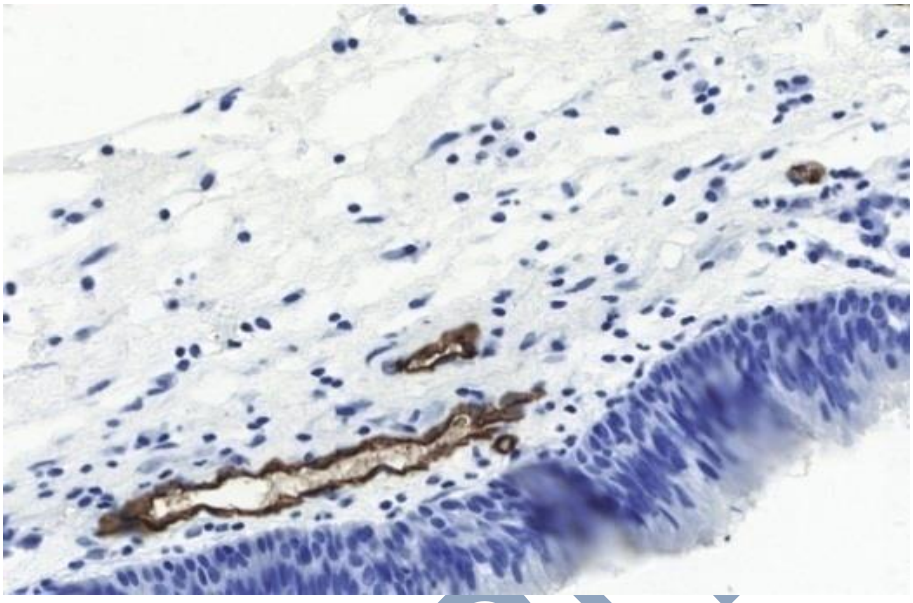


Rice. 13 . Patient Ch., 69 years old, case history No. 14850/754. D/s: Chronic polypous rhinosinusitis "eosinophilic" form . High expression of CD 138 (+++). Immunohistochemical staining. Uv. OK. 10x, vol. 40x .

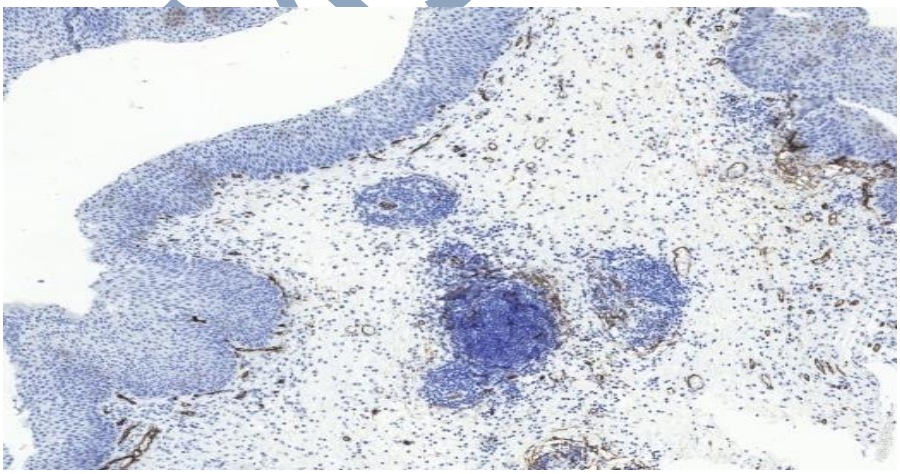


Rice. 14 . Patient Z., 54 years old, case history No. 7945/359. D/s: Polypous rhinosinusitis "neutrophilic" form . High expression of CD 138 (+++). Immunohistochemical staining. Uv. OK. 10x, vol. 20x.

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2771-2265)
VOLUME 04 ISSUE 11 Pages: 34-53
SJIF IMPACT FACTOR (2021: 5.456), (2022: 5.681), (2023: 6.591)
OCLC –1242424495



Rice. 15 . Patient Ch., 69 years old, case history No. 14850/754. D/s: Chronic polypous rhinosinusitis "eosinophilic" form . Moderate expression of CD 34 (+++). Immunohistochemical staining. Uv. OK. 10x, vol. 40x.



Rice. 16 . Patient Z., 54 years old, case history No. 7945/359. D/s: Polypous rhinosinusitis "neutrophilic" form . High expression of CD 34 (+++). Immunohistochemical staining. Uv. OK. 10x, ob.20x .

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2771-2265)
VOLUME 04 ISSUE 11 Pages: 34-53
SJIF IMPACT FACTOR (2021: 5.456), (2022: 5.681), (2023: 6.591)
OCLC –1242424495

Thus, both the mucous tissue and the stroma of polyps differ in the form of CPRS, which implies ¬different tactics for managing patients with this pathology. The immunohistochemical study revealed the formation of difficult-to-reversible changes in the nasal mucosa, leading to the loss of its functional activity and creating the preconditions for frequent relapses of CPRS.

Clinical example: Patient Ch., 69 years old, case history No. 14850/754. He was undergoing inpatient treatment in the department of ENT diseases of the 3rd clinic of the Tashkent Medical Academy from 10/09/2019. until 10/14/2019 with a diagnosis of Chronic polypous rhinosinusitis. Complaints upon admission: difficulty in nasal breathing, lack of sense of smell, mucous discharge from the nose, sneezing, itching in the nose, headaches, general weakness.

From the anamnesis: he considers himself sick for 9 years. He associates his illness with frequent colds and allergies. In the last 5 years, the patient was operated on 3 times by ENT doctors at his place of residence, and polypotomy was performed. In connection with the above complaints, the patient went to the ENT clinic of the 3rd clinic of the Tashkent Medical Academy, where he was examined and hospitalized in the department of ENT diseases on October 09, 2019.

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

Status localis : facial deformity none. Anterior rhinoscopy reveals hyperemia of the nasal mucosa and mucous discharge in both nasal cavities. Transparent polypous formations are identified, completely obstructing both nasal cavities. Nasal septum in the midline.

Results of the examination of the patient: CT scan of the paranasal sinuses - CT signs of polypous darkening of both sides of the maxillary, ethmoid, frontal, main sinuses and nasal cavity.

By decision of the council on October 10, 2019. The operation was performed: Bilateral polypotomy, maxillary sinusotomy, frontotomy, ethmoidotomy and sphenoidotomy. During surgery, polyps were removed, but based on the principles of functional endoscopic sinus surgery, polyposis-altered mucous membrane of the nose and paranasal sinuses was left. The removed polyps were multiple with clear contours, soft consistency, smooth surface, and transparent.

Results of histological examination No. 5613-18: Fibrous polyp with cystic changes against the background of chronic inflammation.

Morphometry results: polyp with a predominance of eosinophilic infiltration.

Immunohistochemical study results: Gordon-Sweet staining - swelling, degradation and destruction of reticular fibers are noted , VEGF indicator - positive +++, high, Ki -67 - positive +++, high , Vimentin - positive +++, high, CD 45 - positive +++, high, CD 68 - positive +, low, CD 34 - positive +++, high, CD 138 - positive +++, high.

In the postoperative period for the purpose of prevention from 10/12/2013 to 10/22/2019. The patient was given a course of antibiotic therapy. To treat the underlying disease, a short course of systemic corticosteroids was administered. From 10/12/2019 until December 30, 2019 The patient was prescribed long-

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2771-2265)
VOLUME 04 ISSUE 11 Pages: 34-53
SJIF IMPACT FACTOR (2021: 5.456), (2022: 5.681), (2023: 6.591)
OCLC –1242424495

term use of fluticasone furoate insufflation, 1 dose in each half of the nose once a day (daily ¬dose 27.5 mcg).

During dynamic observation, a recurrence of the polypous process was noted at a period of 18 months. The patient was re-prescribed a short course of systemic corticosteroids and long-term 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; there has been no relapse of the polypous process for 3 years.

Clinical example: Patient Z., 54 years old, clinical case No. 7945/359. He was hospitalized in the ENT Department of the 3rd Clinic of the Tashkent Medical Academy from May 23, 2019. until 05/27/2019 with a diagnosis of polypous rhinosinusitis.

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

From the anamnesis: he considers himself sick for 3 years. He associates his illness with frequent colds. Over the past 2 years, the patient was treated conservatively by ENT doctors at his place of residence, but was not satisfied. In connection with the above complaints, the patient went to the ENT clinic of the 3rd clinic of the Tashkent Medical Academy, where he was examined and hospitalized in the ENT diseases department on May 24, 2019.

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

Status localis : facial deformity none. With anterior rhinoscopy, the nasal mucosa is pale pink in color, purulent mucous discharge in both nasal cavities. A dense, fibrous polypous formation is detected in the right nasal cavity, occluding 1/3 of the nasal cavity. Nasal septum in the midline.

Results of the examination of the patient: CT scan of the paranasal sinuses - CT signs of polypous darkening of both maxillary sinuses.

By decision of the council on May 24, 2019. An operation was performed: Bilateral maxillary sinusotomy. During surgery, polyps were removed, but based on the principles of functional endoscopic sinus surgery, polyposis-altered mucous membrane of the nose and paranasal sinuses was left. The removed polyps were single with clear contours, dense consistency, smooth surface, and pale.

Results of histological examination No. 1376-83: Chronic polypous sinusitis, inflammatory polyp.

Morphometry results: polyp with a predominance of neutrophilic infiltration.

Immunohistochemical study results: Gordon-Sweet staining - tight junction of reticular fibers is noted , VEGF indicator - positive ++, moderate, Ki -67 - positive +, low, Vimentin - positive +++, high, CD 45 - positive +++ , high, CD 68 - positive +, low, CD 34 - positive +++, high, CD 138 - positive +++, high.

In the postoperative period for the purpose of prevention from May 24, 2019. until 06/04/2019 The patient received a course of antibiotic therapy and insufflation of intranasal corticosteride. For the treatment of the underlying disease from June 4, 2019.

INTERNATIONAL JOURNAL OF MEDICAL SCIENCE AND PUBLIC HEALTH RESEARCH (ISSN – 2771-2265)
VOLUME 04 ISSUE 11 Pages: 34-53
SJIF IMPACT FACTOR (2021: 5.456), (2022: 5.681), (2023: 6.591)
OCLC –1242424495

on December 29, 2019, the patient was prescribed long-term use of low doses of the macrolide roxithromycin 75 mg, 1 tablet 1 time per day orally after meals according to the regimen for 2 months.

The patient is under our supervision; during dynamic observation, no relapse of the polyposis process was observed for 3 years.

CONCLUSION

Summarizing this study, it follows that a morphological and immunohistochemical study revealed the formation of irreversible changes in the nasal mucosa, leading to the loss of its functional activity and creating the preconditions for accelerated ¬relapse. The revealed polymorphism in the structure of the ciliated epithelium is of great practical importance, since currently most endonasal operations are performed without taking into account the peculiarities of the morphological structure of the nasal mucosa. Often, in order to create a wide connection between the affected sinus and the nasal cavity, a large volume of functionally important areas of the ciliated epithelium is removed.

Taking into account the results of the morphological study, we can say that the division of polyps according to their histological structure into “eosinophilic” and “neutrophilic” forms is justified, as it is confirmed by the predominance of one or another cellular composition. From the data obtained it is clear that the samples of all patients (100%) with “eosinophilic” forms of polyps and the majority (83.8%) of “neutrophilic ¬” ones had the expression of proteins detected by Gordon-Sweet staining, this indicates a high activity of the formation of reticular fibers in fabrics. A 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, within which there were a large number of red blood cells. This circumstance indicates a good blood supply to the tissue of polyps of both forms.

Detection of VEGF expression in ¬mesenchymal accumulations indicates the formation of endothelial cells, which will subsequently participate in the formation of neoangiogenesis ¬. In the absence of a developed vascular network, it is possible to ¬form new vessels. The appearance of new blood vessels in ¬lip tissue may further contribute to the formation of fibrous tissue. A positive reaction of the proliferation marker Ki-67 in polyp tissue indicates active division ¬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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VOLUME 04 ISSUE 11 Pages: 34-53
SJIF IMPACT FACTOR (2021: 5.456), (2022: 5.681), (2023: 6.591)
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VOLUME 04 ISSUE 11 Pages: 34-53
SJIF IMPACT FACTOR (2021: 5.456), (2022: 5.681), (2023: 6.591)
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