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# THE USE OF IMMUNOHISTOCHEMICAL METHODS IN THE STUDY OF MORPHOFUNCTIONAL FEATURES OF THE HUMAN PARANASAL SINUSES: LITERATURE REVIEW

## ZASTOSOWANIE METOD IMMUNOHISTOCHEMICZNYCH W BADANIU MORFOFUNKCJONALNYCH CECH ZATOK PRZYNOSOWYCH U CZŁOWIEKA: PRZEGLĄD PIŚMIENICTWA

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### ABSTRACT

**Introduction:** Chronic inflammatory diseases of the mucous membrane of the nose, paranasal sinuses, and pharynx are the most widespread pathology of the upper airways. The thorough study of the features of the organization of local immune protection of the mucous membrane of the paranasal sinuses is crucial for the deep understanding of the causes of the onset and development of this and other pathologies of the paranasal sinuses, the choice of methods of diagnostics and treatment. Consequently, immunohistochemical studies are of great potential and have become preferable for great number of researchers.

**The aim:** The paper was aimed at the analysis of the publications on the use of immunohistochemical methods in the study of the structural and functional features of the paranasal sinuses.

**Materials and methods:** The bibliosemantic method has been used during the study. Findings of the current research works on the use of immunohistochemical methods in the study of the paranasal sinuses have been analyzed.

**Review:** The findings of the analysis shows that the use of immunohistochemical methods in the otorhinolaryngology is becoming more and more popular in the study of both morphofunctional features of the paranasal sinuses and in various experimental studies.

**Conclusion:** The use of immunohistochemical methods in the study of the paranasal sinuses in both clinical otorhinolaryngology and theoretical morphology is relevant to date and is considered reasonable and perspective.

**KEY WORDS:** paranasal sinuses, mucous membrane, local immune protection, immunohistochemistry

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### INTRODUCTION

Currently, paranasal sinus diseases account for about a third of all ENT-pathology. Chronic inflammatory diseases of the paranasal sinuses are the common pathology of the upper airways to date [1-4]. The thorough study of the features of the organization of local immune protection of the paranasal sinuses is crucial for the deep understanding of the causes of the onset and development of this and other pathologies of the paranasal sinuses, the choice of methods of diagnostics and treatment. Consequently, immunohistochemical studies are of great potential and have become preferable for great number of researchers.

### THE AIM

The paper was aimed at the analysis of the publications on the study of the features of the local immune protection organization of the mucous membranes of the paranasal sinuses using the immunohistochemical methods.

### MATERIAL AND METHODS

The bibliosemantic method has been used during the study. Findings of the current research works on the use of immunohistochemical methods in the study of the paranasal sinuses have been analyzed.

### REVIEW AND DISCUSSION

Immunohistochemistry is a method of identifying the exact localization of the cellular or tissue component (antigen) using the immunological and histochemical reactions; in this way the immunological analysis of the tissue sections or cytological material is carried out in conditions of preservation of the morphology of the cells.

Currently, immunohistochemical methods are widely used in various biological studies. In particular, they are successfully used in the veterinary practice. Immunohistochemistry is an integral technique in many veterinary

laboratories for diagnostic and research purposes. In the last decade, the ability to detect antigens (Ags) in tissue sections has improved dramatically, mainly by countering the deleterious effects of formaldehyde with antigen retrieval (AR) and increasing sensitivity of the detection systems [5].

In practical medicine immunohistochemistry is a promising method of research. Immunohistochemical methods can have a decisive role in establishing of the histogenesis of tumors, differentiation of various tissue components of compound tumors, prognostic assessment of the progress of oncological pathology and the choice of treatment. If there is a difficulty in determining the histogenetic appropriateness of tumor tissue, then immunohistochemical studies permit to evaluate the organospecificity of the remote metastases. They are conducted using the antibodies, which specify the antigenic properties of the cells of different organs: PSA antibodies detect prostate cancer; presence of receptors to estrogens and progesterone in the tumor tissue presupposes metastases from the mammary gland or endometrium; antibodies to thyroglobulin are revealed in the tumor cells of the follicular thyroid cancer, etc. [6]. IGH is used to define the markers of proliferation in the thyroid carcinoma [7]. It is the immunohistochemistry that is often crucial in the diagnosis of breast tumors. Noteworthy that after immunohistochemical study the primary histological diagnosis changes in 20%-40% of cases, and determination of the expression of estrogen and progesterone receptors in breast cancer permits to decide the further management [8].

Since immunohistochemical study allows carrying out differential diagnostics of tumor processes and enables to assess the malignant potential of each neoplasm, it is essential for the oncootorhinolaryngology. Diagnosis and timely treatment of patients with inverted papilloma and cancer of the nasal cavity and paranasal sinuses is of significant clinical interest. The use of immunohistochemistry in oncootorhinolaryngology permits early detection of benign tumors and initial stages of malignant processes, to determine malignant potential of these tumors, to predict the progress of the disease and to define the approach to patient's management. Since the ciliary epithelium of the mucous membrane of the nasal cavity and paranasal sinuses is represented by the layers which are different in their structure of cells, and the cellular proliferation is observed only in the lower layers of the epithelium, the immunohistochemical markers are detected in 400 cells of four layers: the basal layer and the three layers, located immediately above it. Squamous cell carcinoma has a marked tissue atypia that violates the layered structure of the squamous epithelium. This makes it almost impossible to determine the cellular layers, and, therefore, 4 zones of distribution of 400 cells are explored: from the basal to the middle of the thickness of the epithelium. Ki-67 index of proliferation is used as an indicator of the proliferative activity, which is defined in each layer of cells by the percentage share of stained nuclei. P53 immunoreactivity index is calculated by the ratio of the amount of cells with the stained nuclei to the total amount of cells. The total level of the proliferative

activity of the epithelial cells in the intact epithelium is low (4.7%) and is more pronounced in papillomas of mucous membranes (25%) [9, 10].

The current publications report that the use of immunohistochemical methods is becoming more and more popular to study morphofunctional features of the paranasal sinuses and in various experimental studies. Particularly, they were successfully used to study the reaction of the glands of the maxillary sinus mucosa on the drugs action [11, 12].

The use of immunohistochemical method has found that the mucous membrane of each wall of sphenoid sinus had certain cytological features. The medial and lateral walls contain a large number of ciliated cells, whereas the goblet cells prevail on the anterior wall at different stages of secretion, and the posterior wall is characterized by the presence of the growth zones. Certain localization of the Ki-67 marker is detected in the medial and lateral walls of sphenoid sinus in elderly people. Short and long intercalated cells, located on the basal membrane, does not have or have poorly marked expression of the Ki-67 marker, while the nuclei of the microvillous and ciliated cells intensely express the Ki-67 immunohistochemical marker. In the submucous layer the endothelial cells of microvessels have enhanced Ki-67 expression, indicating about their ability to proliferation. In elderly people in the pseudostratified ciliated cylindrical epithelium with mainly goblet cells a high expression to the Ki-67 proliferation marker is detected in microvillous cells and partially in goblet cells, whilst the intercalated cells have only isolated expression of this immunohistochemical marker. Deep vegetation of the epithelial complexes into the subjacent submucous layer is detected in the growth zones of the pseudostratified ciliated cylindrical epithelium. In elderly people the enhanced expression of the Ki-67 marker is observed in both short and long intercalated and microvillous cells, and sometimes in the goblet cells. It has been established that the medial, lateral and anterior wall, that contain a large number of highly differentiated cells are characterized by the sufficiently active processes of mitosis, whereas on the posterior wall and growth zones this marker is observed only in the cells located on the basal membrane (short and long intercalated cells). This indicate that the intercalated cells are the precursor cells of the microvillous cells, and, subsequently, ciliated and goblet cells. However, the latter cells support their amount also due to the own mitosis [13-16].

The findings of the immunohistochemical studies of different areas of the mucous membrane of the human sphenoid sinus using the CD-68 marker permitted to establish the regularities of the location of intraepithelial macrophages in the pseudostratified ciliated cylindrical epithelium: most of the macrophages are located in the areas, represented by the ciliated cells. The areas, represented by the goblet cells and in the growth zones, have a smaller number of macrophage cells that, in the opinion of the authors, is explained by the immune surveillance due to the integration of multiple lymphocytes [17].

Immunohistochemical studies also have a big potential in the analysis of the state of the local immune system of the mucous membranes of the paranasal sinuses and their glandular apparatus. The analysis of the immunological protection of the paranasal sinuses is crucial for deep understanding of the causes of their inflammation, choice of the methods of diagnostics and treatment [18].

The resulting immunohistochemical studies of the mucous membrane of the maxillary sinus in sinusitis indicate about mainly B-cell composition of the lymphoid infiltration and its reactive nature. The “lymphoid nodes”-type masses are composed of CD20+ B-lymphocytes with clusters of the CD3+ T-lymphocytes at the periphery in the form of vaguely defined mantle, diffusely in the stroma of the mucous membrane mucosa and in the composition of the interepithelial lymphocytes. During the experiment application of the Sinuforte nasal phyto spray induced the change of the B- and T- lymphocytes ratio in the lymphoid infiltrates in favor of T-cells. Myeloperoxidase-positive cellular elements were found only in the foci with histologically visible eosinophilic cellular infiltration [18, 19].

In odontogenous maxillary sinusitis that lasts more than 3 months, the content of the CD4 / CD8 immunocytes in the mucous membrane of the sinuses gradually increases. In the clinical course of over 6 months the content of CD4 cells decreases and, simultaneously, the level of CD8 cells increases in both the epithelial lamina and on the surface of the mucous membrane [20].

The findings of immunohistochemical studies have revealed CD 3-positive cells in the stroma of the glands of mucous membrane of all walls of the frontal sinus, which are the elements of the local protective barrier. The largest number of the periacinar T-lymphocytes has been detected in the septum mucosa and periductal ones have been found on the inferior wall. The amount of the CD 20-positive cells is insignificant in the periacinar connective tissue of all walls. Numerous B-lymphocytes have been found in the periductal stroma of all walls, mostly in the mucosa of the anterior wall of the human frontal sinus. A significant number of plasmocytes have been detected in the periacinar stroma (the largest number were on the inferior wall) of both serous and mucous glands of the mucous membrane of the human frontal sinus. The amount of CD 138-positive cells in the periductal connective tissue was less than in the periacinar one, but in the mucous membrane of the posterior wall the number of the periductal plasmocytes was significant [21-23].

The catheterization of the human frontal sinus mucosa with the CD 68 transmembrane glycoprotein has revealed a very strong level of the marker expression by the free macrophages, which were localized diffusely in the connective tissue, surrounding the acini and ducts [24-26].

To sum up, the literature review shows that the use of immunohistochemical methods in the study of the paranasal sinuses in both clinical otorhinolaryngology and theoretical morphology is relevant to date and is considered reasonable and perspective.

## CONCLUSION

Currently, the use of immunohistochemical methods of study is of great potential for the analysis of the structural and functional features of the paranasal sinuses, state of the local immune protection of their mucous membranes and glandular apparatus that contribute to the better understanding of the causes of the onset of these masses, to determine the optimal methods of diagnostics, prophylaxis and treatment.

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