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ETIOPATHOGENETIC ASPECTS OF PRECANCEROUS DISEASES OF THE LARYNX

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Abstract. The palatine tonsils are part of a collection of lymphoid tissues that are located at the entrance to the respiratory and digestive tracts. Anatomically, the structure of their crypts greatly increases the epithelial surface area available for contact with environmental agents, which, together with their strategic location, makes the tonsils the first part of the immune system to respond to antigens [1,2,3]. Chronic tonsillitis is a very common disease among adults and children, and is also part of hereditary diseases, or so-called multifactorial diseases. In this regard, to clarify the reasons for the development of this pathology, it is not unimportant to study the heredity of the development of chronic tonsillitis [4,5]. Some researchers believe that the cause of the development of chronic tonsillitis is a hereditary factor, while others pay more attention to the genetic factor in the development of this disease [6,7].

Keywords: chronic tonsillitis, hereditary factor, genetic factor.

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ЭТИОПАТОГЕНЕТИЧЕСКИЕ АСПЕКТЫ ПРЕДРАКОВЫХ ЗАБОЛЕВАНИЙ ГОРТАНИ

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Аннотация. Небные миндалины являются частью совокупности лимфоидных тканей, которые расположены у входа в дыхательный и пищеварительный тракты. Анатомически строение их крипт значительно увеличивает площадь поверхности эпителия, доступную для контакта с агентами окружающей среды, что, наряду с их стратегическим расположением, делает миндалины первым звеном иммунной системы, реагирующим на антигены [1,2,3].

Хронический тонзиллит является очень распространенным заболеванием среди взрослых и детей, а также является частью наследственных заболеваний, или так называемых многофакторных заболеваний. В связи с этим для выяснения причин развития данной патологии немаловажным является изучение наследственности развития хронического тонзиллита [4,5]. Некоторые исследователи считают, что причиной развития хронического тонзиллита является наследственный фактор, в то время как другие уделяют больше внимания генетическому фактору в развитии этого заболевания [6,7].

Ключевые слова: хронический тонзиллит, наследственный фактор, генетический фактор.

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RELEVANCE

According to GLOBOCAN 2012 data, 600 thousand newly diagnosed cases and 300 thousand deaths from cancer of the oral cavity, hypopharynx and larynx are registered annually. In Russia in 2015, the prevalence of RG was 30.2 per 100 thousand population, 44,099 patients were registered for this pathology. The problem remains in making a diagnosis in the later stages of the disease, despite the spread of endoscopic examination techniques. Thus, according to statistics, in Russia, 39% of

laryngeal cancers are detected at stages I-II, 41% at stage II, 12% at stage IV, while within one year the mortality rate reaches 23%, 5-year survival rate for cancer detected at Stages I and II - 80-90%; when diagnosed at later stages of the disease, survival rate is halved.

According to the source "Health and Medical Statistics", the incidence of laryngeal cancer in the Republic of Uzbekistan is 1.0 per 100 thousand population. Among all newly identified patients with malignant neoplasms in 2009, the number of

which was 19,005, laryngeal cancer was diagnosed in 268, of which 197 were men, 71 were women (3:1). In 2009, 70 patients with laryngeal cancer were hospitalized at the Republican Oncology Research Center of the Ministry of Health of the Republic of Uzbekistan. The largest number of patients came from Tashkent and Fergana region: 12 (17.1%), the smallest from Namangan, Jizzakh and Samarkand regions. Patients from the Andijan region were not admitted to the Russian Cancer Research Center for treatment, although the incidence rate in this region is 1.4 per 100 thousand population.

Thus, an analysis of modern data on the prevalence of inflammatory tumor-like and tumor diseases of the larynx confirms that only malignant lesions of the larynx are sufficiently covered.

Thus, immunological studies and determination of the association of HPV and EBV will help to identify precancerous conditions of the larynx in the early stages of their occurrence with the identification of risk groups for morbidity, which will subsequently allow timely diagnosis and treatment of chronic inflammatory and tumor-like diseases of the larynx, which will significantly reduce the number of cases of GC and will improve the quality of their timely treatment, as well as the costs of complex mutilating operations for laryngeal cancer.

PURPOSE OF THE STUDY

To develop a comprehensive method for early diagnosis of laryngeal cancer in patients with precancerous diseases of the larynx.

MATERIAL AND METHODS

This study includes data from a retrospective analysis of medical histories and outpatient records of patients who were diagnosed and treated at the clinic department of the Andijan State Medical Institute for the period from 2010 to 2019. with pathology of the ENT organs. The total number of patients during the study period was 28,030, of which 22,028 were admitted on a planned basis, for emergency indications - 6,002, men - 15,608, women - 12,422, various pathological lesions of the larynx - 770 patients, of which women - 302, men - 468.

The analysis made it possible to distribute patients depending on the type of localization of the pathological process in the larynx, presented in Table 1.

The study was carried out under local anesthesia (lubrication or spraying) of the mucous membrane with a 10% lidocaine solution in a specially equipped endoscopy room. Fiberendoscopy was performed with the patient in a sitting position.

Research was carried out through natural routes (mouth, nose). No complications were observed during or after the manipulation; the manipulation was tolerated painlessly.

All preparations were subjected to morphometry. Morphometric parameters were determined by counting the number of CD-positive cells in several fields of view at magnification 400. with the derivation of the arithmetic mean. The most typical visual fields for a given preparation were selected for calculation. The work used MAbs and polyclonal antibodies with the following characteristics according to CD markers:

1. Anti-CD3 mAb, Dako; total T-lymphocyte populations;
2. MAT to CD4, Dako, T-helper subpopulations;
3. MAT to CD8, Dako, clone C8/144B, mouse anti-human, Code N1592, subpopulation of T-cytotoxic lymphocytes;
4. MAT to CD20, Dako, B-lymphocytes;
5. MAT to CD56, Dako, natural killer cells;

Immunological studies were carried out in the laboratory of Health care medical laboratories LLC (head: B.A. Abdunabiev, head of the department of immunology N. Startseva).

The following tables provide data on the localization of the pathological process depending on their development on various anatomical structures of the larynx. (Table 2.)

The larynx, as a multifunctional organ, should be studied in comparative aspects with clinical, morphological and immunological parallels, with the characteristics of various lesions and diagnostic features. Currently, there are few scientific works studying inflammatory tumor-like diseases in combination with preventive goals, as well as early diagnosis of precancerous and cancerous lesions of the larynx.

RESULTS AND DISCUSSION

The study of the morphological substrate in the study groups made it possible to determine the following morphological variants of chronic laryngitis: lymphoproliferative, myxomatous, granulating, granulomatous, papillomatous.

Table 1.

Distribution of patients depending on the type of localization of the process

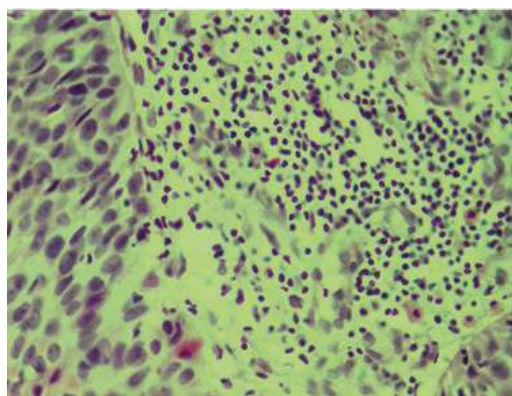
types of pathological process	all observations		localization of the pathological process					
		vestibular	middle		section subglottic			
	a6c.	%	a6c.	%	a6c.	%	a6c.	%
Polyps	48	6,2	-	-	46	95,8	2	4,2
Singing nodules	11	1,4	-	-	11	100	-	-
Cysts	21	2,7	18	85,7	3	14,3	-	-
Nonspecific granuloma	9	1,2	9	100	-	-	-	-
Inflammatory and tumor processes	681	88,4	295	43,3	306	44,9	80	11,7

Table 2.

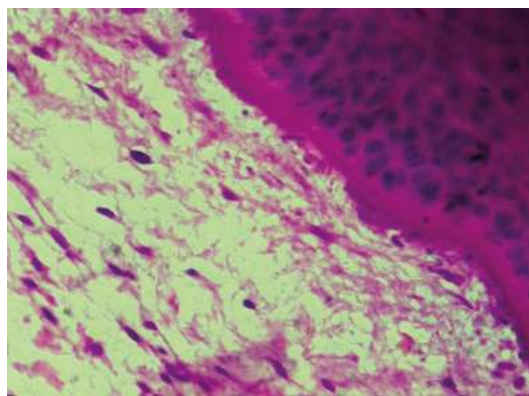
Localization of the pathological process on various anatomical structures of the larynx

Localization	Tumor-like diseases				
	chronic inflammatory benign and malignant processes	singing nodules	polyps	cysts	nonspecific granulomas
anterior and middle thirds of the vocal fold	181	11	4		
- one-sided	80	9	3		
- bilateral	101	2	1		
The superior or inferior surfaces of the edges of the vocal fold	95		22		
Medial edges of the vocal fold	10		5		
Inferior surface of the vocal fold	9		2		
Distributed over the entire surface of the vocal fold	50		1		
Free edge of the vocal fold	20		5		
Epiglottis	76		9	10	
aryepiglottic folds	70			2	
Lingual surfaces of the epiglottis	76			8	
vestibule	54			1	2
In the area of the vocal processes of the arytenoid cartilages	40				7
Total	681	11	48	21	9

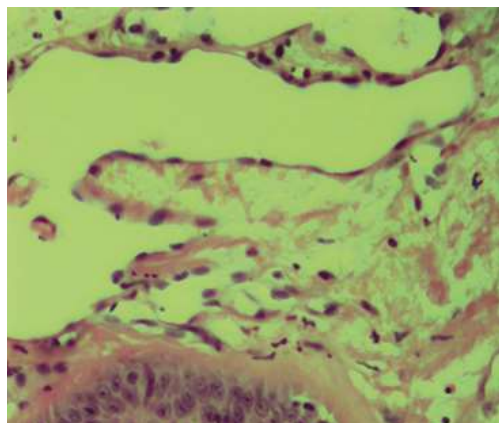
Lymphoproliferative chronic laryngitis (LPL). Diffuse lymphoid infiltration of the stroma. Color: G-E. X: 10x40



Stromal myxamatos, stellate connective tissue cells, thickening of the basement membrane. Color: G-E. X: 10x40



Lymph vascular cyst of the larynx. Cavernous dilatation of lymphatic vessels. Color: G-E. X: 10x40



Myxamatus polyp of the larynx. Loose stroma due to edema and myxamatos, Edema of the cytoplasm of the integumentary epithelial cells. Color: G-E. X: 10x40.

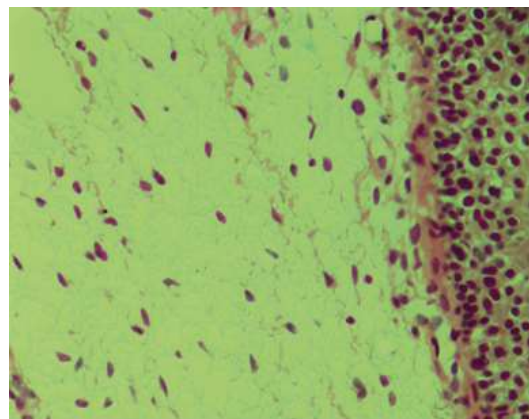


Table 3.
Determination of reference values for immunoglobulin concentrations in healthy individuals

Indicators	concentration in blood serum, g/l	
	norm	median norm (M)
IgG	10,18 - 13,01	12,02
IgA	1,79 - 2,61	2,41
IgM	0,82 - 1,51	1,14

Study of α 2MG concentration levels in study groups (g/l)

Table 4.

groups	α 2MG concentration	(M \pm m)
I-group (PGG)	1,28 - 1,56	1,48 \pm 0,04
II-group (RG)	2,09 - 2,18	1,98 \pm 0,07
III-group (GL)	1,49 - 1,83	1,73 \pm 0,03

One of the methods for differential diagnosis of benign neoplasms of the larynx is undoubtedly histological examination. For this purpose, a biopsy sample is taken from the larynx during fibrolaryngoscopy, indirect or direct microlaryngoscopy. If a patient has a specific process, additional methods for diagnosing the underlying disease, mandatory histological and immunological studies are required.

For this purpose, clinical, morphological and immunological studies were carried out in 82 patients. During the study, patients were divided into three groups: Group I – precancerous processes of the larynx (PPG) (n=38); Group II – laryngeal cancer (LC) (n=21); Group III - control healthy individuals (HL) (n = 23), the average age of the examined patients was 65.3 ± 4.5 years, while with precancerous processes of the larynx they were at a younger age, in comparison with the second group - from 27 to 53 years old (61.3%); the majority of patients with laryngeal cancer were in the age category from 55 to 61 years (53.7%), this indicates the presence of a long period from the onset of the disease to the occurrence of malignancy of the process, as well as initial changes in the form of benign and precancerous processes of the larynx at a young age, which may be due to the presence of any risk factors for the occurrence of the disease (hereditary, carcinogenic, bad habits, virus carriage, etc.) requiring detailed study.

According to a retrospective analysis, changes in the levels of immunoglobulins IgG, IgA, and IgM were studied in the study groups, assessing their relationship with the systems of cytokines and immunoregulatory proteins.

The primary study examined the concentrations of immunoglobulins in healthy individuals in the control group in order to determine the reference values of norms (Table 3).

Study of the level of the marker- α 2-macroglobulin, which determines the immunological status and its changes in precancerous processes and laryngeal cancer.

In this regard, in this work, we studied changes in the levels of α -2MG concentration in the blood serum during PPG and RG.

In order to obtain reference values for the concentration level of α -2MG in blood serum, its determination was carried out in the III control group - healthy individuals, which averaged 1.49 - 1.83 g/l.

Next, a comparative assessment of the marker was carried out in patients with PPG and RG, presented in Table 4.

Based on the data obtained, it is possible to determine the significance of α -2MG for the early diagnosis of precancerous conditions of the larynx, and also recommend its study in conjunction with other cells of the immune system that provide adequate protection of the body from damaging influences - immunoglobulins, interleukins, tumor necrosis factor, qualitative and quantitative cells – T- and B-lymphocytes, providing a complete cellular immune response.

CONCLUSION

Thus, morphological changes in the larynx are closely related to the processes of embryogenesis, immunobiological characteristics of the whole organism, the influence of the central and peripheral nervous, as well as endocrine systems. Numerous diseases of a functional and organic nature often develop due to the insufficiency of these links. When analyzing the pathogenesis and studying the etiological factors of various diseases of the larynx, comparative differential diagnosis with the definition of pathogenesis often plays a decisive role in order to select and justify complex treatment.

Based on the data obtained, it is possible to determine the significance of α -2MG for the early diagnosis of precancerous conditions of the larynx, and also recommend its study in conjunction with quantitative and qualitative analysis of cells of the immune system that provide adequate protection of the body from damaging influences - immunoglobulins, interleukins, tumor necrosis factor, – T- and B-lymphocytes, providing a complete cellular immune response.

CONFLICT OF INTERESTS

The authors declare the absence of obvious and potential conflicts of interest related to the publication of this article.

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AVAILABILITY OF DATA AND MATERIALS

All data generated or analysed during this study are included in this published article.

AUTHORS' CONTRIBUTIONS

All authors contributed to the design and interpretation of the study and to further drafts. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All applicable international, national, and/or institutional guidelines for the care and use of animals were followed.

CONSENT FOR PUBLICATION

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КОНФЛИКТ ИНТЕРЕСОВ

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов.

ИСТОЧНИКИ ФИНАНСИРОВАНИЯ

Авторы заявляют об отсутствии финансирования при проведении исследования.

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ДОСТУПНОСТЬ ДАННЫХ И МАТЕРИАЛОВ

Все данные, полученные или проанализированные в ходе этого исследования, включены в настоящую опубликованную статью.

ВКЛАД ОТДЕЛЬНЫХ АВТОРОВ

Все авторы внесли свой вклад в подготовку исследования и толкование его результатов, а также в подготовку последующих редакций. Все авторы прочитали и одобрили итоговый вариант рукописи.

ЭТИЧЕСКОЕ ОДОБРЕНИЕ И СОГЛАСИЕ НА УЧАСТИЕ

Были соблюдены все применимые международные, национальные и/или институциональные руководящие принципы по уходу за животными и их использованию.

СОГЛАСИЕ НА ПУБЛИКАЦИЮ

Не применимо.

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