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STATE OF CELL DEATH AND PROLIFERATION OF SCAR TISSUE UNDER CONDITIONS OF MECHANICAL IRRITATION

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ABOUT ARTICLE

Key words: larynx, cicatricial narrowing, inflammation.

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Abstract: Chronic inflammatory diseases of the larynx (CIAG) are a collective concept of a fairly large number of diseases with different etiologies. Nosological forms of diseases of the larynx are presented in a wide range - from functional disorders leading to respiratory failure, benign formations of the larynx to severe, long-term cicatricial stenoses that require complex reconstructive operations.

МЕХАНИК ҚЎЗҒАЛИШДА ЧАНДИҚ ТЎҚИМАСИ ХУЖАЙРА ПРОЛИФЕРАЦИЯСИ ҲОЛАТИ

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МАҚОЛА ҲАҚИДА

Калит сўзлар: ҳиқилдоқ, чандиқли торайиш, яллиғланиш.

Аннотация. Ҳиқилдоқнинг сурункали яллиғланиш касалликлари (ҲСЯК) турли хил этиологияга эга бўлган жуда кўп сонли касалликларнинг умумий тушунчасидир. Бу ҳолда ҳиқилдоқ касалликларининг нозологик шакллари кенг доирада тақдим этилади - нафас етишмовчилигига олиб келадиган функционал бузилишлардан тортиб то мураккаб реконструктив операцияларни талаб қиладиган қўпол, узоқ муддатли чандиқли стенозларгача.

СОСТОЯНИЕ КЛЕТОЧНОЙ ГИБЕЛИ И ПРОЛИФЕРАЦИИ РУБЦОВОЙ ТКАНИ В УСЛОВИЯХ МЕХАНИЧЕСКОГО РАЗДРАЖЕНИЯ

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О СТАТЬЕ

Ключевые слова: гортань, рубцовые сужения, воспаления.

Аннотация: Хронические воспалительные заболевания гортани (ХВЗГ) представляют собой собирательное понятие достаточно большого количества заболеваний с различной этиологией. Нозологические формы заболева-ний гортани при этом представлены в широком диапазоне - от функци-ональных расстройств, приводящих к дыхательной недостаточности, доброкачественных образований гортани до грубых, длительно существующих рубцовых стенозов, требующих проведения сложных реконструктивных операций.

INTRODUCTION

Pathological assessment of this condition of the larynx is primarily associated with the presence of chronic inflammation of the mucous membrane and elements of the larynx, including the submucosal layer, as well as the muscles and cartilages of the larynx [1-4]. Most often, chronic inflammation of the larynx is localized in the region of the vocal cords, the subvocal region of the larynx with the transition to the cervical trachea and is a secondary manifestation of the damaging factor [2].

Despite the apparent differences associated with localization and etiology [16], all of these diseases have one common component, characterized by damage to the mucous membrane and elements of the larynx [17]. The mucous membrane of the laryngotracheal part of the respiratory tract reacts differently to the influence of one or another damaging factor and leads to the development of one of the pathologies [5-9]. When the region of the vocal folds is involved, this is manifested by hypertrophic growth or atrophy [15]. Damage to the underlying sections leads to melting of the cartilage of the larynx and trachea and contributes to the formation of scars [10-14,18]

In this regard, the solution of the problem of restoration of the mucous membrane and elements of the larynx and trachea as a result of the intervention, as well as options for preventing their damage, are priority in the treatment of the above diseases.

To understand the processes of mucosal inflammation, it is necessary to know the physiology of the mucosa. In order to understand how, with what actions and what medicinal substances to treat inflammation, it is necessary to know the mechanism of inflammation development.

THE MAIN RESULTS AND FINDINGS

It is known that in practice, in order to eliminate stenosis of the larynx, they often resort to surgical removal of scar tissue, and this intervention is carried out repeatedly. Despite the surgical removal of scar tissue, leading to stenosis of the laryngotracheal region, it is not always possible to achieve the expected result, sometimes restenoses of the larynx and trachea develop. Therefore, in this section, we have made an attempt to study the mechanisms of inefficiency of surgical removal of pathological tissue and to determine the significance of the mechanical effect on scar tissue in the genesis of re-stenosis.

For these purposes, 20 rabbits were selected.

A model of cicatricial stenosis of the larynx was created for all animals according to the method described above (Chapter II). Animal management did not differ from the previous study. All animals in the early postoperative period received anti-inflammatory therapy with daily toileting of the laryngotracheostomy area. However, despite careful care of the animals in compliance with all the rules of management, 4 rabbits died in the first 3 days and 2 more in a longer period. Thus, a study group of 14 rabbits was formed.

The animals were observed for 28 days, followed by gentle excision of young scar tissue from the area of the subvocal region of the larynx. The isolated tissue was subjected to morphological and IHC studies according to the method described above (Chapter II).

Morphological examination of the biopsy revealed the presence of granulation connective tissue containing fibrin clots and destroyed cellular elements. The stroma was imbibed with blood, dead cellular elements, and contained a huge number of mostly oriented blood vessels. In some preparations, the connective tissue was represented by cellular elements with a high density of cellular infiltration (neutrophils were in a state of evolution). In other words, the biopsy was mainly represented by young connective tissue with inflammatory and dyscirculatory disorders (Fig. 1).

It was noteworthy that the morphological picture fully corresponded to the timing and nature of the lesion, and at the same time served as a comparative control. subsequent manipulations on the larynx.

The results of IHC studies of biopsy materials are presented in Table 1.

Table 1

Comparative characteristics of apoptosis and proliferation processes in animals with laryngeal stenosis

Group and impact	MI, ‰	AI, %	Necrosis, %	PCNA H- scores	p53 H- scores
A-control (young scar tissue) n =4	4.5±0.65	5.2±0.70	8.1±0.86	220±17.2	180±14.2
B - experienced (secondary scar tissue) n =4	2.8±0.52	5.8±0.73	12.0±1.02*	160±13.4*	158±12.9*
S-experimental (secondary scar tissue after repeated irritation) n = 3	5.5 ± 0.72	6.9±0.80	11.8±1.02*	280±16.8*	190±15.4*

*- $p< 0.05$

As can be seen from the results presented in the table, the values of the indicators of apoptosis and proliferation in tissue samples did not differ significantly, although the MI index was 1.5 times lower in the secondary scar than in the control scar tissue, however, these differences were not statistically distinguishable ($p >0.05$).

As at the beginning of the study, the animals after excision of pathological tissue from the larynx in the early postoperative period received anti-inflammatory therapy.

At this stage of the study, 3 rabbits died due to suppuration of the wound of the larynx and subsequent asphyxia. The remaining animals were conditionally divided into 2 groups of 7 (group I) and, respectively, 4 rabbits (group II). Thus, 2 groups of studied animals were created: experimental, after repeated intervention on the mucous membrane of the larynx, and control.

In the I group of experimental animals, mechanical irritation of the wound area with a needle from a syringe was performed on days 7 and 21. On the 7th day, all animals of the group (B-experimental) were subjected to this procedure, and on the 21st day, repeated manipulation was performed in 3 rabbits (C-experimental).

II (A-experimental) group was observed for the next 28 days without any external influence.

The study was conducted on the 28th day after the last excision. The choice of the timing of the study was due to sufficient time for the maturation of secondary scar tissue, the possibility of morphological and IHC assessment of the presented changes, as well as the need to study the process of re-scarring in the dynamics of the study.

After the end of the experiment, the biopsy materials were subjected to pathomorphological and IHC studies.

For convenience of presentation, the material was identified as:

A. scar tissue of the subvocal region of the larynx after a single excision (control);

B. secondary scar tissue after repeated excision;

C. secondary scar tissue after its mechanical irritation;

A comparative morphological study of samples A and B of pathological tissue, basically revealed the same changes in terms of maturation in each of the groups of animals. At the same time, morphologically, the picture of the experimental group of animals with secondary scar tissue

after repeated excision was characterized by a more pronounced inflammatory reaction with dense infiltration of lymphohistiocytic elements. The fibers are thin, edema is expressed between their bundles. The lumens of blood vessels are wide with thinned walls.

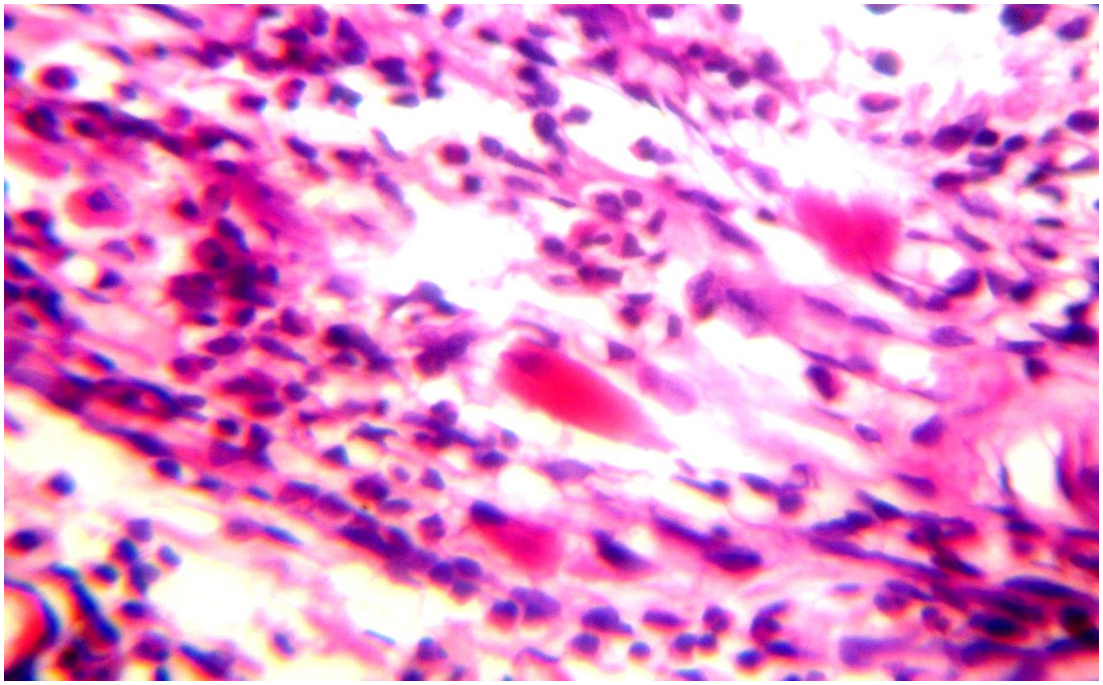

Fig.1. Connective tissue infiltrated with lymphohistiocytic elements with a predominance of neutrophils. Hematoxylin and eosin. SW. 200x

Oriented thin collagen fibers are revealed between clusters of cells. There are also areas represented by a coarser fibrous tissue with symptoms of fiber edema and an arrangement of spindle-shaped elongated fibroblasts with rod-shaped nuclei.

More visible changes were presented in the samples of group C. On the preparation, connective tissue was determined, in places densely infiltrated with lymphohistiocytic elements, among which neutrophils predominated in areas.

The entire tissue was permeated with a large number of blood-filled capillaries. All of the above characterized the high proliferative activity of the tissue of the presented samples.

CONCLUSION

The morphological changes revealed during the experimental study correlated with the subsequent IHC study of the same tissue samples. As can be seen from the data presented in Table 4..5., in the group of tissue samples C, the AI and MI values are noticeably higher with a relatively equivalent level of cell necrosis. However, PCNA protein expression was markedly higher compared to tissue sample groups A and B.

Therefore, our results indicate an increase in the proliferation of scar tissue fibroblasts under conditions of mechanical stimulation. This circumstance, to a certain extent, allows us to explain

why the number of cases of laryngeal restenosis increases in the conditions of repeated surgical interventions.

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