Reaction of Tonsils Epithelium in Hypoxia

A. V. Kuznetsov a,*, I. S. Irhina b, A. G. Verzhbitsky c

1 Department of Human Anatomy Novosibirsk State Medical University: Krasny Prospect, 52, Novosibirsk 91, Russia, 630091.
2 Municipal Clinical Hospital 25: A. Nevskogo 1A, Novosibirsk 75, Russia, 630075.
3 Regional Hospital 14 named after Shanaurin: Bolnichnaya 20, Kazanskoe, Tyumenskaya region, Russia, 627420.

*Corresponding author at A. V. Kuznetsov, Department of Human Anatomy Novosibirsk State Medical University: Krasny Prospect, 52, Novosibirsk 91, Russia, 630091, Tel: 007 383-222-32-04 E-mail address: alexapex@yandex.ru (A. V. Kuznetsov)

Abstract:

The aim of the research was to detect tonsils reaction as epithelial hyperplasia in patients with hypoxia-inducing diseases. Three groups of males and females (aged from 60 to 80) were investigated: 1 - patients with larynx cancer and lymphoma; 2 - chronic heart failure; 3 – without larynx cancer and heart failure. A scrape from the medial surface of the palatine tonsil was taken with a spatula. The specimens of cells were transferred (as smears) to microscopic slide, stained by Giemsa and studied with a light microscope. Epithelial cells proliferation in smears of scrapes from the palatine tonsils of all the patients with cancer of larynx, lymphoma and heart failure was revealed side by side with usual epithelium. The proliferating cells of the patients with heart failure had a rounded form, the same size and intensive staining of nucleus and cytoplasm. The cells proliferation clustered like oblong ribbons or round islands. The proliferation of epithelial cells in group 1 was more expressive than it was in group 2. No cells proliferation in smears of scrapes from tonsils of patients without cancer of larynx, lymphoma and heart failure was found. Palatine tonsils hypoplasia in heart failure was revealed.

This study demonstrated that palatine tonsils are able to respond to larynx cancer, lymphoma and heart failure with proliferation of their own epithelium despite tonsils involution. This finding suggests that proliferation of epithelium of tonsils is a universal reaction to the diseases inducing hypoxia and immune dysfunctions. The proliferation/hyperplasia reflects the reaction of palatine tonsils to hypoxia and immunity dysfunctions in patients with heart failure, oncology diseases and can be a marker of these changes and health-related quality of life in the patients with cancer and chronic heart failure during treatment. It is necessary to keep on the research by using HIFs-markers.

1. Introduction

Hypoxia demonstrates the ability of inducing proliferation/hyperplasia of epithelium. Chaudhary et al [1], Weng et al [2] and Hodson et al [3] reported hyperplasia of oral epithelial, proliferation of alveolar epithelial cells and caroid body proliferation, correspondingly. Li et al [4] and Deng et al [5], Hayashy et al [6] revealed proliferation of pulmonary artery smooth muscle cells and Comes [7] showed proliferation of neuroendocrine cells correspondingly. Hypoxic and ischemic injuries are closely associated with disturbed BBB function and the contribution of perivascular cells to hypoxic/ischemic barrier regulation has gained increased attention. It was established too that higher sensitivity coincided with rapid and significant stabilization of HIF-1α and its downstream targets (VEGF, GLUT-1, MMP-9 and PHD2), early disruption of the actin cytoskeleton and metabolic impairment in conditions where the perivascular cells remain largely unaffected. Additional adaptation (suppression) of proliferation also likely contribute to astrocytic and pericytic tolerance during severe injury conditions [8]. Hypoxia inducible factor-1α (HIF-1α) is known to be essential in tumorigenesis, as it regulates the expression of numerous factors that are involved in angiogenesis, cellular proliferation and apoptosis [9]. Noman et al [10] reviewed new evidence indicating that the efficacy of the cell-mediated cytotoxicity (CTLs and NK) may be dependent on hypoxia induced miRNA and microvesicles in the tumor microenvironment by inhibiting the efficacy of natural host anti-tumor immune response and improving the ability of tumors to avoid immunosurveillance. Some data indicated that HIF-1α siRNA is important in the inhibition of non-small cell lung cancer (NSCLC) cells. The effects of HIF-1α siRNA may be strengthened by DDP, which suggests that HIF-1α siRNA may be combined with DDP for the treatment of tumors [9]. Chaudhary et al [1] observed the relationship between the expression of HIF-1α in oral submucous fibrosis (OSMF), oral squamous cell carcinoma (OSCC) and OSCC with OSMF. Hypoxia-inducible factor 1 (HIF-1) is a critical regulator for cellular oxygen balance. Myocardial hypoxia can induce the increased expression of HIF-1α [11].

So proliferation/hyperplasia of epithelium of any immunologic organ can be a diagnostic criterion of hypoxia. The study was designed to reveal the most typical changes of cells of palatine tonsils in patients with hypoxia of different geneses: in oncology and cardiology. The purpose was to detect tonsils reaction as epithelial hyperplasia in patients with hypoxia-inducing diseases.

2. Methodology/Algorithm

The patients both males and females (aged from 60 to 80) including smokers, nonsmokers, alcoholics and sober were studied in subgroups within three investigated groups: Group 1 - patients with cancer of larynx (T1), who underwent radiotherapy (5) and lymphoma (3); Group 2 – patients with chronic heart failure II-III stage (27); Group 3 – patients without cancer of larynx and heart failure (20), 5 of them had chronic tonsillitis. After the informed consent was obtained, each patient sat or lay with the month opened and the tongue protruded. A limited scrape from the medial surface of the palatine tonsil (right or left) was taken with a spatula. The specimens of cells were transferred (as smears) to microscopic slide, stained by Giemsa and studied with a light microscope. The patients of groups land 2 did not have tonsillitis. There were no complications after the procedure. The patients’ diagnoses were made by specialists both otolaryngologists and cardiologists.

3. Results and Discussion

Side by side with usual cells of epithelium proliferation of cells in smears of scrapes from the palatine tonsils of all the patients with cancer of larynx, lymphoma (Group 1) and heart failure (Group 2) was revealed. The proliferating cells of the patients with heart failure had a rounded form, the same size and intensive staining of nucleus and cytoplasm. The
proliferation of cells clustered like oblong ribbons or round isles. It is clear from figure 1 and 2. Figure 3 illustrates proliferation of epithelium in the patients with lymphoma. The proliferation of epithelial cells of patients in group 1 was more expressive than it was in group 2. Some proliferating cells were hyperchromatic, they were of large size and had large blue nucleus like in dysplasia. There was no proliferation of cells in smears of scrapes from the palatine tonsils of patients (Group 3) without cancer of larynx, lymphoma and heart failure. Hypoplasia (involution) of palatine tonsils in patients with heart failure was strongly revealed. In this study, proliferating epithelium of palatine tonsils is a universal feature in human pathophysiology because it occurs in clinical conditions such as circulatory shock, myocardial ischemia and stroke.

Figure 1: The proliferation/hyperplasia of tonsil cells clustered like oblong ribbons of patients with heart failure (Giemsa x 400)

Figure 2: The proliferation/hyperplasia of tonsil cells clustered like round isles of patients with heart failure (Giemsa x 400)

Shyu et al [16] found that hypoxia-inducible factor-1 alpha is tightly regulated in the ventricular myocardium in heart failure. The findings confirm the results Doki et al [17] obtained earlier: background squamous cell carcinoma of the esophagus (ESCC) is radiosensitive; however, surgeons frequently encounter ESCC that survives radiotherapy to grow more rapidly and invasively. This alteration of tumor behavior may result from hypoxia induced by radiotherapy. Tumor hypoxia would induce ulcerative and invasive growth, which is a great obstacle to clinical treatment of residual or relapse after radiotherapy. The obtained results show that activation of hypoxia inducible factor-1 (HIF) is a hallmark in hypoxia-induced pulmonary hypertension (PHH) [5]. The proliferating cells are probably cells of profound layers of epithelium of palatine tonsils in patients with heart failure. Obtaining of cytologic material from palatine tonsil of patients by “scraping” is relatively easy and safe. This method is not expensive and is done within 40 minutes. Aagaard et al [18] reported that in clinical practice a method for assessment of tissue vitality is a sought-after tool.

Figure 3: The proliferation/hyperplasia of tonsil cells of patients with lymphoma (Giemsa x 400)

4. Conclusions
This study demonstrates that palatine tonsils are able to respond to cancer of larynx, lymphoma and heart failure with proliferation/hyperplasia of their own epithelium despite tonsils involution. At the same time this finding suggests that proliferation of epithelium of tonsils is a universal reaction to the diseases inducing hypoxia and immune dysfunctions. The proliferation reflects the reaction of palatine tonsils to hypoxia and immunity dysfunctions in patients with heart failure, oncology diseases and can be a marker of these changes and health-related quality of life in patients with cancer and chronic heart failure during treatment. It is necessary to keep on the research by using HIFs-markers.

Acknowledgement
The author thanks Galina Igorevna Kuznetsova for help in translation of the manuscript.

References
[4]. X. W. Li, X. M. Wang, S. Li, J. R. Yang: Effects of Chrysins (5,7-dihydroxyflavone) on Vascular Remodeling in Hypoxia-induced Pulmonary Hypertension in Rats, Chinese Medicine,10(4), eCollection 2015.


