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DISTURBED CELL PROLIFERATION AND APOPTOSIS IN PATIENTS WITH CHRONIC PERIODONTITIS AGAINST THE BACKGROUND OF GASTROESOPHAGEAL REFLUX DISEASE

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ABSTRACT — This study aimed to examine the indicators of gum epithelial cell proliferation in patients with chronic periodontitis against gastroesophageal reflux disease (GERD). The clinical, endoscopic, immunohistological and morphological studies revealed that diseases affecting the esophagus facilitate the development and the progression of periodontal issues. Enhanced apoptosis due to insufficient proliferation of periodontal tissues contributes to the progression of inflammatory and destructive changes in the tissues, against the background of reduced regeneration due to a decrease in the Ki-67 immunopositive cells.

KEYWORDS — periodontitis, gastroesophageal reflux disease, proliferation, apoptosis, Ki-67, Bcl-2

INTRODUCTION

The issues related to the pathogenesis, diagnostics and treatment of inflammatory periodontal diseases still remain relevant due to their prevalence (98%) worldwide, which makes them a serious socio-economic issue [1]. There have been a number of somatic factors identified currently, which add to the development and progression of periodontal diseases, which, in turn, result in stereotypic response revealed as structural shifts once subjected to the effect of various somatic changes in the body [2–6]. The inflammatory periodontal issues incidence in patients with gastroesophageal reflux disease reaches 85.7% of cases [2, 7–9]. Disturbed cell proliferation and apoptosis determine the transition from chronic gingivitis to periodontitis, contributing to chronic diseases progression [10]. Currently, an important role in apoptosis regulation and cell proliferation belongs to the proliferating cells marker — Ki-67, anti-apoptotic protein Bcl-2, and apoptosis [11, 12]. The study of proliferation and apoptosis of gum epithelial cells in periodontal diseases against esophageal pathology will expand the scope of pathogenesis issues, improve early diagnostics of the said diseases, and improve treatment.

Aim of study

to analyze the expression of cell proliferation markers and apoptosis of gum epithelial cells in chronic periodontitis with gastroesophageal reflux disease.

MATERIALS AND METHODS

100 patients were examined; 40 patients had periodontitis on the GERD background; 40 patients had periodontitis with no esophageal pathology; the comparison group included 20 patients with intact periodont. All the patients underwent a comprehensive clinical and instrumental examination with the following index indicators identified: OHI-s (Green J.C., Vermillion J.R., 1964), PMA (Parma, 1960), PI (Russel A.L., 1956) as well as dentition radiological diagnostics. The diagnosis of GERD was given based on the outcomes of a comprehensive clinical and morphological examination. The patients were monitored subject to a single program, including general clinical examination, ultrasound abdominal examination, fibrogastroduodenoscopy, general morphological and cytological, as well as immunohistochemical examination.

The material for morphological diagnostics was taken from the gingival margin mucous membrane, the gingival papillae, as well as the mucous membrane in the transitional gingival fold area. An immunohistochemical study was done using monoclonal mouse antibodies to the proliferating cell marker, Ki-67 and Bcl-2 (Sigma, St. Louis, USA, titer 1: 200). The number of expressing cells was counted in 30 fields within view, and at the indicated magnification; the digital data were counted as per 1 mm^2 using the Video Test-Morphology 4.0 application morphometric software package.

RESULTS AND DISCUSSION

The clinical and instrumental analysis focusing on the periodontal tissues status revealed that periodontal diseases were observed in all (100%) the examined patients with GERD, while the issues were

more severe than in patients without somatic pathology. The anamnesis analysis showed that the severity of the chronic periodontitis course correlates with the GERD history. In case the duration of GERD exceeded 10 years, periodontal diseases of moderate and severe severity were observed in 63.6% of the cases.

Patients with chronic periodontitis complained of bleeding gums, slight pain, and halitosis. An objective examination allowed detecting hyperemia, swelling, bleeding gums. It is to be noted that, at basically equal values in the individual hygiene levels (OHI-s 2.94 ± 0.053), the inflammatory process in the periodont against the GERD background was higher: the PMA index (66.11 ± 1.64); Muhlemann (3.88 ± 0.45); and PI (3.74 ± 0.11), were statistically differed from indicators in patients with periodontitis with no somatic pathology: (OHI-s 2.36 ± 0.34) PMA (33.95 ± 2.35); Muhlemann (1.64 ± 0.28); and PI (1.60 ± 0.13) ($p < 0.05$).

An analysis of the gums immunohistochemical study outcomes revealed that in healthy people, periodontal epithelium shows a low potential for proliferative and anti-apoptotic activity (Ki-67 9.53 ± 0.19); (Bcl-2 2.88 ± 0.10); apoptosis index (Iapt 0.38 ± 0.04). Chronic periodontitis without esophageal pathology featured an increase in the expression of (Ki-67 = 28.88 ± 1.42) and (Bcl-2 8.26 ± 1.19), with a relatively low apoptosis index (Iapt 0.54 ± 0.03). In patients with periodontitis against the GERD background, there was a multiple increase in the gum epithelial cells proliferative potential, which manifested itself through an increase in the number of cells immunopositive to (Ki-67 20.19 ± 0.37). At the same time, apoptosis also increased (Iapt 1.40 ± 0.12); however, the degree of its increase did not correspond to the epithelial cells proliferative activity. The latter could be accounted for by genetic rearrangement of individual cells with them gaining an ability to express an anti-apoptotic molecule (Bcl-2 5.23 ± 0.32). Thus, in patients with inflammatory periodontal diseases observed against the GERD background, cell renewal reveals an epithelial cells apoptosis lagging progressively behind the proliferation rate. The obtained data are consistent with the results obtained through previous studies, which showed that apoptosis increases accordingly to an increase in the severity of periodontal disease inflammatory changes [13, 14]. Activated apoptosis and inhibited proliferation disturb both the physiological and the regenerative function in the mucous membrane of the oral cavity and the stomach.

CONCLUSION

Our data indicate that esophagus diseases contribute to the progression of periodontal disease. The dental status analysis in patients with periodontitis against the GERD background indicates a more pronounced inflammatory lesion of the periodontal complex, if compared with patients without esophageal pathology. An important risk factor triggering and facilitating the course of periodontal disease in people suffering from GERD is the history of the esophagus issue.

The obtained changes in cell proliferation processes and apoptosis largely determine the degree of inflammatory and destructive lesions in periodontal disease against the GERD background, and correlate with the severity of inflammatory periodontal diseases. The leading role in the progression of inflammatory and destructive changes in periodontal tissues against the GERD background belongs to Ki-67, which describes the degree of processes, Bcl-2, which reflects the severity of anti-apoptotic activity, and the apoptosis index, which shows the degree of destruction in the periodontal tissues.

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