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Comprehensive Analysis Of Oral Pre-Cancerous Diseases

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Abstract: High morbidity and mortality from oral cancer, which occupies one of the leading positions among oncological diseases of the head and neck. Despite modern achievements in diagnostics and therapy, most cases are detected in later stages, which significantly worsens the prognosis and patients' quality of life. The study included 122 patients with precancerous conditions who underwent treatment at the Department of Hospital Stomatology of the Tashkent State Medical Institute from 2016 to 2023. Molecular, immunological, immunohistochemical, and statistical research methods were used.

Keywords: Precancerous diseases, oral mucosa, treatment, markers, immunohistochemistry.

Introduction: In modern dentistry and oncology, early diagnosis and assessment of the risk of transformation of precancerous changes in the oral mucosa into malignant neoplasms are of great importance. For effective prevention and treatment, it is necessary to comprehensively understand the morphological, molecular, and immunological characteristics of these conditions. This chapter presents the results of an analysis conducted in several key areas: characteristics of precancerous types and forms, their area, and the age of patients, as well as etiological factors such as HPV infections. Special attention is paid to assessing the expression of oncogenic and angiogenic markers such as p53, VEGF, and EGFR, as well as the state of local immunity and the level of cellular proliferative activity expressed by the Ki-67 indicator. The obtained data not only allows for a deeper understanding of the pathogenesis of precancerous diseases but also for identifying indicators capable of serving as prognostic markers of malignancy risk, which is important for developing individualized diagnostic and treatment strategies.

We conducted a sex analysis depending on the characteristics of the precancer.

Analysis of the sex distribution of patients with precancerous changes in the oral mucosa revealed a correlation between sex and the morphological characteristics of the pathological process. In the study group, three main parameters were identified:

precancerous type, precancerous form, and area of lesion, which provides a comprehensive assessment of the morphological variability of these diseases in the context of gender.

The results showed that no statistically significant differences were found between the sex and precancerous type (p = 0.264). The sex distribution in patients with leukoplakia, CPL, and erythroplakia was characterized by approximately the same proportions: in women - about 47-62%, in men - about 38-53%. This indicates a uniform distribution of the precancerous type among men and women and the absence of gender preference for specific morphological variants.

Analysis of the precancerous form (simple, erosive, and erosive-ulcerative) also did not reveal statistically significant differences in sex (p = 0.289). In men and women, the proportions relative to the precancerous form were approximately the same, indicating that the morphological features of lesions do not depend on sex.

The most significant differences were revealed when analyzing the area of damage. In this category, there are statistically significant differences (p = 0.022). In particular, men predominate in patients with focal lesions (30.2%), while women predominate in patients with subtotal lesions (54.0%), while men's proportion decreases to 37.5% in patients with total lesions. In pairwise comparisons: focal lesions - subtotal (p = 0.047) and focal lesions - total (p = 0.048), significant differences were also recorded. These data indicate that men are more likely to be diagnosed with localized focal lesions, while women are more likely to have extensive, total lesions.

Summarizing the results, it can be concluded that sex is not a significant factor in determining the type and form of precancerous disease, but it is significantly related to the scale of the lesion: in men, limited lesions are more common, in women - wider and more severe. These observations are important for understanding the pathogenesis and clinical picture of precancerous diseases, and can also be considered when planning diagnostics and treatment tactics, focusing on the prevalence of the pathological process depending on gender.

An analysis of the spread of human papillomavirus (HPV) depending on the type of precancerous changes in the oral mucosa was conducted to identify possible associations between the presence of the virus and the precancerous type. In particular, the presence of HPV types 16 and 18 in patients with leukoplakia, CPL, and erythroplakia was studied. According to the obtained data, when assessing the influence of HPV type 16, it was found that 80.6% of patients with leukoplakia (72 out of 58) and 79.1% with CPL (43 out of 43) did not have the virus, while among patients with erythroplakia, the presence of HPV16 was detected only in 100% of patients (7 out of 7). Similarly, according to HPV type 18, statistics show that 72.2% of patients with leukoplakia (72 out of 52) and 83.7% with LPL (43 out of 36) had no virus, while HPV 18 was present in 85.7% of patients with erythroplakia.

Statistical analysis using Pearson's Chi-square methods showed that the differences in the presence of HPV 16 and 18 between precancerous types are statistically insignificant (p=0.414 and p=0.312 respectively). This means that the identified differences in the prevalence of the virus in different groups do not exceed the random level, and within the framework of this study, no reliable relationships were found between the precancerous type and the presence of HPV 16 and 18.

The absence of statistical significance of these differences can theoretically indicate that at this stage of precancerous changes development, the influence of HPV types 16 and 18 is homogeneous and does not depend on the specific type of precancer. This allows us to assume that viral infections associated with HPV-16 and HPV-18 can play a role in the pathogenesis of precancerous oral mucosa, regardless of the type of change, or that in this sample, the influence of the virus has not yet reached the level necessary for statistical significance. It should also be noted that the size of subgroups, especially in patients with erythroplaxis, was small (only 7 cases), which reduces the statistical power of the analysis and may prevent the identification of possible associations.

Overall, the results of this analysis emphasize the need for further research with an expansion of the sample and the use of additional diagnostic methods to clarify the role of HPV types 16 and 18 in the development of precancerous oral mucosa diseases, as well as to determine possible therapeutic and preventive measures aimed at eliminating the viral component and reducing the progression of precancerous conditions.

Analysis of the molecular-biological characteristics of precancerous changes in the oral mucosa was conducted to identify possible differences in the expression of key oncogenes and angiogenesis factors depending on the type of precancer. Three subgroups of patients were identified in the study group: patients with leukoplakia, patients with CPL, and patients with erythroplakia, which made it possible to assess the possible features of the pathogenesis and the prognostic significance of these molecular indicators in each of the states.

The first indicator analyzed within the framework of

the study was the expression of genes encoding P53, VEGF, and EGFR proteins, as these molecules are widely studied in the context of the development and progression of malignant processes. In particular, according to P53, most patients, regardless of the type of precancerous disease, demonstrated no expression of this gene - in 62.5% (72 out of 45) patients with leukoplakia, 60.5% (43 out of 26) with CPL, and 57.1% (7 out of 7) with erythroplakia. Similarly, the presence of this protein expression was noted in 37.5% (72 out of 27) in leukoplakia, 39.5% (43 out of 17) in CPL, and 42.9% (7 out of 7) in erythroplakia. Statistical analysis using the Pearson's chi square method showed that there is no significant difference in p53 expression between the groups ($p = 0.948$). This indicates that within this sample, the expression or absence of p53 expression is not directly related to the type of precancerous disease, which is consistent with data on the high prevalence of absence of mutations of this gene in precancerous conditions.

Further, the expression of the VEGF factor, responsible for regulating angiogenesis processes - a crucial component of tumor and precancerous progression - was considered. Analysis showed that in 81.9% of patients with leukoplakia, VEGF expression was absent, while in 74.4% with LPL and 57.1% with erythroplakia, its presence was noted. In the erythroplakia group, VEGF expression is more pronounced (42.9%), which may indicate more active vascular formation processes and potential malignant transformation. However, despite these observations, statistical analysis showed no significant difference between the groups ($p = 0.255$).

Finally, the expression of the EGFR receptor associated with cell growth and differentiation regulation was evaluated. Overall, the presence of EGFR expression was recorded in 59.7% of patients with leukoplakia, in 20.9% with CPL, and in 42.9% with erythroplakia. There were trends in differences, but their statistical significance was also not achieved ($p = 0.091$).

Overall, the analysis of molecular properties showed that among the studied genes and proteins, no significant statistically significant differences were found between precancerous types ($p > 0.05$ for all indicators). This indicates the high heterogeneity and complexity of the pathogenetic mechanisms involved in the formation of precancerous changes, as well as the need to expand research to identify more specific molecular markers for prognostic and therapeutic use. The obtained data confirm that the expression of P53, VEGF, and EGFR within this sample is not a determining factor for the differentiation of precancerous types, however, further research, taking into account molecular and genetic characteristics, as well as an expanded analysis of marker combinations, can contribute to the development of individual approaches to diagnosis and therapy.

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