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Perspectives

Potentially premalignant disorder/lesion versus potentially premalignant patient: Relevance in clinical care

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ABSTRACT

This communication presents a discussion of patient risk factors and outcomes for potentially malignant and malignant lesions in contrast to lesion assessment and lesion management. The shift in consideration may have implications for research and clinical intervention. This compact review discusses several local and systemic components that contribute to the development of malignant changes and discusses whether patients instead of lesions should be defined as having a potentially premalignant condition.

Introduction

Carcinogenesis is conceptualized as multistep process through the continuum from normal epithelium to invasive carcinoma [1,2]. Within this continuum, oral epithelial dysplasia is considered as a histological indicator of the risk of malignancy [3,4]. The presence of both epithelial architectural disturbance and cytological atypia is required to define dysplasia, which is generally classified as mild, moderate and severe according to thickness of involvement of the epithelium [3]. However, rather than separate stages, the histologic changes represent a gamut of molecular and cytologic changes within the epithelial layers of oral mucosa, which can either progress or regress in time [3].

A premalignant condition/lesion has been defined as "the histopathologic changes seen in a chronic, progressive, and premalignant disorder of oral mucosa which may present itself clinically as leukoplakia, erythroplakia, or leukoerythroplakia, or may also be seen in verrucous or papillary leukoplakias, in the margins of a chronic mucosal ulcers, or in the adjacent mucosa of invasive squamous cell carcinoma" [5]. This term also refers to unpredictable diversity of risk and variable biology and pathogenesis of potential precursor lesions to cancer [6]. However, it is also noted that the severity of dysplasia within a potentially premalignant lesion/condition may imply the malignant potential of that particular lesion rather than the clinical presentation [4,5,7]. Thus, it may be suggested that oral potentially premalignant lesions/conditions can be better understood as the clinical manifestations of various degrees of oral mucosal epithelial dysplasia either at the molecular or histological level, resulting from the alterations of the epithelium and the cellular microenvironment (oral surface and microbiology and connective tissue) and immune function [8].

Discussion

The process of carcinogenesis is a broad and multi-dimensional process than the changes in the epithelial cells. This statement is included in discussions regarding the role of dysplasia and risk of progression to cancer; as some reports describe a risk of progression to cancer that is unrelated to the severity of dysplasia [9–12], while others revealed that the degree of dysplasia is associated with a risk of progression [5,13–15]. Unexpected transformation may be attributable to the unreliable nature of histological grading of epithelial dysplasia [10,16], or to the presence of invasion which may occur without any histological evidence of prior full-thickness change in the overlying epithelium [10]. Additionally, malignant transformation of a dysplastic lesion may have many other important components, including host dependent or behavioral factors and genetics [17–19], tobacco and alcohol consumption [20–22], inflammatory conditions [23,24], microbial factors [25–28], systemic disorders or medication use which in turn alter the cellular metabolism and immunosurveillance of the host [29,30], oral hygiene status [31,32] and nutritional conditions [31,33]. All these components may contribute to the development of malignant changes within and around an epithelial cell; thus, connective tissue signaling and immunosurveillance (related to either innate or adaptive immunity) are increasingly recognized as critical in pathogenesis [8]

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and potentially in management. Considering the complex and unpredictable nature of the transformation of oral epithelial cells from normal to malignant and the absence of a single etiological entity responsible for this alteration, today may be the time to discuss "'whether patients instead of lesions should be defined as having a potentially premalignant condition". This discussion would not only assist to clarify the actual status of a patient, but also help to determine the approaches to management [10,12,22,32,34–39]. The appropriate treatment is usually determined by both the lesion related factors such as the degree of dysplasia, location and size [10,12,34], and the patient related factors such as the age [12], general health status [36,37], oral conditions [32,35], and anticipated compliance of the patient to follow-up. However, as malignant transformation may also occur in non-dysplastic or low-grade lesions [12], all lesions require follow-up and the search for effective prevention and intervention is needed.

Considering that the immune function and tissue microenvironment and general health of the patient including habits and nutritional assessment play critical roles in pathogenesis and response to treatment, it may be time to address the conventional attitude towards prediction of malignant transformation of a lesion in oral cavity and analyze the patient as a whole, including genetic, endocrine, psychological, nutritional and oral aspects which are patient specific. A patient with a history of malignancy in the family, consumption of tobacco and alcohol, poor oral hygiene, various systemic diseases, having high level of stress and inadequate nutrition may be considered as a "high risk patient" and may deserve a thorough examination, including evaluation of some established biomarkers for malignant transformation of oral mucosal lesions (eg. EGFR, mTOR, LOH) and continuing clinical follow up. In this case, mild dysplasia identified in a "high-risk patient" may be treated with more aggressive treatment approaches and follow up than an analogue lesion noted in a "low risk patient". The potential for new interventions based upon molecular change and tumor microenvironment in addition to current approaches directed primarily to the epithelial changes may change future management of the premalignant patient.

Conclusion

Consideration of the patient's genetic, general, emotional and behavioral health components, and integration of tissue changes, microenvironment, proteomics, and growth factors and inflammatory biomarkers into this judgement process would eventually lead to "patient-unique treatment decision" which may impact management approach of potentially premalignant and malignant patient.

Conflict of interests

None declared.

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