Site-specific Oral Cancers are different Biological Entities

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INTRODUCTION

One of the imperative features of the oral cavity is the presence of different areas, which are characterized by unique sets of tissue organization. These regions are divided into lining mucosa (buccal mucosa, labial mucosa, alveolar mucosa, mucosa lining the ventral surface of the tongue, floor of the mouth, and soft palate) and masticatory mucosa (hard palate, attached gingiva, and dorsal surface of the tongue).1 Variations are present not only in terms of tissue composition, but also marked disparity has been noted in molecular marker expressions and epithelial turnover rates. It is widely acknowledged that the expression of epidermal growth factor, keratinocyte growth factor, interleukin-1, and transforming growth factors alpha and beta is attributed to the variation in the site-specific epithelial turnover rate.2

Oral squamous cell carcinoma (OSCC) is the most common malignancy of the oral cavity, which usually is preceded by myriads of oral potentially malignant disorders.3 Oral squamous cell carcinoma can be omnipresent in the oral cavity, affecting any site. Geographic variations in the site predilection of OSCC have been reported in the literature. For example, in many South and Southeast Asian countries including India, the intraoral distribution of oral cancer revealed buccal mucosa to be the most common site, followed by anterior two-thirds of the tongue. However, in Europe and other Western countries, contrastingly, tongue cancer is encountered more frequently than cancer of buccal mucosa.4 Molecular alterations are an integral part of malignant transformation of OSCC, which has been very well elucidated in our recently proposed definition.5 Looking at the turnover rate and molecular expression variability at different sites of the oral cavity, a sense of wonder usually arises on the possibility of molecular heterogeneity in OSCC arising at distinct spots. If site-wise heterogeneity exists in OSCC, then it would have an immense impact on the future of development of targeted drug therapy.

Literature search revealed scarce studies on the comparative analysis of molecular expression in OSCCs at different sites.6-8 It has been established that p16 and p21 expressions were significantly different in buccal and tongue carcinomas. In combined analysis, simultaneous downregulation of p16 and p21 was seen in 47% of tongue cancer cases as against 28% in buccal mucosa carcinomas.6 Telomerase activity has been reported to be significantly diverse among the tumors in the nonkeratinizing mucosa (buccal mucosa, alveolus, and floor of mouth) and tongue.8 In another study, expression of cyclin D1 displayed a significant variation with respect to site, with higher manifestation in tongue tumors as compared with buccal mucosal OSCC.7

Site-wise heterogeneity in molecular expression is quite likely and could have an impact on the development of personalized cancer medicine in the future. Literature search depicts not enough studies, and there is a dire need for additional more examinations on larger sample size. Expressions related to cell survival and proliferation have been studied till date. However, future studies on the molecular expression of invasion, migration, and
angiogenesis are recommended to fully comprehend and appreciate the biological behavior of OSCCs at distinct sites. It is evident from the published literature that there is a vague comparison between buccal mucosa and tongue as primary sites for OSCC, while other sites have been overlooked or the data are not well elucidated. We believe that OSCCs of gingiva, labial mucosa, floor of mouth, retromolar triangle, and palate also carry potential for site-specific heterogeneity in molecular expression. Literature suggests that the prognosis of the patient varies depending upon the involvement of different sites. The 5-year survival rate and neck control are better in buccal mucosa as compared with tongue OSCC. Hence, we recommend that all the future studies on molecular expression should be complemented with the results of patient outcome.

REFERENCES