SHORT COMMUNICATION

Filling in the Gaps in Histopathological Reporting of Oral Squamous Cell Carcinoma for Better Diagnosis and Prognostic Outcomes.

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Abstract

Introduction: Oral squamous cell carcinoma (OSCC) remains a significant global health challenge with poor survival rates. This necessitates an update of the diagnostic and reporting system to enhance understanding of the disease. Histopathology reports play a crucial role in OSCC management, influencing treatment decisions and providing prognostic information. However, there is a need to improve and refine the current reporting parameters to reduce ambiguity. Recent advancements propose incorporating additional parameters such as tumor budding and tumor-stroma ratio, which have demonstrated significant roles in prognosis.

Management: Considering the process of epithelial-mesenchymal transition (EMT) at the tumor invasive front can provide valuable insights into tumor behavior and outcomes. Updating the histopathology reporting system for OSCC can contribute to better treatment planning and improved patient outcomes.

Conclusion: The integration of these novel parameters in routine histopathology reports can provide a comprehensive understanding of OSCC, enabling personalized treatment strategies and improved clinical outcomes.

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Introduction

Oral squamous cell carcinoma (OSCC) has established itself as one of the most persistent health calamity across the globe which remains unconquered even with most advanced therapeutics and a multidisciplinary diagnostic and management approach with 5 year survival rate of less than 60%.[1,2] Pondering on the above statement it can be clearly made certain, that possibly the current diagnostic and reporting system also has to be meticulously reviewed and updated with the newer parameters identified rather than the age old parameters for bringing out better understanding of the nature of the pathology.[2,3]

Importance of histopathology Report (H/P) in OSCC

The practice of histopathology reporting is often underrated as most of them usually are based upon the clinico-pathological correlation and thereby this "gold standard" diagnostic modality remains just as a confirmatory tool of the diagnosis. However, it is a well- studied fact that management of OSCC both surgical as well adjuvant therapies such as chemotherapy and radiotherapy is influenced to a great extent by the histopathology report of both incisional and excisional biopsies of OSCC.[3,4] As also, prognosis as well as behaviour of malignancy is also gauged to a large extent by the histological parameters.[4] Thereby, we as pathologists hold moral responsibility of delivering accurate, detailed and updated reports.

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Routine Parameters of H/P in OSCC

The ideal updated report of excisional biopsy according to American Joint Committee on Cancer (AJCC 8) for diagnosing the OSCC along with its grade differentiation comprises of -type of growth, depth of invasion (DOI), tumor thickness (TT), status of surgical margins, lymph vascular invasion, perineural invasion, lymph node involvement which consists of number of positive nodes as well as extra capsular spread and extranodal extension.[5]

Independent assessment of the AJCC 8 reporting parameters revealed room for improvement due to subjective and arbitrary parameters like DOI and TT, leading to reporting

ambiguity.[1] Thereby, few literature studies are coming forth to give certain alternate parameters to DOI. One such paper by Kalele et. al. have suggested more research to evaluate the utility of Muscle Invasion (MI) as a more predictable as well as simple parameter to predict the outcomes and prognosis of OSCC. 6

Advancements in reporting coming into limelight-

The present AJCC 8 reporting system has both merits and deficits. Researchers like Jakobsson et al., Anneroth et al., and Bryne et al. have proposed a more complex and detailed reporting system. This system considers various factors, including tumor differentiation, cellular detailing, architectural aspects of the invasive front, and tumor-stroma relationship. By taking into account the cross-talk between epithelial and stromal tissues, this multifactorial system provides a comprehensive understanding of the biological behavior and outcomes of tumors.[7]

Detailed reporting is cumbersome, necessitating a focus on specific parameters, particularly tumor invasive fronts, to provide valuable insights into behavior, prognosis, and therapeutic response.

Recently, a study done by Pallavi. K et al.1 have evaluated parameters such as pattern of invasion (POI), Tumor budding TB, lymphocytic host response (LHR), tumor-associated tissue eosinophilia (TATE), and muscular invasion (MI) alongwith traditional parameters including DOI, TT, lymphovascular invasion and perineural invasion. Their study reported significant role of tumor budding along the invasive front of the malignancy and its prognosis. This novel parameter in the tumor cells can be considered as an independent marker for discohesion and active invasion and is associated with poor prognosis. Dourado et al.[8] emphasized the importance of Tumor Stroma Ratio (TSR) and tumor budding in outcomes of OSCC. They found that both TSR and TB were associated with reduced cancer-specific survival and independently linked to cancer mortality and recurrence in early and advanced stages. Therefore, it is crucial to include these histopathology parameters in routine reporting.

However, TB, which is gaining considerable importance, actually symbolizes the process of epithelial-mesenchymal transition (EMT) at the invading front of the tumor which is known to facilitate tumor invasion and metastasis. [1]

EMT as a new potential histopathological prognosticator

EMT is an important biological event which is characterized by loss of cohesive properties and polarization of epithelial cells and their transformation into non-polarized mesenchymal-like cells which are highly motile.[9]

EMT plays a pivotal role in cancer progression, but its impact on prognosis is not extensively explored. A study by Costa et al.[9] reported reduced E-cadherin expression, a hallmark of EMT, along the invasive fronts of OSCC. Decreased E-cadherin expression correlated with lower disease-free rates, increased recurrence, higher lymph node metastasis, and higher mortality rates. Vimentin, another EMT marker, also showed correlation with tumor invasiveness. Previous studies have similarly reported positive associations between EMT markers and invasiveness, local infiltration, metastasis, recurrence, and overall outcomes.[10,11]

EMT is concerning due to its association with radiotherapy resistance in cancer. It promotes radio resistance in cancer cells undergoing radiation therapy and is a major factor in enhancing resistance to radiotherapy. Many radio-resistant cells exhibit EMT phenotypes.[12]

EMT plays a crucial role in cancer, from initiation to therapy failure. However, its reporting is often absent in routine histopathological reports, mainly due to the financial and technical challenges associated with using immunohistochemical markers for EMT assessment. However, Kalele et al. 13 in their latest research have given five histological parameters to diagnose EMT in routine hematoxylin and eosin stained sections under light microscope. Following are the parameters used to diagnose EMT-

- Loss of apical to basal polarity
- Loss of cell adhesion
- Cell individualization
- Establishment of front back polarity in cell
- Dense inflammatory cell infiltration

These easily identifiable parameters can provide valuable diagnostic information, particularly regarding the presence of EMT along the tumor invasive fronts, in addition to traditional parameters.

Conclusion

The present brief discussion suggests updating of the present histopathology reporting of OSCC which can contribute to better understanding of tumor behavior and outcomes. The prognosticators discussed in the present paper can be a potential top ups for routine parameters to provide prognostic index and help the oncologists in planning customize treatment of every tumor based on its clinicohistological phenotype for best outcomes in the disease.

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