Preface to the series on oral pre-cancer and cancer

Oral cancer and oral potentially malignant disorders (OPMDs) are one of the most well-explored topics related to oral pathology. A majority of research on oral cancer, especially oral squamous cell carcinoma (OSCC) has revolved around its potential risk factors including tobacco products, alcohol, microbial agents, etc. Among these, tobacco products such as cigarette are well-established as an independent risk factor and thus has been heavily sanctioned by global health agencies in an attempt to curb their sale. Despite valiant efforts by the health agencies, the tobacco industry has found innovative methods to sustain its product flow through the introduction of novel tobacco products including E-cigarettes (1). Unlike conventional cigarettes, the potential health hazards of the E-cigarette is relatively unexplored. Thus, without adequate information on E-cigarette induced health effects, it is not possible to implement sanctions restricting their sale.

In addition to well-established risk factors, there are several potential risk factors such as microbial agents, environmental agents, wherein there is a lack of conclusive evidence for causal inference. Researchers have focussed on exploring the overall microbiome profile in oral cancer patients (2). In such cases, it is vital to determine if the microbial profile noted in the cancer patients were a risk factor for the initiation and progression of oral cancer or is the microbial profile secondary to oral cancer. Several microbial agents including HPV and EBV have been implicated in cancer of the oropharynx and nasopharynx but their association with oral cancer has been inconclusive (3,4). The lack of clarity in associating a microbial agent to oral cancer is due to the presence of several confounding factors such as tobacco, alcohol consumption, etc. Thus, in such cases, it is not possible to assess the specific microbial agent as an independent risk factor. Also, studies exploring the association between a microbial agent and cancer have largely used a wide variety of diagnostic tools to detect the microbe. The variations in the sensitivity and the specificity of these diagnostic tools have in turn led to conflicting results.

In addition to etiopathogenesis, recent studies have given much importance to assess the quality of life among oral cancer patients. Anti-cancer treatments often have a cytotoxic effect which can lead to both systemic and local manifestations. Thus, the patients must be given additional prophylactic care to reduce the overall morbidity associated with the therapeutic regimen (5). Also, such oral cancer patients have relatively greater difficulty in adapting to post-therapeutic oral rehabilitation including oral prosthesis (6). Thus, it is heartening to see a surge in the number of articles exploring the quality of life of oral cancer patients. It is vital to understand that in addition to preventing mortality from cancer, it is also in the duty of the clinician to improve the quality of life of oral cancer patients by limiting the associated morbidity.

The Tumour micro-environment is a major factor determining the overall tumor behavior. Thus, studies have constantly explored the various components of the tumor micro-environment including the inflammatory cells (7). Exploring the molecular profile of the stromal micro-environment of both oral cancer and OPMDs could aid in understanding the factors determining the tumor behavior including malignant potential.

The major reason for the increasing number of OSCC cases is due to the inability to prevent the malignant transformation of an OPMD. Thus, studies have tried a wide range of diagnostic markers to asses the malignant risk associated with OPMDs. Despite the identification of a large number of potential salivary and serum diagnostic markers (8), their prognostic ability has remained largely poor.

The WHO has provided clear definitions for the majority of OPMDs along with their etiopathogenesis and diagnostic criteria. Despite these clear delineations, there are few entities such as the oral lichenoid dysplasia (OLD), whose natural history remains to be elusive (9). By definition, OLD is a primary epithelial dysplasia with secondary lichenoid (stromal inflammatory) features. The controversy of OLD is due to its close resemblance to oral lichen planus (OLP), and oral lichenoid lesion (OLL). Both OLP and OLL have the lichenoid component (stromal inflammation) as the primary pathology. Most authors agree that the OLL could have a secondary epithelial dysplastic component. Unlike OLL, there is a lack of consensus as to the presence of epithelial dysplasia in OLP. Authors supporting the presence of epithelial dysplasia in OLP, consider the entity to have malignant potential. Authors rejecting the presence of epithelial dysplasia in OLP, do not believe OLP to have malignant potential. Thus, at present, there is a general lack of consensus as to the natural history of these enigmatic group of lesions.

Surgery, chemo, and radiotherapy have remained to be the major therapeutic modalities for cancer. The recent innovations including targeted therapy have aimed to reduce the morbidity associated with the conventional therapeutic regimens. Among

the recent cancer therapeutic innovations, much importance is being given to gene-editing tools such as the CRISPR-Cas gene (10). Although at a relatively incipient stage, there is an increasing number of studies exploring the potential application of CRISPR-Cas gene tools in cancer, including oral cancer. Such novel cancer therapeutic tools although, could be of immense translational value, require a cautious approach.

The series on oral pre-cancer and cancer included articles analyzing the etiopathogenesis, the tumor micro-environment, diagnostic markers, and therapeutic innovations for oral cancer (1-4,7,8,10). The natural history of enigmatic entities such as oral lichenoid dysplasia has been explored in-depth (9). Also, the series includes articles assessing the quality of life of oral cancer patients both during anti-cancer treatment and during prosthetic rehabilitation (5,6).

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