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Letter to the editor

Co-existing 'Oral Potentially Malignant Disorders' – A high risk clinical entity?

Tobacco 'chewers' and 'smokers' form distinct groups with characteristic oral mucosal changes [1]. Tobacco and areca nut chewers are chiefly found in South Asian countries, and are exposed to a relatively higher carcinogen load due to 'direct-contact' of quid with oral mucous membrane. Moreover, in countries like India, industries often combine tobacco and areca nut into one potential formulation (eg: gutka, mawa, mainpuri, etc.). Prolonged chewing of such dual preparations can result in multiple 'oral potentially malignant disorders' like 'leukoplakia' and 'oral sub-mucous fibrosis' (OSF) in the same patient. Their co-existence might further raise the likelihood of oral squamous cell carcinoma (OSCC) development? Co-existing OPMDs (c-OPMD) have not received enough attention in oral oncology literature and require due consideration by clinicians. It is logical to presume the cumulative 'malignant transformation rate' as additive when two carcinogenic products 'tobacco' and 'areca nut' are chewed simultaneously, and particularly high when distinct OPMDs like leukoplakia and OSF co-exist synchronously?

In a retrospective study of 3056 OPMD patients from a Taiwan registry, 'OSF and leukoplakia' were shown to have a higher rate of malignant transformation (MT) [2]. The 5 year MT rate was 5%, and 10 year MT rate was 10% [2]. The mean duration of MT in another Taiwan based study was 5.1 years for non-OSF, 2.7 years for OSF alone, and 2.2 years for 'OSF with leukoplakia', [3]. More such longitudinal studies, with a minimum of 5–10 years follow-up, are needed to document the true potential of dual OPMDs, 'OSF and leukoplakia' [4].

Individuals who develop 'OSF and leukoplakia' may have a higher grade of dysplasia, because 'oral epithelium' is exposed to hypoxia and metabolic stress due to fibrotic lamina propria [5]. Additionally, epithelium is also exposed to tobacco and sharp pieces of areca-nut, which might accentuate OSCC development due to constant mechanical trauma? [5,6] This two way additive effect of 'hypoxia' and 'direct carcinogen exposure' leads to a conducive milieu favoring oral carcinogenesis. The phenomenon of dual OPMDs/c-OPMDs must therefore raise serious concerns to patients and clinicians.

Even in individuals chewing mainly 'areca nut', c-OPMD may occur as some also follow smoking and/or chew tobacco simultaneously. In such cases, milder versions of leukoplakia may occur in a more solid background of OSF. The clinical/histological grade of 'OSF and leukoplakia' (c-OPMD) depends on the degrees of exposure to areca nut and tobacco. The highest incidences of OSCC recorded in South Asian countries may be attributed to the higher incidence of high risk c-OPMDs?

'Smokeless tobacco' and 'areca nut' use is rampant among many Indian homemakers [7]. In working men, they are frequently consumed by truck drivers to increase 'alertness at work'! [7] In this context, 'sedentary life style' and 'occupational stress' can elevate consumption through different mechanisms. Depending on 'type of product', 'time period' and 'frequency' of consumption, patients can present with OPMD, c-OPMD or OSCC. Also, a large number of tobacco and areca nut chewers belong to a lower socio-economic order. As a consequence of poor educational background, weak national policies and inadequate representation in electronic and print media, this group have poor knowledge about deleterious habits, and display grave initial presentations! Patients have either advanced OPMD/c-OPMD, or advanced OSCC at the time of presentation. OPMDs are initially asymptomatic lesions, with high potential for complete regression following habit cessation and supportive therapy. Unfortunately, many individuals pay no attention to asymptomatic presentations, and are careless about habit withdrawal and timely screening, reverting back to their habits in no time! It is important to develop realistic counseling sessions, particularly at peripheral centers which are accessible to many patients living at remote locations.

Since c-OPMDs develop years after habit inception and take several years to transform, clinicians have a sufficient 'therapeutic window' to arrest them. During this window clinicians can implement potential approaches that might effectively reduce MT rate if instilled with habit cessation. More efforts are needed for identifying suitable 'topical chemotherapeutic agents' and 'dietary chemo-preventive' strategies as OPMDs/c-OPMDs are chiefly 'epithelial conditions' (~1–2 mm deep), amenable to direct interception!

Regular consumption of herbal remedies (eg: green tea, curcumin), may decrease MT rate because of 'transepithelial percolation' of their respective active ingredients [8]. c-OPMDs often demonstrate red and white elements. The 'white elements' correlate with keratin accumulation, and 'red elements' correlate with atrophy and erythema. Antioxidants within herbal remedies can percolate through the atrophic areas more strongly over areas showing thick keratin barrier? The atrophic and erythematous areas are the zones that display a 'higher grade of dysplasia', which need to be effectively targeted.

A great deal of attention is also needed to thoroughly screen c-OPMDs, because they present as wide lesions extending several centimeters in many cases. It is extremely difficult to choose representative *'site of biopsy'* in such wide lesions. Therefore, it is important to utilize effective screening methods to bio-monitor such lesions for early signs of MT. Thorough screening/bio-monitoring is possible with developments in 'exfoliative cytology', 'light' and 'saliva' based methods. Among the various light based strategies 'auto-fluorescence' based screening is a relatively simple, easy-to-use clinical adjunct that could potentially improve OSCC detection [9].

Due to obliterated mouth opening in OSF, and presence of wide mucosal coverage in leukoplakia and OSF, c-OPMDs should be considered as 'diagnostically and therapeutically challenging entities'. Owing to the large number of c-OPMD cases reported world-wide, it is crucial to address them separately, and their malignant potential should not be underestimated by clinicians…

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