Review Article

An update on precancerous lesions of oral cavity

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ABSTRACT

Oral cancer is the most common head and neck cancer, found in 270,000 patients annually worldwide. Some cancers develop from precancerous lesions; however, there is no definitive clinico pathological factor or biomarker that reliably enables malignant transformation to be predicted in an individual patient. Early detection and early treatment of oral cancer are important for improving the survival rate of patients; prevention of oral cancer will clearly contribute most to decreasing its death rate. So correct diagnosis and timely treatment of premalignant lesions with high risk of malignant transformation may help to prevent malignant transformation.

***Keywords**: Oral premalignant lesions, potentially malignant lesions, leukoplakia, erythroplakia, malignant transformation, epithelial dysplasia*

Introduction

Premalignancy include group of diseases that acts as precursors of the squamous cell carcinoma. Premalignant lesions are clinically and histologically distinct lesions preceding malignant changes. Not all malignancies arise from premalignancies. The concept of oral pre-cancers is especially relevant to Indian subcontinent because of the cultural habit of Betel nut, betel leaf chewing reverse smoking.[1, 2] The assault of oral mucous membrane starts from a young age due to highly spicy food habits. Oral pre-cancer is an intermediate clinical state with increased cancer risk, which can be recognized and treated, obviously with a much better prognosis compared to the full blown malignancy. [3, 4]

Definitions: Premalignant or precancerous lesion is defined by the World Health Organization (1978) as “a morphologically altered tissue which cancer is more likely to occur than its normal counterpart. [5]

At a workshop coordinated by the WHO Collaborating Centre for Oral Cancer and Precancer in the UK: The term, "**potentially malignant disorders**', was recommended to refer to precancer as it conveys that not all disorders described under this term may transform into cancer.

Potentially malignant disorders: A lesion or condition, in which risk of malignancy, being present at the time of initial diagnosis or at a future date. [6, 7]

Potentially malignant lesions include:

- Leukoplakia
- Erythroplakia
- Palatal changes among reverse smokers.

LEUKOPLAKIA (leuko - white; plakia - patch**)** Number of definitions of leukoplakia came since 1978 to 2007. Earlier leukoplakia was defined as "a white patch or plaque that cannot be characterized clinically or pathologically as any other disease" (WHO, 1978) [5]

Latest, Warnakulasuriya et al in 2007 defined it "should be used to recognize white plaques of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer". [8, 9]

History:

- In 1818 - Alibert termed it as Ichthyosis
- 1851 - Sir James Paget termed it as leuko keratosis and smoker's patch
- And finally in 1877 – Schwimmer termed it as Leukoplakia.

Etiology:

- Tobacco (smoke and smokeless)
- Alcohol
- Candida albicans
- Viral antigens (HPV strains 16, 18)
- Levels of Vit A, B12, C, beta-carotene, folic acid and syphilis are associated. [10, 11]

Molecular changes:

Lesions that progress to squamous cell carcinoma (SSC) appear to differ genetically from non-progressing lesions although they may not differ on the basis of histomorphologic findings. Progressing early lesions are genetically different from morphologically similar non-progressing lesions and molecular analysis may therefore become necessary in diagnosis. Loss of heterozygosity on 3p and/or 9p has a 3.8 times relative risk for developing SCC, and if additional sites of LOH are present (4q, 8p, 11q, 13q, or 17p), a 33-fold increase in risk of progression to cancer is seen. [12]

Pathogenesis:

When a cell is exposed to a carcinogen it probably tries to adapt to it. An increase in cell proliferation, diminishing the cytosolic volume and the associated organellar load, could be an attempt in this direction. In the context of oral epithelium, an accelerated growth phase depicted by broadening the progenitor compartment (hyperplasia) is the earlier sequelae and when the irritant still persists, the epithelium shows features of cellular atrophy, again a well characterized feature of adaptation (atrophy). At a later stage when the stages of adaptation and reversible cell damage surpasses, the cells progressively slips into a stage of irreversible cell damage; manifest either as cell death or neoplastic transformation. The accelerated pace of cell division noted at the earlier stages of transformation as a part of adaptive response (to replace the damaged cell pool) is, in a way, facilitative of the accumulation of further genetic damage, thereby driving the cells further along the path of transformation. [13, 14]

Clinical classification: [15]

- Mehta et al 1971 homogenous, ulcerated and nodular leukoplakia
- WHO in 1980 Homogeneous and Non Homogeneous

- Banoczy in 1982 Leukoplakia simplex, Leukoplakia verrucosa, Leukoplakia erosiva
- WHO in 1998 thin/pre leukoplakia / homogenous, thick/smooth/fissured/homogenous,nodular/granular/ rough / Verruciform, speckled / non homogenous/ erythro leukoplakia
- WHO in 2002
    - Phase I: thin, smooth leukoplakia – better prognosis.
    - Phase II: thick, fissured leukoplakia.
    - Phase III: proliferative verrucous leukoplakia (PVL) – higher malignant trans-formation rate.
    - Phase IV: Erythro-leukoplakia – poor prognosis. [10]

The current "gold standard" for predicting the malignant potential of premalignant lesions is the presence and degree of dysplasia. [16]

Various grading systems of dysplasia

1. Smith and Pindborg grading system: no dysplasia, mild dysplasia, moderate dysplasia, severe dysplasia. [17]
2. Conventional grading system: mild dysplasia, moderate dysplasia, severe dysplasia and carcinoma in situ. [18, 19]
3. Ljubljana grading system: simple hyperplasia, abnormal hyperplasia, atypical hyperplasia, carcinoma in situ. [20, 21]
4. WHO system: low, moderate, severe and carcinoma in situ. [22, 23, 24]

A Modified Classification and Staging System for Oral Leukoplakia:

A proposal for a modified classification and staging system for oral leukoplakia (OLEP) has been presented by Van der Waal el al, 2000 in which the size of the leukoplakia and the presence or absence of epithelial dysplasia are taken into account. Altogether four stages are recognized:

LI - Size of leukoplakia < 2 cm
L2 - Size of leukoplakia 2-4 cm
L3 - Size of leukoplakia >4cm
Lx - Size not specified
P - Pathology
PO - No epithelial dysplasia
PI - Distinct epithelial dysplasia
Px - Dysplasia not specified in the pathology report.

OLEP Staging System

Stage I - L1 PO
State II - L2 PO
Stage III - L3POorLlL2Pl
Stage IV - L3 P1

Malignant transformation rate is 0.13 – 17.5 %. [25, 26]

ERYTHROPLAKIA

The term erythroplakia in 1978 was defined analogously to designate lesions of the oral mucosa that present as ''bright red, velvety plaques which cannot be characterized clinically or pathologically as being due to any other condition''. In 1994 it was also used analogously with leukoplakia to designate lesions of the oral mucosa that present as ''red areas and cannot be diagnosed as any other definable lesion''**.** In 1997 it was defined as ''A fiery red patch

that cannot be characterized clinically or pathologically as any other definable lesion'' The term erythroplakia should be used analogously to leukoplakia to designate lesions of the oral mucosa that present as ''a predominantly red lesion of the oral mucosa that cannot be characterized as any other definable lesion''. [27]

The word is an adaptation of the French term "**erythroplasia de Queyrat**," which describes a similar-appearing lesion of the glans penis with a comparable premalignant tendency.

Etiology: Although the etiology of erythroplakia is uncertain, most cases of erythroplakia are associated with heavy smoking, with or without concomitant alcohol abuse. [2]

Clinical features: Several clinical variants of erythroplakia have been described, but there is no generally accepted classification. Shear described "homogeneous erythroplakia, erythroplakia interspersed with patches of leukoplakia, and granular or speckled erythroplakia"; most authors consider this last category to be identical to speckled leukoplakia. Many of these lesions are irregular in outline, and some contain islands of normal mucosa within areas of erythroplakia, a phenomenon that has been attributed to the coalescence of a number of pre-cancerous foci. It occurs predominantly in older men, in the 6th and 7th decades of life. Erythroplakias are more commonly seen on the floor of the mouth, the soft palate, and the tonsillar fauces, all prime areas for the development of carcinoma. These lesions are commonly described as erythematous plaques with a soft velvety texture. [4]

Histological features: The epithelium shows a lack of keratin production and is often atrophic. This lack of keratinization especially when combined with epithelial thinness, allows the underlying microvasculature to show through, thereby causing the red color. The underlying connective tissue often demonstrates chronic inflammation. Differentiation of erythroplakia with malignant change and other early squamous cell carcinomas from benign inflammatory lesions of the oral mucosa can he enhanced by use of 1 per cent toluidine blue (tolonium chloride) solution applied topically with a swab or as an oral rinse.

Malignant transformation is found to be 18-50%. This may be due to severe epithelial dysplasia, epithelial atrophy, and lack of keratin with location which is at floor of the mouth. [2]

PALATAL CHANGES ASSOCIATED WITH REVERSE SMOKING

Reverse chutta smoking practiced especially among females of Srikakulam district of Andhra Pradesh, (Daftary, et al, 1992). Palatal involvement was noted in 422 (85 per cent) of the 497 leukoplakia cases and of course in all of the cases of leuko keratosis nicotina palati. Palatal changes associated with reverse smoking thus exhibited a spectrum of clinical changes, and it was not satisfactory to group them under leukoplakia, pre leukoplakia or leuko keratosis nicotina palati. The annual age-adjusted incidence rates of palatal changes were 24.9 per 1,000 among men and 39.6 per 1,000 among women and the peak incidence was in the 55-64 year age group.[2]

Clinical Aspect: Palatal changes comprise several components:

- Keratosis—diffuse whitening of the entire palatal mucosa.

- Excrescences—1-3 mm elevated nodules, often with central red spots.
- Patches—well defined, elevated white plaques
- Red arms—well defined reddening of the palatal mucosa.
- Ulcerated areas—crater-like areas covered by fibrin
- h areas—areas of palatal mucosa that are devoid of pigmentation.

Palatal changes remain stationary, regress, recur, or progress to cancer. Some 75% of the palatal changes remain stationary, 14% regress spontaneously, about 11% show variable characteristics, i.e. they regress, recur, and regress again. The regression rates were higher when the habit was discontinued or reduced substantially.

Malignant transformation is found to be 0.3 %. [4, 11]

Conclusion

Correct diagnosis and timely treatment of potentially malignant lesions with high risk of malignant transformation may help to prevent malignant transformation**.** Potentially malignant lesions can be treated based on the clinical and histological staging. Various treatment modalities are suggested in the literature; from cessation of the habit to surgical reconstruction. But among this early diagnosis of the lesion and cessation of habit is the best line of treatment.

References

1. Parkin DM, Bray F, Ferlay J et al. Global cancer statistics. Cancer J Clin 2002; 55:74-108.
2. Shafer's Hine Levy**.** A Text book of Oral Pathology. 4th Edition. Philadelphia: Saunders Elsevier; 2006.p.1058-65.
3. Amagasa T. Oral premalignant lesions. Int J Clin Oncol 2011; 16:1–4
4. Neville Damm Allen Bouquot**.** Oral & Maxillofacial Pathology. 2nd Edition. Philadelphia: Saunders Elsevier; 2002: 5055-08.
5. Kramer IRH, Lucas RB, Pindborg JJ et al. Definition of leukoplakia and related lesions: an aid to studies on oral precancer. Oral Surg Oral Med Oral Pathol1978; 46:518–39.
6. Axell T, Holmstrup P, Kramer IRH et al. International seminar in oral leukoplakia and associated lesions related tobacco habits. Commun Dent Epidemiol 1984; 12:145–54.
7. Axell T, Pindborg JJ, Smith CJ et al. Oral white lesions with special reference to precancerous and tobacco-related lesions: conclusions of an international symposium held in Uppsala, Sweden, May 18–21 1994. J Oral Pathol Med 1996; 25:49–54.
8. Warnakulasuriya S, Johnson NW, vanderwaal I. Nomenclature and classification of potentially malignant disorders of the oral mucosa J Oral Pathol Med 2007; 36:575–80.
9. Warnakulasuriya S, Reibel J, Bouquet J, Dabelsteen E. Oral epithelial dysplasia classification systems: predictive value, utility, weaknesses and scope for improvement. J Oral Pathol Med 2008; 37: 127–33.
10. Cabay RJ, Morton TH, Epstein JB. Proliferative Verrucous Leukoplakia and its progression to oral carcinoma: a review of literature. JOPM 2007: 36, 255-61.

11. Sapp, Eversal, Wysock**.** Oral and maxillofacial pathology. 2nd Edition. Missouri: Mosby Elsevier; 1997.p.400-02
12. Mithani, Mydlard, Grumbine, Smith, Califano. Molecular Genetics of Premalignant oral lesions. Oral Ds 2007; 13:126-33.
13. Izumo T. Oral premalignant lesions: from the pathological viewpoint Int J Clin Oncol 2011; 16:15–26.
14. Amagasa T, Yamashiro M, Uzawa N. Oral premalignant lesions: from a clinical perspective. Int J Clin Oncol 2011; 16:5–14.
15. Pindborg JJ, Reichart PA, Smith CJ et al. Histological typing of cancer and precancer of the oral mucosa, 2nd ed. Berlin: Springer.
16. Van der Wall I. Potentially malignant disorders of the oral mucosa and oropharyngeal mucosa; terminology, classification and present concepts of management. Oral Oncol 2009; 45:317–23.
17. Pindborg JJ, Reibel J, Holmstrup P. Subjectivity in evaluating oral epithelial dysplasia, carcinoma in situ and initial carcinoma. J Oral Pathol 1985; 14:698–708.
18. Abbey L, Kaugars GE, Gunsolley JC et al. Intraexaminer and interexaminer reliability in the diagnosis of oral epithelial dysplasia. Oral Surg Oral Med Oral Pathol 1995; 80:188–91.
19. Karabulut A, Reibel J, Therkildsen MH et al. Observer variability in the histologic assessment of oral premalignant lesions. J Oral Pathol Med 1995; 24:198–200.
20. Gale N, Kambic V, Michaels L et al. The Ljubljana classification: a practical strategy for the diagnosis of laryngeal precancerous lesions. Adv Anat Pathol 2000; 7:240–51.
21. Hellquist H, Cardesa A, Gale N et al. Criteria for grading in the Ljubljana classification of epithelial hyperplastic laryngeal lesions. A study by members of the Working Group on Epithelial Hyperplastic Laryngeal Lesions of the European Society of Pathology. Histopathology 1999; 34:226–33.
22. Hellquist H, Lundgren J, Olofsson J. Hyperplasia, keratosis, dysplasia and carcinoma in situ of the vocal cords a follow up study. Clin Otolaryngol 1982; 7:11–27.
23. Amagasa T, Yokoo E, Sato K et al. A study of the clinical characteristics and treatment of oral carcinoma in situ. Oral Surg Oral Med Oral Pathol 1985; 60:50–5.
24. Shimizu M, Nagata K, Yamaguchi H et al. squamous intraepithelial neoplasia of the esophagus: past, present, and future. J Gastroenterol 2009; 44:103–12.
25. Amagasa T, Yamashiro M, Ishikawa H. Oral leukoplakia related malignant transformation. Oral Sci Int 2006; 3:45–55.
26. Silverman S Jr, Gorsky M, Lozada F. Oral leukoplakia and malignant transformation: a follow-up study of 257 patients. Cancer 1984; 53:563–8.
27. Reichart PA, Philipsen HP. Oral erythroplakia—a review Oral Oncology 2005; 41: 551 61.

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