Case Report

Bilateral oral leukoplakia: A case report and review on its potential for malignant transformation

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Abstract

Oral leukoplakia (OL) is considered as a most common potentially malignant disorder (PMD) affecting the mucosa of the oral cavity. With the passage of time, the definitions of OL kept evolving. Leukoplakia usually presents after the fourth decade of life and is one of the most common oral PMDs affecting the oral cavity. Based on the macroscopic features of OL, it can be classified into two subtypes: homogeneous and nonhomogeneous.

Keywords: Homogeneous leukoplakia, malignant transformation, oral leukoplakia, treatment

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INTRODUCTION

One of the most common oral potentially malignant disorders (PMDs) affecting the oral cavity is oral leukoplakia (OL). In the first international conference on OL (1984) in Malmo, Sweden, OL was defined as "a white patch or plaque that cannot be characterized clinically or pathologically as any other disease and is not associated with any physical or chemical causative agent except use of tobacco." In the year 1997, the WHO defined leukoplakia as "a predominantly white lesion of the oral mucosa that cannot be characterized as any other definable lesion. van der Waal in 2007[1] suggested a new definition that includes histological confirmation, but this has not been yet assessed by the WHO, "A predominantly white lesion or plaque of questionable behaviour having excluded, clinically and histopathologically, any other definable white disease or disorder.[1]" Consumption of alcohol along with other tobacco products has a synergistic effect and is thought to be a causative factor in OL. On an average, the rate of malignant transformation of OL has been estimated to be 1.36%.[2] This case report emphasizes on the treatment aspects of OL and to further prevent its malignant progression.

CASE REPORT

A 49-year-old male patient reported to the department of oral medicine and radiology with a chief complaint of a whitish area in his right inner side of the cheek for the past 6 months. On eliciting personal history, the patient has a habit of smoking cigarettes since the last 7 years, 5 cigarettes per day. On clinical examination, no abnormalities were detected extraorally. Inspection of the lesion intraorally revealed an irregular whitish plaque on the right buccal mucosa at the line of occlusion, measuring approximately 1 cm × 2 cm at its greatest

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diameter [Figure 1]. The lesion extends anteriorly 1 cm away from the commissure of the lip up to 4 cm short of retromolar trigome region posteriorly, superiorly 3 cm below the upper buccal vestibule, and inferiorly 4 cm short of lower buccal vestibule. The boundaries of the lesion appeared to be well defined. Similarly, an irregular whitish plaque was noted on the left buccal mucosa at the line occlusion, measuring approximately 1.5 cm × 1.5 cm at its greatest diameter [Figure 2]. The lesion extends anteriorly 1 cm away from the commissure of the lip and extending 4.5 cm short of retromolar trigome region posteriorly. Superiorly, the lesion was present 2.5 cm below the upper buccal vestibule and inferiorly 4 cm short of lower buccal vestibule. The lesion had well-defined boundaries. The surface over the lesion appeared to be rough and wrinkled, giving it a cracked mud appearance. The surrounding mucosa appeared to be brownish-black suggestive of postinflammatory melanin pigmentation. On palpation of both the lesions, all inspectory findings were confirmed with respect to size, shape, and extent. The lesions were nonscrappable and nontender. It was raised 0.5 mm over the surface. No bleeding from the site was noticed. Based on the history and clinical examination, a provisional diagnosis of bilateral homogeneous leukoplakia was considered. The differential diagnosis of frictional keratosis and plaque type of lichen planus was given. The patient was advised a routine hematological investigation which reported to be normal followed by toluidine blue staining which revealed retentive areas within the lesion [Figure 3]. Patient motivation and counseling with respect to tobacco cessation was done. Excisional biopsy of both the lesions was performed and the specimen was submitted for histopathological examination which revealed OL. A final diagnosis of OL was confirmed based on the history, clinical examination, and histopathological report. The patient was recalled after 1 week for suture removal and follow-up. Healing of the biopsy site was adequate [Figure 4].

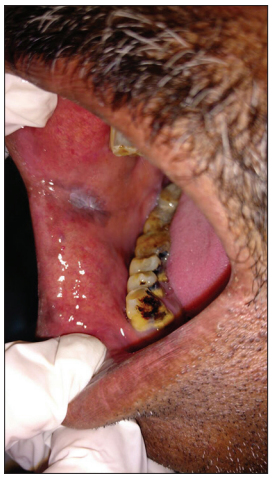

Figure 1: Oral leukoplakia affecting the right buccal mucosa

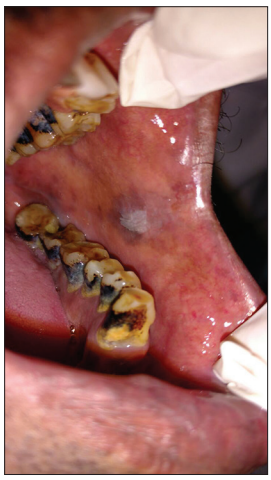

Figure 2: Oral leukoplakia affecting the left buccal mucosa

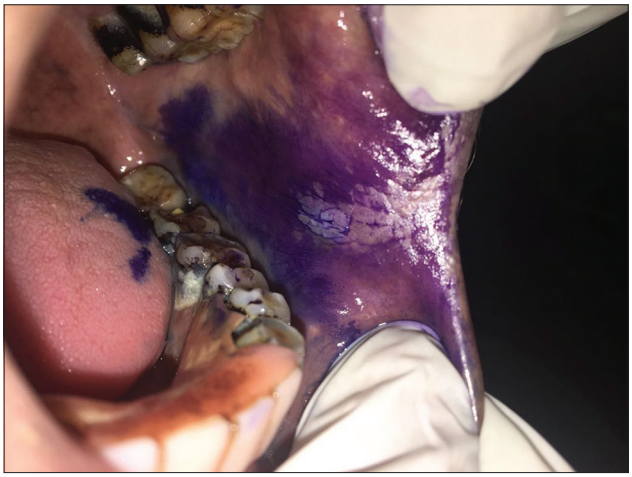

Figure 3: Toluidine blue staining shows retentive areas within the lesion

DISCUSSION

In 2007, Warnakulasuriya *et al*.[1] proposed in a report that: "Oral Leukoplakia should be used to recognise white plaques of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer."

Etiology

Smoking has been proved to be the dominant etiological factor in OL. The etiology of leukoplakia is believed to be a causal affiliation between prolong mechanical trauma, candidiasis, human papillomavirus (16 and 18 types), Epstein–Barr viruses, herpes simplex viruses, HIV viruses, and also reduced serum concentrations of β-carotene and Vitamin A.[3,4]

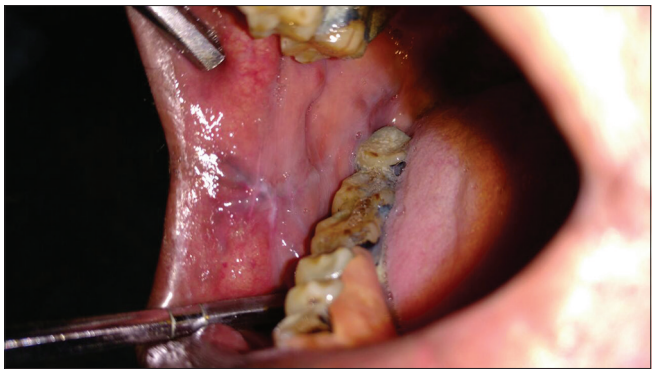

Figure 4: Healing of the biopsy site noticed

Clinical manifestation

Based on the macroscopic features of OL, it can be classified into two subtypes: homogeneous and non-homogeneous.[2,3] In our case, the lesion clinically manifested like a whitish plaque with a wrinkled surface texture, typically characterizing, homogeneous leukoplakia.

Histopathology

Leukoplakia is a clinical terminology and does not have any particular or specific histological appearance. Histopathologically, leukoplakia shows signs of hyperkeratosis, acanthosis, atrophy, and may exhibit various degrees of epithelial dysplasia. Histological changes can be appreciated when there are signs of dysplasia. It may be followed by loss of architectural integrity of epithelial cells. These findings distinguish OL into dysplastic and nondysplastic lesions. Higher risk of malignant transformation to oral cancer has been associated with the presence of dysplasia in histological examination.[5]

Management

The strongest predictor for malignant transformation is the dysplastic changes as are seen within the epithelium. Studies have been reported that all OL lesions should be treated irrespective of the presence of any dysplastic changes. Multiple treatment modalities have been documented including both nonsurgical approaches. Nonsurgical modalities help to prevent malignant transformation. They serve as conservative management, in particular within patients that entail a larger area concerning the oral mucosa, or in those medically compromised patients pertaining to high surgical risks. Consumption of carotenoids (β-carotene, lycopene); Vitamins A, C, and K; and fenretinide, bleomycin, and photodynamic therapy have shown significant regression of the lesion, but randomized controlled trials for nonsurgical treatment have not shown much of evidence in the prevention of malignant transformation and recurrence.[3] Surgical approaches encompass conventional surgery, electrocauterization, laser ablation, or cryosurgery. Conventional surgical procedures entail excision of the lesion. It can be accompanied with or without the placement of skin graft or any other dressing material. It is often not practicable for widespread lesions or those in complex anatomical locations. The associated morbidity of surgery also makes it less appealing for extensive lesions. The related dismalness of surgery additionally makes it less engaging for broad lesions.[5]

Malignancy

A few variables have been related with an increased risk of malignant transformation in OL.[6] Multivariate investigation has proposed that sort of lesion, age, site, and dysplasia are considered as independent risk factors.[3,5]

Appearance

As stated earlier,

- Homogeneous leukoplakia has fewer chances for malignant transformation, low-risk lesions
- Varied red and white lesions, as seen in speckled leukoplakia, possess intermediate risk for malignant transformation
- Complete red lesions (erythroplakia) are at higher risk for malignant transformation.

However, the clinician cannot completely rely upon the macroscopic features for diagnosis. Histological analysis is obligatory to assess the biological potential of the lesion.

Site and age:

The site and age are predictive indicators for malignant transformation.

- It has been reported that the lesions affecting the tongue or floor of the mouth have higher chances for malignant transformation
- In addition, in lesions that are of larger diameter (>200 mm) and in nonsmokers, the risk is higher
- Patients >60 years of age with the site of the lesion on the lateral border of the tongue or on the ventral surface and those who presents with nonhomogeneous type macroscopically with high grade of dysplastic changes correlate with an increased risk of malignant transformation.

Dysplasia

Epithelial dysplasia has been viewed as a standout among the most vital indicators of malignant potential. It has been revealed that dysplastic OL conveys a 5-fold more serious risk of malignant transformation than that of nondysplastic OL, and its prescient value relies upon the predominance of leukoplakia in a given populace. Throughout the years,

it has been recommended that DNA content (DNA ploidy) is an imperative indicator for malignant transformation of leukoplakia or erythroplakia. When a multivariate analysis was performed in a case–control study, it showed that anomalous DNA content was a significant indicator for progression to malignancy with a hazard ratio (HR) of 3.3 (95% confidence interval: 1.5–7.4) redressed for site and grade of dysplasia.[7] Bremmer *et al.* conducted a study which showed that DNA aneuploidy was concomitant with the progression of cancer (HR: 3.7, 54% sensitivity and 60% specificity). It was concluded from their study that DNA aneuploidy has a higher risk for malignant transformation as compared to DNA diploid lesions.[8] Few biomarkers have been reported which said to be significant predictors for malignant transformation such as Ki-67 (Mib-1) and bromodeoxyuridine, combined biomarker score of chromosomal polysomy, p53, and loss of heterozygosity.[9] The events that take place at a molecular level to induce transformation of a premalignant lesion to carcinoma are have not been known yet. Overexpression (or underexpression) of any biomarkers is considered to have a significant predictive value over standard histological examination. Oral cytological examination has been proven efficient for the examination of dysplastic lesion, but its high variability in the results as false positive and false negative has been its limitation.[10] Though the prevalence rate of OL is estimated to be 1.4%–22%[11] and is found to be six times higher in smokers as compared to nonsmokers, its early recognition and management is necessary as it carries a potential for malignant transformation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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