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A CASE REPORT ON ORAL LEUKOPLAKIA WITH MODERATE DYSPLASIA, & ITS MANAGEMENT

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INTRODUCTION

The term Leukoplakia is a clinical diagnostic entity which means white patch. It was used by a Hungarian dermatologist, ErnoSchwimmer, in 1877. Oral leukoplakia is a potentially malignant, non-scrapable, well demarcated, keratotic, white lesion of the oral mucosa which may show a cracked-mud appearance or proliferative & verrucous surface texture. It generally remains asymptomatic & has been found to be associated with tobacco usage or idiopathic in nature in some cases& has a higher male predilection [1 2]. Carcinogens such as tobacco may induce hyper keratinization, with the potential to revert following cessation,but at somestage, mutations will lead to an unrestrained proliferation and cell division.Activation of oncogenes and deletion and injuries to suppressor genes and genes responsible for DNArepair will all contribute to a defective functioning of thegenome that governs cell division. The diagnosis should be limited exclusively to the clinical context by the exclusionof other white lesions (chronic cheek-bite, frictional keratosis, tobacco-induced keratosis, nicotine stomatitis, leukoedema and white sponge nevus), which present as plaques, & are related differential diagnostic terms[1 2 3]. A biopsy is advised in case of long

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standing, recurrent lesions, or when the lesion reveals a suspicious malignant or dysplastic change.

Regarding treatment strategies, multiple approaches have been proposed & practiced, depending on lesion stage & prognostic factors, e.g. habit cessation & strict surveillance, surgical excision, photodynamic therapy, cryosurgery, laser surgery, topical & systemic drug administration ranging from retinoids, lycopene, bleomycin, imiquimod & other antioxidants with variable results.

In the following case report, three treatment modalities have been used, i.e. diode laser excision, systemic retinoids & topical Imiquimod 5% therapy on a sequential basis with favourable results.

Case history:A 51 year old male patient from Vashi, Navi Mumbai , reported to the Oral Medicine OPD, with a complain of white patch on his front lower gum region since 15 days.

History reveals, patient noticed a white coloured patch on his front lower gum & lip region around 2 months ago which showed a moderate increase in size since 2 weeks, till the present condition. The lesion is asymptomatic in nature. Patient visited a private medical practitioner with the above complaint & has been prescribed topical triamcinolone, clotrimazolem.p, SM Fibro capsule & zytee gel. But there was no sign of regression of the white lesion. Patient did not apply the candid mouth paint as advised. Later patient was referred to our OPD for further management.

Past medical historyrevealed no significant & relevant comorbidities.

Past dental history revealed treatment procedures like ultrasonic scaling, conservative restorations & dental extraction around 2 years back.

Lifestyle evaluation: tobacco with slaked lime chewing habit & quid placement on the lower anterior labial vestibule, 6-7 times/day for the past 30 years. Habit quit since few weeks.

General & maxillofacial examination showed normal features.

Intraoral examination: *On inspection*, lower labial mucosa & anterior gingival surface revealed a well demarcated, wide spread , white homogenous plaque having irregular margin, extending from 44 to 35 region, *(fig.1).*

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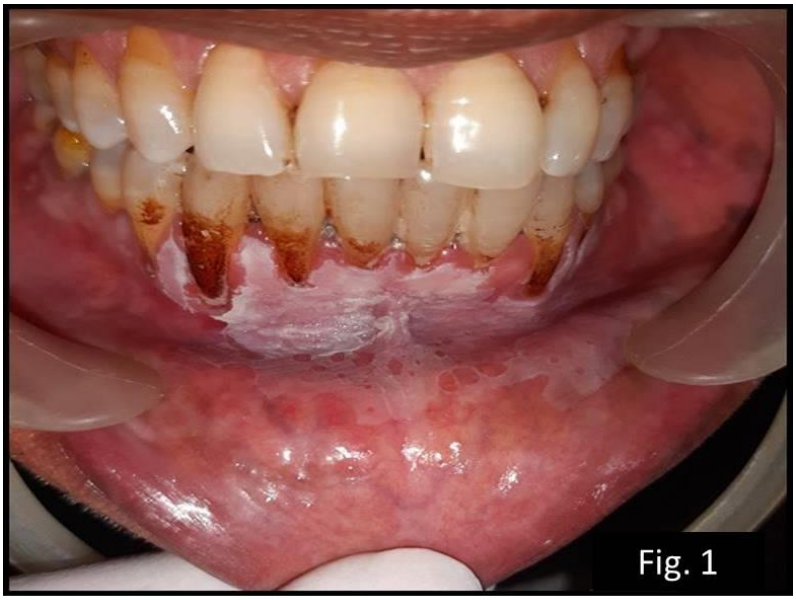

fig 1. White leathery lesion on the lower anterior gingiva & labial mucosa

Surface texture appeared to be leathery & fissured. Size of the lesion > 4cm. The lesion is asymptomatic in nature.

*On palpation*the lesion appeared to be mostly non-scrapable, non-tender, soft in consistency & doesn't blanch on compression. However few areas of the lesion showed peeling off of the white membrane when rubbed with dry cotton.

Upper Labial mucosa, R/L buccal mucosa , hard & soft palate & floor of the mouth did not reveal anyabnormality on examination

Dorsal tongue surface shows multiple fissures or groove of varying depth & size. Few are inter-connected, *fig.2(a)*.

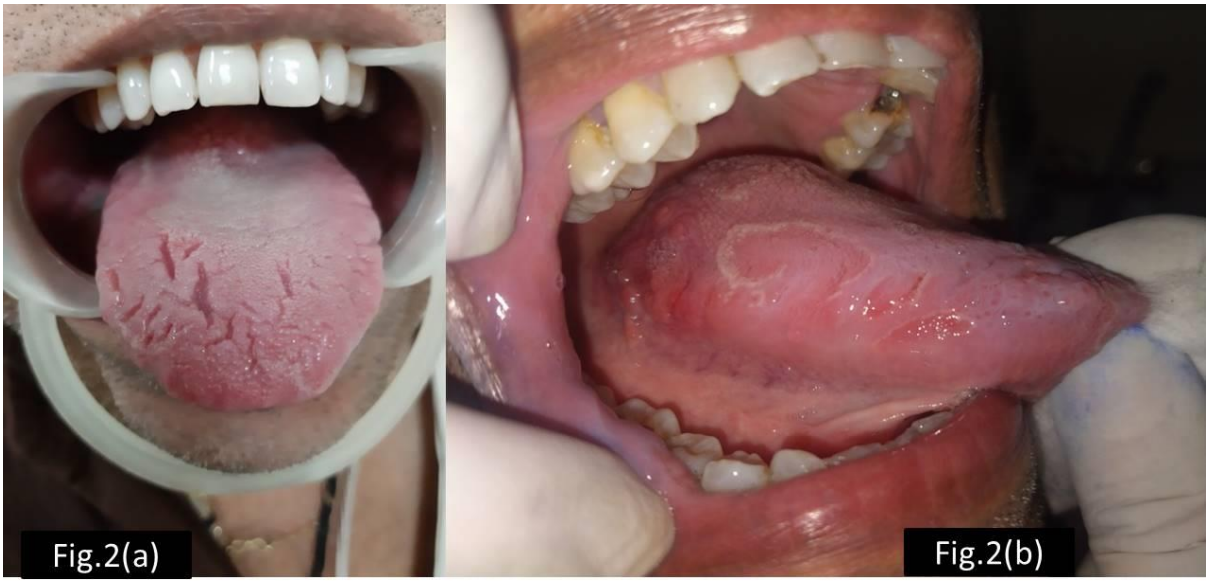

fig 2(a,b). Clinical images of fissured tongue and benign migratory glossitis respectively

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Right lateral surface showed well-demarcated white serpenginous line/striation with surrounded zone of smooth, eryhthematous depapillated mucosa *fig.2(b).*

Based on the above clinical features, a provisional diagnosis of *Homogenous Leukoplakia (fissured) with Candida super-infection* on lower anterior gingiva & labial mucosa i.r.t 35 to 44 has been derieved. **(DD**: KUS, hyperplastic candidiasis, chronic phase of discoid lupus erythematosus, white sponge nevus.) & *Benign Migratory Glossitis (geographic tongue) associated with fissured tongue (lingua plicata)*

To achieve a confirmed diagnosis, toluidine blue staining followed by incisional biopsy, *fig.3 (a), fig.3(b),*was performed for histopathological diagnosis.

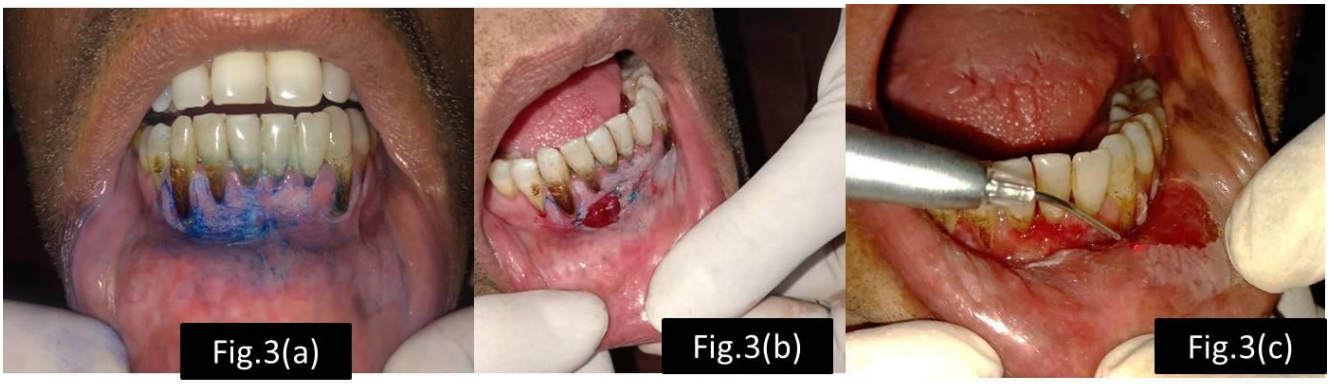

Fig 3: retention of toluidine blue stain (a), incisional biopsy site (b), diode laser ablation (c)

Histopathology evaluation confirmed a **hyperkeratotic lesion with mild to moderate dysplasia & inflammatory infiltrate.**

Final disgnosis: *Homogenous Leukoplakia (fissured) with epithelial dysplasia & Candida super infection* on lower anterior gingiva & labial mucosa i.r.t 35 to 44, Stage IV : L3 P1 (van der Waal,2000).

Benign Migratory Glossitis (geographic tongue) associated with fissured tongue (lingua plicata).

Treatment plan:

- Tobacco cessation counselling was done
- Oral prophylaxis advised
- Diode Laser ablation of the affected area, *fig.3(c),* in three incremental sessions.

Pharmacotherapy

- Cap. Lycored , BD PC x 2 months
- Tab. Vitamin A (retinoic acid-palmitate) 50,000 I.U. chewable,
  as loading dose – 1 tab daily x 2 weeks, followed by
  1 tab every alternate day x 4 weeks

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½ tab every alternate day x 4 weeks

- Candid mouth paint for topical application, TDS x 2 weeks
- **Imiquimod 5% cream** (after complete surgical wound healing post laser ablation therapy) - 1 sachet OD for topical application x 7 days
- Recall & follow-up

Discussion

Oral Leukoplakia which is one of the most common pre-malignant lesions, has been broadly divided into homogenous & non-homogenous types based on surface texture of the lesion[1]. Development of such white lesions with a history of tobacco habits is nothing but a reactionary or resistance phenomenon of the healthy oral mucosa to adapt against the chronic mechanical & chemical irritants. Habit withdrawal following tobacco cessation counselling & periodic follow-up of such cases generally results in significant remission of the lesion, specially in case of homogenous variety. Non-homogenous forms (erythroleukoplakia, verrucous, etc.) requires aggressive treatment & strict monitoring due to its higher tendency to transform into malignancy or show dysplastic features.The main objective of treatment is to prevent carcinogenesis in the presenting lesion or to arrest epithelial dysplasia.

Regarding treatment, surgical approach is one of the most widely used method, that includes cold knife excision & laser surgery, but does not guarantee the development of squamous cell carcinoma during future recurrence[2]. Similarly, under non-surgical treatment, using topical & systemic medications, quite a significant cases showed relapse with epithelial dysplasia &/or OSCC. This may be explained by the concept of field cancerization, i.e., genetic defects in clinically normal mucosa which is caused by simultaneousgenetic instabilities in the epithelium of several extra lesional sites that may lead to squamous cell carcinomas[1]. In such scenarios, in addition to surgical excision, an anti-neoplastic topical agent or a chemo-preventive systemic drug provides favourable results due to synergism.

In a systematic review, conducted by *Giovanni Lodi, Roberto Franchini, S. Warnakulasuriya, et.al,* in 2016[4], that consisted of 14 studies (RCT) including 909 participants, they concluded that no single treatment regimen can be proposed to be superior &100 percent curative without any relapse. However, systemic vitamin A therapy, carotenoids & topical bleomycin, proved to show some benefits in healing the lesion & prevention of OSCC.

In an experimental model study, *Vasiliki Gkoulioni, Anna Eleftheriado, et.al,* 2010[5], the efficacy of Imiquimod on dysplastic lesions of the oral mucosa were studied, which showed favourable results specially in case of HPV associated lesions.

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In the year 2021, *Swati Mane, Bhakti Patilsoman, et.al,* conducted a pilot study[6] in Maharashtra,to evaluate the efficacy and tolerability of **topical 5% Imiquimod** in cases of Oral Leukoplakia, which concluded that, this topical application provided good clinical response& may be considered as the best alternative to conservative management& surgical excision, with lesser morbidities & relapse. Bleomycin is another chemotherapeutic agent used widely, as topical solution or intra-lesional injection for the treatment of leukoplakia with dysplasia or Ca in-situ & shows promising results. *A.S. Ribeiro, Patricia Salles, et.al. 2010,* conducted a review on non-surgical treatment of oral leukoplakia[7], consisting of 20 studies with interventions such as alfa-tocopherol, beta-carotene, Isotretinoin, vitamin A, bleomycin, lycopene & photodynamic therapy, where they concluded & recommended the systemic administration*1,3-c Retinoic acid* due to its superior efficacy, compared to other forms of vitamins & anti-oxidants.

Imiquimod is a synthetic small neuclotide-like molecule belonging to the family of Imidazoquinolinamines. This topical drug is an immune response modifier which has both antiviral and antitumor effects, mediated by Toll‑like receptors (TLR7 & TLR8)[8]. Imiquimod therapy has been widely used by dermatologist all across the globe for treating actinic keratosis, superficial basal cell carcinoma, anogenital warts, etc.

In this case, we have used a combination of three treatment modalitiescomprising, diode laser ablation, systemic Vitamin A (retinylpalmitate) 50,000 I.U. &Imiquimod 5% cream along with Clotrimazole mouth paint based on the clinical response(as described above in pharmacotherapy). Follow up evaluation within a period of 3 months (*fig.4a,4b,4c*)

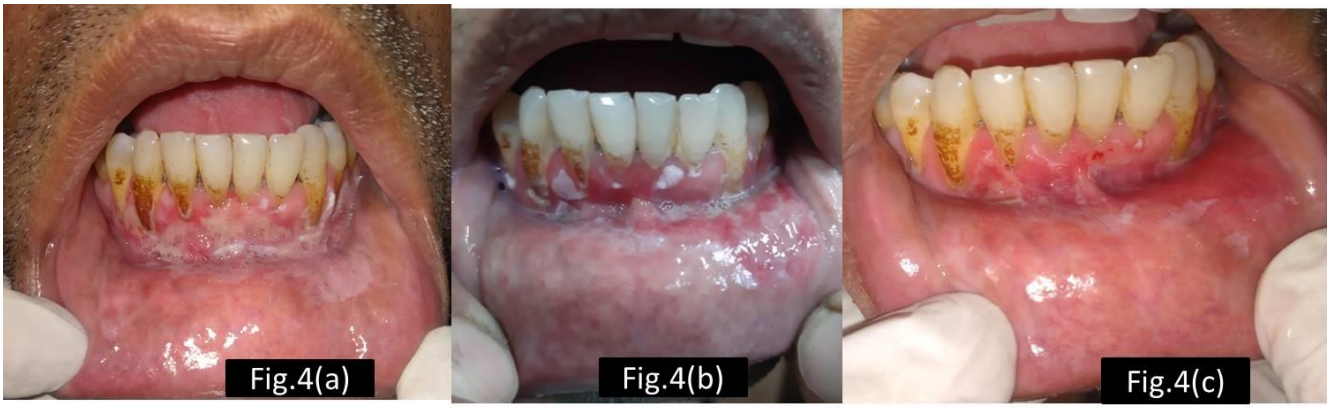

Fig 4: healing mucosa post laser ablation (a), recurrence of lesion (b), regression of white plaque after initiation of topical Imiquimod 5% (c).

& 9 months from the date of intervention revealed near complete remission of the lesion without any adverse effects (*fig.5*).

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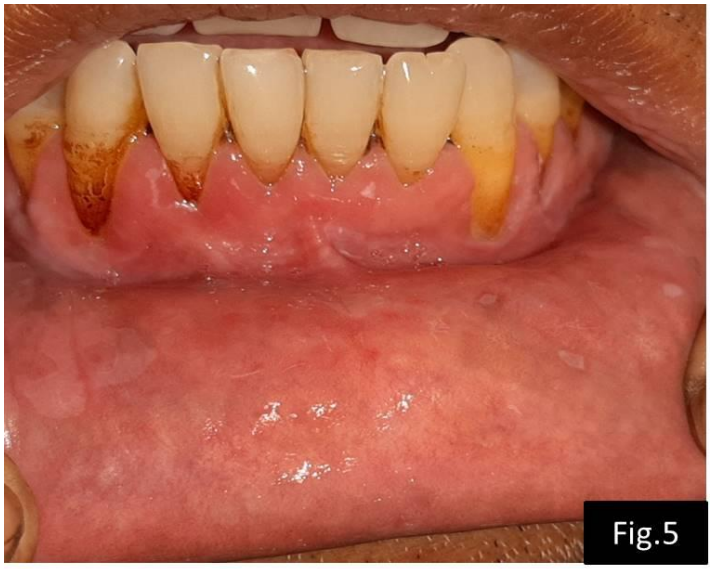

Fig 5. significant remission during 9 month follow-up.

Conclusion: There is no specific evidence based treatment regimen for leukoplakia, hence it may be challenging for the oral physician to treat such potentially malignant cases with associated epithelial dysplasia. Treatment plan may vary depending on clinical scenario & demography. The objective of any such interventions should primarily be focused on habit cessation & prevention of carcinogenesis.

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