Malignant Transformation of Oral Lichen Planus

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ABSTRACT
Oral lichen planus (OLP) is a chronic inflammatory mucocutaneous disease that frequently involves the oral mucosa. It has been regarded by many authors as a premalignant condition. There has been a continuous debate regarding the possible malignant potential of OLP, and these patients have been recommended to have their lesions monitored two to four times annually. A case of a lichen planus transformed into malignancy is reported here. This case does not provide answers to the ongoing controversy about the innate propensity of OLP to become malignant. However, in view of common occurrence of OLP and unresolved issue regarding its malignant potential (MP), this case report illustrates the need for histologic confirmation and close follow-up of patients with clinical lesions that have lichenoid features.

Keywords: Squamous cell carcinoma, Oral lichen planus, Premalignant, Recall, Malignant transformation.

INTRODUCTION
Lichen planus (LP) is a mucocutaneous disease, characterized by a nonspecific chronic inflammatory process, which leads to an intense destruction of the basal layer of the epithelium.1,2 OLP may be preceded by and or associated with dermal LP and affects 1 to 2% population. Considerable controversy exists in the literature as to whether OLP has an inherent predilection to become malignant.3

The world health organization (WHO) classifies OLP (erosive/atrophic), leukoplakia and erythroplakia as potentially malignant disorders. The risk of OLP converting into malignancy is lower than the risk of leukoplakia and erythroplakia.1 The factors that influence this rate of malignant transformation (MT) are still questionable. The overall prevalence of OLP is 1.5%. Moreover it is highest, i.e. about 3.7% in those people with mixed oral habits and found to be lowest 0.3% in nonusers of tobacco.1

Here we are presenting a case of OLP involving left buccal mucosa, which was under follow-up twice a month for 6 months with no change, however about 18 months later developed neoplastic growth in the pre-existing lesion.

CASE REPORT
A 30-year-old man reported to Modern Dental College and Research Center, Indore, Madhya Pradesh in August 2008, with the chief complaint of pain and burning sensation in right and left cheek mucosa. History revealed recurrent episodes of remission and recurrence of the lesions involving both buccal mucosae with 2 to 3 weeks interval, which were associated with burning sensation and pain and for that he was taking analgesics. He denied cutaneous, nasal and/or genital involvement. There was no clinical evidence of lymphadenopathy. Intraoral examination exhibit irregular erosion covered with pseudomembrane with reticular or finely radiating keratotic striae at the periphery in the right and left buccal mucosa of approximately 3 to 5 cm in size (Fig. 1). His medical history was noncontributory and had the habit of chewing gutkha (Vimal) 10 to 15 pouches/day since 4 to 5 years. On incisional biopsy, it revealed to be erosive LP (Figs 2 and 3). He was prescribed antioxidants, topical steroids and advised to quit the habit. The lesion on right cheek mucosa subsided following the treatment. The patient was under follow-up twice a month for 6 months with no change. Furthermore after about 18 months, there was a proliferative growth (Fig. 4) in the left cheek mucosa of 3 × 3 cm at the level of occlusal plane, 2 cm distal to corner of mouth and 2 cm anterior to the retromolar region. On palpation it was tender to touch and firm in consistency. There was no regional lymphadenopathy.
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Fig. 2: 10X showing hyperkeratotic epithelium with saw tooth rete ridges, liquefaction degeneration of basal cells and subepithelial band of CHR inflammatory reaction

Fig. 3: Ulceroproliferative growth involving left cheek mucosa

Fig. 4: 10X showing parakeratinized epithelium with severe dysplasia covering the tissue with invasive islands of malignant squamous cells

lymphadenopathy. Considering the small size, excisional biopsy was performed and sent for histopathology, then it was diagnosed as moderately differentiated squamous cell carcinoma (SCC). Since it was a SCC, patient was planned for further radiotherapy. The patient is under regular monthly follow-up since one year.

DISCUSSION

LP is a chronic autoimmunne, mucocutaneous disease, which can affect the oral mucosa, skin, genital mucosa, nails, conjunctival, esophageal, or laryngeal mucosa. The disease most often reported in middle-aged patients more commonly in female than male in the ratio of about 1.4 : 1. It was first described by Erasmus Wilson in 1869 and is thought to affect 0.5 to 1% of the world’s population affecting all races. About half of the patients with skin lesions have oral lesions, whereas about 25% present oral lesions alone. In contrast to cutaneous LP, the oral form may persist for up to 25 years.

Though the precise etiology of OLP is unknown, several predisposing factors have been implicated in the pathogenesis. These include drugs like anti-malarials, angiotensin converting enzyme inhibitors, diuretics, β-blockers, oral hypoglycemics, gold salts, nonsteroidal anti-inflammatory drugs, penicillamine, antituberculosis, and diabetes. Dental materials, chronic liver disease and hepatitis C virus, stress, genetics, tobacco chewing, graft vs host disease have all enact in causation of OLP. Though familial cases are rare an association has been observed with HLA-A3, A11, A26, A28, B3, B5, B7, B8, DR1, DRW9.

Of all these etiological factors tobacco (gutkha) chewing was one of the predisposing factors in the present case.

OLP clinically may manifest in various forms like linear, reticular, annular, vesicular, bullous, erosive, ulcerative, atrophic, hypertrophic. In the present case lesions were erosive surrounded by fine radiating striae.

Lesions are usually characteristically bilateral, commonly involving the buccal mucosa, tongue, gingiva, palate, floor of mouth or lips. Present case too displayed bilateral buccal mucosal involvement.

The best evidence of the potentially malignant nature of LP currently available is from the follow-up studies and retrospective incidence studies. It shows slightly higher incidence of oral SCC in patients with OLP than in the general population. Though actual overall frequency of MT is low, it varies between 0.3 to 3%, 0.27% per year, 1% in mean 5 years. The cause of increased oral cancer risk in OLP patients is unknown, although it is stated that the oral mucosa affected by OLP may be compromised to the extent of being more sensitive to exogenous mutagens in tobacco, alcohol, betel quid and Candida albicans. Therefore patients with LP should be advised to eliminate tobacco and alcohol consumption. However, less than 5% of OLP patients, who does not use tobacco products develop SCC, most frequently in atrophic, erosive and plaque lesions of OLP, therefore erosive/atrophic OLP is considered a premalignant condition by several authors and a recall system for OLP patients have been recommended to facilitate the early diagnosis of oral cancer with the aim of reducing morbidity and mortality from oral cancer arising in
Approximately 12% erosive and atrophic lesions can be converted into reticular lesions using topical steroids, thereby decreasing the risk of MT, as most oral cancers arising in OLP patients are associated with erosive, atrophic and plaque lesions. In the present case lesion on right cheek mucosa subsided following the treatment. However with regard to plaque like OLP lesions, the effect of treatment on the risk of oral cancer is unclear. Further it is emphasized that the chronic inflammatory response and simultaneous epithelial wound healing response in OLP may increase the likelihood of cancer forming gene mutations. Additionally the link between chemical mediators of T cells and tumorogenesis elucidates that macrophage migration inhibitory factor (MIF) released from T cells and macrophages, suppresses the transcriptional activity of the p53 tumor suppressor protein. p53 functions mainly in the prevention of many cancers including oral SCC. Hence blocking p53 function by MIF (and possible other inflammatory mediators) may underlie the increased risk of oral cancer in OLP patients.

OLP patients should be advised that a nutritious diet including fresh fruits and vegetables may help reduce the risk of oral cancer by providing vitamins, minerals and antioxidants. Due to the potential role of *C. albicans* in the development of oral SCC, fungal infection should be eliminated with topical antimycotics. OLP patients should be advised to attend whenever there is an exacerbation of symptoms or a change in lesion presentation. Such changes most often indicate a phase of increased disease activity, although neoplasia must be excluded.

OLP patients should have regular follow-up examination 2 to 4 times annually. An established recall system must be based on 2 important basic assumptions: (i) It is possible to identify patients with an increased risk of cancer development and (ii) It is possible to reduce cancer morbidity and /or mortality as a result of the recall program. Any chronic and/or refractory lesion should be considered for a biopsy to establish a diagnosis and subsequently to rule out malignancy. Periodic biopsies are indicated for persistent lesions as there is a potential for MT. The reported incidence of MT is approximately 2 to 5%. The mean length of time for LP to transform to SCC is 7.2 years. These figures indicate the need for long-term, appropriate follow-up and monitoring.

**CONCLUSIONS**

Systemic drugs, contact allergens, bacterial products, mechanical trauma and psychological stress may trigger or exacerbate OLP. The risk of oral cancer in LP patients may be reduced by the elimination of exogenous carcinogens, effective treatment of atrophic, erosive lesions and consumption of a nutritious diet including fresh fruit and vegetables. Patients must be advised to attend, whenever there is an exacerbation of symptoms or a change in lesion presentation. Patient education may improve the outcomes of LP therapy and further reduce the risk of oral cancer in LP patients. Although OLP may in many cases is diagnosed clinically, appropriate specialist referral is required for: (i) histological diagnosis; (ii) assessment of causative/exacerbating factors, associated diseases and oral cancer risk; (iii) patient education and management; (iv) medical treatment; and (v) long-term 6 monthly review and rebiopsy as required.

**REFERENCES**