Original Article

Evaluation of oral epithelial dysplastic features in oral lichen planus: The diagnostic difficulties

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ABSTRACT

Background: Lichen planus (LP) is chronic, mucocutaneous, autoimmune disease which can affect oral mucosa, skin, scalp, nails, and genital mucosa. The prevalence of oral LP (OLP) varies with different geographic distribution. It presents symmetrical and bilateral or multiple lesions with varying clinical types accompanying with burning sensation and sometimes pain. Due to its potentially malignant nature, the evaluation of cell proliferation brings important information regarding diagnosis and prognosis of several types of cancer. **Materials and Methods:** Sixty-four cases of OLP were retrieved and were histologically assessed under 10× and 40× magnifications for valuation of the dysplastic features. The grading was done by the criteria followed by Odukoya *et al*. The data obtained were tabulated and subjected for the statistical analysis. **Results:** Epithelial dysplasias were observed in 60 cases of OLP which Grade I had 9 cases, Grade II 27 and Grade III 24 cases. Four cases of OLP did not show any dysplasia. The interrater reliability was found to be in strong or substantial agreement in assessing few of the dysplastic features. Male:female ratio was 1.2:1 with buccal mucosa being the most common site. **Conclusion:** Our study showed the importance to establish a correct diagnosis of OLP based on the history, clinical presentations, and histopathology. Furthermore, the long-term follow-up of the patient with OLP is mandatory when dysplasia is encountered on histopathology.

Key words: Dysplasia, epithelia, lichen planus, pathology

INTRODUCTION

Lichen planus (LP) a chronic inflammatory mucocutaneous disease with a wide-ranging population prevalence from 0.1% to 2.2%. Being the most frequent dermatological disease, it also involves the oral cavity of middle-aged and elderly people with female:male ratio of about 2:1.2. The prevalence rates of oral LP (OLP) vary from 0.5% to 2.6% of the world population. The diagnosis of OLP is based on a combination of its characteristic clinical findings, history, and the histopathology. OLP shows various clinical variants presenting as asymptomatic hyperkeratotic reticular, papular or plaque-like lesions or symptomatic atrophic, erythematous, erosive or ulcerative lesions. Buccal mucosa is considered to be the most common location for OLP followed by the tongue, lips, floor of the mouth, and gingiva.[1-3]

Many factors have been implicated for the cause of OLP, but it still remains unknown. It has been suggested that it runs a benign course, but the possible malignant transformation of OLP is still the subject of contrasting views. Previous studies have supported that OLP is a premalignant disease, and currently, the World Health Organization (WHO) classifies it under potentially malignant disorders.[3-5]

The characteristic histological features of OLP includes hyperkeratosis, presence of civatte bodies, liquefaction degeneration of the basal layer, saw tooth rete ridges and a subepithelial band of inflammatory cell infiltrate.[4-6] Macdonald and Rennie[7] have reported to observe epithelial atypia in OLP cases which was later supported by various other authors.[4,8,9] Hence, the present study aimed to retrospectively study the prevalence of oral epithelial dysplastic features in OLP cases and inform pathologists about the difficulties surrounding its histopathological diagnosis. We also aim to establish the importance of long-term follow-up of patients with OLP.

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MATERIALS AND METHODS

A retrospective study was conducted on patients with a confirmed diagnosis of OLP based on medical history and physical and histopathological examination. Special attention was given toward the clinical variant of OLP, site of involvement, age, sex, duration, habit (tobacco smoking and alcohol), histopathology and prior treatment [Flow chart 1].

A total of 64 cases of OLP were obtained, and all the cases were reassessed independently by three examiners, following the histopathological criteria suggested by Eisenberg[10] [Figure 1 and Table 1]. After confirming the cases, the hematoxylin- and eosin-stained sections were studied under low power (10×) and high power (40×) magnifications for valuation of the dysplastic features [Table 2]. The stained sections were then graded, and the method followed for grading of the dysplastic features included the criteria suggested by Odukoya *et al*.[9] [Table 3 and Flow chart 2]. The data obtained were subjected for the Chi-square statistical analysis.

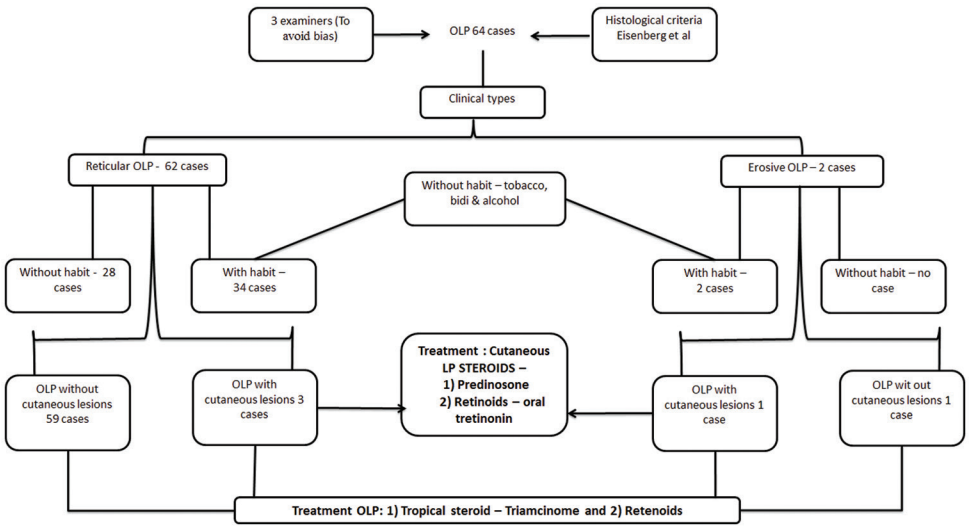
RESULTS

Of 64 cases of OLP, 35 (54.7%) were males and 29 (45.3%) were females with 1.2:1 male:female ratio. The age ranged from 16 to 75 years with a mean of 45.5 years. The subjects were grouped under 6 age groups which included 5 cases in 16–25 years, 8 cases in 26–35 years, 28 cases in 36–45 years, 13 cases in 46–55 years, 8 cases in 56–65 years, and 2 cases in 66–75 years of age. The most common site of occurrence of OLP is buccal mucosa with 38 cases (59.4%) followed by the tongue and retromolar area with each 8 cases (12.5%). Palate, gingival, floor of the mouth and labial mucosa showed 4 case (6.2%), 3 (4.7%), 2 (3.1%), and 1 case (1.6%), respectively [Graph 1].

Sixty-two (96.87%) of OLP cases presented clinically with the reticular pattern whereas 2 (3.12%) OLP cases clinically showed erosive type [Figures 2 and 3]. Four of the patients (3 with reticular OLP and 1 with erosive OLP) presented with bilateral cuteneous lesions on the flexor surface of legs. All 4 patients were under treatment (corticosteroids) for cutaneous LP from past 5 years. Three of the patients with the reticular pattern were unaware of the OLP, as it was accidentally encountered while restoring the tooth whereas erosive form of OLP presented with a history of pain and burning sensation.

Grading of dysplastic features in OLP: Among 64 cases of OLP, 4 cases (6.2%) did not show any dysplastic feature but Grade I was observed in 9 cases (14.1%), Grade II in 27 (42.2%) and Grade III in 24 (37.5%). Individual dysplastic features assessment in OLP showed 54 cases (84.4%) with basal cell hyperplasia, prominent nucleoli in 45 (70.3%), pleomorphism in 42 (65.6%), increased nuclear-cytoplasmic ratio in 36 (56.2%), abnormal stratification and loss of polarity in 16 (25%) and mitotic figures in 15 (23.4%) of cases. Whereas 38.33% of cases showed other features such as hyperchromatism, loss of cohesion, individual cell keratinization, and drop-shaped rete ridges.

The interrater reliability analysis using the interclass correlation coefficient suggested by Landis and Koch,[11] was performed between all the three observers for consistency, in assessing grade level and for each individual epithelial dysplastic features. The interrater reliability was found to be in strong or substantial agreement (0.719) for assessment of the presence of basal cell hyperplasia, hyperchromatism, mitotic figures, individual cell keratinization, and loss of cohesion [Graph 2].



Flow chart 1: Clinical description of oral lichen planus cases

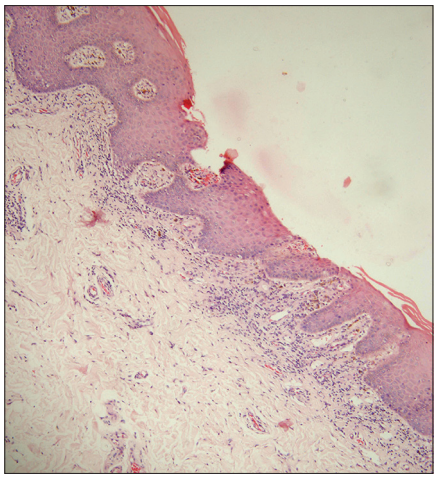
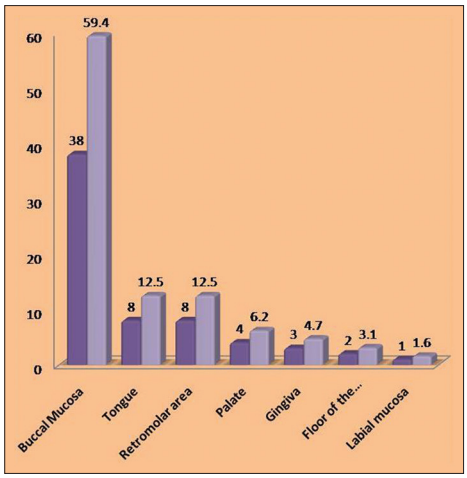


Figure 1: Photomicrography showing H and E stained section of oral lichen planus at 10×



Graph 1: Graphical representation of the distribution of oral lichen planus cases

Table 1: Histological criteria suggested by Eisenberg

Essential features
Basal cell liquefaction
Band-like lymphocytic infiltrate at epithelial-the stromal junction with obfuscation of basal cell region
Normal epithelial maturation pattern
Other features
"Candle-dripping," spindly rete ridges
Parakeratosis
Civatte bodies
Ragged separation of the epithelium from lamina propria due to basal cell destruction
Exclusion features
Nuclear enlargement or hyperchromasia
Prevalent dyskeratosis
Increased numbers of mitotic figures; aberrant mitoses
Blunted, droplet-shaped rete ridges
Absence of basal cell liquefaction
Stratification disarray
Heterogeneous lichenoid infiltrate
Deeper submucosal extension of infiltrate beyond superficial stroma
Perivascular infiltration

Table 2: Epithelial dysplastic features

Epithelial atypias
Loss of polarity of basal cells
Basal cell hyperplasia
Increased nuclear-cytoplasmic ratio
Drop shaped rete pegs
Irregular epithelial stratification
Increased number of mitotic figures
Abnormal mitotic figures
Nuclear hyperchromatism
Cellular pleomorphism
Enlarged nucleoli
Loss of cellular cohesion
Individual cell keratinization

DISCUSSION

Oral lichen planus, a potentially malignant disease, as described by the WHO, is a matter of serious controversy. Various studies have been done by many authors from 1958 to 2007, which showed varied rate of malignant transformation ranging from 0% to 10%.[3] Hallopeau in 1910 reported a case of OLP with malignant degeneration.[12] Krutchkoff *et al*.[13] in their study reviewed 223 cases and suggested that only 7% of OLP adequately shows malignant transformation. The criticism by Krutchkoff *et al*. on the malignant transformation of OLP was disapproved by van der Meij *et al*.[14] in 1999.

The initial histopathological diagnosis of OLP was further debated due to a significant inter- and intra-observer variations in the interpretation, regardless of the criteria suggested by Shafer *et al*., Regezi and Sciubba, Eversole and WHO.[5-7,13] The importance of epithelial dysplasia is not always clearly and carefully detailed in the histopathological reports of OLP. This causes discrepancy and difficulty in comparing the results of different studies. In the present study, interrater reliability showed strong/substantial agreement between raters in the identification of few of the dysplastic features in OLP. The obtained result is entirely subjective as there was difficulty in accuracy of evaluating and quantifying the features of dysplasia. Some differences which were observed between the observers might suggest the possibility that influences the interpretation of dysplasia by the oral pathologists.

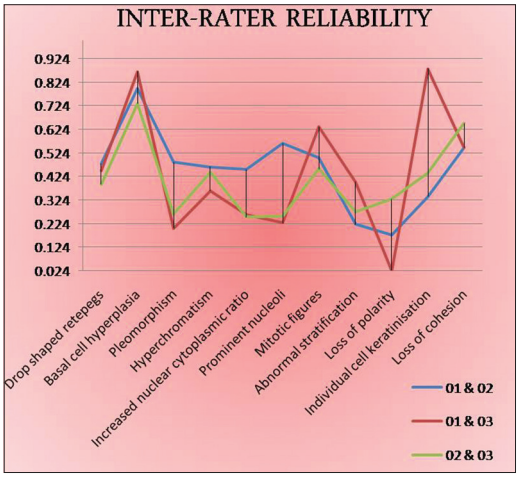
In the present study, the age of the subjects ranged from 16 to 75 years. This is in accordance with the study of De Jong *et al*.,[8] McCarthy and Shklar[15] and Allen *et al*.[16] Male predominance was observed in our study with male:female ratio of 1.2:1, which is in correlation with the study of Girish *et al*.[17] and Kövesi and Bánóczy.[18] Study by Scully *et al*.,[19] Lacy *et al*.[20] and Neville *et al*.[21] reported female predominance whereas Shafer *et al*.,[4] Regezi and Scuiba[6] reported no sex predilection in their study. In the present study, buccal mucosa (59.4%) showed bilateral involvement and is the most common site of involvement of OLP

followed by lesions on tongue and retromolar area, palate, gingival, floor of the mouth and labial mucosa. This finding is in correlation with Batsakis *et al*.[22] and Gorsky *et al*.[23]

The presence of epithelial dysplastic features in OLP, causes obstacle in histopathological diagnosis as some cell disorders such as increased nuclear-cytoplasmic ratio, nuclear hyperchromatism, and irregular chromatin distribution, is indicative of malignant disease which may be seen in cases of epithelial dysplasia or OLP. OLP is a lesion at risk for malignant change due to the dysplasia observed. We have assessed the epithelial dysplastic features in the diagnosed cases of OLP, by following the criteria of Odukoya *et al*.[9] Most of the OLP cases had fallen into Grade II (42.2%) followed by Grade III (37.5%), Grade I (14.1%), and Grade 0 (6.2%). The reason for this could be due to surveying of multiple sections and study of those sections which showed more dysplastic features.

Table 3: Grading of the dysplastic features by Odukoya *et al.*

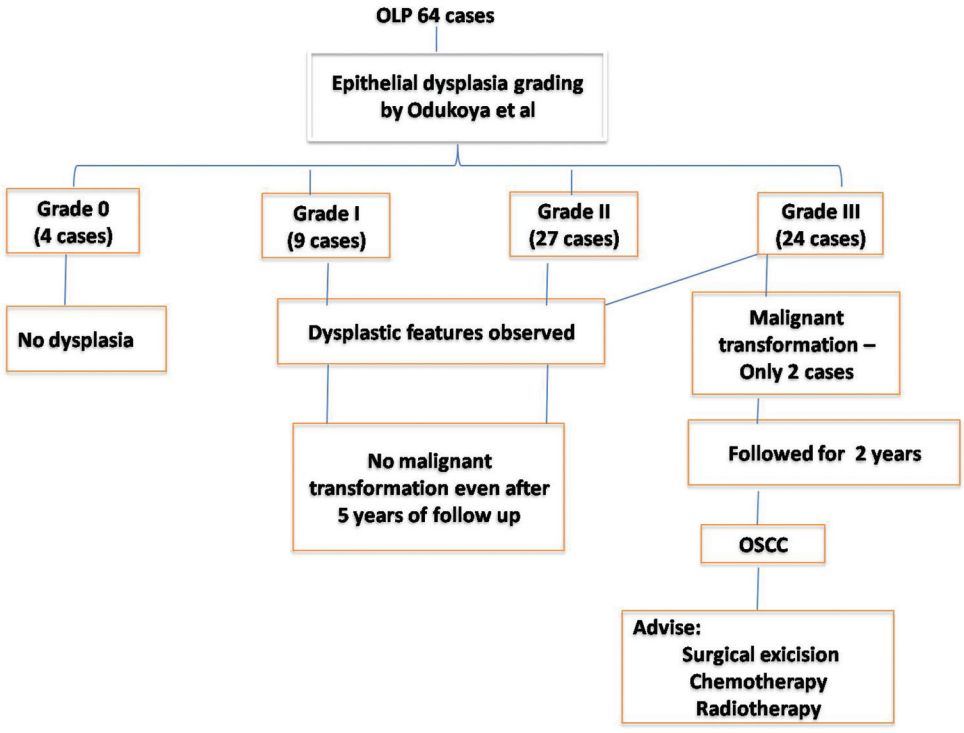
Grades	Epithelial dysplasia
0	No feature of dysplasia seen
I	One or two feature of dysplasia seen
II	Three or four features of dysplasia seen
III	More than four features of dysplasia seen



Graph 2: Interrater reliability with respect to epithelial dysplastic features in oral lichen planus

Age and sex distribution based on the grading of epithelial dysplasia in OLP showed that Grade 0 and Grade I had patients in their second decade of life whereas Grades II and III had patients in their third and fourth decade of life. This finding is supported by the literature.[7-9] Male predominance is observed in patients showing Grades 0, I and III whereas Grade II category showed female predominance. This disparity could be due to external contributing risk factors such as stress, mechanical trauma, nutritional factor, habits, irritation or allergy or other environmental factors.[16]

The dysplastic features observed in Grade II included basal cell hyperplasia, pleomorphism, prominent nucleoli, hyperchromatism, and loss of polarity [Figures 4 and 5a]. Grade III presented additional features such as mitotic figures, abnormal stratification, individual cell keratinization, and



Flow chart 2: Epithelial dysplasia grading in oral lichen planus

Figure 2: Clinical photograph showing reticular form of oral lichen planus

Figure 3: Clinical photograph showing erosive form of oral lichen planus

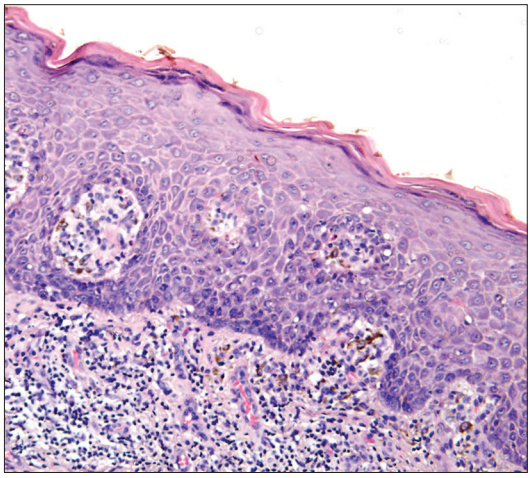


Figure 4: Hyperkeratosis, hyperchromatism, prominent nucleoli, and pleomorphism, 40×

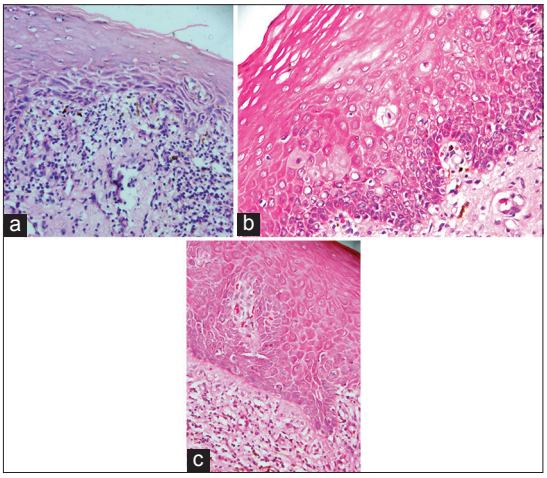


Figure 5: (a) Loss of polarity 40× (b) Individual cell keratinization, 40× (c) Mitotic figures, 40×

loss of cohesion [Figure 5b and c]. The observation of our study is similar to the study of Odukoya *et al*., Girish *et al*., De Jong *et al*. and Macdonald and Rennie. The presence of these features inferred that dysplastic features could be observed in OLP.

All the 64 patients revealed different history of symptoms ranging from painless reticular type to painful erosive type. It is suggested that erosive OLP tends to undergo malignant transformation because erosive forms predispose the oral mucosa to damage from various carcinogenic agents. In our retrospective study 2 of the erosive OLP cases with Grade III epithelial dysplastic changes showed malignant transformation to oral squamous cell carcinoma with the malignant transformation rate of 3.1% in 2.6 years of follow-up. This finding is in correlation with the finding of Silverman and Bahl.[24] The mechanism behind malignant transformation remains unknown but the suggested possible cause could be that chronic OLP can progress to become oral squamous cell carcinoma or the epithelial surface of OLP might be more sensitive to irritants, viruses, or carcinogens.

CONCLUSION

Our study showed the importance to establish a correct diagnosis of OLP based on the history, clinical presentations and histopathology. The exact incidence of oral squamous cell carcinoma in patients with OLP is difficult to establish, due to low number of cases and difficulty in assessing the contributing external risk factors. Furthermore, the presence of epithelial dysplastic features in OLP makes the diagnosis harder; thereby emphasizing the importance of long-term follow-up of such patients not only because of malignant transformation but due to possible mistakes made in diagnosing OLP lesions.

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