Controversies regarding oral lichen planus and lichenoid-dysplastic lesions

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ABSTRACT

Objective: Oral lichen planus (OLP) is an immune-mediated condition featuring chronic inflammation. The World Health Organization (WHO) classifies OLP as potentially malignant, but it is believed that the malignant transformation of OLP occurs in lesions with both lichenoid and dysplastic features (LD). This review discusses the issues surrounding OLP and LD, including their malignancy, classification and categorization, and whether lichenoid inflammation causes dysplastic changes in LD, or vice versa. **Methods:** English full-text literature addressing either OLP, LD and/or dysplasia were reviewed from PubMed, CINAHL, and Google Scholar. **Results:** Thirty-six publications including original research articles, reviews, meta-analyses, books, reports, letters, and editorials were selected. **Discussion:** Research suggests that OLP has malignant potential, although small, and that LD should not be disregarded. Dysplasia presenting with or without lichenoid features has a risk of cancer. There is also disagreement regarding the classification and categorization of LD. Different names have been used to classify these lesions, including "lichenoid dysplasia", OLP with dysplasia, and dysplasia with lichenoid features. Moreover, in LD, does dysplasia or lichenoid infiltration appear first? Is inflammation a response to dysplasia or is dysplasia a response to the persistent inflammation? – The answers are still unknown. The main limitation in the literature is the inconsistency and subjective nature of histological diagnoses. This can lead to interobserver and intraobserver variation, ultimately resulting in the inaccurate diagnosis of OLP and LD. **Conclusion:** Although further research is required to understand OLP and LD, both lesions should be considered potentially malignant and should not be disregarded.

Keywords: Oral lichen planus, oral epithelial dysplasia, oral lichenoid dysplasia, malignant transformation, neoplasms, risk, mouth

CDHA Research Agenda category: risk assessment and management

INTRODUCTION

Oral lichen planus (OLP) is an immune-mediated condition characterized by chronic inflammation.[1] It has a global prevalence of 1.01% and is highly prevalent in the middle-aged population, especially among women.[2–4] The most common clinical presentations of OLP are bilateral white lesions, with variants including reticular, papular, plaque-like, erosive, atrophic or erythematous, and bulbous forms.[2,3] OLP is most commonly located on the buccal mucosa, tongue, and gingiva, with the tongue being associated with the highest rates of malignant transformation.[2,5,6]

Histologically, mucosal lesions with a band-like area of lymphocytic infiltrate in the subepithelium and liquefactive degeneration in the basal cell layer of the tissue are called lichenoid lesions.[3,7,8] These include not only OLP, but also lupus erythematous, graft versus host disease, and lichenoid mucositis. OLP is often confused with oral lichenoid mucositis.[9–11] Not only is oral lichenoid mucositis histologically similar to OLP, but it can also have a similar or indistinguishable clinical appearance to OLP.[12,13] OLP however is a chronic condition, whereas lichenoid mucositis resolves after removal of allergens from factors such as dental filling material to systemic drug intake.[9,10] To further confuse the issue, the terms lichenoid mucositis and lichenoid lesion are used interchangeably and the actual meaning would only be clear with the context.[12,13]

The World Health Organization (WHO) considers OLP a potentially malignant condition, although this is controversial.[10] Others believe that only OLP *with dysplasia* is a potentially malignant variant of OLP.[14,15] They suggest that previous reports of the malignant transformation of OLP had occurred in lesions with both lichenoid *and* dysplastic features (LD).[14,15] This review aims to provide clinicians and researchers further understanding on the issues surrounding OLP

and LD, including malignancy, classification and categorization, and the possibility of lichenoid inflammation causing dysplastic changes in LD, or vice versa.

METHODS

PubMed, CINAHL, and Google Scholar were searched for full-text literature using the key words oral lichen planus, lichenoid dysplasia, lichenoid, dysplasia, oral cancer, malig*, progression, and transformation. No restrictions were placed for publication dates in order to identify the progression of information. To encompass various views, opinions, and evidence on this controversial topic, no restrictions were placed on types of literature selected. Articles not published in English were excluded.

RESULTS

Sixteen original research articles (1 case series, 1 case-control, 4 cohort, and 10 cross-sectional studies); 10 literature, narrative, and scoping reviews; 2 systematic reviews, 1 systematic review with meta-analysis, 1 meta-analysis, 1 book, 2 case reports, 2 reports, 1 letter to the editor, and 1 editorial regarding OLP, LD and/or dysplasia were selected. Literature shows that both OLP and LD have malignant potential, but there is still a lack of agreement on the classification and categorization of LD. It is also still unclear whether inflammation is a response to dysplastic change or if inflammation induces dysplastic change.

DISCUSSION

MALIGNANT PROFILE OF OLP AND LD

Is OLP malignant?

The controversy surrounding the malignant potential of OLP persists due to the lack of uniform and distinct clinical and histopathological diagnostic criteria.[10] In 1978, Krutchkoff et al. published a review examining 223 reported malignant transformations of OLP.[14] Due to the unreliable diagnostic criteria, they proposed that the malignant cases of OLP may have been dysplastic lesions with lichenoid features, hence raising the rate of OLP transformation.[14] In 1989, Lovas et al. analyzed three cases of clinically and histologically diagnosed OLP.[15] Two cases of OLP were in fact epithelial dysplasia with lichenoid infiltrate. The authors claim that the malignant transformation of OLP may instead be the transformation of dysplastic lesions that clinically and histologically mimic OLP.[15] To create a more distinct criterion for OLP, van der Meij and van der Waal modified the 1978 WHO diagnostic criterion in 2003 to exclude cases of LD.[7,8] The modification required the histopathological absence of epithelial dysplasia for a diagnosis of OLP.[7,8] The American Academy of Oral and Maxillofacial Pathology supports this criterion and adds that both clinical and histopathological criteria should be fulfilled for a diagnosis of OLP.[16] Specifically, a histopathological diagnosis of OLP should require the absence of verrucous epithelium.[16] However, the dispute regarding the malignant potential of OLP continues to persist.

Malignant transformation of OLP

Literature shows that the malignant transformation rate (MTR) of OLP without dysplasia ranges from 1 to 1.5%.[2,6,17] Case selection may play a large role in the controversy surrounding

the malignant progression of OLP. In their systemic reviews, Fitzpatrick et al. and Giuliani et al. selected studies that excluded epithelial dysplasia on initial diagnosis of OLP.[6,17] Lesions with both dysplastic and lichenoid features can result in false positive cases of malignant OLP.[6,17] Aghbari et al. stated in their meta-analysis that the diagnosis of OLP was based on a defined criterion, preferably including a histological examination.[2] However, they did not explicitly mention whether epithelial dysplasia was excluded.[2] Of the 7806 cases of OLP studied by Fitzpatrick et al., 85 developed oral squamous cell carcinoma (OSCC), resulting in a MTR of 1.09%.[6] In the study by Giuliani et al., 87 of the 6353 cases of OLP developed OSCC, which resulted in a MTR of 1.37%.[17] Aghbari et al. selected 19,676 cases of OLP; 280 of which developed OSCC (1.42% MTR).[2] These authors demonstrate the possible malignant potential of OLP. Table 1 shows the MTR for OLP and LD across different studies.

Coexistence of lichenoid and dysplastic features

As stated previously, it is believed that the malignant transformation of OLP occurs in lesions with both lichenoid and dysplastic features. Several authors have studied the coexistence of these features.[18,19] Fitzpatrick et al. studied 352 cases of mild to moderate dysplasia, severe dysplasia or carcinoma *in-situ* (CIS), and OSCC.[18] They found that 29% of all cases had three or more of the five lichenoid features included in this study focally present (Table 2). Specifically, 39% of mild to moderate dysplasia, 16% of severe dysplasia or CIS, and 34% of OSCC cases showed three or more lichenoid features focally present.[18] Patil et al. retrospectively reviewed cases of OLP and oral epithelial dysplasia (OED) and found that 8 of the 54 OLP cases had epithelial dysplasia, whereas 22 of the 95 cases of OED presented with lichenoid features.[19] These studies demonstrate that both lichenoid and dysplastic features can coexist, even at higher grades of dysplasia and SCC.[18,19] In higher grades of premalignancy and malignancy, it may be

possible for pathologists to exclude reports of lichenoid features as the diagnosis of the lesion may depend on which histologic and cytologic characteristics are considered more important.[20]

Malignant transformation of OLP and LD

Several authors have studied the malignant transformation of OLP and LD. In their retrospective study, Shearston et al. reviewed OLP and LD.[21] They referred to LD as *oral lichenoid dysplasia* and categorized this lesion separately from OLP. For *oral lichenoid dysplasia*, Shearston et al. required the presence of OED in OLP, or OED associated with lichenoid infiltrate.[21] Bornstein et al., Irani et al., and Bandyopadhyay et al. also retrospectively studied the malignant progression of OLP.[1,22,23] Unlike Shearston et al., LD was classified as part of OLP, and not as a separate entity such as *oral lichenoid dysplasia*.[1,21–23] In their study, Bornstein et al. included cases of OLP and cases of LD on initial diagnosis.[22] The cases of OLP in the study by Irani et al. did not present with dysplasia on initial diagnosis but dysplasia developed in some cases of OLP after the initial diagnosis.[23] Bandyopadhyay et al. did not specify whether dysplasia was present on initial diagnosis or had developed afterwards.[1] In these studies, lesions with lichenoid and dysplastic features were found to progress to OSCC more frequently than OLP.[1,21–23]

Shearston et al. examined 206 cases of OLP with 1 case progressing to OSCC, resulting in a MTR of 0.49%. In comparison, 3 of the 44 *oral lichenoid dysplasia* cases developed OSCC, resulting in a MTR of 6.81%.[21] Bornstein et al. included 141 OLP patients in total; 138 cases of OLP without dysplasia and 3 cases of OLP with dysplasia.[22] One patient diagnosed with OLP without dysplasia developed OSCC simultaneously in three separate sites (0.71% MTR). All three cases of OLP with dysplasia developed OSCC (100% MTR).[22] Irani et al. studied 112 cases of OLP, 100 without dysplasia and 12 with dysplasia.[23] None of the cases without dysplasia

developed OSCC (0% MTR), while one case with dysplasia developed OSCC (8.33% MTR).[23] Bandyopadhyay et al. selected 143 patients with OLP, 132 without dysplasia and 11 with dysplasia.[1] Like Irani et al., none of the cases without dysplasia developed OSCC (0% MTR), whereas two cases with dysplasia developed OSCC (18.18% MTR).[23] Overall, literature shows that the MTR of OLP (without dysplasia) ranges from 0 to 1.5%; whereas the MTR of LD ranges from 6 to 100% (Table 1).[1,2,6,17,21–23] Although the number of cases of LD is small and the MTR range of these cases is large, the higher MTR as compared to OLP (without dysplasia) shows that LD has a higher malignant potential, and thus dysplastic changes should not be disregarded.

Rock et al. compared the MTR of dysplasia with and without lichenoid mucositis.[24] In their study, lichenoid mucositis referred to lesions with lichenoid features.[13] Progression was defined as progression to severe dysplasia, CIS, or SCC.[24] Six of the 73 cases of dysplasia with lichenoid mucositis progressed (8%), whereas 49 of the 373 cases of dysplasia without lichenoid mucositis progressed (13%) (Table 1). The progression rate between the two groups was found to be not significantly different. There was also no significant difference between the 3- and 5-year progression rate for these two groups. This study demonstrates that dysplasia whether presenting with or without lichenoid mucositis has a similar risk of cancer, further supporting that LD should not be disregarded.[24]

CLASSIFICATION AND CATEGORIZATION OF LD

There is disagreement in the literature regarding the classification and categorization of LD. Various names have been used to classify these lesions, including “lichenoid dysplasia”, OLP with dysplasia, and dysplasia with lichenoid features.[1,21–23,25–29] In addition to the confusing names, there has also been no agreement in the categorization of these lesions.

"Lichenoid dysplasia"

In 1978, when Krutchkoff and Eisenberg first proposed the term "lichenoid dysplasia", they regarded it as a distinct histopathological entity from OLP (Table 3).[25] "Lichenoid dysplasia" describes lesions with both clinical lichenoid and histopathological lichenoid and dysplastic features. The presence of two or more dysplastic features in the epithelium (Table 4) rules out the diagnosis of OLP no matter how many lichenoid features are present.[25]

There is little agreement on what constitutes "lichenoid dysplasia". Lodi et al. associates "lichenoid dysplasia" with two groups of conditions: 1) presents clinically as OLP and histologically with dysplasia and 2) presents with no clinical signs of OLP but has lichenoid and dysplastic features histologically.[26] The first group may represent early stages in the malignant transformation of OLP, and the second group refers to various clinical conditions associated with lichenoid histology.[26] To confuse matters further, Sanketh et al. state that *oral lichenoid dysplasia* are *epithelial dysplastic lesions with lichenoid features* and uses these two terms interchangeably.[27] Although there are similar histological characteristics between *oral lichenoid dysplasia* (or *epithelial dysplastic lesions with lichenoid features*) and OLP, in their opinion, *oral lichenoid dysplasia* is not equivalent to OLP. *Oral lichenoid dysplasia* or *epithelial dysplastic lesions with lichenoid features* is clinical leukoplakia or erythroplakia that histologically present with dysplastic and lichenoid features, whereas OLP histologically presents with lichenoid features and may have dysplasia, but clinically appears as lichen planus.[27]

Other classifications

Other authors indicate that the term "lichenoid dysplasia" should not be used. The WHO does not use the term "lichenoid dysplasia".[10] They describe LD in terms of oral lichenoid

lesions or OLP with or without dysplasia.[9] Czerninski et al. believe that OLP with dysplasia is part of the OLP spectrum, and should not be classified into the separate category "lichenoid dysplasia".[28] In contrast, van der Meij and van der Waal regard the presence of epithelial dysplasia as an exclusion criterion for the histopathological diagnosis of OLP, but also refrain from using the term "lichenoid dysplasia".[7] Muller also avoids diagnosing dysplastic lesions presenting with lichenoid histological features as "lichenoid dysplasia" or OLP.[30]

Interestingly, Raj et al. proposed two subtypes for LD.[31] The first subtype is primary OED with lichenoid features, which presents with dysplasia and inflammatory infiltrate regardless of basal cell degeneration. The second subtype is primary OLP with secondary dysplastic features, which clinically, has a bilateral presentation and minor reticular component, and histologically, dysplasia, lymphocytic infiltrate, and basal cell degeneration.[31] Table 5 presents a summary of the various classifications and categorizations of LD.

DOES DYSPLASIA CAUSE INFLAMMATION OR VICE VERSA?

In lesions with both dysplastic and lichenoid features, does epithelial dysplasia cause lichenoid inflammation? Or does lichenoid inflammation cause dysplasia? Or is there no relationship between the inflammation and dysplasia observed?

#1: Inflammation is a response to dysplasia

Lichenoid inflammatory infiltrate can represent an immunologic response to antigenic modification of the epithelium.[32–34] In dysplastic epithelium, the infiltrate may represent an immune response to neoantigens present.[33] In OLP, the infiltrate is dominated by T lymphocytes, whereas in LD, the infiltrate is composed of a mixture of lymphocytes and plasma cells.[30] Eisenberg states that the nature of the antigen controls the composition of the lichenoid infiltrate,

and thus the infiltrate must be carefully examined as it may indicate whether a lesion has malignant potential.[33]

The ratio of T lymphocytes may also be an important feature to note. Flores-Hidalgo et al. found that in OED with lichenoid features, there is an increased CD8+ to CD4+ lymphocyte ratio, while in OLP, there are similar quantities of each cell type.[29] The inflammatory infiltrate changes from a regulatory or suppressive function in OLP to a cytotoxic function in OED with lichenoid inflammation as the CD8+ cells try to eliminate epithelial cells undergoing malignant transformation. This suggests that dysplasia may initiate infiltrate that is specific to lesions with lichenoid and dysplastic features. As a result, OED with lichenoid features may have greater malignant potential than OLP due to differences in cellular activity.[29] Other authors also support the belief that lichenoid inflammation is an immune response to dysplasia.[18,35,36] Of interest, Fitzpatrick et al. observed a loss of lichenoid features as the grade of dysplasia in LD progressed from low to high.[18]

#2: Dysplasia is a response to inflammation

Some authors believe that the inflammatory hallmark of OLP, the lichenoid infiltrate, can induce histologic features similar to dysplasia.[26] Inflammatory actions via inflammatory cells (e.g. certain macrophage types, mast cells, neutrophils, and B and T lymphocytes) were once thought to eliminate tumours, but these responses may have an opposite effect through enhancing tumourigenesis and progression.[32] T lymphocytes, which are expressed in OLP inflammatory infiltrate, release inflammatory factors related with cancer initiation, progression, and invasion.[37] It has been hypothesized that the inflammatory infiltrate may produce oxidative stress, cytokines, and transcription factor signals that can cause abnormal cellular replication, DNA damage, and disordered epithelial integrity.[37] The liquefactive degeneration of the basal cells as well as

apoptosis would increase cell proliferation, which is positively correlated with cellular mutation. These events can lead to epithelial changes associated with dysplasia and cancer over time, resulting in the malignant transformation of OLP.[37,38]

#3: Lichenoid lesion develops dysplasia

It is possible that there is no cause-and-effect relationship between the inflammation and dysplasia observed in a lesion. Lichenoid lesions could develop dysplasia when the mucosa is exposed to a carcinogen, such as tobacco.

GAPS IN THE RESEARCH

The greatest limitation in the literature concerning oral lesions, including those with lichenoid and dysplastic features, is accurate diagnosis.[2,18,19] Fischer et al. suggest that the presence of inflammation, such as inflammation in lichenoid lesions, may reduce a pathologist's ability to observe dysplastic changes.[39] The subjective nature of histologic diagnoses often results in interobserver and intraobserver variation, which can result in the inaccurate diagnosis of dysplastic and lichenoid features.[40–42] The diagnostic variability between pathologists and within a pathologist results from the lack of objectivity in diagnostic criteria.[42] In addition, clinical information about the lesion, although needed, may be missing when tissue specimens are submitted for diagnosis.

Several authors have assessed the presence of interobserver and intraobserver variability in the diagnosis of dysplasia and OLP with the majority showing greater intraobserver agreement than interobserver agreement.[20,40,43,44] In Abbey et al.'s study, agreement with the original diagnosis for the presence of dysplasia was around 80%.[40] When pathologists diagnosed the same biopsies again several months later, intraobserver agreement was also 80%.[40] In the study

by Karabulut et al., there was poor to moderate interobserver agreement in grading tissue from an absence of dysplasia to CIS.[20] Van der Meij et al. assessed interobserver variability in the diagnosis of OLP using the WHO definition of OLP.[43] Likewise to the diagnosis of dysplasia in other studies, there was poor to moderate interobserver agreement (0.20 to 0.51) for the diagnosis of OLP. Intraobserver agreement was greater with moderate to substantial agreement (0.50 to 0.67).[43] In the study by Zohdy et al., they studied the interobserver and intraobserver variability in the diagnosis of dysplasia in OLP and oral lichenoid lesions.[44] The results of four examiners were compared, as well as individual results 3 months later. Similar to the above studies, there was low interobserver reliability among the four examiners, but fair to substantial intraobserver reliability. They suggest the possible use of a binary system of evaluating dysplasia in such oral lesions. Interestingly, grade of dysplasia was diagnosed higher in oral lichenoid lesions than OLP.[44] Future research aiding accurate histological diagnosis of LD and OLP is required to help reduce the controversies surrounding LD and OLP in the literature.

CONCLUSION

The malignant potential of OLP, a condition characterized by chronic inflammation, is subject to controversy as some authors argue that the malignant progression occurs in LD rather than OLP. Systemic reviews and retrospective studies of OLP and LD have demonstrated that the MTR of OLP ranges from 0 to 1.5%, suggesting that OLP does have malignant potential, although small. LD has malignant potential based on the range of its MTR (6 to 100%) and should not be disregarded. However, there is still debate on the classification and categorization of LD. Various names have been used, including “lichenoid dysplasia”, OLP with dysplasia, and dysplasia with lichenoid features. Some authors consider these lesions as part of the distinct entity “lichenoid dysplasia”, part of the OLP spectrum, neither part of OLP or “lichenoid

dysplasia", or part of both OED and OLP. Furthermore, in LD, does epithelial dysplasia or lichenoid infiltrate appear first? Is the inflammation a response to dysplastic changes in the epithelium? Vice versa? Or both? – The answers to these questions are still unknown. Regardless of which change appears first, or which change induces the other, both features appear to be associated with malignancy. Currently, the main limitation in research is the inaccurate diagnosis of OLP and LD due to the subjective nature of histologic diagnoses, which often results in interobserver and intraobserver variation. Although more research is required to understand the relationship between OLP and LD, and their malignant risk, both lesions should be considered potentially malignant and should not be disregarded in clinical practice.

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CONFLICTS OF INTEREST

The authors have declared no conflicts of interest.

PRACTICE RELEVANCE

- Increasing familiarity with the literature and controversies surrounding the malignant potential of oral lichen planus and lesions with both lichenoid and dysplastic features can help increase awareness of such lesions
- Understanding the malignant potential of oral lichen planus and lesions with both lichenoid and dysplastic features can raise the importance of monitoring and following-up such lesions to promote early prevention and detection of oral malignancy

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Table 1. Malignant transformation rate (MTR) of oral lichen planus (OLP) and lesions with both lichenoid and dysplastic features (LD)

	OLP			LD			Total
	Cases	Progressed cases[a]	MTR (%)	Cases	Progressed cases[a]	MTR (%)	Cases
Fitzpatrick et al., 2014[6]	7806	85	1.09	N/A	N/A	N/A	7806
Giuliani et al., 2019[17]	6353	87	1.37	N/A	N/A	N/A	6353
Aghbari et al., 2017[2]	19,676	280	1.42	N/A	N/A	N/A	19,676
Shearston et al., 2019[21]	206	1	0.49	44	3	6.81	250
Bornstein et al., 2006[22]	138	1	0.71	3	3	100.00	141
Irani et al., 2016[23]	100	0	0	12	1	8.33	112
Bandyopadhyay et al., 2017[1]	132	0	0	11	2	18.18	143
Rock et al., 2018[24]	N/A	N/A	N/A	73	6[b]	8.22	73

[a]Progression to oral squamous cell carcinoma unless otherwise indicated
[b]Progression to oral severe dysplasia, carcinoma *in-situ*, or squamous cell carcinoma

Adapted from Fitzpatrick et al., 2014;[6] Giuliani et al., 2019;[17] Aghbari et al., 2017;[2] Shearston et al., 2019;[21] Bornstein et al., 2006;[22] Irani et al., 2016;[23] Bandyopadhyay et al., 2017;[1] and Rock et al., 2018.[24]

Table 2. Five histological lichenoid features included in the study by Fitzpatrick et al., 2014

1. Band-like infiltrate immediately subjacent to the epithelium.
2. Sawtooth rete ridges formation.
3. Interface stomatitis, or the infiltration of the basal layer of epithelium by lymphocytes.
4. Formation of Civatte (colloid) bodies.
5. Degeneration of basal layer.

Adapted from Fitzpatrick et al., 2014.[18]

Table 3. Histological diagnostic criteria of oral lichen planus by Krutchkoff and Eisenberg, 1985

Requisite features	Liquefactive degeneration of basal cells.
	Bandlike infiltrate of lymphocytes within lamina propria that intimately intermingles with basal cell region of surface epithelium.
Additional features	"Saw-toothed" rete pegs; a common variation is the presence of slender, indistinct, tapered rete pegs.
	Hyperkeratosis or parakeratosis.
	Separation of surface epithelium from underlying connective tissue with ragged, uneven plane of cleavage.
	Isolated individual cell keratinization within the prickle cell region (formation of so-called "Civatte bodies").
Disqualifying features (features that, if present, preclude a definite diagnosis of lichen planus)	Topographic and cytologic features of dysplasia; these include any or all of the following: a. Significantly increased nuclear size (usually manifests as increased nucleus/cytoplasm ratio). b. Cellular pleomorphism. c. Altered or disturbed epithelial maturation. d. Nuclear hyperchromasia (beyond the range of normal). e. More than sporadic foci of premature or abnormal keratinization. f. Abnormal mitotic figures. g. Notable intercellular fluid accumulation or edema that accompanies any of the six preceding parameters.
	Presence of heterogeneous round cell inflammatory infiltrate within the lamina propria; the presence of substantial numbers of plasma cells, eosinophils, or neutrophils within the "bandlike" infiltrate is considered adequate grounds for disqualification.
	Diffuse extension of infiltrate to involve deeper submucosal tissues or frank perivascular distribution of infiltrate.

Adapted from Krutchkoff and Eisenberg, 1985.[25]

Table 4. Histological features of dysplasia by Krutchkoff and Eisenberg, 1985

Increased nucleus/cytoplasm ratio.
Nuclear pleomorphism.
Nuclear hyperchromasia.
Disturbed or disorderly maturation.
Lack of cellular cohesion, which often manifests as marked intercellular edema.
Increased or abnormal mitoses.
Blunted, club-shaped, or “tear drop”-shaped rete pegs.

Adapted from Krutchkoff and Eisenberg, 1985.[25]

Table 5. Classification and categorization of lesions with both lichenoid and dysplastic features (LD)

"Lichenoid dysplasia"	
Krutchkoff and Eisenberg, 1985[25]	"Lichenoid dysplasia" is a distinct histopathological entity from oral lichen planus (OLP). "Lichenoid dysplasia" describes lesions with both clinical lichenoid and histopathological lichenoid and dysplastic features.
Lodi et al., 2005[26]	"Lichenoid dysplasia" includes two groups: 1. Lesions clinically presenting as OLP and histologically with dysplasia. They represent early stages in the malignant transformation of OLP. 2. Lesions that do not clinically resemble OLP but have lichenoid features histologically. They represent different clinical conditions associated with lichenoid histology.
Sanketh et al., 2017[27]	*Oral lichenoid dysplasia* represents *epithelial dysplastic lesions with lichenoid features*, and these terms are interchangeable. *Oral lichenoid dysplasia* or *epithelial dysplastic lesions with lichenoid features* histologically presents with dysplasia and lichenoid features. OLP histologically presents with lichenoid features but can also manifest with dysplasia. *Oral lichenoid dysplasia* does not represent OLP with dysplasia as *oral lichenoid dysplasia* or *epithelial dysplastic lesions with lichenoid features* clinically presents with leukoplakia or erythroplakia, whereas OLP clinically appears as lichen planus.
Other classifications	
OLP	
Czerninski et al., 2015[28]	OLP with dysplasia is part of the OLP spectrum and should not be classified into the separate category of "lichenoid dysplasia".
Other (not OLP or "lichenoid dysplasia")	
van der Meij and van der Waal, 2003[7]	Epithelial dysplasia is an exclusion criterion for the histopathological diagnosis of OLP. The term "lichenoid dysplasia" should not be used either.
Muller, 2011[30]	"Lichenoid dysplasia" should not be used to describe dysplastic lesions presenting with lichenoid histological features. The presence of dysplasia in a lichenoid lesion should not result in the diagnosis of OLP.
Raj et al., 2018[31]	There are two subtypes for LD: 1. Primary oral epithelial dysplasia with lichenoid features: It presents with dysplasia and inflammatory infiltrate regardless of basal cell degeneration. 2. Primary OLP with secondary dysplastic features: It has a bilateral presentation, minor reticular

	component, dysplasia, lymphocytic infiltrate, and basal cell degeneration.

Adapted from Krutchkoff and Eisenberg, 1985;[25] Lodi et al., 2005;[26] Sanketh et al., 2017;[27] Czerninski et al., 2015;[28] van der Meij and van der Waal, 2003;[7] Muller, 2011;[30] and Raj et al., 2018.[31]