Case Report

JOMP
Journal of Oral Medicine and Pain

pISSN 2288-9272 eISSN 2383-8493
J Oral Med Pain 2015;40(4):163-168
http://dx.doi.org/10.14476/jomp.2015.40.4.163

Lichenoid Dysplasia Misdiagnosed as Oral Lichen Planus: 3-Year Follow-up Case Report

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Received November 25, 2015
Revised December 2, 2015
Accepted December 3, 2015

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This study was supported by research fund from Wonkwang University, 2014.

Lichenoid dysplasia is a lichenoid features with epithelial dysplasia clinically and histopathologically similar to oral lichen planus. It can be clinically mistaken for oral lichen planus, but has histopathologic features of dysplasia and a true malignant predisposition. The clinician should be able to differentiate between oral lichen planus and lichenoid dysplasia for the proper management. We experienced a 75-year-old man with erosive, erythematous lesion on the left buccal mucosa previously diagnosed as oral lichen planus. He underwent surgical excision and the final histopathological result confirmed it to be lichenoid dysplasia with massive candidal infection. We report this case with a review of the related literature.

Key Words: Candidiasis; Epithelial dysplasia; Lichenoid dysplasia; Lichen planus, oral

INTRODUCTION

Lichenoid dysplasia (LD) is a lichenoid features with epithelial dysplasia clinically and histopathologically similar to oral lichen planus (OLP). It can be clinically mistaken for OLP, but has histopathologic features of dysplasia and a true malignant predisposition.[1,2] The clinician should be able to differentiate between OLP and LD for the proper management. We experienced a case of LD in the buccal mucosa misdiagnosed as OLP at first. We present the case with a review of the related literature.

CASE REPORT

A 75-year-old male visited the Department of Oral Medicine at the Wonkwang University Daejeon Dental Hospital (Daejeon, Korea) with the chief complaint of pain on the left buccal mucosa when eating hot and spicy foods. He had been experiencing the pain for about 1 year, and history taking revealed that he had visited a Department of Dermatology, and had a biopsy about 5 month ago. It led to a diagnosis of OLP. He had been treated with topical steroid for 5 months, including one time intra-lesional injection with corticosteroid. However, the lesion did not regress and the pain did not decrease. The patients reported no habits of smoking and drinking alcohol. Also, he reported no parafunctional habit except left unilateral chewing because of missing of right posterior teeth. The previous medical history revealed that the he suffered from angina pectoris and has been taking anticoagulant.

At intraoral clinical examination, the lesion was localized on the left anterior buccal mucosa and presented with

erosive lesion mixed with whitish and erythematous lesion (Fig. 1A). The tentative diagnosis was oral lichenoid lesion (OLL) because the clinical feature was unilateral lesion and not typical that of OLP. We cannot verify the first feature of the lesion because the feature of first-visit time was that of after biopsied. So, the symptomatic treatment was considered first based on the previous biopsy result. Prednisolone (Solondo; Yuhanmedica Inc., Cheongju, Korea) was administered orally for 3 weeks because the lesion failed to respond to topical corticosteroid measures. The patient also used topical antifungal agent (Diflucan; Pfizer, Paris, France) to prevent opportunistic infection, oral candidiasis. After 4 weeks, he had no particular discomforts. At intraoral clinical examination, the erosive and erythematous lesion was disappeared, but the whitish plaque-like lesion was formed instead. The whitish plaque-like lesion was not peeled off. He had an excisional biopsy and it led to a final diagnosis of moderate epithelial dysplasia with massive candidal infection (Fig. 2A-C). The oral pathologist recommended total complete excision of the lesion, use of antifungal agent, and closed follow-up. Based on this result, the antifungal agent (Diflucan) was orally administered and any other medications were discontinued. Oral pathologist re-read the previous lesional tissue slide to find out whether the presence of epithelial dysplasia or not. It led to a diagnosis of moderate epithelial dysplasia with submucosal lymphoplasmocytic infiltration, i.e., LD. The patient has gotten regularly close followed up for a recurrence for 3 years, and underwent additional four times complete excision. The last excisional biopsy result was hyperkeratosis and acanthosis with mild epithelial dysplasia without candidal infection (Fig. 2D). After the last excision, to date, the buccal mucosa is well maintained without a recurrence (Fig. 1B).

DISCUSSION

OLP is a chronic mucocutaneous disease affecting 1% to 2% of the population. The etiology is not known clearly, but current evidence indicates that OLP is an immunologically mediated disorder. OLP typically results in lesions which are whitish, reticular, but may be papular or plaque-like and associated with red atrophic areas bilaterally. The clinical and histopathological diagnostic criteria of OLP was agreed by World Health Organization (WHO) in 1978.[3] But lack of clinicopathologic correlation in the diagnosis of OLP and the absence of criterion about the presence of epithelial dysplasia made researchers to be confused. So van der Meji and van der Waal[4] proposed modified WHO diagnostic criteria in 2003 (Table 1). They emphasize that a diagnosis of OLP should not be assessed on the histopathological picture alone, but should also be based on distinct clinical criteria. They regard the presence of epithelial dysplasia as an exclusion criterion for the histopathologic diagnosis of OLP to exclude LD and also proposed the diagnostic criteria of OLL. According to modified WHO diagnostic criteria in 2003, our patient should have not been diagnosed as OLP or OLL, but diagnosed as epithelial dysplasia or LD at first. Furthermore, the clinical features was not typical that of OLP and we could not verify the first feature of the lesion because the feature of first-visit time was that of after biopsied. We should have re-biopsied at first before prescribing medications.

LD is similar to OLP clinically and histopathologically,

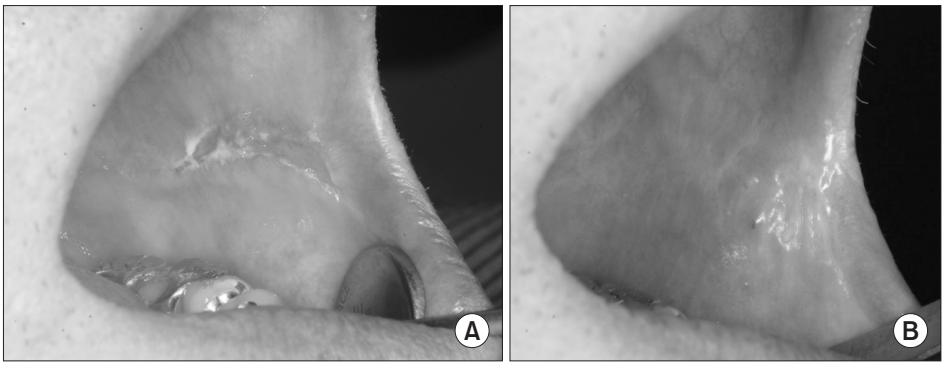

Fig. 1. (A) Left buccal mucosa and post-commissural area were presented with erosive lesion mixed with whitish and erythematous lesion. (B) Intraoral feature after 3 years. The lesion is maintained without a recurrence.

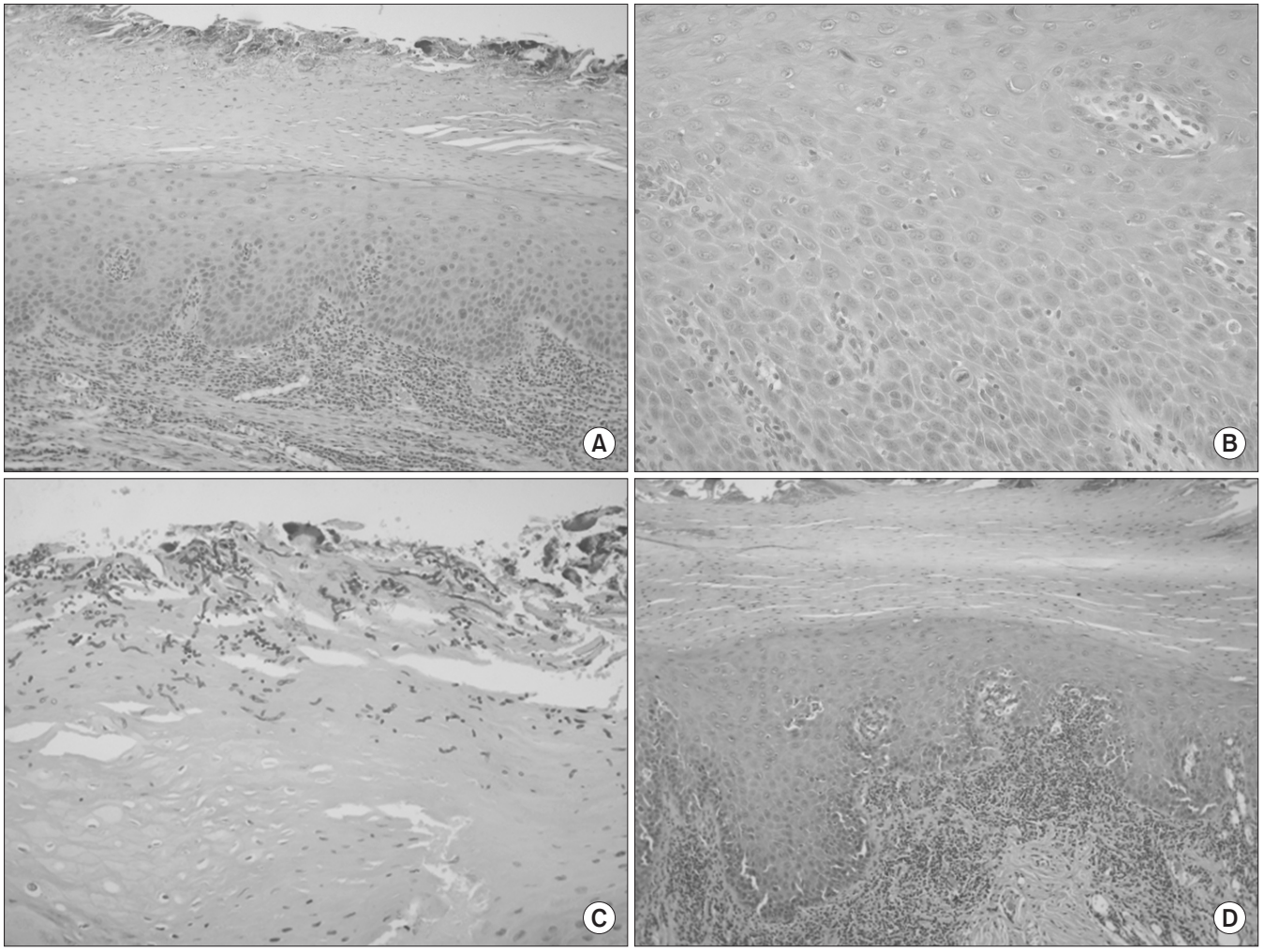

Fig. 2. (A) Moderate epithelial dysplasia. Photomicrograph shows dysplastic changes extended to the midpoint of the epithelium and submucosal lymphoplasmocytic infiltration (H&E staining, ×100). (B) Moderate epithelial dysplasia. Photomicrograph shows dysplastic changes characterized by nuclear hyperchromatism, pleomorphism, scattered mitotic figures, and cellular crowding (H&E staining, ×200). (C) Candidiasis. High-power photomicrograph shows the tubular hyphae and ovoid yeasts of *Candida albicans* embedded in the parakeratin layer (PAS staining, ×200). (D) Mild epithelial dysplasia (the latest excisional biopsy, after 3 years). Photomicrograph shows the alterations limited to the basal layers with hyperkeratosis and acanthosis (H&E staining, ×100).

first defined by Krutchkoff and Eisenberg,[1] has been used to describe lichen planus-like histopathological aspects in dysplastic epithelium. This term dose not imply the presence of dysplastic epithelial changes in OLP but it may have actually epithelial dysplasia with a secondary lichenoid inflammatory features that mimicked lichen planus. They insisted LD as a distinct histopathologic entity and LD is obvious precancerous lesion that should be differentiated with OLP.

Krutchkoff and Eisenberg[1] proposed strict histopathologic criteria to help distinguish among epithelial dysplasia, OLP, and specific and nonspecific inflammatory conditions of the oral mucosa. The crucial determinant that allows separation of LD from OLP is the additive presence of dysplastic features with the overlying epithelium in the LD. Such features include increased nuclear size and nuclear-cytoplasmic ratios; nuclear pleomorphism; nuclear hyperchromasia; disturbed or disorderly maturation; lack of cellular cohesion; increased or abnormal mitoses; and blunted, club-shaped, or "tear drop"-shaped rete pegs. The presence of any two or more of these histopathologic features in lichenoid lesion mandates separate consideration.

OLP and LD can appear with similar and overlapping microscopic features that often make accurate hisopathologic diagnosis to be a difficult problem. Some sought possible

Table 1. Modified World Health Organization diagnostic criteria of OLP and OLL (2003)[4]

Clinical criteria
• Presence of bilateral, more or less symmetrical lesions
• Presence of a lace-like network of slightly raised gray-white lesions (reticular pattern)
• Erosive, atrophic, bullous, and plaque-type lesions are only accepted as a subtype in the presence of reticular lesions elsewhere in the oral mucosa.
• In all other lesions that resemble OLP but do not complete the aforementioned criteria, the term "clinically compatible with" should be used.
Histopathologic criteria
• Presence of a well-defined band-like zone of cellular infiltration that is confined to the superficial part of the connective tissue, consisting mainly of lymphocytes.
• Signs of liquefaction degeneration of the epithelial basal layer (apoptosis keratinocyte)
• Absence of epithelial dysplasia
• When the histopathologic features are less obvious, the term "histopathologically compatible with" should be used.
Final diagnosis OLP or OLL
To achieve a final diagnosis, clinical as well as histopathologic criteria should be included:
• OLP - A diagnosis of OLP requires fulfillment of both clinical and histopathologic criteria
• OLL - The term OLL will be used under the following conditions:
1. Clinically typical of OLP but histopathologically only compatible with OLP
2. Histopathologically typical of OLP but clinically only compatible with OLP
3. Clinically compatible with OLP and histopathologically compatible with OLP

OLP, oral lichen planus; OLL, oral lichenoid lesion.

immunohistochemical distinction among OLLs that would provide a simple and reliable means for establishing more accurate diagnoses. They focused on the exploration of a possible unique marker of keratinocyte differentiation such as filaggrin, 50 and 58 kDa keratin classes, involucrin, and etc. Among these, involucrin, a single protein, has greater immunostaining specificity for squamous epithelium. According to Eisenberg et al.,[5] the involucrin reactivity was generally uniform within superficial strata and the expression is very high in OLP. By contrast, the involucrin reactivity was not uniform and the expression is not high in LD. They suggest that in some cases a distinction can be made between OLP and LD by careful evaluation and comparison of their respective involucrin reactivity patterns.[5]

The clinician should differentiate with OLP and LD. The OLP is an immunologically mediated mucocutaneous disorder and the management primarily includes topical or systemic corticosteroids. On the other hand, the LD is an epithelial dysplasia with lichenoid features and distinct precancerous lesion. LD exhibiting moderate epithelial dysplasia or worse should be removed completely and closed long-term follow-up after removal is extremely important because recurrences are frequent and additional dysplastic change may develop in LD.[6]

Another reason for differentiating with OLP and LD is the uncertainty of potentially malignant nature of OLP. Although the WHO currently considers OLP to be a disease that may evolve to cancer, the potential of malignant transformation of OLP has been one of the most debated topics over the years since first reported in 1969.[7] One of the reasons of the debates and variation of prevalence of malignant transformation (0%-12.5%)[8,9] is due to lack of uniform clinical and histopathological criteria for OLP. OLP, OLL, and LD (epithelial dysplasia with lichenoid features) were diagnosed by different diagnostic criteria in each case. According to Krutchkoff and Eisenberg,[1] many of the OLP cases eventually evolved to oral squamous cell carcinoma (SCC) were actually LD cases which were misdiagnosed as OLP, more specifically when in their early stages. These misdiagnosis and different diagnostic criteria can influence of prevalence of malignant transformation of OLP. To avoid confusion, all lesions that resemble OLP but exhibit epithelial dysplasia were excluded in modified WHO diagnostic criteria of OLP and OLL. However, this may be lead to an underestimation of the rate of malignant transformation of OLP. If OLP per se is a potentially premalignant disorder, dysplasia may represent a valid stage in the development of SCC.[10] It is still unclear whether a patient with OLP per se has an independent risk of malignant transformation to SCC, or whether areas of oral epithelium with

a premalignant potential—molecular changes manifesting clinically as normal or histologically with unrecognized atypia that is not yet dysplasia—evoke a nonspecific lichenoid response.[11] Future studies should address the concept of LD that may help to resolve any controversies with regard to the malignant potential of OLP.

Patients with OLP can have superimposed candidal infections or can be secondarily infected with candida from corticosteroid therapy.[8] *Candida* species are common mouth commensals, but it can proliferates if the local ecology of the mouth changes or if immune defenses fall. *Candida* typically colonizes mucocutaneous surfaces and these can be portals for entry into deeper tissues. Chronic candidal infection (chronic hyperplastic candidiasis; candidal leukoplakia) is common in speckled leukoplakia and *Candida albicans* can cause or colonize other keratoses, particularly in smokers, and is especially likely to form speckled leukoplakia at commissures. Chronic candidal infection causes cellular changes including hyperplasia, mild to severe dysplasia, and ultimately carcinoma in situ or invasive carcinoma.[12] The probable role of fungal infections in oral carcinogenesis remains unclear,[13] but various investigators have demonstrated a significant correlation between epithelial dysplasia and fungal invasion. According to Hebbar et al.,[14] as the degree of dysplasia increased, a significant increase in PAS positivity was noted. Leukoplakia with candidal infection has been shown to have a higher rate of malignant transformation than in those not infected with candida.[15] Furthermore, alcohol consumption and tobacco smoking have an important role in oral carcinogenesis when the candida species existed in the pathologic lesion.[16-18] Ethanol becomes oxidized into acetaldehyde that is a highly reactive and toxic compound recently reclassified as a group 1 carcinogen by the International Agency for Research on Cancer.[19,20] OLP and candidiasis together provide a fertile background for malignant transformation of oral epithelium, acting synergistically and/or additively in progression to oral SCC. Our patients had a massive candidal infection in the lesion. He was misdiagnosed as OLP at first, and he had gotten topical corticosteroid therapy for 6 months. During this period, the lesion might have superimposed candidal infections. At intraoral clinical examination after 8 weeks, the whitish plaque-like lesion formed and the clinical feature was more similar to candidal leukoplakia than OLL. Candidal infection might be influence on the degree of epithelial dysplasia. Control of candidal infection in OLP treatment may be able to help prevent transformation to epithelial dysplasia and exacerbations of the lesion.

In conclusion, OLP and LD can appear with similar and overlapping histopathologic features that often make accurate histopathologic diagnosis to be a difficult problem. The clinician should differentiate with OLP and LD by early diagnosis with uniform clinical and histopathological diagnostic criteria for the proper treatment. It is very important to control the candidal infections in the OLP and LD management. Closed follow-up and long-term evaluation after the removal of LD is important due to high recurrence rate.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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