Oral Manifestations of Dermatologic Disease: A Focus on Lichenoid Lesions

Susan Müller

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Abstract Lichenoid changes in the oral mucosa can be encountered in a wide range of lesions with varied etiologies including immune-mediated disorders, reactions to systemic medications and to dental materials. Dysplasia of the oral cavity can exhibit a lichenoid histology, which may mask the potentially cancerous component. Another unusual clinical disease, proliferative verrucous leukoplakia, can often mimic oral lichen planus clinically requiring careful correlation of the clinical and pathologic features.

Keywords Lichen planus · Lichenoid reactions · Oral dysplasia · Proliferative verrucous leukoplakia

Introduction

An immune mediated disease of unknown etiology oral lichen planus (OLP) is a chronic inflammatory disease of variable severity that can wax and wane over a long period of time. A number of clinical as well as microscopic mimics of OLP exist making diagnosis challenging at times. Oral lichenoid lesions from systemic drug exposure or local allergic contact hypersensitivity are well documented [1]. Other immune-mediated diseases including mucous membrane pemphigoid, graft versus host disease, and lupus erythematosus can share common clinical and

histological features with OLP [2]. Oral lichenoid lesions requires that both the clinician and pathologist have broad experience of the varied clinical presentations to develop an accurate differential diagnoses. The exact incidence of malignant transformation of OLP is unknown although there have been a few well-documented cases [3]. An important diagnostic consideration to pathologists however, is oral epithelial dysplasia with a “lichenoid” pattern. Similar to lichen planus, lichenoid dysplasias exhibit a prominent band-like, chronic inflammatory cell infiltrate subjacent to the basal cells. On closer examination abnormal maturation, mitoses and/or dyskeratosis may be appreciated, features of epithelial dysplasia and not oral lichen planus [4]. Proliferative verrucous leukoplakia, both a clinical and microscopic mimic of OLP needs to be considered when a patient with multiple oral lichenoid lesions shows histologically varying degrees of dysplasia, verrucous carcinoma, or conventional squamous cell carcinoma [5].

Discussion

Oral Lichen Planus

Lichen planus is a relatively common immune-mediated disease and next to cutaneous lichen planus, the oral lesions are the most common presentation. [6]. OLP is the only disease manifestation in up to 35% of patients and is nearly always bilateral or multifocal [1]. In the oral cavity there are three major clinical presentations: reticular, erythematous, and erosive (Fig. 1) [7].

A clinician familiar with both the clinical and histologic features of lichen planus can be of great assistance to the pathologists. Because the diagnosis of lichen planus

S. Müller (✉)
Department of Pathology and Laboratory Medicine, Emory
University School of Medicine, 1364 Clifton Road NE, Atlanta,
GA 30322, USA
e-mail: susan.muller@emory.org

S. Müller
Department of Otolaryngology Head and Neck Surgery, Emory
University School of Medicine, Atlanta, GA, USA

Fig. 1 Erosive oral lichen planus involving the gingiva and buccal mucosa (arrow). Note that adjacent to the areas of erythema, white reticulated/lacelike features are present

Fig. 2 Low power photomicrograph of oral lichen planus illustrating the hallmark histologic feature of a band-like lymphocytic infiltrate. At the right edge of the image a subepithelial separation is apparent

requires evaluation of the basement membrane zone, biopsies of OLP ideally include intact epithelium rather than just the ulcerative component.

The microscopic features of OLP are highly variable and depend in some part to whether the biopsy was from a hypertrophic, atrophic, or erosive lesion. A “sawtooth” pattern of the rete can be observed in OLP, but the epithelium can also appear acanthotic or atrophic corresponding to the clinical presentation (Fig. 2). Interface dermatitis is a hallmark of OLP. Hydropic degeneration of the basal cells with scattered dyskeratotic keratinocytes (Civatte, colloid, hyaline, or cytoid bodies) along the epithelial interface is seen (Fig. 3); [8]. At the basement zone, hugging the basal cells is a band-like, predominately T lymphocyte, inflammatory cell infiltrate. Generally the inflammation is superficial rather than deep and perivascular inflammation is not generally noted. Biopsies of erosive OLP lack many of the histologic hallmarks of

Fig. 3 High power photomicrograph of oral lichen planus exhibiting “saw-toothed” rete, Civatte bodies (arrows), as well as prominent hydropic degeneration of the basal cells resulting in the subepithelial split

lichen planus and arriving at a definitive diagnosis can be difficult. In fact it has been reported that as many as 50% of OLP cases lack clinicopathologic correlation [9].

Malignant transformation of oral lichen planus to squamous cell carcinoma has been reported, ranging from 0.04 to 1.74%, although the exact incidence is unknown [4, 7, 10–12]. The well-documented cases of malignant transformation in long-standing OLP often occurred in poorly controlled erosive or atrophic form [4]. Some reported cases of malignant transformation of OLP were based on clinical features alone and never had pathologic confirmation. In this author’s opinion the presence of dysplasia in a lichenoid lesion should not be diagnosed as lichen planus and rather be diagnosed as epithelial dysplasia. One exception is the presence of a superimposed candidal infection that can cause reactive epithelial atypia.

Drug Related Oral Lichenoid Lesions

Many systemic medications can cause oral lichenoid reactions (OLR) although the exact incidence is unknown and the pathogenesis is unclear [1–3]. The onset of a drug related lichenoid reaction and initial medication use vary widely, from weeks to over a year [13]. No standardized criteria for the diagnosis of OLR exist, however if a temporal relationship can be identified discontinuing the offending medication is recommended. OLR lesions can take many months or longer to resolve. Similar to OLP, OLR can present clinically with either reticular or erosive patterns but unlike OLP that is a multifocal and/or bilateral disease, OLR lesions often present as a single lesion. Commonly reported medications that cause can cause OLR include antihypertensives, nonsteroidal inflammatory drugs, antimalarials, and HIV antiretrovirals [14, 15].

The microscopic features of drug-related lichenoid lesions share many similarities to OLP with notable differences. The inflammatory infiltrate in OLR is more diffuse and extends deeper into the lamina propria rather than the band-like infiltrate seen in OLP. In addition to lymphocytes both plasma cells and eosinophils may be seen [2, 14]. Increased numbers of dyskeratotic keratinocytes (colloid or Civatte bodies) may be present in OLR compared to OLP. A perivascular chronic inflammatory cell infiltrate can be seen in drug related lichenoid lesions, which is an uncommon finding in OLP. However, these microscopic features are not specific and rely on clinical information including a temporal association with any systemic medications.

Oral Lichenoid Contact Reaction

There are a variety of agents that are known to cause an oral lichenoid contact reaction including dental materials and flavoring agents [16, 17]. Most lesions can mimic OLP clinically although the lesions occur at the site of contact with the offending material. Amalgam restorations can cause lichenoid lesions and are found on the buccal mucosa or the tongue in direct contact with the amalgam. Cinnamon can induce stomatitis that has a characteristic histology. In oral lichenoid contact reactions when the offending agent is removed the lesions quickly resolve.

The pathology of oral lichenoid contact reactions is not specific and overlaps with OLP. Amalgam associated oral lichenoid reactions however, can have such a dense lymphocytic infiltrate that lymphoid follicles called tertiary follicles may form [15] (Fig. 4a). Cinnamon-induced oral

lichenoid lesions demonstrate marked epithelial acanthosis with elongated rete ridges and unlike OLP, the inflammatory infiltrate contains plasma cells, histiocytes and eosinophils in addition to lymphocytes [17] (Fig. 4b). Interface mucositis may be evident in cinnamon stomatitis and a deep perivascular infiltrate is seen.

“Lichenoid Dysplasia”: Oral Dysplasia and Proliferative Verrucous Leukoplakia

An unusual form of leukoplakia that is a clinical and pathologic mimic of OLP is proliferative verrucous leukoplakia (PVL). PVL was first described in 1985 and can be a diagnostic challenge, especially in its' early presentation [5]. The demographics and clinical presentation share similarities to OLP. Most reported patients are older females, many without a history of tobacco or alcohol abuse who present with oral lesions of long standing [18, 19]. The lesions are multifocal similar to oral lichen planus and have a propensity for the gingiva, palate, tongue and buccal mucosa [18] (Fig. 5). The hard palate can be involved which is an unusual location for OLP, however similar to OLP the ventral tongue and floor of mouth is uncommon location. The lesions vary in appearance ranging from hyperkeratotic plaques to erythematous atrophic areas or frank ulceration.

Microscopically, oral dysplasia can sometimes exhibit a band-like inflammatory infiltrate which on low-power can mimic lichen planus [12] (Figs. 6, 7). This type of dysplasia has sometimes been called “lichenoid dysplasia” although the use of this term is discouraged to avoid clinical mismanagement [4, 7]. The inflammatory infiltrate is usually composed of both lymphocytes and plasma cells with migration of inflammatory cells through the

Fig. 4 **a** Amalgam associated lichenoid reaction forming tertiary lymphoid follicles. The melanosis seen subjacent to the basal cells is consistent with post-inflammatory hyperpigmentation. **b** Cinnamon mucositis shares some histologic features with oral lichen planus including epithelial acanthosis with elongated rete, but the inflammatory infiltrate is mixed and extends into the deeper lamina propria

Fig. 5 Proliferative verrucous leukoplakia presenting as a thickened white plaque involving the attached gingiva. This is a typical clinical presentation and can slowly progress to involve a majority of the gingiva

Fig. 6 Biopsy of oral dysplasia what shows a lichenoid appearance on low-power including a band-like inflammatory infiltrate and a sub-epithelial separation

Fig. 7 Higher magnification of Fig. 6 shows the dysplastic epithelial changes of budding of the rete and scattered mitoses (*arrows*). The inflammatory infiltrate is composed of both plasma cells and lymphocytes

epithelium. Varying degrees of cytologic atypia is present [18]. Compared to OLP, the malignant transformation rate is reportedly higher in oral lichenoid lesions that do not have all the typical clinical and histologic features of OLP [20]. These studies again emphasize the importance of both clinical and pathologic correlation in making the diagnosis of oral lichen planus.

PVL can exhibit a wide range of histologic features; from hyperkeratosis without dysplasia, to more lichenoid features with a band-like lymphocytic infiltrate, to dysplasia, verrucous carcinoma or conventional type squamous cell carcinoma [16]. Early lesions can have a unique pattern referred to as atypical epithelial (verrucous) hyperplasia with varying degrees of keratosis with little to no dysplasia (Fig. 8). There is some histologic overlap with verrucous carcinoma, however the rete are usually not as

Fig. 8 Atypical verrucous leukoplakia in a patient with proliferative verrucous leukoplakia. Marked acanthosis with elongated bulbous rete is seen. The mixed inflammatory cell infiltrate is not as dense as in oral lichen planus and can extend into the deeper lamina propria. Despite the lack of dysplasia, the overall architecture is worrisome for progression to cancer

bulbous as verrucous carcinoma. Unlike conventional oral squamous cell carcinoma, often the site of malignant transformation in PVL is the attached gingiva, palate, or dorsal tongue.

Conclusions

Oral lichenoid lesions can be a diagnostic challenge for the pathologist due to the tremendous overlap in the clinical and pathologic presentation of many inflammatory, reactive, and immune-mediated disorders than commonly involve the oral mucosa. Ideally good clinical information will accompany the biopsy specimen including site, presentation and other relevant information as an accurate diagnosis cannot be made in a vacuum. It is critical that dysplastic changes in lichenoid lesions not be overlooked to ensure appropriate treatment for the patient.

References

- Schlosser BJ. Lichen planus and lichenoid reactions of the oral mucosa. *Dermatol Ther.* 2010;23:251–67.
- van der Waal I. Oral lichen planus and oral lichenoid lesions; a critical appraisal with emphasis on the diagnostic aspects. *Med Oral Patol Oral Cir Bucal.* 2009;14(3):E310–4.
- Farthing PM, Speight PM. Problems and pitfalls in oral mucosal pathology. *Curr Diagn Pathol.* 2006;12:66–74.
- Eisenberg E, Krutchkoff DJ. Lichenoid lesions of oral mucosa. Diagnostic criteria and their importance in the alleged relationship to oral cancer. *Oral Surg Oral Med Oral Path.* 1992;73: 699–704.

5. Hansen LS, Olson JA, Silverman S Jr. Proliferative verrucous leukoplakia. A long-term study of thirty patients. *Oral Surg Oral Med Oral Pathol*. 1985;60:285.
6. Thornhill MH. Immune mechanisms in oral lichen planus. *Acta Odontol Scand*. 2001;59(3):174–7.
7. Eisen D. The clinical features, malignant potential, and systemic associations of oral lichen planus: a study of 723 patients. *J Am Acad Dermatol*. 2002;26:207–14.
8. Van der Meij EH, Reibel J, Slootweg PJ, et al. Interobserver and intraobserver variability in the histologic assessment of oral lichen planus. *J Oral Pathol Med*. 1999;28:274–7.
9. Van der Meij EH, van der Waal I. Lack of clinicopathologic correlation in the diagnosis of oral lichen planus based on the presently available diagnostic criteria and suggestions for modifications. *J Oral Pathol Med*. 2003;32:507–12.
10. Van der Meij EH, Mast H, van der Waal I. The possible premalignant character of oral lichen planus and oral lichenoid lesions: a prospective five-year follow-up study or 192 patients. *Oral Oncol*. 2007;43:742–8.
11. Van der Waal I. Potentially malignant disorders of the oral and oropharyngeal mucosa; terminology, classification and present concepts of management. *Oral Oncol*. 2009;45:317–23.
12. Krutchkoff DJ, Eisenberg E. Lichenoid dysplasia: a distinct histopathologic entity. *Oral Surg Oral Med Oral Pathol*. 1985;60:308–15.
13. McCartan BE, McCreary CE. Oral lichenoid drug eruption. *Oral Dis*. 1997;3:58–63.
14. Al-Hashimi I, Schifter M, Lockhart PB, et al. Oral lichen planus and oral lichenoid lesions: diagnostic and therapeutic considerations. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;103(Suppl S25):e1–12.
15. Thornhill MH, Sankar V, Xu XJ, et al. The role of histopathological characteristics in distinguishing amalgam-associated oral lichenoid reactions and oral lichen planus. *J Oral Pathol Med*. 2006;35:233–40.
16. Issa Y, Duxbury AJ, Macfarlane TV, Brunton PA. Oral lichenoid lesions related to dental restorative materials. *Br Dent J*. 2005;198:361–6.
17. Miller RL, Gould AR, Bernstein ML. Cinnamon-induced stomatitis venenata. Clinical and characteristic histopathologic features. *Oral Surg Oral Med Oral Pathol*. 1992;73(6):708–16.
18. Bagan JV, Murillo J, Poveda R, et al. Proliferative verrucous leukoplakia: unusual locations of oral squamous cell carcinomas, and field cancerization as shown by the appearance of multiple OSCCs. *Oral Oncol*. 2004;40:440–3.
19. Silverman S Jr, Gorsky M. Proliferative verrucous leukoplakia: a follow-up study of 54 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1997;84:154–7.
20. Van den Haute V, Antoine JL, Lachapell JM. Histopathological discriminant criteria between lichenoid drug eruption and idiopathic lichen planus: retrospective study on selected samples. *Dermatologica*. 1989;179:10–3.