# Oral Complications of Dermatologic Disorders

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#### **KEYWORDS**

• Autoimmune dermatologic oral conditions • Oral lichen planus • Mucous membrane pemphigoid • Pemphigus vulgaris

#### **KEY POINTS**

- The oral lesions in dermatologic diseases may be the early aspects of the disease itself, the most significant clinical appearance, or the only sign or symptom; sometimes lesions can occur simultaneously in the skin and in the oral cavity.
- Although in most instances cutaneous lesions of lichen planus are self-limiting, causing merely itching, oral lesions are persistent, potentially premalignant, hardly ever undergo spontaneous remission, and are habitually a source of morbidity.
- From a diagnostic and therapeutic point view, it might be of significant advantage to discriminate a clinical subset of mucous membrane pemphigoid, termed oral pemphigoid, in which the disease is mainly limited to the oral cavity and patients have a better prognosis compared with other variants.
- Gingival lesions caused by autoimmune dermatologic disorders are described with diffuse erythematous lesions, blisters, erosions, or ulcerations, mainly located on the attached gingiva and on the palate; the occurrence of epithelial desquamation, erythema, and erosive lesions on the gingival tissue is described in literature as "desquamative gingivitis."
- Oral manifestations and dental involvement of epidermolysis bullosa vary in frequency and severity according to the form. Intraoral manifestations include multiple carious lesions affecting almost the entire dentition, with severe gingival inflammation, microstomia, ankyloglossia, and obliteration of oral vestibule.

#### Introduction

Skin and oral mucosa are analogous and comparable structural tissues, composed of specialized stratified epithelium functioning as a first-line barrier against dissimilar types of chemical or physical injuries. Stratified squamous epithelia are complex compound structure, mainly comprising of keratinocytes (KCs) adherent to each other, and to the underlying epithelial basement membrane and connective tissue. Cohesion among KCs is needed for preserving the tissues' structure and epithelial functions. Three functional types of junctional structures interconnect KCs: (1) anchoring junctions (including desmosomes and adherens junctions), (2) occludens junctions (tight junctions), and (3) nexus junctions (gap junctions). Much of the oral mucosa is resulting embryologically from an invagination of the ectoderm and, not surprisingly, it may become involved in disorders that are mostly associated with the skin.

The oral lesions in dermatologic diseases may be the early aspects of the disorder itself, or the most significant clinical appearance; other times, they are the only sign or symptom, or sometimes lesions can occur simultaneously in the skin and in the oral cavity. A wide range of dermatologic disorders

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can affect the mouth, although the more common are oral lichen planus (OLP), mucous membrane pemphigoid (MMP), pemphigus vulgaris (PV), epidermolysis bullosa (EB), and psoriasis.

The proper diagnosis of this oral condition should be made through clinical findings, assessment of subepithelial or intraepithelial blister by histopathology, detection of autoantibodies in the mucosal samples by direct immunofluorescence, and binding to the roof and/or floor of the blister of salt-split skin by indirect immunofluorescence. Commercially available enzyme-linked immunosorbent assays, based on proteins involved in dermoepidermal or chorioepithelial adhesion, are also usually used for serologic diagnosis.

#### Oral lichen planus

OLP is a chronic inflammatory disease, affecting roughly 1.5% to 2% of the total population, women almost more than twice as men. Patients of all ages could be interested, frequently in the fifth to sixth decades of life, usually at an earlier age in men. Patients with OLP usually show no increased prevalence of cigarette smoking or alcohol consumption.

To date, the defined cause remains unknown. Immune dysregulation plays a critical role in the development and progression of this disease; however, it is unlikely to be caused by a single antigen, given that studies of T-cell receptor variable region genes from lesional OLP T cells have not revealed the use of a restricted number of different variable region genes. Probably, OLP is the outcome of the influence of a limited range of extrinsic antigens or altered self-antigens. In a

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minority of patients, precipitating factors have been identified, including dental materials, medications (eg, nonsteroidal anti-inflammatory drugs and angiotensin-converting enzyme inhibitors), stress, trauma, and various infectious agents. Different authors have demonstrated an association of OLP and hepatitis C in southern Europe and in Asia, reporting that viral sequences could be also discovered in the serum of patients with OLP; moreover, the virus was also shown to occasionally replicate in OLP tissues. The possible association of hepatitis C virus infection with OLP may necessitate the importance of virus screening in such patients, especially in some regions.

The oral manifestations of OLP are satisfactory recognized. To date, six clinical forms of have been described (white [reticular, plaque-like, popular], or red [atrophic, erosive, and bullous]). Although white forms are generally asymptomatic (counting usually for 60% of total cases) (Fig. 1), atrophic and erosive (Fig. 2) lesions could result in profound discomfort. The gingiva is one of the most prevalent oral sites (Figs. 3 and 4), after the buccal mucosa and the tongue (Fig. 5). Skin lesions characteristically present as flat-topped, polygonal, violaceous papules regularly covered by a network of fine lines affecting usually wrists, ankles, and genitalia. Although in most instances cutaneous lesions of lichen planus are self-limiting, causing merely itching, oral lesions are persistent, potentially premalignant, hardly ever undergo spontaneous remission, and are habitually a source of morbidity. One of the most important complications of OLP is the potential development of an oral squamous cell carcinoma (Fig. 6), although this is a reasonably controversial matter. The rate of transformation in individual studies ranged from 0% to 3.5%. However, it should be judicious for clinicians to pursue continued regular observation and follow-up in patients with OLP with these conditions, even if they do not fit a traditional high-risk category for oral cancer (eg, female and nonsmokers). In patients followed up for a long period, it has been published that less than 3% of them had a complete and definitive healing of oral lesion, whereas most showed a stable clinical appearance (more than 75%) and a minority of patients got worse (less than 10%).

Numerous drugs have been used to treat this condition, with variable results; however, even if the best treatment remains high-potency topical corticosteroids, management is commonly empirical, with no adequate control groups or corrected study designs. Treatment is usually undertaken with the goal of achieving control of symptoms with minimal side



Fig. 2 Oral lichen planus. Red erosive lesion on the right buccal mucosa.

effects. Clobetasol propionate 0.05% seemed to be one of the most effective topical steroids, because in an adhesive base it led to complete remission in almost 75% of patients with symptomatic forms, but strong evidence on its efficacy is lacking. However, independently from the active principle used and the way of administration, more than half of the responsive patients showed yet again active painful disease, and can need a new therapeutic approach, confirming the OLP chronic course and the symptomatic character of therapeutic treatments. Moreover, some patients are refractory to steroid medication and could need a different approach. The nonsteroidal topical calcineurin inhibitors are important treatment option and are indicated in cases where the use of topical steroids is unsuitable, or have failed to adequately control OLP, especially in the acute phase, similarly to other dermatologic conditions. Pimecrolimus and tacrolimus ointments seemed to be a treatment of choice, safe and easy, for patients with atrophic-erosive OLP, previously treated with topical steroids but unresponsive. Low-level laser therapy (LLLT) is an approach increasingly used in medicine, which also has potential biostimulating effects if applied to oral tissues by improving wound healing. LLLT has also been showed to be a feasible treatment choice for patients with unresponsive symptomatic OLP, but small data from limited studies are available.



Fig. 1 Oral lichen planus. White reticular lesions on the left buccal mucosa.



**Fig. 3** Diffuse gingival involvement (desquamative gingivitis) in a patient with diagnosed oral lichen planus (mainly erythematous).

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