Mucocutaneous diseases of the oral cavity

Kristina Perschbacher

Abstract

There are several immune mediated inflammatory mucocutaneous diseases that affect the oral cavity, most of them presenting clinically with varying degrees of blistering, sloughing, erosions, ulcerations and pain. These conditions may have serious sequelae if left untreated therefore early and proper diagnosis is crucial for patient management. Knowledge of the clinical presentation of these conditions can help the histopathologist when reporting mucocutaneous diseases of the oral cavity. This review will focus on common and clinically significant oral mucocutaneous diseases and is intended to be a supplement to specialist texts and resources.

Keywords chronic graft-versus-host disease; erythema multiforme; lichen planus; mucous membrane pemphigoid; oral mucocutaneous diseases; pemphigus vulgaris

Introduction

The most clinically significant mucocutaneous diseases of the oral cavity are inflammatory dermatoses. These conditions are typically ulcerative or blistering diseases with an autoimmune or immune mediated inflammatory pathogenesis. They often present with painful intraoral lesions and may have serious sequelae if left untreated. This article will review the most common and clinically significant oral mucocutaneous diseases: oral lichen planus, mucous membrane pemphigoid, pemphigus vulgaris, erythema multiforme and chronic graft-versus-host disease. In this review, the clinical presentation, histopathologic features and treatments for each of these diseases will be discussed.

Lichen planus

Lichen planus was first described as a chronic disease affecting skin, scalp, nails and mucosa by Erasmus Wilson in 1869.[1,2] It has been established that lichen planus has a T-lymphocyte directed, immune-mediated pathogenesis. The trigger for the inflammatory immune response is unknown and may be a self-antigen or an exogenous antigen.[2–4]

Clinical presentation

OLP affects approximately 0.1%–2% of the population with a 3:1 ratio of female to male patients.[5] This condition often presents in middle age (>40yrs) however, there have been cases of OLP diagnosed in patients as young as 15yrs.[1,3,5]

Oral lichen planus (OLP) can have a wide variety of clinical presentations ranging from subtle white reticular patterns to severe erosions and ulcerations with intense erythema and white striae. The lesions of OLP are typically multifocal in presentation, affecting bilateral mucosal surfaces and involving the gingiva in multiple quadrants of the maxilla and mandible (Figure 1). Patients presenting with lichen planus may be asymptomatic and unaware of the condition or they may have pain and complain of burning discomfort and sores, especially noticeable when eating spicy or acidic foods.[1,3,4,6]

There are lichenoid lesions that look both clinically and histologically like OLP, however they can be linked to a causative agent or underlying disease. These lichenoid lesions can be classified into the following categories[4,7]:

- Oral lichenoid contact lesions occur as a result of allergic contact stomatitis (delayed type IV hypersensitivity reaction) to dental restorative materials, in particular amalgam.
- Oral lichenoid drug reactions may be seen coinciding with the taking of certain medications, such as ACE inhibitors, oral hypoglycemic agents, and non-steroidal anti-inflammatory agents.
- Oral lichenoid lesions of graft-versus-host disease, (discussed later in this paper).
- Oral lichenoid lesions of discoid or systemic lupus erythematosus.

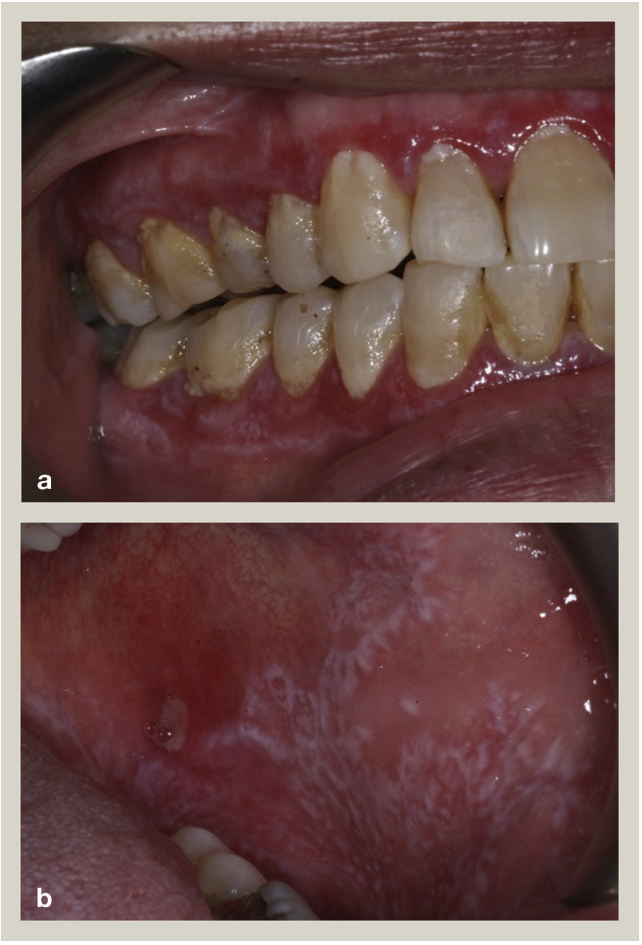

Figure 1 Lichen planus (**a**) Maxillary and mandibular gingiva with diffuse erythema and white reticular striations. (**b**) Buccal mucosa with mostly white lace like, reticular striations and at the posterior extent there is increased erythema with an ulceration.

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The WHO diagnostic criteria for OLP were revised in 2003 by van der Meij and van der Waal to include more correlation between the clinical and histopathological features.[5,8,9]

Histopathologic features

OLP has a characteristic histologic presentation featuring hyperkeratotic stratified squamous epithelium with either acanthosis or atrophy. There is a dense band of inflammation, predominantly lymphocytic, within the connective tissue directly below the epithelium. Fibrinogen can be present at the basement membrane zone. The basal cell layer shows hydropic degeneration. Rete ridges may become thinner and sharper, often described as "saw toothed". Within the epithelium there may be colloid bodies (Civatte bodies)[1,6,10] (Figure 2).

OLP has been surrounded by controversy with regards to its premalignant potential. Atypia is not a usual histologic feature of OLP and if present then the diagnosis of lichenoid dysplasia should be given and treatment based on the severity of the dysplasia is recommended.[1,11,12] A recent meta-analysis has shown that 1.1% of patients with OLP develop oral squamous cell carcinoma.[13] Given the uncertainty regarding the risk of malignant transformation of OLP, long term follow-up and management of patients with OLP is recommended.

Treatment

Patients who are either symptomatic or who present with more erosive or ulcerated OLP usually respond well to treatment with topical corticosteroids. These medications can be delivered in either a mouthwash, ointment or gel formulation. The rare cases that are not responsive to topical corticosteroids may require alternative treatments such as systemic steroids, calcineurin inhibitors, and retinoids.[2,3,6]

Mucous membrane pemphigoid

Mucous membrane pemphigoid (MMP), previously known as cicatricial pemphigoid, is a chronic autoimmune vesiculobullous disease that primarily affects the ocular and oral mucosa. It is caused by autoantibodies directed against hemidesmosomal components within the basement membrane zone. The immune deposits of MMP have been shown to consist of IgG and C3.[3,14,15]

Clinical presentation

The oral lesions of MMP are often the initial site and are present approximately 85% of the time with conjunctival lesions occurring in approximately 64% of patients.[16] There are reports of involvement of the nasal areas, nasopharynx, pharynx, esophagus, larynx, trachea, vagina and anal canal. Cutaneous involvement is less common but can affect the face, neck, scalp, axilla, trunk and extremities.[6,14,15]

The most common presentation of MMP in the oral cavity has been described as "desquamative gingivitis", however this clinical presentation is also seen in other autoimmune oral diseases such as erythema multiforme, dermatitis herpetiformis, pemphigus vulgaris, erosive oral lichen planus and allergic stomatitis. It is also the classic clinical description for chronic periodontal disease.[14]

Patients complain of redness, soreness, bleeding, peeling of the mucosa and dysphagia. A positive Nikolsky sign can be elicited by lateral palpation by either a finger, mouth mirror, or periodontal probe. A blister will develop at the site of pressure which quickly ruptures leaving a yellowish pseudo-membrane covered irregular shaped erosion or ulcer surrounded by an erythematous halo and white necrotic sloughing mucosal tissue. These lesions can occur anywhere on the oral mucosa and gingiva[14,16] (Figure 3).

Histopathologic features

Diagnosis is based on the history, clinical examination, biopsy for routine histopathology and direct immunofluorescence (DIF). Histopathology for MMP shows a sub-basilar split of the epithelium away from the connective tissue with a chronic inflammatory infiltrate containing eosinophils, lymphocytes, and some neutrophils in the lamina propria.[10] (Figure 4) DIF should be performed on perilesional tissue that has been placed in Michel's solution or snap-frozen on liquid nitrogen. DIF confirming MMP will show a homogeneous linear deposition of IgG and C3 in the basement membrane zone.[16]

Treatment

The treatment for MMP, when it is limited to the oral cavity, is topical anti-inflammatory agents. Patients can often be managed with topical corticosteroids or topical tacrolimus and

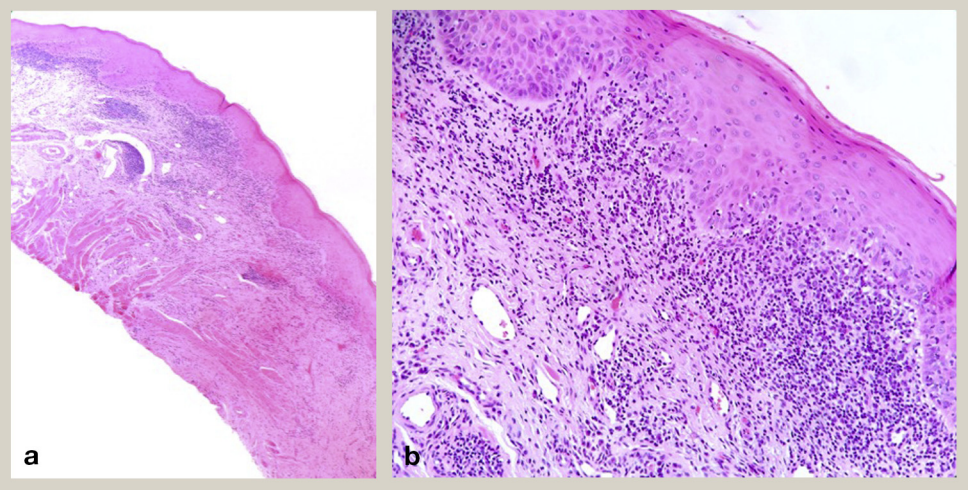

Figure 2 Lichen planus histology (**a**) Low power image showing hyperkeratotic stratified squamous epithelium and a dense band of inflammation in the connective tissue directly below the epithelium. (**b**) High power view shows hydropic degeneration of the basal layer of the epithelium.

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