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Oral lichen planus

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Abstract Lichen planus is an inflammatory mucocutaneous disease that can affect the skin, hair, nails, and mucosal surfaces. Mucosal sites of involvement include oral, genital, ocular, otic, esophageal, and, less commonly, bladder, nasal, laryngeal, and anal surfaces. Oral lichen planus is a mucosal variant of lichen planus, which tends to affect women more often than men, with a typically more chronic course and potential for significant morbidity. Treatment can be challenging, and there is potentially a low risk of malignant transformation; however, therapeutic benefits can be obtained with various topical and systemic medications. Clinical monitoring is recommended to ensure symptomatic control. Increasing awareness and recognition of this entity have continued to fuel advances in therapy and in our understanding of the disease.

Introduction

Lichen planus (LP) is an inflammatory mucocutaneous disease that can involve the skin, hair, nails, and mucosal surfaces.[1] The worldwide prevalence is estimated to be less than 5% without an obvious gender predilection. Mucosal sites of involvement include oral, genital, ocular, otic, esophageal, and, less commonly, bladder, nasal, laryngeal, and anal surfaces.[2] Although the clinical range of LP manifestations is broad, the skin and oral cavity are the major sites of involvement. Oral lichen planus (OLP) is a mucosal variant of LP, which tends to be chronic, often requiring long-term treatment and clinical surveillance. Given the potential for multisite involvement, thorough physical examination of all cutaneous areas, mucosal sites, hair, and nails is warranted. Management is often multidisciplinary; dentists and dental specialists, dermatologists, gastroenterologists, gynecologists, otorhinolaryngologists, and ophthalmologists may all play a role in care depending on sites of involvement.[2]

Etiology and risk factors

The pathogenesis of OLP is not fully understood. It is considered to be a T-cell–mediated chronic inflammatory tissue reaction with both antigen-specific and nonspecific mechanisms hypothesized.[3] Antigen-specific mechanisms include antigen presentation by basal keratinocytes, activation of $CD4^+$ helper T cells, and cytokine release, resulting in a cytotoxic reaction against the epidermal basal cell layer. This supports the finding that the inflammatory infiltrate is primarily composed of cytotoxic $CD8^+$ T cells. Proposed pathways for $CD8^+$ T-cell–mediated cytotoxicity in OLP include: (1) activated $CD8^+$ T-cell secretion of tumor

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necrosis factor α (TNF-α), secretion of granzyme B, or Fas-Fas ligand interactions inducing keratinocyte apoptosis; and (2) activated $CD8^+$ T-cell production of chemokines, which recruit inflammatory cells, promoting continued inflammation.[3] Nonspecific mechanisms include mast cell release of proinflammatory mediators and proteases and upregulation of matrix metalloproteinases in OLP lesions, which results in T-cell infiltration into the superficial lamina propria, disruption of the basement membrane, entry of immune cells into the epidermis, and keratinocyte apoptosis.[3]

Genetic factors influencing immune function may contribute to OLP pathogenesis. A significant increase in genetic polymorphism of the first intron of the promoter gene of interferon γ was found in patients with OLP compared with controls,[4] and a Chinese study found an association between a polymorphism in the TNF-α gene and genetic risk for OLP in a subset of patients.[5] These provide potential targets for treatment modalities, and as discussed later in this chapter, molecular markers may play a future role in assessing risk for malignant transformation.

Multiple factors have been identified as potentially contributing to the pathogenesis; however, a causative role for these factors has not been confirmed. Stress has been identified as the most common cause of acute exacerbations of OLP.[6] The Koebner phenomenon, whereby lesions develop in sites of prior trauma, is observed in both cutaneous and OLP. Dental procedures, irritation from tobacco products, friction from sharp teeth, rough dental restorations, poorly fitting dental prostheses, and oral habits, such as lip and cheek chewing, are exacerbating factors.[6] Dental plaque may worsen gingival LP and is associated with a higher incidence of erythematous and erosive gingival lesions.[7] When OLP lesions are confined to areas in close contact with dental restorations, an allergy or reaction to a dental material, such as amalgam or gold, should be considered (Figure 1).[6,8] Certain medications, such as nonsteroidal antiinflammatory agents and angiotensin-converting enzyme inhibitors, may also produce oral lichenoid reactions.[9,10] These hypersensitivity lichenoid reactions to materials and medications may clinically and histologically resemble LP but have an identifiable etiology. Patch testing in the case of suspected dental restoration allergy can be helpful in identifying the specific dental material, and removal may lead to considerable improvement.[11]

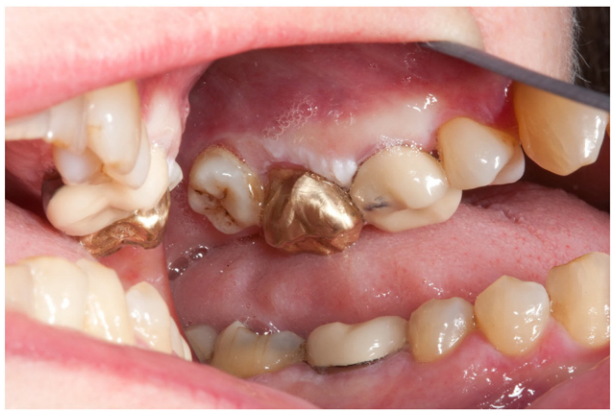

Fig. 1 Oral lichen planus of the left upper alveolar ridge adjacent to a gold crown.

The association between liver disease and LP has been debated in the literature; however, a meta-analysis found a strong association between hepatitis C virus (HCV) infection and LP in some geographic locations, such as Japan and Mediterranean regions.[12] HCV antibodies have been found in a small but statistically significant percentage of patients with cutaneous LP in the United States compared with controls.[13] In addition, HCV sequences have been found in the serum of patients with OLP and in oral tissue samples.[12,13] An Italian study identified the HLA-DR6 allele as a potential risk factor for HCV-associated OLP.[14] Although the association between HCV and LP may be dependent on many factors, such as geography, screening all patients with LP for HCV has been recommended to prevent transmission of undetected HCV given that LP may be the initial presentation of HCV infection.[12,13]

Clinical findings

Cutaneous manifestations

On presentation, LP may affect one or multiple sites simultaneously. More than 5% of patients with LP have concurrent involvement of three or more sites.[15] The oral cavity and skin remain the most commonly affected sites. Cutaneous LP is typically characterized by polygonal, violaceous, flat-topped, pruritic papules on the trunk or extremities with overlying reticular white striae known as Wickham striae. Although only 16% of patients with predominantly oral LP develop cutaneous lesions,[15] two thirds of patients with cutaneous LP are found to have oral lesions.[2] The severity of oral disease does not usually correlate with extent of cutaneous involvement.[6]

Lichen planopilaris is a variant of LP producing scarring alopecia, characterized by atrophic plaques, perifollicular erythema, and follicular spines. LP of the nails occurs in approximately 10% of patients with cutaneous LP; however, it is an infrequent finding in patients with OLP.[6] Clinical findings of nail LP include thinning, ridging, distal splitting of the nail plate, red lunula, and dorsal pterygium formation.[16]

Oral manifestations

The worldwide prevalence of OLP is estimated to be about 2%.[17] It tends to be more chronic in nature than cutaneous disease, affecting women more commonly than men, with age of onset on average around 60 years. OLP in childhood is rare. The extent of involvement with OLP is