

An oral lesion masquerading as lichen planus

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Abstract

Proliferative verrucous leukoplakia (PVL) is a rare, aggressive form of oral leukoplakia with a substantial risk of malignant transformation. The slowly progressive course and the lack of a single defining histopathologic characteristic for PVL make this entity a diagnostic challenge. We report on a patient who presented with a 7-year history of worsening oral lesions.

Keywords: cancer, malignant disorder, oral, proliferative, verrucous leukoplakia

Introduction

Typically presenting as white oral plaques and occasionally displaying lichenoid changes on biopsy, proliferative verrucous leukoplakia (PVL) lesions are

assumed to represent oral lichen planus (OLP) prompting evaluation by a dermatologist. Patients go undiagnosed and undertreated due to the slowly progressive nature of the lesions and because demographics differ from traditional oral squamous cell carcinoma.

Case Synopsis

A 68-year-old woman presented to the dermatology clinic for evaluation of a 7-year history of worsening oral lesions. There was no prior use of tobacco products or systemic immunosuppressants and there was no relevant family history. She applied topical clobetasol gel to the affected areas for years with minimal improvement. She denied pain, dysphagia, ocular symptoms, or involvement of skin or genitals. On examination, she had confluent sheets of white verrucous plaques involving the right



Figure 1. Clinical images of the oral cavity. White lacy plaques on **A)** the buccal mucosa, and **B)** the upper gingiva.

buccal mucosa and maxillary gingiva with the extension of the plaques into the left mandibular vestibule (**Figure 1**). A plaque on the right buccal mucosa was biopsied (**Figure 2**). Hematoxylin & eosin staining of the biopsy specimen revealed a strip of mucosa surfaced by verrucous and markedly hyperorthokeratotic stratified squamous epithelium without dysplasia (**Figure 2**). Given these histological characteristics and the clinical presentation, a diagnosis of proliferative verrucous leukoplakia (PVL) was made. Because of the substantial risk of malignant transformation, the patient is evaluated by an oral pathologist every three months with biopsy of any suspicious lesions.

Discussion

First described in 1985 by Hansen et al. [1], PVL presents a diagnostic challenge. Proliferative verrucous leukoplakia is a rare, high-risk form of oral leukoplakia characterized by slowly progressive, white, and warty proliferations. Plaques most frequently involve the gingiva, buccal mucosa, or tongue, but can occur at any site [2,3]. Proliferative verrucous leukoplakia may first appear hyperkeratotic or lichenoid and evolve over months to years, progressing to multifocal involvement that is recalcitrant to therapies. Lesions do not always exhibit a verrucous appearance and may range from smooth and erythematous to nodular, indurated, or ulcerated [4]. Due to the variation of histologic appearance of these lesions, criteria for diagnosing

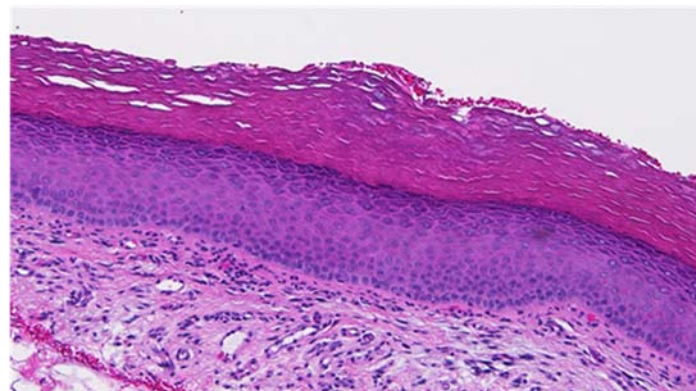


Figure 2. H&E histopathology of buccal mucosa biopsy. Microscopy reveals a strip of mucosa surfaced by verrucous and markedly hyperorthokeratotic stratified squamous epithelium. Mixed chronic inflammation is noted in the connective tissue stroma, 100x.

PVL histologically have not been established [5]. Proliferative verrucous leukoplakia occurs more frequently in women in their sixth or seventh decade [2,3]. There are no associations with tobacco or alcohol use and no validated biomarkers to predict malignant transformation [3]. The evidence demonstrating an association with human papillomavirus infection is variable [6].

For dermatologists, distinguishing between PVL and OLP is crucial given they can look similar clinically and histologically, yet they have distinct outcomes [7]. Interface mucositis with a lymphohistiocytic infiltrate can be observed in early PVL. However, clinicians should be wary of OLP that shows hyperorthokeratosis, as lichen planus in the oral cavity, by definition, should show hyperparakeratosis [7]. Dysplasia also rules out OLP [7].

Proliferative verrucous leukoplakia has a considerable risk of malignant transformation to oral squamous cell carcinoma (OSCC) and oral verrucous carcinoma (OVC). A systematic review commissioned by the most recent World Health Organization consensus meeting found the pooled rate of malignant transformation to be 43.9% [8]. Most patients develop OSCC over OVC [8,9]. Compared to conventional OSCC, PVL-associated OSCC tends to have a lower clinical stage, smaller tumor size, no lymph node or distant metastasis, and better short-term survival [9]. The pooled proportion of mortality for PVL-associated oral carcinoma is 21.3% [9].

There are no Food and Drug Administration-approved therapies and limited clinical trials for the treatment of PVL. A meta-analysis of 25 published studies found that 80% of PVL cases were treated with surgical scalpel excision, 23.8% with radiation, 23% with laser therapy, 5.6% with chemotherapy, 4.8% with photodynamic therapy, and 1.6% with retinoids [6]. A more recent meta-analysis noted that 41.4% of those patients who had surgical excision did so in combination with other treatment modalities, most commonly metisopronol, radiation therapy, or laser ablation [10]. A recently published case report described the use of high-dose brachytherapy to treat a PVL lesion confined to the hard palate and refractory to multiple courses of CO₂

laser excision. This was preferred in this patient in whom surgical resection would have resulted in an extensive defect with denuded bone. The patient remains disease-free at 36 months [11].

Conclusion

Dermatologists will encounter patients with white plaques in the mouth. In these instances, it is important to include PVL in the differential diagnosis

for patients with a long history of progressive, white, and verrucous oral plaques. Proliferative verrucous leukoplakia often shows malignant transformation necessitating close monitoring and interdisciplinary care with oral pathology, and head and neck surgery departments.

Potential conflicts of interest

The authors declare no conflicts of interest.

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