



REVIEW ARTICLE

## Proliferative verrucous leukoplakia: diagnosis, management and current advances<sup>☆</sup>



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### Abstract

**Introduction:** Proliferative verrucous leukoplakia is a multifocal and progressive lesion of the oral mucosa, with unknown etiology, and commonly resistant to all therapy attempts with frequent recurrences. It is characterized by a high rate of oral squamous cell carcinoma and verrucous carcinoma transformations.

**Objective:** To analyze the studies about Proliferative verrucous leukoplakia and develop a concise update.

**Methods:** A Pubmed search identifying studies (laboratory research, case series and reviews of literature) that examined patients with Proliferative verrucous leukoplakia was realized.

**Results:** There are not enough studies about Proliferative verrucous leukoplakia in the literature. The few found studies not present a consensus about its etiology and diagnosis criteria. Although several treatment strategies have been proposed, most of them still show a high recurrence rate.

**Conclusion:** More research about Proliferative verrucous leukoplakia is necessary to understand and treat this disease.

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**PALAVRAS-CHAVE**

Leucoplasia oral;  
 Leucoplasia;  
 Leucoplasia verrucosa  
 proliferativa;  
 Câncer oral;  
 Carcinoma, Célula  
 escamosa;  
 Câncer de cabeça e  
 pescoço

**Leucoplasia verrucosa proliferativa: diagnóstico, conduta e avanços atuais****Resumo**

**Introdução:** Leucoplasia verrucosa proliferativa (LVP) é uma lesão multifocal e progressiva da mucosa oral, com etiologia desconhecida e comumente resistente a todas as tentativas terapêuticas, com recorrências frequentes. É caracterizada por uma alta taxa de transformação em carcinoma de células escamosas e carcinoma verrucoso da cavidade oral.

**Objetivo:** Analisar os estudos sobre LVP e elaborar uma atualização resumida.

**Método:** Foi realizada uma pesquisa na base de dados Pubmed identificando estudos (pesquisas laboratoriais, séries de casos e revisões de literatura) que avaliaram pacientes com LVP.

**Resultados e discussão:** Não há estudos suficientes sobre LVP na literatura. Os poucos estudos encontrados não apresentam consenso quanto aos critérios de etiologia e diagnóstico. Embora várias estratégias de tratamento tenham sido propostas, a maioria ainda apresenta alta taxa de recorrência.

**Conclusão:** Mais pesquisas sobre LVP são necessárias para entender e tratar esta doença.

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**Introduction**

Proliferative verrucous leukoplakia (PVL) is a very aggressive and rare form of oral leukoplakia (OL) with high morbidity.<sup>1</sup> The first description has been made by Hansen et al. (1985) as a distinct form of OL which develops initially as a white plaque that eventually becomes multifocal slow-growing lesions resistant to all therapeutic procedures, including surgery, with a high recurrence rate and an oral cancer transformation trend.<sup>2</sup> With the introduction of the term PVL, the previously used term “oral florid papillomatosis” has disappeared from the literature.<sup>3</sup> Actually, the World Health Organization (WHO) (2005) described PVL as “a rare but distinctive high-risk clinical form of oral precursor lesions”.<sup>4</sup> Several studies have examined PVL characteristics and its propensity to develop into oral carcinoma.<sup>4</sup> Thirty years after its discovery, it is still a challenging disease with no confirmed etiology and efficient treatment. Although there are published papers about PVL diagnosis criteria, they may be imprecise in detecting early disease presentations, either for clinical or histopathological view. The objective of this paper is to analyze the PVL literature and to develop a concise update.

**Review methods**

A PubMed search using the term “Proliferative Verrucous Leukoplakia” was made from 1985 to 2015 (30 years). Additional papers were included based upon the original literature search and references in the selected papers. Papers concerning laboratory research, case series, as well as reviews of literature were also included.

**Results and discussion****Etiology**

Hansen et al. (1985) described PVL as a disease with unclear etiology, but typically associated with tobacco use.<sup>2</sup> However, the role of tobacco in PVL lesions is unknown since these lesions are seen in smokers and nonsmokers (Table 1).<sup>1,2,5-15</sup> Several studies evaluated alcohol use by PVL patients, but the relation between them was not established (Table 1).<sup>1,9,11,13</sup>

In recent years, it has been hypothesized that human papillomavirus (HPV) may influence both potentially and already established oral malignant lesions.<sup>16</sup> Although the association between oral squamous cell carcinoma (OSCC) and HPV is already mentioned, its influence on PVL cases is not confirmed yet.<sup>17</sup> Over the last decades, some studies reported different and contradictory frequencies of HPV DNA detection in PVL (Table 2).<sup>1,7,10,18,19</sup>

About other possible etiologies, there are few studies with PVL that tried to identify the presence of *Candida albicans*. Silverman et al. (1997) reported 19 of 38 specimens with *C. albicans* positivity, but without correlation between the fungal infection and PVL occurrence or progression to carcinoma, characterizing it as a probable secondary infection.<sup>6</sup> Similarly, Hansen et al. (1985) observed that 12 of 30 patients were positive for *C. albicans*.<sup>2</sup> Concerning to Epstein Barr Virus (EBV), Bagan et al. (2008) was the only one to detect EBV in a PVL group (60% of 6 patients).<sup>20</sup> Therefore, none of these studies have yet established the exact role of microbiological agents in PVL pathogenesis.

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