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Case Report

Non-Homogenous Proliferative Verrucous Leukoplakia of the Lateral Tongue: A Case Report

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Abstract

Leukoplakia is an oral potentially malignant disorder of questionable risk. The presence of oral epithelial dysplasia (OED) within a leukoplakic lesion is the most predictive histopathologic marker of malignant transformation. The goal of managing OED is early diagnosis to prevent malignant transformation. This case report describes a female patient with an exophytic verrucous leukoplakic plaque of the left lateral tongue that carries the potential for malignant transformation that was not present on two previous biopsy procedures.

Keywords: Leukoplakia; oral epithelial dysplasia; proliferative verrucous leukoplakia; malignant transformation; biopsy.

INTRODUCTION

Leukoplakia is an oral potentially malignant disorder of questionable risk. [1, 2]. It is defined as a predominantly white plaque that has been characterized clinically and histopathologically by exclusion of other known white lesions or disorders that carry no increased risk for cancer. [1, 3] The estimated worldwide prevalence of leukoplakia is approximately 1.5% to 4.3%. [4]. Oral epithelial dysplasia (OED) is the histopathologic finding within a subset of leukoplakias and is the most predictive independent marker of malignant transformation. It is defined by the World Health Organization (WHO) as a spectrum of architectural and cytological changes in the oral epithelium that carries the potential for malignant transformation to squamous cell carcinoma. [5, 6]. **Table 1**. OED clinically may present as leukoplakia, erythroplakia, or speckled leukoplakia (mixed leukoplakic-erythematous lesions).

The WHO and the WHO Collaborating Centre for Oral Cancer classify this group of clinical conditions as oral potentially malignant disorders (OPMD), which include leukoplakia, erythroplakia, proliferative verrucous leukoplakia (PVL), oral submucous fibrosis, oral lichen planus, oral lichenoid lesions, verrucous hyperplasia, actinic cheilitis, and certain hereditary disorders. [7]. The goal of treatment of OED is early diagnosis to prevent malignant transformation. This case report describes a female patient with an exophytic verrucous leukoplakic plaque of the hyperkeratotic left lateral tongue that has the potential for malignant transformation that was not present on two previous biopsy procedures.

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Table 1. Epithelial Dysplasia Architectural and Cytological Features.

Architectural Features	Cytological Features
Loss of basal cell polarity	Anisonucleosis
Drop-shaped rete ridges	Nuclear pleomorphism
Increased mitotic figures	Anisocytosis
Abnormal superficial mitoses	Cellular pleomorphism
Dyskeratosis (premature keratinization	Increased nuclear/cytoplasmic ratio
Keratin pearls	Increased number and size of nucleoli
Loss of epithelial cell cohesion	Hyperchromasia

From: WHO, 2022

CASE REPORT

A 66-year-old Asian female was referred to the oral and maxillofacial surgeon (CYSL) for evaluation of an exophytic verrucous plaque on the hyperkeratotic left lateral tongue (**Figure 1**). The patient had two incisional biopsies in 2019 (**Figure 2**) and 2024 (**Figure 3**). Both biopsy procedures were diagnosed as hyperkeratosis and negative for malignancy. Oral examination of the left lateral and ventral tongue revealed a homogenous leukoplakic plaque. In the middle-1/3 of the leukoplakic plaque was a thick, raised exophytic verrucous plaque that was not present on the two previous biopsy procedures. The patient was informed of this new clinical finding and of the decision to biopsy the lesion for a definitive histopathologic diagnosis. Under local anesthesia, the entire lesion was excised from the tongue and placed in 10% formalin for histopathologic evaluation.

Figure 1. Clinical photograph of left lateral tongue in 2026. Note the exophytic, verrucous plaque that was not previously present in 2019 and 2024.



Figure 2. 2019 Biopsy of middle 1/3 left lateral tongue. Sections of squamous mucosa show marked hyperkeratosis, acanthosis, and mild chronic inflammation. No evidence of dysplasia or malignancy. (H & E stain, 4x).

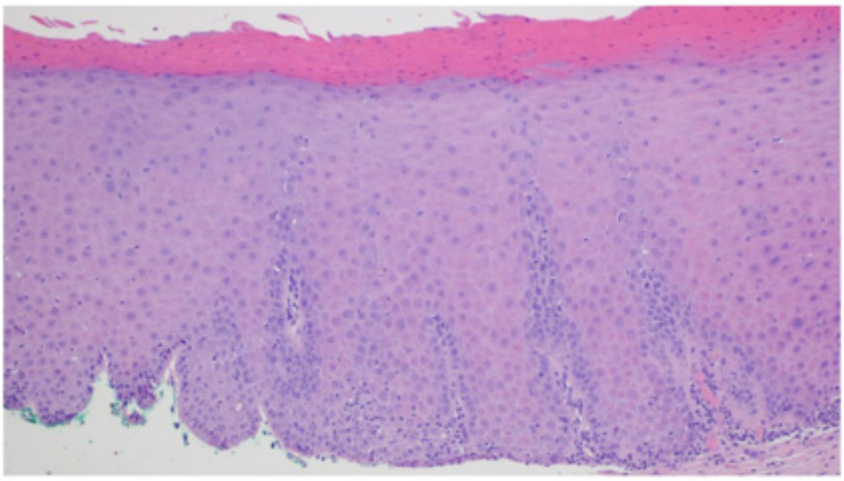
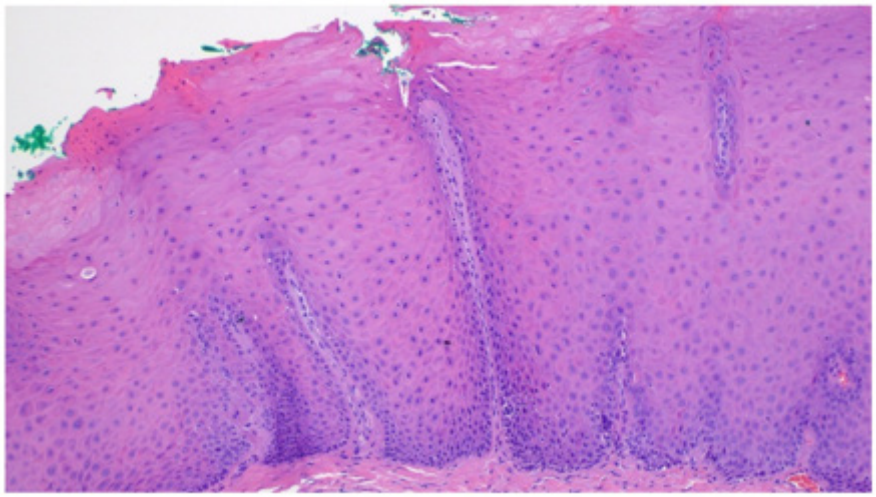


Figure 3. 2024 Biopsy of middle 1/3 of left lateral tongue. Sections of squamous mucosa show marked hyperkeratosis, acanthosis, and mild chronic inflammation. No evidence of dysplasia or malignancy. (H & E stain, 4x).



HISTOPATHOLOGY

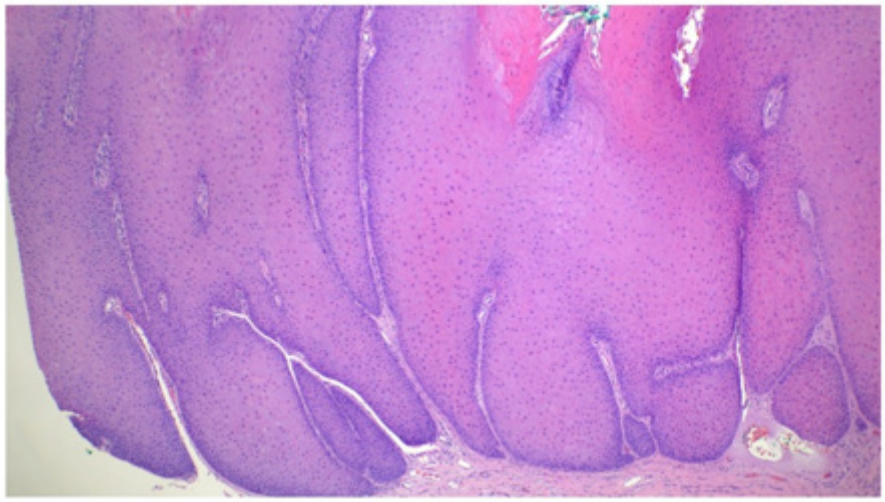
Different histological grading systems have been proposed for stratifying the risk of malignant transformation. The most widely accepted grading system is that of the fifth edition of the World Health Organization Classification of Head and Neck Tumours for the histopathological diagnosis of oral epithelial dysplasia (OED), published in 2022. [8] The WHO classification is based on architectural and cytological features of the oral epithelium and retains the three-tiered system of mild, moderate, and severe dysplasia, with carcinoma in situ combined within the severe category. [5, 8].

Mild dysplasia is defined by changes involving the lower one-third of the epithelium. In moderate dysplasia, changes extend into the middle-third of the epithelium. In severe dysplasia, changes involve the upper third of the epithelium. Grading is additionally informed by the degree of cytological and architectural atypia, which may upgrade a lesion irrespective of the vertical extent of involvement. [8, 9].

RESULTS

Histologic sections of the left lateral tongue biopsy in 2026 revealed an atypical squamous proliferation with architectural atypia characterized by bulbous rete ridges with focal inward bowing of the rete. Focal areas of cytoplasmic change with a glassy appearance are present. Nuclear atypia is minimal to absent. There is no evidence of conventional infiltrative invasion (**Figure 4**).

Figure 4. 2026 Biopsy middle 1/3 of left lateral tongue. Sections of squamous mucosa show an atypical squamous proliferation with architectural atypia characterized by bulbous rete ridges with focal inward bowing of rete. Cytoplasmic changes with glassy appearance are present. Nuclear atypia is minimal to absent. No evidence of conventional infiltrative invasion.
(H & E stain, 4x).



DISCUSSION

Common sites for oral leukoplakia are the tongue, buccal mucosa, floor of mouth, gingiva, and hard palate. [10] Epithelial dysplasia, carcinoma in situ, or squamous cell carcinoma may be found in a substantial proportion of leukoplakic lesions on biopsy, with reported frequencies varying widely across cohorts and lesion sites. [11, 12, 13] In a study by Bagan et al [14] the tongue was a common site for the development of squamous cell carcinoma. The reported five-year survival rate for oral squamous cell carcinoma (OSCC) varies considerably by stage and cohort but is commonly in the range of approximately 50% to 65%, with markedly worse outcomes in advanced-stage disease. [15, 16]. Therefore, early detection and treatment of premalignant lesions are critical to improve patient survival.

Lesions are described not only by their clinical color (leukoplakic, erythematous, speckled leukoplakia) but also as either homogenous or non-homogenous. [17] Homogenous leukoplakic lesions appear as thin, smooth white plaques with well-defined borders. In contrast, non-homogenous leukoplakic lesions have varied surface characteristics: verrucous, nodular, or mixed erythroleukoplakia. [17] Non-homogenous lesions have a higher risk for malignant transformation.

A variant of non-homogenous leukoplakia is proliferative verrucous leukoplakia (PVL). It may appear as multiple irregularly shaped leukoplakic patches or as a single large leukoplakic patch (Figure 1). PVL is more common in females and is frequently not associated with tobacco use. Compared with conventional leukoplakia, which has a relatively low malignant transformation rate, PVL has a markedly higher rate. Reported estimates range from approximately 44% to 48% in pooled analyses and up to 70% to 100% in some cohorts. [18].

Earlier studies, such as those by Silverman et al [19] and Schepman and colleagues [20] reported malignant transformation rates for leukoplakia and OED in the range of approximately 10% to 20%. In more recent series, OED is observed in a substantial proportion of leukoplakic lesions, and the pooled malignant transformation rate of oral leukoplakia is approximately 9.8%, with reported ranges spanning 0.1% to 34%. [12, 13, 21, 22]. All sites of oral leukoplakia have the potential for malignant transformation.

For the clinician, they must be aware that the potential for malignant change can occur without dysplasia. [12, 13, 23] In a study by Speight and colleagues [16], female patients 50 years and older, non-smokers, floor-of-mouth and tongue lesions were among the factors associated with a greater potential for malignant transformation. Furthermore, previously treated areas of leukoplakia may still undergo malignant transformation, with a reported transformation rate of approximately 12%. [24]

CONCLUSION

In our patient, a new lesion appeared on the left lateral tongue at a site where two previous biopsies were consistent with hyperkeratosis. The third biopsy revealed an atypical verrucous proliferation in which verrucous carcinoma could not be excluded. This case underscores the need for ongoing, long-term monitoring of patients with leukoplakic lesions of the tongue given the risk of malignant transformation which may occur despite prior benign histopathology. Clinicians,

including dentists and physicians, must be familiar with the clinical features of leukoplakia and OED because of this malignant potential.

Disclosures

Conflict of Interest:

None

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