

## Leukoplakia of the Marginal Gingiva: A Report of Two Cases

Konstantinos I. Tosios,\* Athanasios Vasilas,† Ioannis Melakopoulos† and Alexandra Sklavounou-Andrikopoulou\*



**Introduction:** Leukoplakia of the marginal gingivae is uncommon and in most cases reported up to date represents a manifestation of proliferative verrucous leukoplakia. The clinical and pathologic features of two cases of leukoplakia confined to the marginal gingiva are described and their biologic significance is discussed.

**Case Presentation:** The cases involved two female patients, non-smokers, aged 82 and 57. The lesions clinically appeared as small, well-demarcated white plaques on the marginal gingiva of posterior teeth. After being totally excised, microscopic examination showed keratosis of unknown significance in the first patient and verrucous hyperplasia in the latter, while immunohistochemistry for p16<sup>INK4A</sup> was negative for both. There was no recurrence in 7 months and 5 months after excision, respectively.

**Conclusion:** A white plaque on the marginal gingiva may be overlooked due to its small size or may be misdiagnosed as frictional keratosis. However, it may represent leukoplakia, a potentially malignant disorder. Therefore, diagnosis and management should follow the established guidelines for leukoplakia. *Clin Adv Periodontics* 2018;8:84–87.

**Key Words:** Mouth diseases; precancerous conditions; leukoplakia, oral; gingiva; gingival diseases.

### Background

Leukoplakia is a potentially malignant disorder associated with an increased risk for transformation to oral squamous cell carcinoma.<sup>1</sup> Although leukoplakia of the gingiva is not uncommon,<sup>2</sup> leukoplakia of the marginal (free) gingivae in most of the cases reported up to date is a manifestation of proliferative verrucous leukoplakia (PVL).<sup>3,4</sup>

We describe the clinical and pathologic features of two cases of leukoplakia confined to the marginal gingivae and discuss their biologic significance.

### Clinical Presentation

#### Case 1

An 82 year old female was referred to one of the authors (KT) in November 2016 for a white gingival lesion. It was

\*Department of Oral Pathology and Medicine, School of Dentistry, National and Kapodistrian University of Athens, Athens, Greece

†Private practice, Athens, Greece

Received May 14, 2017; accepted September 30, 2017

doi: 10.1002/cap.10016

incidentally noticed in May 2015 and provisionally diagnosed as frictional keratosis (Fig. 1a), but although the patient modified her toothbrushing technique, it expanded over the following 18 months. Medications included carvedilol and furosemide for hypertension, and atorvastatin for hyperlipidemia. She had never smoked or systematically consumed alcohol.

Clinical examination showed a well-demarcated oblong white plaque with a slightly granular surface, measuring 0.7 × 0.3 cm, on the facial marginal gingiva of the first left maxillary premolar tooth (Fig. 1b). The rest of the oral mucosa was normal and the dental and periodontal condition was excellent, with a probing depth of <3 mm around the involved tooth.

#### Case 2

A 57 year old female was referred by her oncologist to one of the authors (IM) in February 2017 for a white lesion on the gingiva, incidentally seen during a routine follow-up examination. She had undergone myeloablative megatherapy with autologous hematopoietic cells transplantation for λ-light chain multiple myeloma, 5 years earlier. Medications included levothyroxine sodium for hypothyroidism, metformin for diabetes mellitus, and venlafaxine hydrochloride for depression. She had never smoked or systematically consumed alcohol.



**FIGURE 1** Case 1. Clinical presentation. Well-demarcated white plaque on the marginal maxillary gingiva of the left premolar tooth in (a) May 2015 and (b) November 2016. Notice expansion of the lesion.

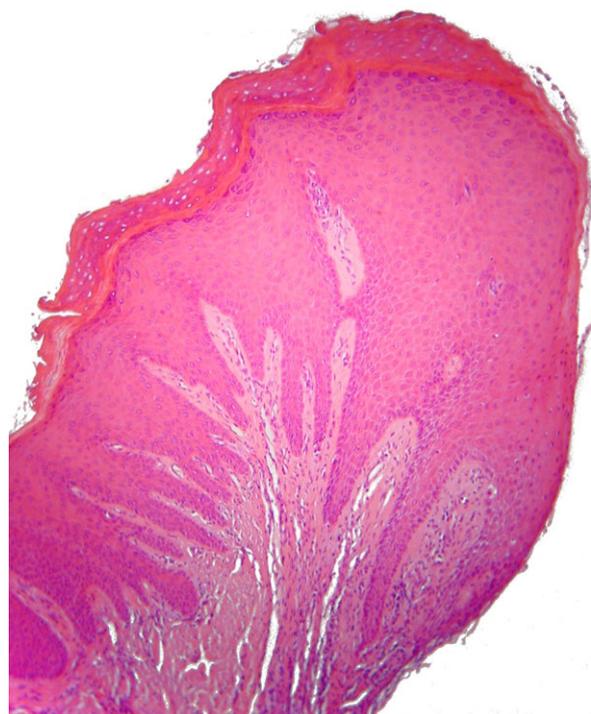


**FIGURE 2** Case 2. Clinical presentation. Well-demarcated white plaque on the marginal palatal gingiva of the first molar tooth.

Clinical examination showed a well-demarcated white plaque with a rough surface, measuring  $0.5 \times 0.2$  cm, on the palatal gingiva of the first molar tooth (Fig. 2). The rest of the oral mucosa was normal and the dental and periodontal condition was excellent, with a probing depth around the involved tooth of  $<3$  mm.

### Biopsy and Histopathologic Features

With the provisional diagnosis of leukoplakia, both lesions were totally excised under local infiltration anesthesia. In case 1, the squamous epithelium presented slight



**FIGURE 3** Case 1. Microscopic features. Slight papillomatosis, hyperkeratosis and focal hypergranulosis, and acanthosis, with tapered, but not confluent rete ridges. Note sharp demarcation from the adjacent normal gingival epithelium (hematoxylin and eosin stain, initial magnification x100).

papillomatosis, hyperkeratosis and focal hypergranulosis, acanthosis, and tapered, but not confluent, rete ridges (Fig. 3). There was a sharp demarcation of the lesion from the adjacent normal gingival epithelium, no features of epithelial dysplasia, while the sulcular epithelium was parakeratotic. The final diagnosis was epithelial hyperplasia consistent with keratosis of unknown significance.<sup>5</sup>

In case 2, there was pronounced papillomatosis, hyperkeratosis and hypergranulosis, acanthosis, and broad, interconnecting rete ridges (Fig. 4a). There was a sharp demarcation from the adjacent normal gingival epithelium (Fig. 4b), no features of epithelial dysplasia, while the sulcular epithelium was spongiotic with long and interconnecting rete ridges, and subepithelial chronic inflammatory infiltrations. The final diagnosis was verrucous hyperplasia.

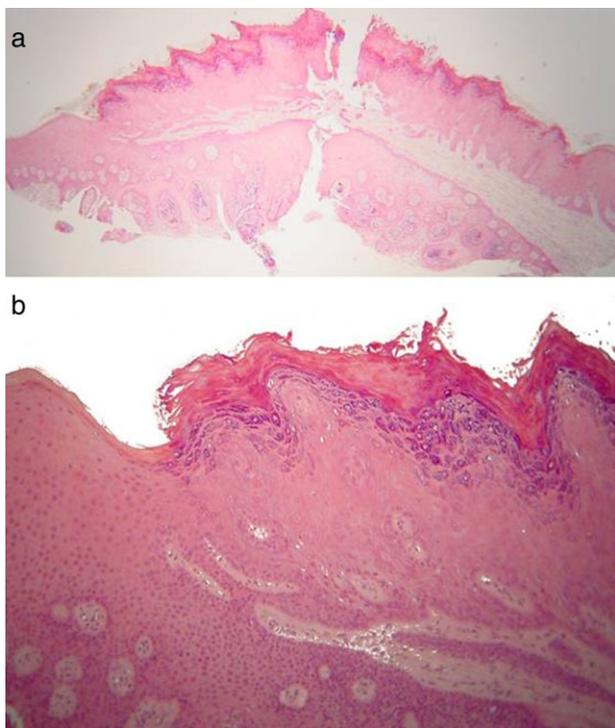
Both cases did not express p16<sup>INK4A</sup> after immunohistochemical staining.

### Clinical Management

The patients were advised to be re-examined every 6 months; seven months and 5 months after excision, respectively, there was no recurrence.

### Discussion

The cases of homogeneous white plaques reported above are uncommon due to their localization on the marginal



**FIGURE 4** Case 2. Microscopic features. **(a)** Pronounced papillomatosis, hyperkeratosis and hypergranulosis, and acanthosis, with broad, interconnecting rete ridges (hematoxylin and eosin stain, initial magnification x25). **(b)** Sharp demarcation from the normal epithelium (hematoxylin and eosin stain, initial magnification x400).

gingivae; both showed microscopic features consistent with leukoplakia.<sup>5</sup> The differential diagnosis included frictional keratosis, a common lesion of the facial maxillary attached gingivae, which has been rarely described occurring on the marginal gingivae of a single tooth.<sup>6</sup> In case 1, modification of the toothbrushing technique did not prevent the proliferation of the lesion during the 18 month observation period, while in both cases the presence of a clearly demarcated border and the absence of similar lesions in other gingival sites were not consistent with frictional keratosis. The preceding hematopoietic cell transplantation for  $\lambda$ -light chain multiple myeloma in case 2 could be suggestive of chronic graft versus host disease, but this is unusual after autologous transplantation and presents with extensive lesions that resemble oral lichen planus.<sup>7</sup>

PVL is common on the gingivae,<sup>3</sup> and PVL of the gingivae (PVLG) is described as a subset of PVL that preferen-

tially involves the anterior gingivae.<sup>4</sup> PVLG may present as solitary, non-descript white plaque on the marginal gingiva of a single tooth, but in 10 of 11 cases described, there was involvement of more than one tooth, as “linear gingival hyperplasia”.<sup>4,8</sup> Diagnosis is usually documented by slow extension over time, change in the clinical and microscopic features, recurrence, and progression into squamous cell carcinoma.<sup>4</sup> As in typical PVL,<sup>9</sup> PVLG cannot be definitely associated with a known risk factor, such as tobacco, human papilloma virus (HPV) or Epstein-Barr virus (EBV) infection, and may present a spectrum of microscopic features, from hyperplasia without epithelial dysplasia to malignancy.<sup>4</sup> The present cases did not fulfill current diagnostic criteria for PVL,<sup>10,11</sup> but the follow-up period was less than the 5 years considered necessary for determining the disease evolution.<sup>10</sup> The same applies for a case of “idiopathic linear gingival hyperplasia”,<sup>12</sup> but involvement of five teeth and two recurrences following excision were features suggestive of PVLG.

Finally, idiopathic gingival papillokeratosis with crypt formation and sanguinaria-related leukoplakia are leukoplakias solely or mostly localized on the gingivae. However, both lesions usually involve the anterior maxillary attached gingivae;<sup>13,14</sup> the former is possibly of developmental etiology, has only been diagnosed in young patients, and on microscopic examination shows parakeratosis and papillary acanthosis with parakeratin-filled crypts;<sup>13</sup> the latter, which usually occurs in the maxillary vestibule, is associated with chronic use of sanguinaria-containing mouthwashes<sup>14</sup> which none of the patients could recall.

No known etiologic factors were identified in the cases presented above, as they were p16<sup>INK4A</sup> negative, precluding the presence of HPV,<sup>15</sup> and none of the patients smoked. Therefore, they may be considered as idiopathic leukoplakias.

Long-term follow-up was suggested, as leukoplakia has an obscure biologic behavior and may undergo malignant transformation,<sup>1</sup> while it cannot be excluded that they could be the initial manifestation of PVL/PVLG.<sup>3</sup>

In conclusion, two cases of white plaques of the marginal gingivae are described that could be easily overlooked due to their small size or be misdiagnosed as frictional keratosis. However, they showed microscopic features consistent with leukoplakia; therefore, diagnosis and management should follow the established guidelines for leukoplakia. ■

## Summary

<b>Why are these cases new information?</b>	■ An unusual location for the development of leukoplakia, a potentially malignant disorder.
<b>What are the keys to successful management of these cases?</b>	■ Management should follow the established guidelines for diagnosis and treatment of leukoplakia.
<b>What are the primary limitations to success in these cases?</b>	■ Due to its small size and unusual location, it may be overlooked or misdiagnosed.

## Acknowledgments

The excellent technical assistance of Mrs. Maria Manou, MTL, MSc, Department of Oral Pathology and Medicine, School of Dentistry, National and Kapodistrian University of Athens, Athens, Greece, is acknowledged. Drs. Tosios, Vasilas, Melakopoulos, and Sklavounou-Andrikopoulou report no conflicts of interest related to these cases.

### CORRESPONDENCE

Konstantinos Tosios, Department of Oral Pathology and Medicine, School of Dentistry, 2 Thivon Street, 11527 Athens, Greece. E-mail: [ktosios@dent.uoa.gr](mailto:ktosios@dent.uoa.gr)

## References

1. Warnakulasuriya S, Johnson NW, van der Waal I. Nomenclature and classification of potentially malignant disorders of the oral mucosa. *J Oral Pathol Med* 2007;36:575-580 <https://doi.org/10.1111/j.1600-0714.2007.00582.x>
2. Bouquot JE, Gorlin RJ. Leukoplakia, lichen planus, and other oral keratoses in 23,616 white Americans over the age of 35 years. *Oral Surg Oral Med Oral Pathol* 1986;61:373-381.
3. Gandolfo S, Castellani R, Pentenero M. Proliferative verrucous leukoplakia: a potentially malignant disorder involving periodontal sites. *J Periodontol* 2009;80:274-281 <https://doi.org/10.1902/jop.2009.080329>
4. Fettig A, Pogrel MA, Silverman S, Jr., Bramanti TE, Da Costa M, Regezi JA. Proliferative verrucous leukoplakia of the gingiva. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;90:723-730 <https://doi.org/10.1067/moe.2000.108950>
5. Woo SB, Grammer RL, Lerman MA. Keratosis of unknown significance and leukoplakia: a preliminary study. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2014;118:713-724 <https://doi.org/10.1016/j.oooo.2014.09.016>
6. Mignogna MD, Fortuna G, Leuci S et al. Frictional keratoses on the facial attached gingiva are rare clinical findings and do not belong to the category of leukoplakia. *J Oral Maxillofac Surg* 2011;69:1367-1374 <https://doi.org/10.1016/j.joms.2010.05.087>
7. Margaix-Munoz M, Bagan JV, Jimenez Y, Sarrion MG, Poveda-Roda R. Graft-versus-host disease affecting oral cavity. A review. *J Clin Exp Dent* 2015;7:e138-145 <https://doi.org/10.4317/jced.51975>
8. Hayes M, Tomson P, Parmar S, Chapple ILC. Proliferative verrucous gingival leukoplakia: A sinister condition. *Perio* 2006;3:205-206.
9. Bagan J, Scully C, Jimenez Y, Martorell M. Proliferative verrucous leukoplakia: a concise update. *Oral Dis* 2010;16:328-32 <https://doi.org/10.1111/j.1601-0825.2009.01632.x>
10. Carrard VC, Brouns ER, van der Waal I. Proliferative verrucous leukoplakia; a critical appraisal of the diagnostic criteria. *Med Oral Patol Oral Cir Bucal* 2013;18:e411-e413.
11. Cerero-Lapiedra R, Balade-Martinez D, Moreno-Lopez LA, Esparza-Gomez G, Bagan JV. Proliferative verrucous leukoplakia: a proposal for diagnostic criteria. *Med Oral Patol Oral Cir Bucal* 2010;15:e839-e845.
12. Sapna N, Vandana KL. Idiopathic linear leukoplakia of gingiva: A rare case report. *J Indian Soc Periodontol* 2010;14:198-200 <https://doi.org/10.4103/0972-124X.75918>
13. Noonan VL, Woo SB, Sundararajan D, Kabani S, Gallagher G. Idiopathic gingival papillokeratosis with crypt formation, a report of 7 cases of a previously undescribed entity: possible unusual oral epithelial nevus? *Oral Surg Oral Med Oral Pathol Oral Radiol* 2017;123:358-364 <https://doi.org/10.1016/j.oooo.2016.10.018>
14. Damm DD, Curran A, White DK, Drummond JF. Leukoplakia of the maxillary vestibule—an association with Viadent? *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1999;87:61-6.
15. Smeets SJ, Hesselink AT, Speel EJ et al. A novel algorithm for reliable detection of human papillomavirus in paraffin embedded head and neck cancer specimen. *Int J Cancer* 2007;121:2465-2472 <https://doi.org/10.1002/ijc.22980>

○ indicates key references.