# Benign alveolar ridge keratosis (oral lichen simplex chronicus): A distinct clinicopathologic entity

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Benign alveolar ridge keratosis is a common benign white papule or plaque that occurs on the keratinized gingiva of the maxillary or mandibular alveolar ridge that is probably traumatic/frictional in origin, with characteristic histologic features, similar to those of lichen simplex chronicus of the skin. This is a retrospective study of 108 consecutive specimens displaying characteristic histopathologic features of benign alveolar ridge keratosis accessioned during a 36-month period. There was a male:female ratio of 3.7:1. It occurred on the attached gingiva, with the retromolar area and the edentulous alveolar ridge involved in 51% and 49% of cases, respectively; 19% were bilateral and all bilateral cases were on the retromolar pad. Detailed clinical information was available on 27 cases by a mail-in questionnaire. Histologically, the lesions were characterized by moderate to marked hyperorthokeratosis and wedge-shaped hypergranulosis. The epithelium exhibited slight surface papillomatosis and acanthosis in the form of long, tapered rete ridges that frequently anastomosed at the base. There was generally insignificant inflammation. These features are similar if not identical to lichen simplex chronicus of the skin, a benign condition caused by chronic irritation. Ten randomly selected cases were immunostained for p16INK4A(p16), a tumor suppressor protein expressed in dysplastic epithelium. All lesions were negative for p16. Benign alveolar ridge keratosis is a specific clinicopathologic entity that should be removed from the category of leukoplakia as is currently the practice for clinical white lesions with a specific, consistently recognizable histologic appearance. ( J Am Acad Dermatol 2008;58:151-7.)

Leukoplakia is a clinical entity defined by the World Health Organization as "a white plaque that does not wipe off and cannot be characterized clinically or pathologically as any other disease and is not associated with any physical or chemical agent except tobacco."[1-3] The histopathologic examination of a leukoplakia serves to exclude other histologically defined lesions (eg, lichen planus, a common white mucosal lesion) or to establish the presence of an epithelial dysplasia, carcinoma in situ (CIS), or invasive squamous cell carcinoma (SCC). Histologically, oral leukoplakia represents a hyperorthokeratosis or parakeratosis with or without acanthosis, with or without inflammation, and most importantly with or without dysplasia.

*Abbreviations used:*

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| BARK: | benign alveolar ridge keratosis |
| CIS: | carcinoma in situ |
| LSC: | lichen simplex chronicus |
| SCC: | squamous cell carcinoma |

The most important aspect of oral leukoplakia is that 9% to 34% of all leukoplakias present with dysplasia, CIS, or invasive SCC at the time of biopsy.[4-7] Nonhomogenous leukoplakia and erythroplakias have a higher incidence of dysplasia, CIS, or invasive SCC at the time of diagnosis (54%-91%).[8-11] Erythroleukoplakic lesions on the floor of the mouth, ventral tongue, and soft palate are more likely to show dysplastic/malignant changes and these are considered high-risk sites.[8,9,12] Furthermore, a form of leukoplakia called proliferative verrucous leukoplakia, which usually appears histologically benign or only mildly atypical, exhibits 70% to 100% carcinomatous transformation over time.[13-15] Therefore, true leukoplakias require long-term and likely lifetime follow-up with periodic biopsies.

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Funding sources: None.

Conflicts of interest: None declared.

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0190-9622/$34.00



doi:10.1016/j.jaad.2007.07.011

The mouth is an environment of chronic, often intense trauma resulting in lesions that are frequently referred to in the literature as "frictional keratoses."[16-18] However, there are no reports to date that define specific histopathologic features for these lesions that are usually submitted with a clinical diagnosis of leukoplakia. These lesions are frequently rendered the histopathologic diagnosis of "hyperkeratosis" or "hyperkeratosis and acanthosis," which places them in the category of leukoplakia, a condition with malignant potential even though such frictional keratoses are histopathologically benign with no malignant potential and do not require further treatment or long-term follow-up.

In this study we report the lesion benign alveolar ridge keratosis (BARK) as a distinct histopathologic and clinical entity that should be separately classified, much like oral lichen planus and other histopathologically defined white/hyperkeratotic lesions. BARK resembles lichen simplex chronicus (LSC) of the skin, a condition caused by chronic frictional injury.[19] We believe that BARK is caused by chronic frictional (masticatory) trauma to the maxillary and mandibular alveolar ridge mucosa and that it should be reported as such, and not as the nonspecific "hyperkeratosis with/out acanthosis" to separate it from oral leukoplakia and its dysplastic connotations.

## METHODS

All cases were accessioned from our surgical pathology reference laboratory files. Cases that were submitted with a clinical diagnosis of "leukoplakia" or "white plaque/lesion" and histologically diagnosed as "hyperkeratosis" with or without "benign epithelial hyperplasia" or "acanthosis" that occurred on the maxillary or mandibular ridge mucosa and that exhibited features similar to the histopathologic features seen in LSC of the skin were accessioned for this study from January 2001 to December 2003 inclusive. For conventional light microscopy, the tissue had been fixed in 10% formalin, embedded in paraffin, cut, and stained with hematoxylin-eosin. All other cases with a clinical diagnosis of "leukoplakia" were also accessioned from the files for the same period to determine the prevalence of other white lesions with a different histopathology from BARK.

### Immunohistochemical analysis

Ten randomly selected cases were selected for immunohistochemical analysis and 9 cases of severe epithelial dysplasia/CIS were used as controls.

For immunohistochemical studies, representative sections of 10 lesions were examined by the avidin-biotin-peroxidase complex technique using appropriate positive and negative controls throughout. The p16-specific mouse monoclonal antibody G175−405 (PharMingen, San Diego, Calif) was used at 2 $\mu$g/mL for all experiments. The results were confirmed using the p16-specific mouse monoclonal antibody JC2 (provided by James Koh, PhD, previous of the University of Vermont, currently at Duke University) at 4 $\mu$g/mL. Rabbit polyclonal anti-p16 antibody C20 (Santa Cruz Biotechnology Inc, Santa Cruz, Calif) was used in some initial experiments at 2 $\mu$g/mL. The immunostaining was performed as described previously.[20]

### Clinical and follow-up information

Mail-in questionnaires were sent to submitting clinicians for all cases. A second mailing was sent out 4 weeks later. Information was requested on the following: use of tobacco (smokeless and smoked); alcohol intake and mouthwash; presence of removable prosthetic appliances on or opposing the lesion; and a detailed clinical description of the lesion with regard to size, color, texture, and bilaterality. Information regarding the recurrence of lesions after excision, progress of lesions after incisional biopsy, and occurrence of dysplasia or cancer at any other site in the oral cavity was obtained for a follow-up period of 24 months.

## RESULTS

### Clinical findings

In all, 108 cases that were diagnosed based on the histopathologic criteria described below were identified for the purposes of the study. The age range was 21 to 75 years (mean 50 years, median 52 years). There were 85 men and 23 women (3.7:1 male:female). Most lesions (72%) occurred in patients in the fifth and seventh decades (Fig 1). In all, 56 lesions (51%) occurred in the retromolar pad area and 52 lesions (49%) on the gingiva/alveolar ridge mucosa. The majority of the lesions associated with the alveolar ridge were present in edentulous areas or sites of previously extracted teeth. Of the 108 lesions, 98 (91%) occurred on the mandibular mucosa. In all, 21 patients (19%) presented with bilateral lesions, all of which occurred in the retromolar pad area. Clinically these lesions appear as a white papule or plaque that did not wipe off and had a slightly rough, warty surface (Fig 2).

### Clinical and follow-up information

Of 108 mail-in questionnaires, 27 (25%) were returned and the data are presented in Table I. In all, 26 of 27 lesions were described as being white with either smooth or rough surfaces with one case exhibiting an area of redness that the clinician had