JAMA Dermatology Clinicopathological Challenge

A White Patch on the Tongue

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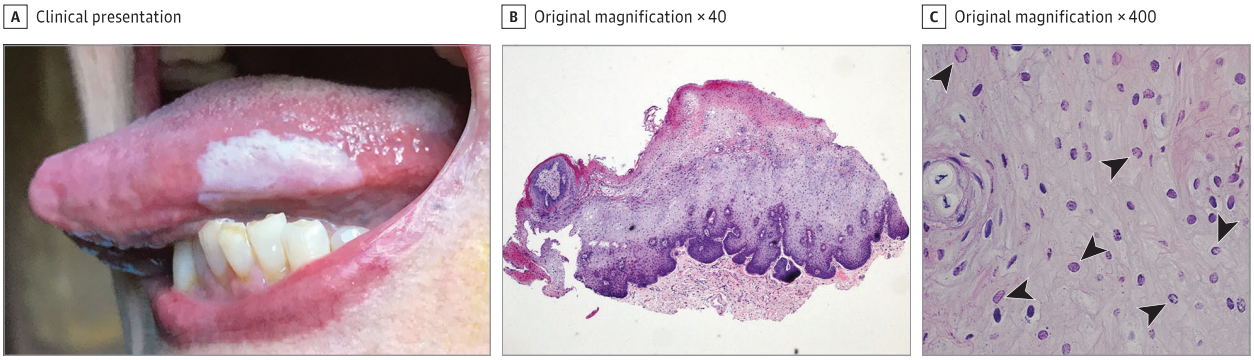

Figure 1. A, A corrugated, nonremovable white lesion on left lateral tongue. B, Histologic image showing hyperkeratotic, acanthotic stratified squamous epithelium exhibiting cells with lightly stained cytoplasm (balloon cells) throughout the stratum spinosum and superficial layer (hematoxylin-eosin). C, Histologic image showing several epithelial nuclei with peripheral chromatin margination also described as chromatin beading (arrowheads) (hematoxylin-eosin).

An 80-year-old white woman presented with an asymptomatic white patch affecting the tongue of 1 month's duration. She had a 15-year history of oral lichen planus (OLP) managed with betamethasone dipropionate, 0.05%, gel twice daily and clotrimazole troches, 10 mg, 3 times daily as needed for symptomatic OLP flares. Medical history revealed stage 1A mycosis fungoides/cutaneous T-cell lymphoma affecting the right calf and left thigh managed primarily with halobetasol, 0.05%, cream owing to intolerance of narrowband UV-B therapy and mechlorethamine, 0.016%, gel. Immunosuppression or history of infectious diseases, including human immunodeficiency virus (HIV), was not reported. A 1.5 × 1.0-cm nonremovable white, plaquelike lesion was observed on the left lateral tongue (Figure 1A). Biopsy specimens were obtained with a 3-mm punch instrument at 3 different sites, which demonstrated similar microscopic findings (Figure 1B and C).

WHAT IS YOUR DIAGNOSIS?

- **A.** Oral frictional keratosis
- **B.** Oral lichen planus
- **C.** Oral hairy leukoplakia
- **D.** Oral squamous cell carcinoma

Diagnosis

C. Oral hairy leukoplakia

Microscopic Findings and Clinical Course

Microscopic analysis of all specimens demonstrated hyperkeratosis and acanthosis with a band of cells characterized by lightly stained cytoplasm (balloon cells). The superficial cells contained nuclei with peripheral chromatin margination or nuclear beading typical of Epstein-Barr virus–infected oral keratinocytes and consistent with oral hairy leukoplakia (OHL). The patient was prescribed valacyclovir 1 g 3 times daily, which she discontinued taking after 3 days owing to medication adverse effects. On reexamination, the tongue lesion had completely resolved (Figure 2).

Discussion

Physicians would consider a clinical diagnosis of oral leukoplakia when they find a white plaque of questionable risk and have excluded other known diseases or disorders that carry no increased risk for cancer.[1,2] Oral hairy leukoplakia was first described in 1984 during the AIDS epidemic and named for its white color and corrugated appearance.[3] Historically, it has been associated with HIV infection and as a sign of disease progression.[3] Recently, several reports describe OHL in non–HIV infected individuals in association with inhaled or topical corticosteroids.[4-6] Epstein-Barr virus is a DNA B-lymphotropic human herpesvirus that infects more than 90% of the world's population and is associated with the etiopathogenesis of OHL.[4,5] Typically, OHLs appear on the lateral borders of the tongue and are asymptomatic. Microscopic analysis of OHLs may demonstrate several histopathologic features: (1) hyperkeratosis and acanthosis, (2) ballooning degeneration of keratinocytes, and (3) little to no inflammatory infiltrate in the lamina propria.[5] However, peripheral chromatin margination or nuclear beading is the only essential diagnostic criteria, and in situ hybridization for Epstein-Barr virus detection is often used to confirm the diagnosis.[5] Although treatment of OHL is not typically warranted, lesions have responded to antiviral agents such as acyclovir and valacyclovir.[3] In the present case, development of OHL may have occurred due to long-term use of topical corticosteroids for OLP

management in the absence of any known systemic immunosuppressive conditions. The patient was recommended for further evaluation of possible immunosuppression. It was indeterminate if OHL resolution was attributed to use of valacyclovir or spontaneous resolution.

Oral frictional keratosis, OLP, and oral squamous cell carcinoma (OSCC) were included in the differential diagnosis owing to clinical similarities. Oral frictional keratosis is considered a benign lesion caused by chronic rubbing between 2 surfaces, occurring at higher frequency in areas prone to mechanical trauma.[7] The characteristic white appearance of oral frictional keratosis is due to generation of keratin filaments from chronic irritation.[8] These lesions have been observed on multiple surfaces, including the tongue, buccal mucosa, gingiva, and alveolar ridges.[7] Oral frictional keratosis lesions typically reduce or resolve within 3 weeks if the causative agent is identified.[7]

Oral lichen planus is a chronic, immune-mediated disorder with prevalence ranging from 0.1% to 2% and predominantly affecting middle-aged women.[8] Oral lichen planus lesions have a wide range of clinical presentations, from mild inflammation with striae to plaque-like lesions to severely painful ulcerations, which can affect multiple areas of the oral cavity.[8] Treatment of OLP may involve topical and/or systemic immunomodulators to manage signs and symptoms of the condition.[8] Routine monitoring of OLP is recommended due to risk of dysplasia and/or malignant transformation to OSCC, which is estimated at approximately 1%.[8]

Oral and oropharyngeal cancer are typically considered collectively, with greater than 48 000 diagnosed cases in the United States annually.[9] Squamous cell carcinoma comprises over 90% of malignancies in this region, and OSCC is thought to be a complex, multistep progressive disorder with an accumulation of both genetic and epigenetic alterations.[9] Oral squamous cell carcinoma often presents as a nonhealing ulcer but can also present as a white plaque and/or red patch.[8] High-risk sites for development of OSCC include the lateral or ventral tongue and floor of mouth, but it may affect any intraoral surface.[8,9] Suspected OSCC lesions must undergo microscopic analysis to confirm the diagnosis, and subsequent therapy may include surgery, radiation therapy, and/or chemotherapy. Overall 5-year survival rate for OSCC is 60%, with poorer prognosis for cancers detected in later stages of disease.[9]

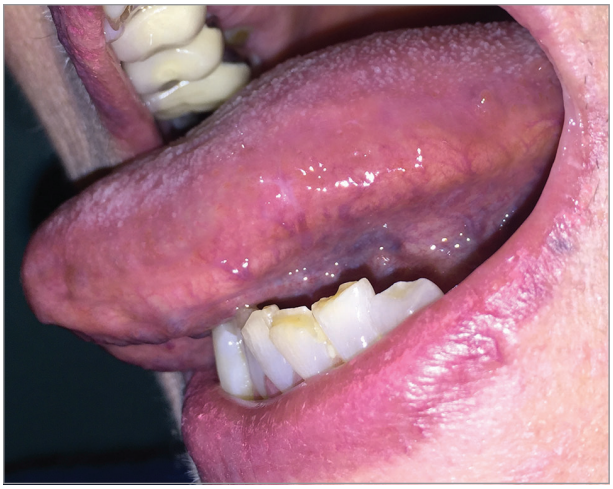

Figure 2. Posttreatment resolution of the lesion.

ARTICLE INFORMATION

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