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Oral Premalignant Lesions: Management Considerations

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Introduction

Oral cancer represents about 3% of all malignancies in men and 2% of all malignancies in women in the United States [1]. The American Cancer Society estimates that 30,000 new cases of oral cancer will be diagnosed in the United States population, of which 90% will be squamous cell carcinomas. Most oral cancers are squamous cell carcinomas because the mutagens in tobacco, alcohol, and viruses have prolonged exposure to the superficial layers of the oral mucosa, creating an opportunity for genetic mutation within the superficial mucosal layers that leads to a phenotypical mucosal premalignant lesion. Oral squamous cell carcinoma (OSCCA) generally arises in middle-aged and older people, with a male to female ratio of greater than 2:1 [2]. This ratio is changing because of increased incidence of tobacco and alcohol use among women. Despite recent advances in surgery, radiation, and chemotherapy, the 5-year survival rate remains between 50% and 55% [3,4].

Because the 5-year survival rate is directly related to the stage of malignancy at the time of diagnosis, prevention and early detection are vital to decrease the incidence and improve the survival odds of individuals who develop the disease. Oral premalignant lesions and early stage malignancies often arise as subtle lesions and require an alert clinician with a high index of suspicion, especially if any of the risk factors are present. Invasive OSCCA usually is preceded by the presence of a clinically detectable premalignant lesion of the oral mucosa. A premalignant lesion is defined as a "morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterpart" [5]. Frequently these lesions can manifest as white lesions, referred to as leukoplakia, or red lesions, referred to as erythroplakia. As these lesions progress, patients or their doctors may notice an ulcer or a mass, which usually is asymptomatic. Occasionally, OSCCA arises from other preexisting mucosal lesions, such as lichen planus, reverse smoker's palate, and tobacco pouch keratosis. This article focuses on relevant aspects of the more common premalignant lesions, leukoplakia, erythroplakia, and lichen planus, with regard to their malignant potential.

Leukoplakia

Leukoplakia is the most common oral premalignant lesion. The World Health Organization (WHO) defines leukoplakia as a "white patch or plaque that cannot be characterized clinically or pathologically as any other disease" [6]. It is therefore a diagnosis of exclusion and only a clinical descriptive term and has no diagnostic or prognostic implication. When clinicians inform patients about identifying leukoplakia in the oral cavity, it is imperative that other entities, such as frictional keratosis, candidiasis, leukoedema, and lichen planus, have been considered and eliminated from the differential diagnosis. The concept of a two-step process of malignancy (ie, initial

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presence of a precursor [premalignant] lesion subsequently developing into OSCCA) is well established and leukoplakia seems to be the best known precursor for OSCCA [7]. One study reveals that between 16% and 62% of OSCCA are associated with leukoplakia at the time of diagnosis. Leukoplakia is identified most frequently in middle-aged and older men, with increasing prevalence with age [8]. It is prevalent in 8% of men over the age of 70 and 2% of women over the age of 70 [8]. The most common sites include buccal mucosa, alveolar mucosa, and lower lip. Lesions arising on the floor-of-mouth, lateral tongue, and lower lip are most likely to show dysplastic or malignant changes, and are considered high-risk sites [9].

Leukoplakia can be classified based on clinical appearance into: (1) early/thin, (2) thick/homogenous, (3) granular/nodular, (4) proliferative verrucous, and (5) speckled leukoplakia types [10]. The early/thin variant appears as a thin, minimally elevated gray-white plaque with either well-defined or poorly defined borders [10]. It gradually progresses to a thick, homogenous lesion with a leathery white fissured surface. Some lesions progress from the early type to the granular/nodular type with pebbly surface irregularities. Some early lesions progress to a widespread multifocal lesion with a papillary surface. This uncommon variant, called papillary verrucous leukoplakia [11,12], will be discussed in a subsequent article.

The malignant transformation rate of oral leukoplakia ranges between 0.5% and 20% in some studies and between 15.6% and 39% by other accounts [6,13]. In one particularly large series, Waldron and Shafer studied 3256 cases of oral leukoplakia and reported that 19.9% had some degree of epithelial dysplasia [9]. Within this subgroup, 3.1% of cases had squamous cell carcinoma, 4.6% had severe dysplasia or carcinoma in situ, and 12% were mild to moderate dysplasia [9]. This study also revealed that the location of leukoplakia had significant correlation with the rate of dysplastic or malignant changes. Floor-of-mouth was the highest risk site with 42.9% of lesions demonstrating either dysplasia, carcinoma in situ, or squamous cell carcinoma [9]. Tongue and lip were also high-risk sites with 24% of lesions demonstrating either dysplasia or carcinoma [9] (Fig. 1).

Clinical appearance of the leukoplakic lesion also indicates a possible relationship with the probability of dysplastic or malignant findings within the lesion. As the lesion increases in thickness, the probability of dysplasia or malignancy increases. Papillary verrucous leukoplakia has the greatest chance of dysplasia/malignancy [11,12] compared with thick leukoplakia, which in turn has a higher dysplastic/malignant potential than the thin lesion [10].

Fig. 1. Tongue leukoplakia with central area of dysplasia.

Speckled leukoplakia (Fig. 2) is a mixed red-white lesion and has the highest malignant potential among all subtypes with a rate of about 44% and a dysplasia rate of 51% according to Pindborg and coworkers' study [13]. Regardless of the subtype or location, all leukoplakias should be considered at risk for malignant transformation and biopsy should be obtained after diagnosis and elimination of other white lesions. Histologic examination of the specimen definitively excludes other white lesions in most cases and establishes the degree of epithelial dysplasia if present. Patients should be educated about avoiding risk factors and the importance of periodic long-term follow-up visits to monitor the lesion should be

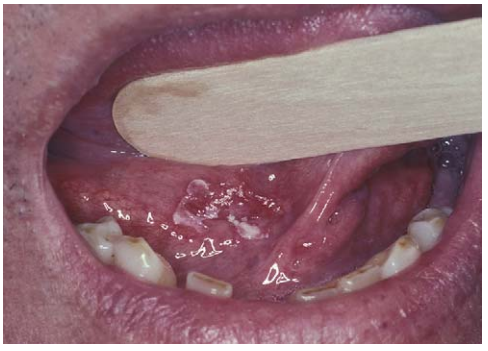

Fig. 2. Speckled leukoplakia of floor-of-mouth.