Oral potentially malignant disorders

BACKGROUND

The umbrella term *oral potentially malignant disorders* (OPMDs) has been used to group a spectrum of oral mucosal disorders that carry an increased risk of malignancy. A more precise term has been proposed, *potentially premalignant oral epithelial lesions (PPOELs)*, that accounts for the fact that these lesions have the potential to become malignant but before malignant transformation they are still potentially premalignant. Most of these disorders are asymptomatic in their early stages and are detected during a routine oral examination. Therefore, oral health professionals must be knowledgeable about the clinical features and diagnostic aspects of OPMDs to carry out the appropriate investigations and referrals to specialists required to manage these conditions before they become malignancies. The primary findings for each of the oral disorders were outlined.

LEUKOPLAKIAS

Leukoplakia

The original definition of leukoplakia denoted any adherent white patch or plaque, but the newest refinement is *predominantly white plaques of questionable risk* once other known disease or disorders carrying no added risk for cancer have been eliminated. Oral leukoplakia can be asymptomatic or benign in appearance, making it difficult to differentiate from reactive or inflammatory disorders.

Most leukoplakias are diagnosed after the fourth decade of life. They are more common in men and smokers, with independent risk factors including alcohol and betel quid. The condition can also be associated with human papillomavirus or be idiopathic. The oral sites involved differ between populations, with Western industrialized populations seeing lesions in the lateral margin of the tongue and floor of the mouth, but Asian populations having lesions in the buccal mucosa and lower buccal grooves. The lesions can vary from small, circumscribed areas to extensive lesions of the oral mucosa.

The 2 main clinical types of leukoplakia are homogeneous and nonhomogeneous, with the nonhomogeneous varieties, which are usually symptomatic, being speckled or erythroleukoplakia (Figure 2), nodular, and verrucous or exophytic. The symptoms seen include discomfort, tingling, and sensitivity to touch, hot beverages, or spicy foods. A red component indicates possible *Candida* colonization and carries an increased risk for dysplasia and/or malignancy.

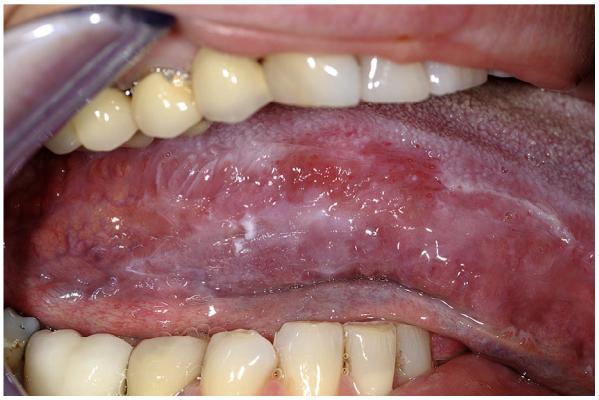

Figure 2. A patch of erythroleukoplakia affecting the lateral margin of the tongue with mixed white-and-red areas within the lesion. Note that the borders are irregular. (Courtesy of Warnakulasuriya S: Clinical features and presentation of oral potentially malignant disorders. *Oral Surg Oral Med Oral Pathol Oral Radiol* 125:582-590, 2018.)

The diagnosis is made after excluding any local traumas as causative and confirming the lesion cannot be scraped off and the color remains with stretching. Tissue biopsy is needed to exclude other pathologic conditions and assess the presence and degree of epithelial dysplasia present, as well as any candida colonization.

Proliferative Verrucous Leukoplakia (PVL)

Clinicians should suspect PVL in leukoplakic lesions that are warty, exophytic, widespread, and recur after treatment. This disorder can involve multiple sites in the oral cavity. The diagnostic criteria include having more than 2 oral sites, usually the gingiva, alveolar processes, and palate; having a verrucous area; including lesions that have spread or enlarged as the disease develops; and involving a recurrence in a previously treated area. Not all PVLs have a verrucous appearance, especially initially.

Erythroplakia

Erythroplakia is usually seen on the soft palate and manifests as irregular but well-defined lesions with surfaces that are bright red and velvety (Figure 6). The surface can also be granular. Erythroplakia must be differentiated from other disorders that appear as red patches. Its well-demarcated, solitary presentation helps to distinguish it. In addition, a diagnostic biopsy is required urgently to establish the lesion is erythroplakia because it is dysplastic and can harbor either carcinoma in situ or frank carcinoma

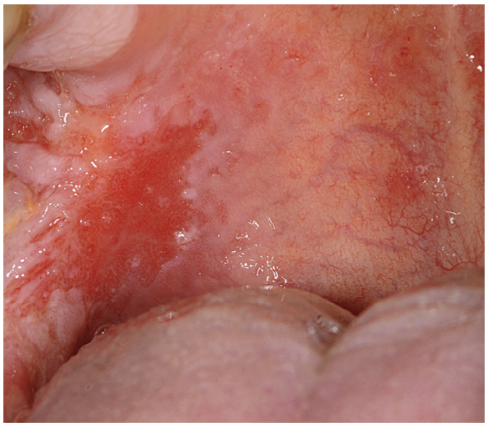

Figure 6. Erythroplakia affecting the soft palate. On biopsy, severe dysplasia was observed in this red patch. (Courtesy of Warnakulasuriya S: Clinical features and presentation of oral potentially malignant disorders. *Oral Surg Oral Med Oral Pathol Oral Radiol* 125:582-590, 2018.)

Erythroleukoplakia

Speckled leukoplakia is now termed erythroleukoplakia, with the red component showing either thinning or speckling. Unlike leukoplakia or erythroplakia, this lesion has irregular margins and causes soreness, often because candida has colonized the area.

ORAL LICHEN PLANUS AND LICHENOID DISORDERS

Oral Lichen Planus (OLP)

The oral manifestations of OLP vary in appearance but tend to be multiple and symmetric in distribution. The subtypes include linear, reticular, annular, papular, plaque, atrophic, and ulcerative, with bullous lichen planus seen only rarely. Often more than one subtype is present simultaneously.

The usual presentation is a bilateral keratotic lace-like network of white striae on the buccal mucosa and lateral margins of the tongue. Most commonly, the reticular type is seen in asymptomatic individuals. When ulceration has occurred, patients usually experience soreness or a burning sensation when eating hot or spicy foods.

The medical history can help identify OLP even when the lesions are cutaneous or in extraoral mucosal sites, such as the genitalia. The diagnosis is generally made clinically based on the lesion's bilateral distribution and presence of classic reticular form with keratotic white striae. It has an extensive differential diagnosis, so a biopsy and histopathologic examination are recommended for a definitive diagnosis. Microscopic evaluation can identify epithelial dysplasia or malignancy, but direct immunofluorescence studies are only helpful in ruling out discoid lupus erythematosus (DLE) or mucous membrane pemphigoid.

OLP can last for several years and consists of flare-ups and remissions. Malignant transformation can occur, but no specific criteria help in evaluating the risk for this occurrence.

Oral Lichenoid Lesions (OLLs)

OLLs are intraoral red and white lesions with a reticular, striated appearance; their clinical features resemble those of OLP, but OLLs result from an underlying causative agent. The various types of OLLs are determined by the cause, which can be sensitivity to a dental restoration, drug related, or associated with chronic graft-versus-host disease (cGvHD).

Ulceration can be present, as can white reticular, linear, or annular striae or plaque-like patches. In erosive OLLs, red and mixed lesions manifest as erythematous atrophic patches, often with ulceration. It can be difficult to differentiate OLL from OLP. The diagnosis depends on the combined findings from the patient's history, clinical examination, skin patch test (when indicated), and microscopic evaluation. Malignant transformation is possible.

MISCELLANEOUS DISORDERS

Graft-Versus-Host Disease (GvHD)

Recipients of allogenic hematopoietic stem cells or bone marrow transplants can develop GvHD as a complication of their transplants. The oral cavity is one of the most frequently affected sites, with lesions becoming widespread in the mouth. Patients experience soreness when eating, keratotic striations, white plaques, or erosive and ulcerative areas in the oral cavity. The buccal mucosa and lateral tongue are often involved, with the dorsum of the tongue sometimes showing papillary atrophy. Patients also experience xerostomia and recurrent mucoceles on the labial and buccal mucosae, tongue, or soft palate. Malignant transformation can occur.

Discoid Lupus Erythematosus (DLE)

DLE can by systemic, drug-induced, or discoid, with the last variant usually involving the skin and mucosal surface of the lips and oral cavity. About 20% of patients with systemic lupus can also have oral lesions. An immune complex deposition in the affected sites causes vasculitis. The discoid variant usually affects the sun-exposed facial and neck areas and can cause a butterfly rash across the nasal bridge. Oral lesions have central zones of ulceration or erythema surrounded by white striations (Figure 10). Immunofluorescence reveals subepithelial immunoglobulin and complement deposition, which can help to distinguish DLE from lichen planus. Erosive areas of DLE can transition to post-inflammatory pigmentation during resolution. The lower lip is most often affected in DLE-related malignant transformation, which is exceedingly rare.

Oral Submucous Fibrosis (OSF)

OSF is a chronic insidious disease of the lamina propria of the oral mucosa, extending deeper as the disease advances. Clinicians should suspect OSF if the patient is Asian, has a history of betel quid chewing, and presents with limited mouth

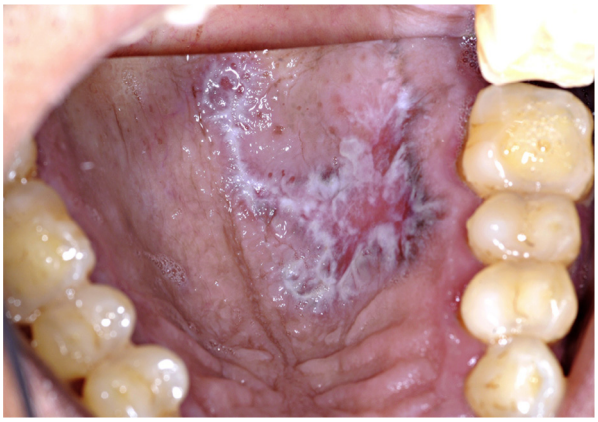

Figure 10. A lupus patch on the palate of a patient diagnosed with systemic lupus erythematosus. The affected area shows irregular keratosis surrounding a zone of central erythema, with some radiating white striae. (Courtesy of Warnakulasuriya S: Clinical features and presentation of oral potentially malignant disorders. *Oral Surg Oral Med Oral Pathol Oral Radiol* 125:582-590, 2018.)

opening. The disease is characterized by a leathery mucosal texture and palpable fibrous bands in the oral mucosa. Early features are blanching of the mucosa, loss of normal pigmentation, and a burning sensation in the mucosa when spicy food is consumed. Clinically, the patient will have sunken cheeks and limited mouth opening. Other signs include a small tongue that has limited mobility and marked loss of papillae; a pale palate with horizontal bands across the soft palate; and a shrunken or deformed uvula. Disease severity is determined by assessing mouth opening and determining whether there are multiple leukoplakia or erythroplakia lesions.

In betel quid users, a new lesion with malignant potential often seen in association with OSF can occur. This mass type lesion has both exophytic and verrucous phenotypes.

Palatal Changes

In reverse smoking, common in India, the Caribbean, Columbia, Panama, Venezuela, Jamaica, Sardinia, and the Philippines, the lit end of a cigar is placed inside the mouth. Mucosal changes include thickened leukoplakic plaques of the palate, mucosal nodularity, excrescences around the orifices of the palatal mucosal glands, yellowish brown staining, erythema, and ulceration. This condition has a potentially malignant nature and can lead to palatal cancer.

Epidermolysis Bullosa (EB)

EB is a skin disease that can manifest as blistering and erosions of the oral mucosa. There are 32 different subtypes, with intraoral soft tissue manifestations in all of them. Malignancies in patients with EB occur in the third decade or earlier. EB is considered a potentially malignant disorder.

Dyskeratosis Congenita (DC)

Patients with this rare inherited bone marrow failure syndrome have a significantly higher risk of malignancy. Oral leukoplakia is the most common presentation and is found in 65% to 80% of patients. A classic triad of signs is seen, including lacy reticular hyperpigmentation of the skin, nail dystrophy, and leukoplakic patches on the dorsal tongue and sometimes the buccal mucosa. Often the tongue is affected from a young age, with oral leukoplakia documented in children and adolescents younger than 15 years. Oral white lesions are rare in children, so finding a white patch on a child's tongue with no other obvious cause must lead the clinician to suspect DC. The condition is attributed to several mutations of genes that help maintain telomeres.

Actinic Cheilitis (AC)

The cause of AC is excessive exposure to solar ultraviolet radiation. Usually the lower lip is involved, and those with fairer skin tend to be at higher risk. Men are more predisposed to AC than women.

The clinical features of AC are commonly white lesions accompanied by crusting, flaking, dryness, or a mottled appearance, which indicates the simultaneous presence of erythema and white patches. Ulcerative lesions can also develop, with inflammation, atrophy, and loss of epithelium.

AC is dose dependent to the amount of ultraviolet radiation the individual has been exposed to. It is not only associated with sun exposure, but also with age, genetic predisposition, geographic local, outdoor occupation, leisure activities, and failure to use protective agents on the lips. The progression of AC to squamous cell carcinoma (SCC) of the lip can be minimized by using appropriate sunscreen when outdoors.

Clinical Significance

OPMDs demonstrate an enhanced risk for developing into oral cancer. Leukoplakia is the most common OPMD seen in clinical practice. Dentists should be aware of the clinical signs and symptoms of all these conditions as well as contributing factors in patients' history that might lead to the development of OPMDs.

Warnakulasuriya S: Clinical features and presentation of oral potentially malignant disorders. *Oral Surg Oral Med Oral Pathol Oral Radiol* 125:582-590, 2018

Reprints available from S Warnakulasuriya, Dept of Oral Medicine, King's College London, Bessemer Rd, London SE5 9RS, UK; e-mail: S.warne@kcl.ac.uk