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Upper Aerodigestive Tract
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Cancer precursor is a term used to describe lesions or systemic states with a high probability of invasive cancer occurrence compared to that in the absence of these conditions. Cancer precursors may consist of morphologically- or genetically-altered localized tissue in which cancer is more likely to occur than in its apparently normal counterpart, or of precancerous conditions, which refer to a generalized state associated with an increased risk of cancer. Identifying those patients with precursors offers a potential strategy to prevent cancer or to detect it early.

The upper aerodigestive tract (UADT) consists of those anatomical regions of the body with shared alimentary and respiratory functions. These include the oral cavity, pharynx, and larynx. Precursors of the UADT are mostly clinically defined entities (Table 6.1). Leukoplakia, erythroplakia and oral submucous fibrosis (OSF) are clinically identifiable oral cancer precursors, which on histology may reveal areas of dysplasia. Laryngeal keratosis and erythrokeratosis are precancerous mucosal changes in the larynx, particularly in the vocal cords, with great similarity to oral leukoplakia. Plummer-Vinson syndrome is a precancerous condition for hypopharyngeal cancer, particularly post cricoid malignancy, and upper esophageal cancer. Plummer-Vinson syndrome is now observed rarely thanks to general improvements in nutrition.

The need for clear definition of the precursors in order to achieve consistency in diagnosis and comparison has long been recognized. There have been efforts to achieve consensus in the definition of oral precursors such as leukoplakia and erythroplakia. Considerable progress has been made in understanding the biology and natural history of cervical cancer precursors. However, this is not the case with UADT precursors. There is a certain paucity of knowledge of the underlying biology and the progression of these lesions. Most of the current understanding of UADT precursors is based on selected case-series from hospitals in different geographical locations, with few population-based studies on oral precancers.

Precursors in the Oral Cavity

Clinical Definition

The term leukoplakia was first used in 1877 by Schwimmer to denote white lesions of the oral cavity. It is now used as a clinical term, without any histological connotation, to characterize a wide range of white, and red and white oral lesions that cannot be rubbed off or diagnosed as another specific disease entity. Leukoplakia has been defined as “a white patch or plaque that cannot be characterized, clinically or histopathologically, as any other disease”, by the WHO Collaborating Center for Oral Precancerous lesions [1].

An international consultation in 1983 modified the above definition as: “Leukoplakia is a whitish patch or plaque that cannot be characterized clinically or pathologically as any other
disease and it is not associated with any physical or chemical causative agent except the use of tobacco” [2]. This implies that the term leukoplakia should be avoided when there is a known etiological factor other than tobacco use. Thus lesions associated with friction, dental restorations, cheek biting, and so on, should not be designated as leukoplakia. It was also proposed that an etiological and clinical description for leukoplakia [2] be established. Etiologically, lesions resulting from tobacco use were designated as “tobacco-associated leukoplakia” and those with unknown etiology as “idiopathic leukoplakia”. Clinically, leukoplakia was categorized as being homogeneous or non-homogeneous, with three subtypes of the latter (erythroleukoplakia, nodular lesions, and verrucous lesions). White lesions with a smooth, corrugated, or wrinkled surface were termed homogeneous leukoplakia, and those with white, or red and white lesions having irregular flat, nodular, or exophytic surfaces were termed as nonhomogeneous.

A new set of guidelines and a clinical staging procedure for oral leukoplakia were proposed in 1994 [3]. The new definition of oral leukoplakia reads as “a predominantly white lesion with a uniformly flat, thin appearance, that may exhibit shallow cracks. It has a smooth, wrinkled, or corrugated surface with a consistent texture throughout.

1. Homogeneous leukoplakia: A predominantly white lesion with a uniformly flat, thin appearance, that may exhibit shallow cracks. It has a smooth, wrinkled, or corrugated surface with a consistent texture throughout.

2. Nonhomogeneous leukoplakia: A predominantly white, or white and red lesion (erythroleukoplakia) that may be irregularly flat, nodular, or exophytic. The nodular lesions have slightly raised, rounded, red and/or white excrescences, and the exophytic lesions have irregular blunt or sharp projections.

It was also proposed that oral leukoplakia could be diagnosed provisionally or definitively, depending on the circumstances under which subjects are examined. The provisional diagnosis is always a clinical diagnosis, while definitive diagnosis is based on histopathological examination and exclusion of other definable lesions. If carcinoma-in-situ or invasive carcinoma, or other definable lesions such as lichen planus, papilloma, or pseudomembranous candidiasis are found in a biopsy of oral leukoplakia, then a provisional diagnosis of oral leukoplakia should be replaced by the definitive diagnosis obtained histopathologically.

In spite of these attempts to formulate uniform terms and definitions, other terms such as preleukoplakia (white lesions of less than 5 mm), ulcerative leukoplakia, speckled and erosive leukoplakia (the latter three are nonhomogeneous lesions) have been frequently used by workers in different countries. Many reports in the literature do not specify whether a diagnosis of leukoplakia has been reached on the basis of a clinical examination only, or after a histopathology report on a biopsy. It is likely that most reports contained both, with a predominance of clinically diagnosed lesions.

We prefer to classify oral leukoplakia mainly as homogeneous or nonhomogeneous, since these are clinically more definite categories, without any further attempt to subclassify nonhomogeneous lesions. This may result in descriptive categories with considerable misclassification between the subcategories. However, we do encourage the identification of nonhomogeneous lesions with nodular or exo-