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Oral submucous fibrosis: an overview of the aetiology, pathogenesis, classification, and principles of management

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Abstract

Oral submucous fibrosis (OSMF) is a complex, debilitating, and precancerous condition. Formerly confined to the Indian subcontinent, it is now often seen in the Asian populations of the United Kingdom, USA, and other developed countries, and is therefore a serious problem for global health. The well-known causative agent of the disease, areca-nut is now recognised as a group one carcinogen. We review and discuss all components of OSMF, including the terminology, presentation, aetiology, and pathogenesis, and provide a brief overview of its management.

Keywords: Oral submucous fibrosis; Areca-nut; Gutkha; Aetiology; Pathogenesis; Review

Introduction

Oral submucous fibrosis (OSMF) is a chronic, debilitating disease characterised by juxtaepithelial fibrosis of the oral cavity. It is regarded as a precancerous and potentially malignant condition.[1,2] The most widely accepted definition of the disease by Pindborg and Sirsat[3] is one of an insidious, chronic disease that affects any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by, or associated with, formation of vesicles, it is always associated with a juxtaepithelial inflammatory reaction followed by fibroelastic change of the lamina propria and epithelial atrophy that leads to stiffness of the oral mucosa and causes trismus and an inability to eat.[3]

The definition by the World Health Organization (WHO) of an precancerous oral condition: "a generalized pathological state of the oral mucosa associated with a significantly increased risk of cancer" fits well with the characteristics of OSMF.[4,5] The condition is thought to be multifactorial in origin with a high incidence in people who chew areca-nut,[6] and a significant malignant transformation rate (7–30%)[7] poses global problems for public health. The physical effects, which include a burning sensation in the mucosa and progressive trismus, can also have psychological and social implications for patients.

Terminology

In 1952, Schwartz described a condition in 5 Indian women that he called "atrophia idiopathies (tropica) mucosae oris" (Schwartz J. Atrophia idiopathica (tropica) mucosae oris. Presented at the Eleventh International Dental Congress, London, 1952); Joshi coined the term "submucous fibrosis of the palate and pillars".[8] Other names suggested include "diffuse oral submucous fibrosis", "idiopathic scleroderma of the mouth", "idiopathic palatal fibrosis", and "sclerosing stomatitis".[3,4] Pindborg and Sirsat used the term "submucous fibrosis" although they suggested that a more appropriate

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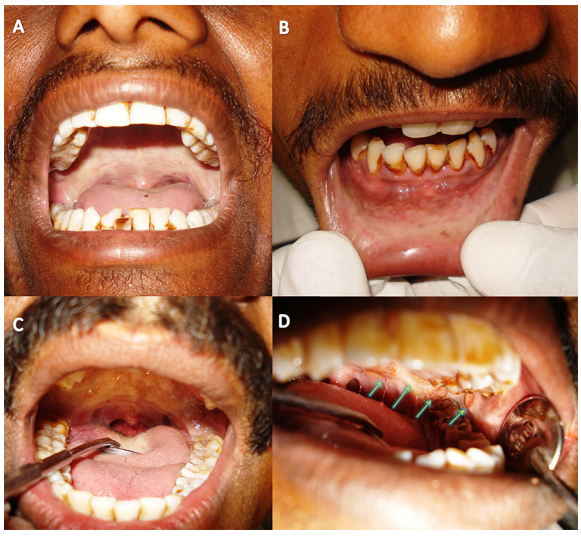

Fig. 1. Clinical appearance of oral mucosa in oral submucous fibrosis (A–C) and malignant changes in the condition (marked with arrows in D).

name would be "juxtaepithelial fibrosis".[3] Its premalignant nature was first described by Paymaster in 1956.[9]

Clinical presentation

Clinical presentation depends on the stage of the disease.[10] Initially, most patients present with a burning sensation or intolerance to spicy food, and they may have vesicles, particularly on the palate. Ulceration and dryness of the mouth is later followed by fibrosis of the oral mucosa, which leads to rigidity of the lips, tongue, and palate, and trismus.[10]

Petechiae, in the absence of blood dyscrasias or systemic disorders, are found in about 22% of patients with OSMF, and occur most often on the tongue followed by the labial and buccal mucosa.[4,11]

A useful clinical sign is pain on palpation in the sites where submucosal fibrotic bands are developing,[11] and trismus is caused mostly by fibrosis in the dense tissue around the pterygomandibular raphae.[11] Fibrosis of the eustachian tube may lead to deafness.[7,12] When the fibrosis involves the nasopharynx or oesophagus, patients may experience referred pain to the ear, a nasal voice, and dysphagia to solids; usually these are features of more advanced disease.[7,11]

The most obvious clinical signs include blanched, opaque oral mucosa with palpable fibrous bands (Fig. 1).[10,13,14] Furthermore, the overlying epithelium may become dysplastic and malignant. Restricted mouth opening interferes with examination of the oral mucosa, and makes early diagnosis of cancer a daunting task.[10,15–17]

Epidemiology

Geographically, OSMF has a specific distribution and affects predominantly Asians (and particularly Indians) from the southern states, and Taiwanese.[10,18] Other series of OSMF in Europe, the Far East, and the Pacific Rim have been reported.[7,10,18] An estimate from 1996 indicated that globally, about 2.5 million people have OSMF,[7] but studies have found that over 5 million people are affected in India alone (0.5% of the Indian population).[1,7,19] It is also estimated that up to 20% of the world's population use betel nut in some form, so the incidence of OSMF is likely to be much higher than current estimates suggest, and it is regarded as a public health issue in the Indian subcontinent, the UK,[1,20] and South Africa.[1,7,21] It is predominantly seen in the second or third decade, and recent data suggest a male predominance; however, both sexes are equally at risk.[10,18] Oral cancer that arises in those who chew betel quid is one of the most common malignancies in south and southeast Asian countries,[1,22] and with immigration from the Indian subcontinent to the UK, USA, and South Africa, oral and maxillofacial surgeons in these countries are likely to encounter the disease more often in future.[7]

Aetiology

At first, OSMF was thought to be idiopathic, but it was later concluded to be multifactorial in origin, and possible aetiological factors include capsaicin in chillies, iron, zinc, and deficiencies in essential vitamins.[6,18,23,24] Various autoantibodies and specific human leucocyte antigens (HLA) in some patients have indicated an autoimmune role as well as a genetic predisposition for the disease.[25] However, various epidemiological studies, large cross-sectional surveys, case–control studies, and cohort and intervention studies have provided overwhelming evidence that areca-nut is the main aetiological factor in OSMF.[21,25–34] The nut is the endosperm of the fruit of the *Areca catechu* palm tree.[7] A range of case–control studies have given convincing evidence that there is a definite dose-dependent relation between areca-nut and causation of the disease, and it is well known that the onset of the disease is directly proportional to the concentration, incidence, and duration of chewing the nut (without tobacco).[25,29,32,34] Generally, younger patients develop clinical features of OSMF within 3.5 years from onset of the habit while in older patients it takes 6.5 years.[25,27]

Currently, in India, Pakistan, and Bangladesh, betel quid and gutkha are the most commonly used commercially freeze-dried areca-nut products. Gutkha (also spelled gutka or guthka, thought to be derived from Hindi meaning "a shred or small piece") is a light brown, grainy powder available in compact storable sachets (Fig. 2). It consists mainly of areca-nut, tobacco, and flavours, and is typically taken to relieve stress. When chewed it dissolves quickly in saliva and provides central stimulation, which is said to be more intense than tobacco.

Gutkha has replaced most of the commercial areca-nut preparations, and contains the nut in high concentrations