Oral Squamous Cell Carcinoma in Background of Oral Submucous Fibrosis: A Case Report

P Balaji1, Poornima Govindraju2, Ashish Gupta3, Yogesh Pawar3, Nikhat Mukhtar Gazge3
1Professor & Head, Department of Oral Medicine & Radiology, Rajarajeswari Dental College & Hospital, Bengaluru, Karnataka, India, 2Reader, Department of Oral Medicine & Radiology, Rajarajeswari Dental College & Hospital, Bengaluru, Karnataka, India, 3Post-graduate Student, Department of Oral Medicine & Radiology, Rajarajeswari Dental College & Hospital, Bengaluru, Karnataka, India

Oral submucous fibrosis (OSMF) is a well-recognized, potentially malignant disorder of the oral cavity that can affect any part of the oral mucosa, characterized by mucosal rigidity of varying intensity caused by fibro elastic transformation of the juxta epithelial layer of connective tissue. OSMF occurs in Indians and other population of the Indian subcontinent with certain oral habits. Betel quid chewing is a popular oral habit with potential links to the occurrence of oral cancer. In patients with submucous fibrosis, the oral epithelium becomes atrophic and thereby becomes more vulnerable to carcinogens. Since the ingredients of betel quid, tobacco are crucial for tumor initiation, promotion and progression, exposure to these toxicants simultaneously has been shown to markedly potentiate the oral cancer incidence in OSMF patients. The rate of malignant transformation of OSMF has been estimated to be 2-10%. Most cases with malignant transformation in OSMF have occurred gradually over a long period of time. This paper presents a case of oral submucous fibrosis turning into malignancy in a 34-year-old male patient.

Keywords: Areca nut habit, Malignant transformation, Oral squamous cell carcinoma Oral submucous fibrosis

INTRODUCTION

Sushruta, who was a renowned Indian physician mentioned about a condition “Vidari” in his book “mouth and throat diseases.” The features of this particular condition simulate oral submucous fibrosis (OSMF).1 OSMF is a high risk potentially malignant disorder characterized by changes in the connective tissue fibers of the lamina propria and deeper parts leading to a stiffness of the mucosa resulting in restricted mouth opening.2 OSMF is also known as “diffuse OSMF,” “idiopathic scleroderma of mouth,” “idiopathic palatal fibrosis,” “sclerosing stomatitis,” “juxta-epithelial fibrosis,” etc.3 Although OSMF was first described by Schwartz in a group of Indian women from East Africa, there are descriptions of a similar condition occurring in betel chewers in early texts dating back to 1908.4 Submucous fibrosis was also described by Joshi in 1953.5,6 It has been reported mainly from India, but has also been diagnosed in Srilanka, Malaysia, Nepal, South Vietnam, and Thailand.6 Various etiological factors have been proposed for OSMF. Several predisposing factors or causative agents include chilli consumption, nutritional deficiency, areca nut chewing, genetic susceptibility, autoimmunity and saliva. Most of the OSMF patients belong to 20-40 years old age group with a male predominance. In patients with submucous fibrosis, the oral epithelium becomes atrophic and hence becomes more vulnerable to carcinogens. The atrophic epithelium first shows an intercellular edema and later epithelial atypia associated with moderate epithelial hyperplasia. From then on, carcinoma may develop anytime. It is suggested that submucous fibrosis should be regarded as a condition that causes a predisposition to the development of oral cancer. Paymaster first mentioned the possible precancerous nature of OSMF in the year 1956. 87% of males being predominantly affected with a malignant transformation rate of 11.7% is reported with OSMF. Around 7.6% of malignant transformation rate has been reported over a period 17 years in the OSMF.1,4,6,7

CASE REPORT

A 32-year-old male patient (Figure 1a), reported to the Department of Oral Medicine & Radiology of Rajarajeswari Dental College and Hospital, Bengaluru, with a chief complaint of pain in his right upper back tooth region since 3 days.
The patient has given a history of pain in his right cheek region since 3 days. The pain was insidious in onset, intermittent in a nature of moderate intensity, radiating to the right side of the face. Pain aggravated while having hot and spicy food and relieved after taking medication. His medical, surgical, and family history were non-contributory. His personal history revealed that he had the habit of chewing tobacco with betel nut 4-5 times/day since 1½ years. He used to place the quid on the right side of the cheek for 30-45 min and used to spit out. He admitted having quit the habit since 1-year. The patient also gave a history of smoking 4-5 cigarettes per day since 5 years.

General physical examination revealed no abnormality. Extraoral examination revealed palpable solitary right submandibular lymph node that was approximately 5 mm × 5 mm in size, round, firm in consistency, mobile, and non-tender. Mouth opening was 30 mm (Figure 1b). Patient was also not able to blow his cheek and whistle.

On intraoral examination, blanching was present in the right and left buccal mucosa and soft palate. Vertical fibrous bands were palpable in the right and left buccal mucosa and retromolar area (Figure 2a). Proliferative growth was present in the right buccal mucosa, measuring approximately 1 cm × 2 cm, irregular in shape, extending from 16 to the retromolar region anterior-posteriorly. Surface of the growth was erythematous. The Lesion was indurated and tender on palpation (Figure 2b). A solitary ulcer was present in the maxilla at the junction of hard and soft palate which was 1 cm mesial to 18, measuring approximately 5 mm × 5 mm and round. The surface was covered with slough, and surrounding area was erythematous and tender on palpation (Figure 2c).

Based on all the clinical findings a provisional diagnosis of OSMF with malignancy was considered.

Patient was subjected to hematological, radiological investigation, and incisional biopsy of the lesion. There were no significant findings on OPG. Complete hemogram values were within normal limits. Histopathologically, features were suggestive of well differentiated squamous cell carcinoma and OSMF (Figure 3).

Based on all investigations, a final diagnosis of OSMF Stage IVb was given.

**DISCUSSION**

OSMF is defined as an “insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx, occasionally preceded by vesicle formation, always associated with juxta epithelial inflammatory reaction followed by a fibro elastic change of lamina propria with epithelial atrophy leading to stiffness of the oral mucosa, trismus, and inability to eat.” The prevalence rate is reported to be about 0.2-0.5% with a higher percentage being reported from the southern states of India. It has been well-recognized as a potentially malignant disorder of the oral cavity. Besides being regarded as a precancerous condition, it is a seriously debilitating and progressive
Once initiated, the disease is not pliable to reversal at any stage of the disease process, even after cessation of the habit. As the tissues become rigid, it results in terms of loss of mouth function and causes significant morbidity. The mouth opening becomes difficult and leads to mortality when there is a transformation into squamous cell carcinoma.  

The highest risk factor for OSMF is the chewing of betel quid containing areca nut. The development of OSMF depends on the amount of areca nut in betel quid and the frequency and duration of chewing betel quid. It has been observed that gutkha chewing is preferred by people in the younger age group of 11-30 years. The findings that clearly document the hazard of gutkha chewing, is that the onset of OSMF changes occurs earlier with gutkha chewing compared to only areca nut chewing. Since people are used to gutkha chewing at a comparatively younger age and as a shorter duration of chewing is required to precipitate OSMF, there may be an increased risk of developing malignant changes in such OSMF cases.

There is continuous irritation to the oral tissues by direct contact of the quid mixture containing various components, including biologically active alkaloids (arecoline, arecaidine, arecolidine, guvacoline, guvacine), flavonoids (tannins and catechins) and copper. They also modulate lysyl oxidases and collagenases and results in elevation of collagen production and decrease in collagen degradation. This leads to increased fibrosis, thereby causing OSMF. As the copper content of areca nut is high, the possible role of copper as a mediator of fibrosis is been supported by the demonstration of up-regulation of lysyl oxidase in OSMF biopsies.

The tumor-promoting activity of the areca nut ingredients has also been suggested. Chemical carcinogenesis is a multistep process involving the initiation, promotion, and progression of the tumour. The interaction between various carcinogens and cellular macromolecules such as DNA, lipids, and proteins are the most crucial event of chemical carcinogenesis. Exposure to the ingredients of betel quid, tobacco have been known to exert genotoxicity and are crucial for tumor initiation, promotion and progression, simultaneously has been shown to markedly increase the oral cancer incidence in OSMF patients. Since the epithelial atrophy in OSMF patients increases the penetration of carcinogenic ingredients of betel quid and further increases the incidence rate of oral cancer.

The genotoxic agents present in betel quid continuously attack the normal oral mucosal epithelial cells. Reactive oxygen species (ROS) and reactive intermediates conjugates with antioxidants such as N-acetyl-L-cysteine, cellular glutathione (GSH), and enzymes such as catalase, superoxide, and GSH peroxidase, which results in the degradation of reactive toxic species and protects the critical cellular macromolecules. However, the repeated and continuous exposure of oral mucosal cells to betel quid ingredients, will eventually lead to the impairment of cellular defense systems.

Figure 4: The mechanisms of pathogenesis of oral submucous fibrosis and the possible molecules and pathways involved in the pathogenesis of oral submucous fibrosis
A highly large amount of ROS, reactive metabolic intermediates from betel quid and tobacco can cause various kinds of DNA damage by attacking cellular DNA. If the DNA-damaged cells are subsequently induced to replicate by proliferative agents, the DNA damage will remain permanent in the cells. This would lead to the formation of mutated “initiated” cells. The further promotion and progression of such initiated cells can lead to the occurrence of oral pre-cancerous lesions and clinical tumours.17

Figure 4 demonstrates the mechanisms of pathogenesis of OSMF and the various kinds of molecules and pathways are involved in the pathogenesis of OSMF.12 Figure 5 demonstrates the possible events in malignant transformation of OSMF.12

**CONCLUSION**

Oral health plays an important role in the maintenance of general health and wellbeing. The ill-effects of carcinogenic products like tobacco, betel nut quid are still high and results in oral diseases regardless the changes and improvements in the oral health status, particularly in South Central Asian countries. Arecanut being used for consumption in various forms, plays an important role in the etiology and results in OSMF. Various treatment modalities and interventions can be up taken in the management OSMF: Discontinuation of habit, antioxidants, oral physiotherapy, intralesional steroids, and surgical interventions. However, the primary objective should be educating the patients about the harmful effects of betel quid consumption. The public and oral physicians should be aware of the high risk of oral malignancy in potentially malignant disorders induced by consumption of these products.

**REFERENCES**

11. Rajalalitha P, Vali S. Molecular pathogenesis of oral submucous

How to cite this article: Balaji P, Govindraju P, Gupta A, Pawar Y, Gazge NM. Oral Squamous Cell Carcinoma in Background of Oral Submucous Fibrosis: A Case Report. IJSS Case Reports & Reviews 2015;1(12):40-44.

Source of Support: Nil. Conflict of Interest: None declared.