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ORAL SUBMUCOUS FIBROSIS AS A PRECURSOR OF MALIGNANCY - A CASE REPORT

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ABSTRACT

Oral submucous fibrosis (OSF) is a high risk precancerous condition predominantly occurs in Indians and other population of the Indian subcontinent with certain oral habits. Betel quid (BQ) 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 BQ, tobacco are crucial for tumour initiation, promotion and progression, exposure to these toxicants simultaneously has been shown to markedly potentiate the oral cancer incidence in OSF patients. The rate of malignant transformation of OSF has been estimated to be 4.5%. Most cases with malignant transformation in OSF had occurred gradually over a long period of time.

Key words: Oral sub-mucous fibrosis, Betel quid, Areca nut, Chemical carcinogenesis.
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INTRODUCTION:

Oral submucous fibrosis (OSF) is a high risk precancerous condition of the oral mucosa that predominantly affects people of South-East Asian origin [1]. In patients with submucous fibrosis, the oral epithelium becomes atrophic and thereby becomes more vulnerable to carcinogens. The atrophic epithelium shows first an intercellular oedema and later epithelial atypia associated with moderate epithelial hyperplasia [2]. From then on, carcinoma may develop any time. OSF should be regarded as a condition that causes predisposition to the development of oral cancer [2]. The possible precancerous nature of OSF was first mentioned by Paymaster in the year 1956 [2]. A

malignant transformation rate of 11.7% was reported with OSF which was seen predominantly in males (87%) [3]. The malignant transformation rate of OSF has been reported to be around 7.6% over a 17-year period [4]. Here we report a rare case of OSF which had turned into malignancy within a short period of only six months, in a thirty year old patient. The ethical clearance for the publication of the case report was obtained from the patient & from the concerned authority.

CASE REPORT:

A 30 year old male patient reported to our department with a chief complaint of burning sensation in the oral mucosa associated with difficulty in mouth opening since one year. There was difficulty on swallowing food and increased burning sensation on intake of spicy food. He had the habit of chewing gutkha three packets per day, since last six years.

Intraoral examination revealed diffuse blanching of left (Figures 1) as well as the right buccal mucosa and was slightly opaque with presence of thick fibrotic bands which were palpable bilaterally and running in vertical direction. Mouth opening was 20mm along with reduced flexibility of cheek. The area was found to be leathery & non tender on palpation. Incisional biopsy of the left buccal mucosa showed stratified squamous orthokeratinized epithelium with atrophy of the rete ridges, the connective tissue showed dense collagenous tissue with hyalinization suggestive of OSF grade II (Figure 2). Antioxidant was prescribed for the patient. Habit counselling was done for quiting gutka chewing habit. The frequency of gutka chewing habit was reduced following the habit counselling but was not completely stopped. Intralesional steroid injection (Betnesol 4mg/1ml vial) was given biweekly. Also patient was adviced to do mouth exercises. The mouth opening was improved following the intralesional steroid injections and mouth exercises. The patient was under follow up once in a month for 6 months with no further change. Furthermore after about 6 months, there was an ulcerative growth (measuring about 4 × 3 cm) noticed on the left buccal mucosa extending 3cm from the corner of mouth to the retromolar area showing irregular and indurated margins. It was firm in consistency and fixed to underlying tissue. Mouth opening was reduced to one finger width. Left submandibular lymph node was enlarged, fixed, firm and non-tender on palpation. Orthopantomograph showed the presence of alveolar bone loss in relation to lower left second and third molar (Figure 3). Incisional biopsy was performed and was sent for histopathology. It was then diagnosed as well differentiated squamous cell carcinoma (Figure 4). The patient underwent segmental mandibulectomy along with excision of the lesion.

Figure 1: Blanching on left buccal mucosa.

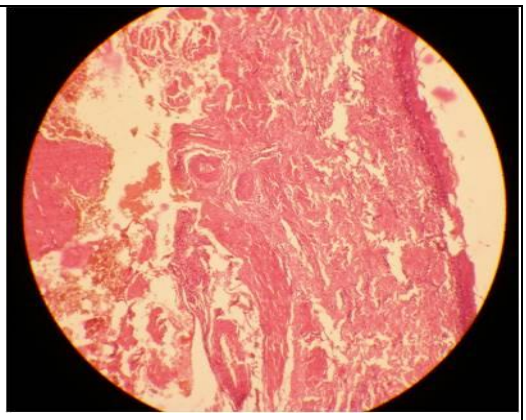

Figure 2: Histopathology showing stratified squamous orthokeratinized epithelium with atrophy of the rete ridges suggestive of grade II OSF

Figure 3: Orthopantomograph showing alveolar bone loss in relation to lower left second and third molar teeth.

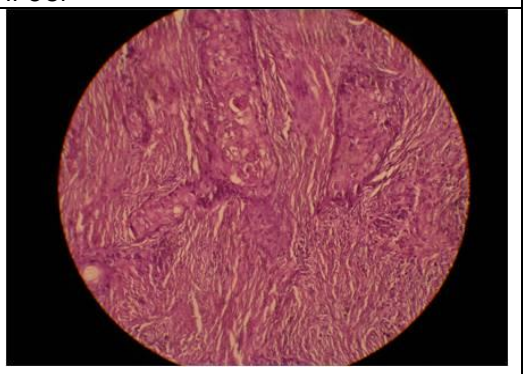

Figure 4: Histopathology shows keratin pearls suggestive of well-differentiated squamous cell carcinoma

DISCUSSION:

OSF is a chronic insidious disease that affects the oral mucosa as well as the pharynx and the upper two-thirds of the oesophagus. It is a well-recognized potentially malignant condition of the oral cavity. Besides being regarded as a precancerous condition, it is a seriously debilitating and progressive disease [5]. Once initiated, the disease is not amenable to reversal at any stage of the disease process even after cessation of the habit. It causes significant morbidity (in terms of loss of mouth function as tissues become rigid and mouth opening becomes difficult) and mortality (when transformation into squamous cell carcinoma occurs) [6].

The strongest risk factor for OSF is the chewing of betel quid (BQ) containing areca nut

[5]. The amount of areca nut in betel quid and the frequency and duration of chewing betel quid are clearly related to the development of OSF [7]. The direct contact of the quid mixture with oral tissues results in their continuous irritation by various components, including biologically active alkaloids (arecoline, arecaidine, arecolidine, guvacoline, guvacine), flavonoids (tannins and catechins) and copper [6]. These chemical components present in areca nut modulate lysyl oxidase enzyme [6]. This increases collagen production and decreases collagen degradation thus leading to an increased fibrosis [6]. The copper content of areca nut is high and the possible role of copper as a mediator of fibrosis is supported by the demonstration of up regulation of lysyl oxidase in OSF biopsies [8]. The fibrosis in the soft tissues leads to trismus, difficulty in eating and even dysphagia as also reported in the present case.

It has been suggested that the areca nut ingredients have tumour-promoting activity [9]. Chemical carcinogenesis is a complex multi-step process including initiation, promotion and progression of tumour [10].

The most important and decisive event of chemical carcinogenesis is the interaction between presumed carcinogens and cellular macromolecules such as DNA, proteins and lipids [11]. Normal oral mucosal epithelial cells are continuously subjected to the attack of genotoxic agents present in betel quid [12]. Antioxidants such as cellular Glutathione (GSH), N-acetyl-L-cysteine (NAC) and enzymes such as glutathione peroxidase, catalase and superoxide dismutase can form conjugates with Reactive Oxygen Species (ROS) and reactive intermediates, thereby degrading reactive toxic species and protecting the critical cellular macromolecules [9]. Repeated and continuous exposure of oral mucosal cells to BQ ingredients, however will lead to the impairment of cellular-defence systems [9].

An excessive amount of ROS, reactive metabolic intermediates from BQ and tobacco can attack cellular DNA and induce various kinds of DNA damage. If the DNA-damaged cells are subsequently induced by proliferative agents to replicate, the DNA damage will remain permanently in the cells, and thereby leading to the formation of mutated “initiated” cells [9]. The further promotion and progression of such initiated cells can lead to the occurrence of oral pre-cancerous lesions and clinical tumours. Since the ingredients of BQ, tobacco have been shown to exert genotoxicity and are crucial for tumour initiation, promotion and progression, exposure to these toxicants simultaneously has been shown to markedly potentiate the oral cancer incidence in OSF patients [13]. Epithelial atrophy in OSF patients increases the penetration of carcinogenic ingredients of BQ and thereby subsequently increasing the incidence rate of oral cancer [2].

It was also observed that gutkha chewing was preferred by people in the age group 11-30 years [14]. It has been reported that the onset of OSF changes occurred earlier with gutkha chewing compared to only areca nut chewing [14]. These findings clearly document the hazard of gutkha chewing.

Since people take to gutkha chewing at a comparatively younger age and as it requires a shorter duration of chewing to precipitate OSMF, there may be an increased risk developing malignant changes in such OSF cases [14].

CONCLUSION:

The case reported here had a history of chewing gutkha which contains both arecanut & tobacco. This has led to the development of OSF and further progression to oral cancer. Documentation of such cases is highly important to make the people aware of the possible hazardous effects of chewing habits and to prevent further progression of OSF to malignancy.

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