

# Oral Submucous Fibrosis in a 15-year-old Boy: The First Case Report in Iran

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## KEY WORDS

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## ABSTRACT

A case of oral submucous fibrosis (OSF) occurring in a 15-year-old Iranian boy is reported. This case is associated with chewing of Supari for a long time. The close association between areca nut chewing and development of OSF with a risk of oral cancer has been demonstrated in many studies. There is no cure for OSF. Education and prevention seem to be the only way to reduce the risk of OSF. This article reviews the etiology, clinical presentation and treatment plan of OSF. This case reveals a correlation between the regular use of Supari (which contains areca nut) and OSF. This association has already been reported among Indian children but in Iran it has not still been reported.

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## Introduction

Oral submucous fibrosis (OSF) is a chronic disease characterized by sub-epithelial collagen deposition with formation of bands involving the oral cavity and adjacent structures. OSF is a precancerous lesion which is associated with chewing of betel quid (Areca catechu, piper-betel, lime and tobacco), Supari and pan which contain areca nut [1-3].

OSF is seen almost exclusively in adults from southern Asia, India and Bangladesh where its occurrence is strongly associated with the oral habit of betel quid chewing. The first clinical sign of OSF is blanching of the mucosal tissues. The presence of the palpable fibrous bands contributes to the diagnosis [1-3].

Progressing fibrosis leads to a reduced oral opening, difficulty in speech, mastication and swallowing as well as impaired tongue function. OSF in women is more common than men [2].

## Case report

A 15-year-old Iranian boy living in Chabahar city was referred to the oral surgery clinic of Zahedan University of Medical Sciences, College of Dentistry, with a complaint of limitation of the oral opening (Figure1-a). He reported that he had chewed Supari and pan since the age of 10. He had used Supari 15 times a day. There was no abnormality on laboratory tests and medical history was normal.

The patient was born in Chabahar, a city in Iran neighboring Pakistan. The patient has visited Zahedan on a regular basis and the first visit was in 2007. He was the eldest of six children. A telephone interview with the parents revealed that there was a long history of tobacco chewing among his parents: the father smokes and chews Supari and the mother consumes chewing tobacco once-twice per day. The patient regularly chews Supari (a sweetened form of areca nut). His family was unaware of



**Figure 1a** Patient with OSF with normal face feature. **b** Sever limitation in oral opening and rigidity of oral mucosa. **c, d** Sever limitation in oral opening.

the harms of Supari or chewing tobacco products, believing that they are natural products which aid indigestion.

Oral hygiene was poor and the dentition required restoration. Intra-oral examination revealed that the buccal mucosa and labial mucosa were pale and fibrous bands could be palpated within the buccal mucosa (Figure 1-b). On examination, mouth opening was restricted to 22 mm as measured from the incisal edges, with an obvious increase in the evidence of fibrosis and banding within the cheeks (Figures 1-c, 1-d). A clinical diagnosis of OSF was made and the patient was once again strongly advised to stop the consumption of Supari.

Management involved reassurance and advice on cessation of arecanut chewing, and use of chlorhexidine 0.2% as a mouthwash twice daily. Regular oral hygiene instruction as well as scaling and polishing were arranged. Treatment plan was surgical intervention but the patient refused. It was only possible to give these instructions directly to the patient. These instructions and further health training advice were given via a telephone interview by the dentist. A follow-up review at the Oral Medicine Clinic was arranged and the patient was referred to the Dental Clinic in Chabahar for routine dental care. Unfortunately, the patient failed to attend several subsequent appointments. He subsequently failed to attend the Oral Medicine Clinic for almost 1 year. However, with a continued history of oral opening limitation he was eventually visited

after one year. At the age of 16, the oral discomfort had led to poor oral hygiene and there was evidence of gingivitis and severe dental caries associated with poor oral hygiene. At that time (August 2008), laboratory tests did not reveal any abnormality.

The patient refused surgical intervention but intra-lesion corticosteroid (dexametasone) was administered. The opening of the mouth improved from 22mm to 26 mm one month after the injection. Unfortunately, he continues to use Supari, and in this respect he accepted that he was at high risk of developing intra-oral Squamous cell carcinoma in the future.

### Discussion

The present study describes the case of oral submucous fibrosis (OSF) in a 15-year-old Iranian boy who used to chew Supari for a long time. The condition predominantly affects Indian women with a female-male ratio of 3:1 which characteristically first presents in adulthood between the ages of 45-54 years [2]. The present report describes an unusual case of OSF presenting in a young Iranian boy who is a resident of Chabahar. Shah [2] also reported a case of OSF in a 11-year-old Bangladeshi girl living in the United Kingdom and Hayes [4] reported OSF in a 4-year-old Indian girl. The etiology of OSF is not well established but there is evidence suggesting that it is multifactorial [1]. A number of irritant factors such as: areca nut chewing [5-8], nutritional factors, genetic disposition and hormo-

nal factors trigger the disease process [2-3].

The areca nut component of betel quid plays an important role in the etiology of OSF [5]. It is chewed throughout India as 'paan supari'. This component is held adjacent to the buccal mucosa and slowly chewed over a long period of time. The present case also chewed Supari for a long time.

Many experimental studies have shown a strong association between OSF and areca nut chewing. A clear dose-dependent relationship was observed for both frequency and duration of chewing areca nut (without tobacco) in the development of OSF [6]. Areca nuts contain alkaloids of which arecoline seems to be a primary etiologic factor. Arecoline has the capacity to modulate matrix metalloproteinase as lysyl oxidases and collagenases, all affecting the metabolism of collagen which leads to an increased fibrosis. During the development of fibrosis, a decrease in the water retaining proteoglycans will occur in favor of an increased collagen type I production [9]. It was revealed that the extracts of arecanut stimulated collagen synthesis by 170% over the control studies [8].

Areca quid chewing habit and the smoking and alcohol consumption alone have been shown to have no effect in the development of OSF [8, 10]. Areca nuts shown to have a high copper content, and chewing areca nuts for 5-30 minutes significantly increases the soluble copper levels in the saliva. This increased level of soluble copper supports the hypothesis that copper acts as an initiating factor in individuals with OSF by stimulating fibrogenesis through up-regulation of copper-dependent lysyl oxidase activity [11]. Further, a gradual increase in the serum copper levels from pre-cancer to cancer patients has been documented [12] which may have a role in the oral fibrosis to cancer pathogenesis.

Iron deficiency anemia, vitamin B complex deficiency, and malnutrition have been implicated in conjunction with other factors. These subjects derange the repair of the inflamed oral mucosa, lead-

ing to defective healing and resultant scarring [1, 13]. The resulting atrophic oral mucosa is more susceptible to the effects of betel nuts and chilies. Although in the present case it was not detected and laboratory tests were normal. Many studies have demonstrated that mucosal atrophy and chronic dysphagia in women who had chronic anemia (sideropenic anemia) has the potential for cancerous change in the oropharynx [2, 14].

There is also evidence of a genetic predisposition of the importance for the etiology behind OSF. Polymorphism of the gene which is coding (coded) for tumor necrosis factor  $\alpha$  caused fibrosis. An increased frequency of HLA-A 10, HLA-B7, DR3 and DR7 has been reported in patients with OSF [1, 2, 12, 14, 9]. There would appear to be a predisposition in females with a female to male ratio of 3:1 [14-15]. Studies have shown increased levels of immunoglobulins such as IgA, IgE and IgD. Autoantibodies to gastric, parietal, and thyroid and anti-nuclear antibodies have been found in 65% of the patients with OSF [1-2, 15].

Some studies have demonstrated increased levels of pro-inflammatory cytokines and reduced anti-fibrotic interferon gamma in patients with OSF, which may be central to the pathogenesis of OSF [16].

Diagnosis of OSF is based on the clinical signs and symptoms including burning sensation (particularly with spicy foods), oral ulceration, blanching of the oral mucosa, and occasional leukoplakia. The most diagnostic feature is the marked vertical fibrous bands formation within the cheeks, and board like stiffness of the buccal mucosa [1-2, 4, 13]. That was detected in the present case. The fibrosis in the soft tissue of the oral cavity results in difficulty eating, trismus, dysphagia to solids (if the esophagus is involved) and limitation in opening of the mouth that was a predominant feature in the present case.

Biopsy of the lesion is rarely performed due to

the observation that such investigation leads to further fibrous scar development and worsening of the symptoms. Thus, the treatment of submucous fibrosis should focus on cessation of the chewing habits. If this is achieved, the early lesions have a good prognosis and might regress. A plethora of treatment strategies have been tried such as topical and systemic steroids, physiotherapy nutritional supplementation with physical devices and surgery.

Successful prevention in the early stages of the condition has been shown to improve the symptoms [1-2, 4, 9, 13]. In this case, intra-lesion corticosteroid injection resulted in an increase in the opening of the mouth. There has been much research concerning administration of topical corticosteroids and improvement of OSF, but this effect is reversible if the patient does not stop the habit [17].

The close relationship between areca-nut chewing and the development of OSF with a risk of oral cancer has been revealed in a number of researches [1-2, 18-20]. A case control study demonstrated that this lesion only occurred among those who chewed areca-nut. However, other factors such as nutrition and genetics play a role. As there is no certain cure for the condition, training and prevention seem the only way to reduce the risk of OSF in the South Asia, India and Bangladesh [21].

The association of this lesion with the development of oral cancer highlights the importance of education in reducing OSF cases. The possible precancerous nature of OSF was first described by Paymaster, who observed the occurrence of squamous cell carcinoma in one third of patients with OSF [19]. Subsequent studies have demonstrated that the occurrence of carcinoma varies in OSF from 2–30% [22]. The chewing of Gutkha (a sweetened mixture of tobacco and betel-nut) and Supari has increased in Chababar. Since Gutkha has widely been available in Chababar for the past 13 years, there is enough evidence indicating the long-term potential adverse effects of this product [23]. The

present case describes the presentation of OSF in teenagers. However, dentists should be reminded of the lesion since it may well be seen more frequently in the future and an active preventive approach is required to hopefully limit the potential for the development of oral malignancy. Therefore, close monitoring of oral mucosa is essential [24].

### Conclusion

OSF in this young boy was difficult to manage due to severe progression of the lesion. In addition, he was found to have a poor attendance and this made managing and monitoring of the condition difficult at the earliest stages. It seems inevitable that his OSF is likely to worsen since he would not appear to be able to stop the use of Supari. If the condition worsens, he may need surgical intervention with grafting in the long term, and there is always the possibility of oral cancer.

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