

CASE REPORT



## Intralesional injections in oral submucous fibrosis - A series of case reports

Tejavathi Nagaraj, Durga Okade, Arundhati Biswas, Poonam Sahu, Swati Saxena

Department of Oral Medicine and Radiology, Sri Rajiv Gandhi College of Dental Sciences, Bengaluru, Karnataka, India

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### Correspondence:

Dr. Arundhati Biswas, Department of Oral Medicine and Radiology, Sri Rajiv Gandhi College of Dental Sciences, Bengaluru, Karnataka, India. Phone: +91-9845451029. E-mail: arundhatibds@gmail.com

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### Abstract

Oral submucous fibrosis (OSMF) is a chronic insidious disease and is well-recognized as a premalignant condition. It is a collagen-related disorder associated with betel quid chewing and characterized by progressive hyalinization of the submucosa. It is a well-recognized potentially malignant condition of the oral and oropharyngeal mucosa with initial inflammation followed by progressive fibrosis of the underlying connective tissues. The aim of this article is to report three cases of OSMF which was treated with intralesional injection of corticosteroids, hyaluronidase, and local anesthesia which showed remarkable improvement in the clinical symptoms.

### Introduction

Oral submucous fibrosis (OSMF) is a chronic, insidious, generalized, and debilitating condition of the oral mucosa predominantly encountered in South-East Asian countries. OSMF is etiologically linked to the consumption of the areca nut in flavored formulations or as an ingredient in the betel quid chewed by the communities in these countries. It is a well-recognized potentially malignant condition of the oral and oropharyngeal mucosa with initial inflammation followed by progressive fibrosis of the underlying connective tissues.

Pindborg *et al.* defined OSMF as, “an insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx, although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxta-epithelial inflammatory reaction followed by fibroelastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat.”<sup>[1,2]</sup>

Is a disease due to a chronic, insidious change in fibroelasticity, characterized by burning sensation in the oral cavity, blanching, and stiffening of the oral mucosa and oropharynx leading to trismus and inability to open the mouth. The symptoms and signs depend on the progression of the lesions and the number of affected sites. It is predominantly seen in Indians and other Asians. Once the disease has developed, there is neither regression nor any effective treatment.<sup>[3]</sup>

### Case Report

#### Case 1

A 50-year-old female reported to the Department of Oral Medicine and Radiology with a chief complaint of reduced mouth opening, discomfort and a burning sensation particularly while eating spicy foods. Patient gave a history of areca nut chewing for 4 years. Patients consumed 6–7 packets for 4 years. Reduced mouth opening was noticed from past 1 month, with discomfort and a burning sensation particularly when eating hot and spicy food. On intraoral examination, diffuse blanched appearance of the oral mucosa was seen. The buccal mucosa was rubbery and inelastic. Vertical bands were palpable in the buccal mucosa with respect to the right posterior molar region on the right side and the retromolar area. Circular band was palpable with respect to the mandibular and maxillary labial mucosa. Oro-dental hygiene was poor. The mouth opening was significantly reduced (measuring 18 mm). The tongue protrusion was significantly reduced. When the patient was asked to blow out air with closed lips, the usual puffed cheek appearance was not seen, suggesting loss of cheek elasticity. General examination was normal. Based on clinical examination, a provisional diagnosis Grade III OSMF was made [Figures 1 and 2]. The patient was treated with biweekly intralesional injections of corticosteroids (2 ml), hyaluronidase (1500 IU), and local anesthesia (2 ml) 8 weeks.



**Figure 1:** Blanching of the left and right buccal mucosa in case 1



**Figure 2:** Restricted mouth opening in case 1

The patient was advised capsules of lycopene 1500 mcg and mouth opening exercises. Patient mouth opening significantly increased (measuring 25 mm) and the burning sensation gradually reduced. Patient was on follow-up for 3 months after the intralesional injections but was lost to follow-up thereafter.

### Case 2

A 40-year-old male reported to the Department of Oral Medicine and Radiology for routine dental checkup. Patient gave a history of pan and betel nut chewing for 15 years. Patients consumed 5–6 pan per day. No history of discomfort and burning sensation was present. On intraoral examination, diffuse blanched appearance of the oral mucosa was seen. Vertical bands were palpable bilaterally in the buccal mucosa with respect to right the retromolar area. The mouth opening was reduced (measuring 25 mm). The tongue protrusion was normal. When the patient was asked to blow out air with closed lips, the usual puffed cheek appearance was not seen, suggesting the loss of cheek elasticity of cheek. Based on clinical examination, a provisional diagnosis of Grade III OSMF was made [Figures 3 and 4]. The patient was treated with biweekly intralesional injections of corticosteroids (2 ml), hyaluronidase (1500 IU), and local anesthesia (2 ml) for 6 weeks. The patient was also advised adjuvant therapy of antioxidant and mouth opening exercises. Patient mouth opening significantly increased (measuring 35 mm). Patient was on follow-up for 1 year after the intralesional injections but was lost to follow-up thereafter.



**Figure 3:** Blanching of the left and right buccal mucosa in case 2



**Figure 4:** Restricted mouth opening in case 2

### Case 3

A 34-year-old male patient reported to the Department of Oral Medicine and Radiology with chief complaint of dislodge restoration. Patient gave a history of gutka chewing for 6 years. Patients used to consume 4–5 pack per day. On eliciting the history, discomfort and a burning sensation while eating hot and spicy food were revealed. Intraoral examination revealed diffuse blanching of the oral mucosa. Vertical bands were palpable bilaterally in the buccal mucosa with respect to the right and left retromolar area. The mouth opening was 36 mm. The tongue protrusion was normal. No loss of cheek elasticity was seen. General examination was normal [Figures 5 and 6]. Based on clinical examination, a provisional diagnosis of Grade II OSMF was made. The patient was treated with biweekly intralesional injections of corticosteroids (2 ml), hyaluronidase (1500 IU), and local anesthesia (2 ml) for 6 weeks. The patient was also advised to take SM fibro 2 times a day for 1 month. Burning sensation and discomfort gradually reduced. Patient was on follow-up for 6 months after the intralesional injections but was lost to follow-up thereafter.



**Figure 5:** Blanching of the left and right buccal mucosa in case 3



**Figure 6:** Restricted mouth opening in case 3

## Discussion

OSMF is a premalignant disorder associated with the chewing of areca nut (betel nut). It is seen that in South Asian populations betel chewing is prevalent and nowadays it also recognized in Europe and North America. Significant morbidity is associated with OSMF and also responsible for mortality after carcinomatous transformation. It is reported in literature that prevalence of OSMF is 2.01% and malignant transformation rate of 2.3–7.6% has been reported in the literature OSMF is associated with inflammation which is followed by hypovascularity and fibrosis, giving the initial appearance as blanching of oral mucosa also called marble-like appearance. This appearance may be diffuse, localized, or reticular. OSMF can also appear as erosions which occurs due to rupture of vesicles.<sup>[4]</sup> In the later stage due to severe fibrosis, there is restriction of mouth opening causing trismus which is characteristic of OSMF. Further problems occur due to submucosal fibrosis of cheeks, pharynx, and upper third of the esophagus leading to dysphagia. Development of fibrous bands in the lip leads to thickening and rubbery appearance. It becomes difficult to retract or evert the lips, which transform into an elliptical shape.<sup>[5]</sup>

Etiology of OSMF is areca nut, chillies, and micronutrient deficiencies of iron, zinc, and essential vitamins. Demonstration of various autoantibodies has given a possible autoimmune

basis to the disease. Genetic predisposition has also been proposed.<sup>[6-10]</sup>

Exact pathogenesis of OSMF is not well established. It is known to be multifactorial in origin. Mechanisms involve increased collagen production and stabilization or decreased breakdown of collagen.<sup>[11]</sup>

There are several factors associated with fibrosis. Increased collagen production is due to production of genetically different fibroblast under the influence of areca nut. Increased cross-linking of collagen through upregulation of lysyl oxidase activity in fibroblasts. Upregulation of lysyl oxidase occurs due to presence of copper in betel nut. Catechin and tannins from the areca nut help stabilization of collagen structure.<sup>[12,13]</sup> Procollagen genes increase collagen production while tissue inhibitor of metalloproteinases and plasminogen activator inhibitor genes inhibit collagenase and thereby decreases collagen degradation, which result in an increase in insoluble form of collagen. Polymorphisms of the genes coding for tumor necrosis factor alpha increase the risk of OSMF. Various studies have shown raised autoantibodies and immune complexes, which tend to indicate the autoimmune basis of the disease.<sup>[11]</sup>

Various classifications have been purposed depending on the clinical features such as by Wahi *et al.*<sup>[14]</sup> who classified OSF on the basis of clinical features, severity, and extent of involvement into three clinical groups; another classification was by Sirsat and Pindborg<sup>[1]</sup> who classified the histological picture of OSF into four stages. Khanna and Andrade<sup>[15]</sup> categorized OSF into different stages considering the clinical features, histological features, and mouth opening of the patients. More *et al.*<sup>[16]</sup> in 2011 provided a clinical staging of OSMF considering the symptoms of the disease and presence of the palpable fibrous bands. Lai *et al.*<sup>[17]</sup> classified patients on the basis of mouth opening. We have staged our patients as per the classification of More *et al.*

Despite so much of progress is done understanding the pathogenesis and treatment of OSF but no known cure is effective. Initial treatment starts with complete stoppage or even reduction of the habit of areca nut chewing. If this is achieved, the early lesions have a good prognosis and might regress with improvement in symptoms. The three main treatment modalities available to treat the patients of OSMF are medical therapy, surgical treatment, and oral physiotherapy. The list of treatment modalities is extensive and includes the use of micronutrients and minerals, CO<sub>2</sub> laser, pentoxifylline, lycopene, interferon gamma, turmeric, hyalase, chymotrypsin, and placental extracts. As fibrosis cannot be reversed when mouth opening is severely reduced, surgical interventions such as myotomy, coronoidectomy, and excision of fibrotic bands have also been reported in literature. Alternatively, procedures such as insertion of stent, physiotherapy, local heat therapy, and mouth opening exercises with acrylic carrots and ice cream sticks have been tried with variable success rates. Kakar *et al.* reported that patients treated with hyaluronidase showed quicker improvement in symptoms but a combination of corticosteroids gave better and long-term results.<sup>[18]</sup> Steroids are well-known immunosuppressive agents for suppression of fibroproductive inflammation found in OSMF.



Hyaluronidase degrades the fibrous matrix promoting the lysis of fibrinous coagulum and activating specific plasmatic mechanism. Relief of symptoms like stiffness in oral cavity occurs through softening and diminishing fibrous tissue.<sup>[7,19,20]</sup> In the above case reports intralesional corticosteroid injection with injection hyaluronidase and local anesthesia was given biweekly to make the treatment easily acceptable by the patient, for better compliance, and it also becomes cost effective for them. The patients showed an increase in mouth opening, relief from symptoms of burning sensation to spicy food, and reduction in oral discomfort along with reduction in stiffness of buccal mucosa which can be taken as a subjective symptom after administration of injections biweekly for 6–8 weeks.

## Conclusion

The cases demonstrate the significant morbidity and mortality associated with OSMF. It highlights the importance of intralesional injection which can comfort the patient and also can effectively reduce the disability and also is cost-effective. Due to the significant cancer risk among these patients, periodic biopsies of suspicious regions of the oral mucosa are essential for the early detection and management of high-risk oral premalignant lesions and prevention of cancer.

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