

## Treatment of Oral Submucous Fibrosis: A Case Report

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### Abstract

**Background:** Oral submucous fibrosis (OSF) is a progressive and inflammatory mucosal fibrosis disease with cancerous tendency. Even though the exact etiology and pathogenesis of OSF have not yet been elucidated totally, the currently recognized pathogenic factor is areca nut. The typical symptoms of OSF patients with limited mouth opening directly affect life quality. Treatments focus on reducing inflammation and improving mouth opening to improve a patient's quality of life. Steroids and corticosteroids are used to treat OSF for a long time because of preventing inflammatory response, reducing fibroblast proliferation, and alleviating collagen deposition. It was also reported that Chinese medicine formulas such as salvia/miltiorrhiza have certain effects in OSF treatment by means of activating blood circulation, removing blood stasis and softening the stiffen oral mucosa.

**Case Presentation:** This case report describes the patient with limited month opening and the 3 years history of chewing areca nuts. The diagnosis of oral submucous fibrosis was confirmed with histopathological examination. With the combined treatment of sublingual compound Danshen dropping pills and topical triamcinolone acetonide for mouth rinse, the patient achieved curative effects of obviously improved mouth opening and soften oral mucosa. And the mechanism of the treatment was discussed.

**Conclusions:** The combined treatment of topical triamcinolone acetonide and sublingual compound Danshen dropping pills may get good effects for OSF patients but need further study.

**Keywords:** Case Report; Compound Danshen Dropping Pills; Oral Submucous Fibrosis; Treatment

**List of Abbreviations:** CBC- Complete Blood Count;  $\text{NaHCO}_3$  - Sodium Bicarbonate; OSF- Oral Submucous Fibrosis

### Background

Oral submucous fibrosis (OSF) is a chronic and latent malignant disease, which poses a global and regional problem to public health, especially in East and Southeast Asia where areca nut chewing is popular. The malignant transformation rate of OSF to oral squamous cell carcinoma ranges from 1.2 to 23% worldwide [1-2]. Current epidemiological studies and evidence indicate that betel nut chewing is one of the most significant risk factors for OSF. The most abundant alkaloid in areca nut, has been proven to induce buccal mucosa fibroblast activation [2-3]. Simultaneously, it can also increase the tissue inhibitors of matrix metalloproteinase-1 which reduces collagen degradation and induces extracellular matrix deposition [1-3]. In addition,

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it has antiproliferative and cytotoxic effects on endothelial cells, which may lead to impaired vascular function, thus participating in the pathogenesis of OSF [1-3]. While the collagen deposition alters in oral mucosa, the compact tissue oppresses the capillaries and block the blood flow that produces a hypoxic environment suitable for the promotion of malignant cell growth [1-3]. According to statistics, OSF generally progresses to oral cancer 3–16 years after the OSF diagnosis [1]. The clinical features of OSF include whitening of the mucous membrane, stiffness, burning sensation, and appearance of characteristic fibrous bands, which are related to the gradual inability to open the mouth. Prodromal symptoms contain a burning sensation in the mouth when eating spicy food, ulcers or recurrent stomatitis, impaired taste, and occasionally dry mouth with blistering pain [1-3]. It should be noticed that many patients with OSF have anxiety, depression, and stress and show weak social interaction, and the incidence is proportional to the severity of the disease [1-3]. The diagnosis of OSF is mainly based on subjective clinical diagnosis, while histopathological examination is still the gold standard [3-4]. Pathological features include chronic inflammation, excessive collagen deposition in the submucosal connective tissue of the oral mucosa, local inflammation in the lamina propria or deep connective tissue, and degenerative changes in muscle [3-4]. For the treatment of this disease, the first choice is to fast betel nut, spicy, tobacco and other stimulants. However, it is difficult to reverse the disease simply by quitting the habit of chewing areca nut in most OSF patients with moderate to severe disease. Steroids and corticosteroids are commonly used to treat OSF. It is reported that Chinese medicine formulas such as salvia/miltiorrhiza have certain effects in OSF treatment [3-5]. Compound Danshen dropping pills are mainly composed of panax notoginseng, borneol and salvia miltiorrhiza, commonly is used by sublingual administration in clinic to promote blood circulation and remove stasis according to Traditional Chinese Medicine [5-10]. This case report describes the OSF patient achieved curative effects with combined treatment of sublingual compound Danshen dropping pills and topical triamcinolone acetonide for mouth rinse, and. There were no similar reports before.

### Case Presentation

A 20-year-old man presented the stomatology department with progressively limited mouth opening, dry mouth and burning sensation. The limitation of mouth opening made it difficult for his daily routine oral cleaning, speaking, and eating. The patient had about 3 year's history of areca nut chewing. The patient denied history of diabetes, hypertension, drug allergy history and family cancer. Oral examination showed that the whitening and stiffen oral mucosa with the appearance of fibrous bands. The mucosa becomes markedly tough on palpation, inelastic and opaque, especially at the sites of premolar region, buccal, soft palate and the pharynx.

The maximum interincisal mouth openings was 30mm. Figure 1 and 2 showed the manifestations of the oral cavity.

Laboratory examination revealed complete blood count (CBC), liver and kidney function, blood lipid and blood glucose were normal. The fungal smear of the oral mucosa and the lesions tested negative. Histological findings: Biopsy of the buccal mucosa on hematoxylin and eosin staining sections showed excessive collagen deposition in the submucosal connective tissue of the oral mucosa and hyaline degeneration of collagen fibers. Figure 3 and 4 showed the histological findings.



Figure 1: whitened and stiffen oral mucosa.

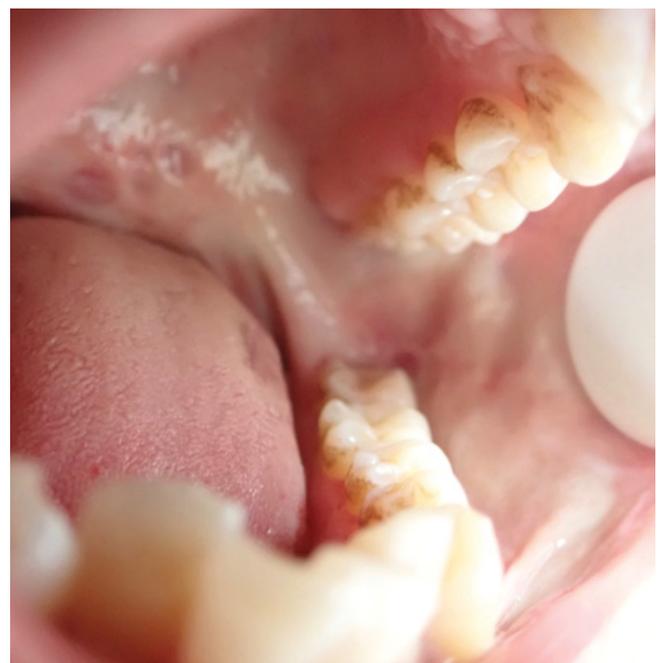


Figure 2: whitened and stiffen oral mucosa.

## Diagnosis

The diagnosis of oral submucous fibrosis was made according to the history of areca nut chewing, the clinical manifestation and histopathological demonstration.

## Treatment

The patient was treated with sublingual compound Danshen dropping pills and topical triamcinolone acetonide for mouth rinse. The therapeutic schedule included sublingual 10 pills of compound Danshen dropping pills each time firstly, and then 0.08% topical triamcinolone acetonide for mouth rinse for 20 minutes, and finally 2% sodium bicarbonate ( $\text{NaHCO}_3$ ) for mouth rinse for 1 minute. Three times daily.

## Follow-up and Outcomes

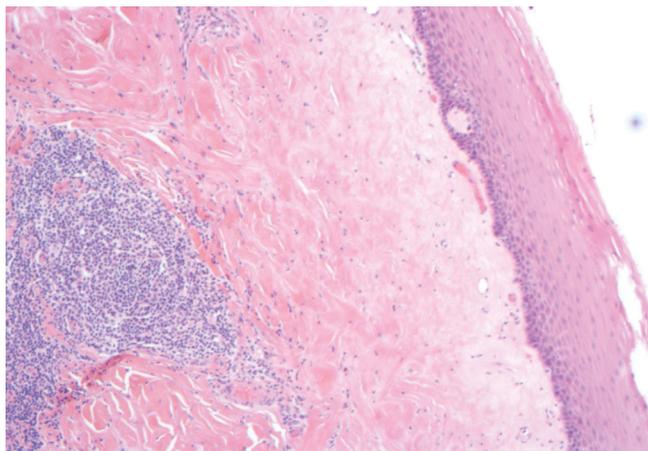
After 3 weeks treatment, the whitening and stiffen oral mucosa started to become pink and soften, the maximum mouth opening improved to 45mm from 30mm. Figure 5 and 6 showed the manifestations of the oral cavity after 3 weeks treatment. And the follow up was continued.



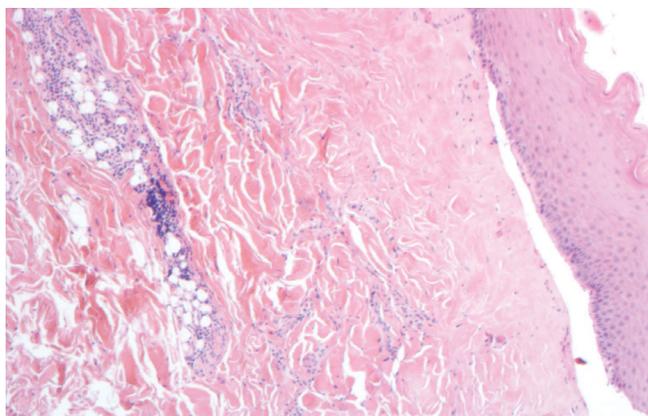
**Figure 5:** After 3 weeks treatment, the whitening and stiffen oral mucosa became pink and soften.



**Figure 6:** After 3 weeks treatment, the whitening and stiffen oral mucosa became pink and soften.



**Figure 3:** Hematoxylin and eosin staining showing collagen deposition in the submucosal connective tissue.



**Figure 4:** Hematoxylin and eosin staining showing hyaline degeneration of collagen fibers.

## Discussion

Oral mucosa whitening is an important clinical feature in the early stage of OSF. In the late stage, mouth opening limitation is caused by fibrosis of oral mucosa area. The maximum average mouth opening of 18–30 years is 56.60 mm for men and 51.04 mm for women in healthy individuals [3]. On functional staging/classification of OSF, the maximum interincisal mouth openings are divided into >20 mm, 11–19 mm, and <10 mm for stage 1 to stage 3, respectively [3]. In this case, the maximum interincisal mouth openings of the patient was 30mm at the beginning. Commonly used drugs include steroids and corticosteroids. Steroids to suppress the inflammatory response in damaged tissues is considered a reliable strategy to limit the development of fibrosis. It was also reported that Chinese medicine formulas such as salvia/miltiorrhiza have certain effects in OSF treatment [3,5]. Compound Danshen dropping pills are mainly composed of panax notoginseng, borneol and salvia miltiorrhiza, which has the effects of regulating Qi, relieving pain, promoting blood circulation and removing stasis according to Traditional

Chinese Medicine [5-10]. This traditional Chinese medicine commonly is used by sublingual administration in clinic to treat cardiovascular diseases such as coronary heart disease. Compared with oral administration, sublingual compound Danshen dropping pills could obtain faster absorption rate and directly acting on the lesions of oral mucosa. It is reported that compound Danshen dropping pills can not only promote the patients' capillary network and microcirculation, accelerate blood circulation, enhance the body's ability to resist hypoxia, but also activate fibrinolysis system and inhibit platelet aggregation [5-10].

The patient's therapeutic schedule was firstly sublingual compound Danshen dropping pills to accelerate blood circulation and improve microcirculation, then followed by 0.08% topical triamcinolone acetonide for mouth rinse for 20 minutes for anti-inflammation. And finally, 2% sodium bicarbonate ( $\text{Na}_2\text{HCO}_3$ ) for mouth rinse for 1 minute to avoid oral fungal infection induced by topical triamcinolone acetonide. After 3 weeks treatment, the patient's symptoms of whiten and harden oral mucosa and mouth opening limitation were obviously relieved. The most common reason for OSF patients to see doctors is the difficulty of mouth opening due to oral mucosal rigidity. The treatment must improve the elasticity of the oral mucosa and mouth opening distance. In this case our combined therapeutic schedule achieved the purpose of alleviating the symptoms of OSF rapidly, with less side effect of triamcinolone acetonide due to topical triamcinolone acetonide administration compared with commonly oral or intralesional injection administration. But there is no doubt that we need further study and more evidence about the combined treatment.

## Conclusions

The combined treatment of topical triamcinolone acetonide and sublingual compound Danshen dropping pills may get good effects for OSF patients but need further study.

## Declarations

### Ethical Approval and Consent to Participate

Not applicable

### Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

### Availability of Data and Materials

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

### Competing Interests

The author has declared that no competing interest exists.

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## Author Contributions

Min Zhao performed the physical examination, oral cavity examination, follow-up visits and multidisciplinary consultation. Min Zhao was the contributor in the biopsy of the tongue and writing the manuscript.

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