

2.5 ORAL SUBMUCOUS FIBROSIS

Introduction

Oral submucous fibrosis is a high risk precancerous condition that predominantly occurs amongst Indians, Indians settled outside India, to a lesser extent in other Asiatics, and sporadically in Europeans. This condition was first reported in India in 1953. In the literature a number of factors that include chillie consumption, areca-nut chewing, autoimmunity, and genetic predisposition have been implicated in the pathogenesis of submucous fibrosis. Now there is convincing epidemiologic evidence implicating areca nut as a causative factor in the pathogenesis of this condition. Some substantiation of this finding from epidemiologic and tissue culture studies is available. The prevalence of submucous fibrosis in random samples of the population in India is up to 0.4%. This indicates that there may be millions of individuals suffering from submucous fibrosis in the country. Although hard data are not available, indications are that this disease is increasing rapidly in India, corresponding to the current upsurge in the popularity of various manufactured areca-nut preparations such as maw a and pan masala (see Appendix 1). Submucous fibrosis affects all parts of the oral mucosa and occurs in both sexes over a wide age range. Nevertheless, there are significant and specific regional variations in this regard.

Definition and criteria

Submucous fibrosis is' a chronic mucosal condition affecting any part of the oral mucosa, characterized by mucosal rigidity of varying intensity due to fibroelastic transformation of the juxtaepithelial connective tissue layer. The presence of palpable fibrous bands is a diagnostic criterion for submucous fibrosis. The fibrous bands occur especially in the buccal mucosa (Fig. 1), retromolar areas, and around the rima oris. When the tongue is affected, it is devoid of papillae



Fig.1. Submucous fibrosis of the right buccal mucosa and the retromolar area in a betel-quinid chewer.

and becomes smooth (Fig. 2). Its mobility, especially the protrusion, is impaired. The opening of the mouth is restricted. In severe submucous fibrosis, the patient cannot protrude the tongue beyond the incisal edges and there is a progressive closure of the oral opening (Fig. 3). Submucous fibrosis must be diagnosed only if palpable fibrous bands are present. Otherwise, other mucosal pathologies such as anemic states are likely to be misdiagnosed as submucous fibrosis.

Clinical aspects

The most common initial symptoms of submucous fibrosis are burning sensation of the oral mucosa aggravated by spicy food (42%), followed by either hypersalivation or dryness of the mouth (25%). The most common and initial clinical sign as well as a regular feature of this disease is blanching, i.e., marble-like appearance of the oral mucosa.



Fig. 3. Shrunken tongue, and the maximal oral opening in a female who has advanced submucous fibrosis.

Localized blanching : Blanching is caused by the impairment of the local vascularity. The disease often starts as a blanched area and palpable fibrous bands develop over time.



Fig. 2. Involvement of the tongue in submucous fibrosis. Note the depapillation.



Fig. 4. Localized blanching in the left buccal mucosa of a female betel- quid chewer who has submucous fibrosis.



Fig. 5. Diffused blanching in the left buccal mucosa of an individual who has submucous fibrosis.

Blanching may be localized (Fig. 4), i.e., limited to an area, diffuse or reticular. The period between the initiation of the habit and the development of submucous fibrosis (incubation period) may range from few months to several decades. This variation may be due to the type of areca-nut chewing habit in addition, of course, to variation in individual response and other unknown factors. For example, in those persons who chew only areca nut (supari), the incubation period is comparatively short, while in betelquid chewers, it is generally long.

Diffused blanching: In diffused blanching a greater part of the oral mucosa is involved (Fig. 5). Blanching may be asymptomatic or accompanied by a burning sensation of the oral mucosa, and salivary changes.

Reticular blanching: Reticular (lace-like) blanching consists of blanched areas with intervening, clinically normal mucosa (Fig. 6), giving it a lace-like appearance. Over a period of time, one type of blanching may

change into another. Microscopically, biopsies from the blanched mucosa without palpable fibrous bands(not yet categorized as submucous fibrosis) show features



Fig. 6 . A reticular blanching in the right buccal mucosa. This form of blanching must be distinguished from reticular lichen planus.

Fig. 7 . Labial mucosal involvement characterized by blanching and pigmentation changes.



suggestive of early submucous fibrosis. Nevertheless, to avoid over-diagnosis, submucous fibrosis should be diagnosed only on the basis of the presence of palpable fibrous bands.



Fig. 8 . Elliptical oral opening in a patient with moderately severe submucous fibrosis.

Submucous fibrosis at different intraoral locations

Labial mucosa: Submucous fibrosis can affect any or all parts of the oral mucosa. However, in certain geographic areas of India, some intraoral sites are more frequently affected than others. Overall, the labial mucosa is involved in about 36% of the cases. The affected mucosa is blanched, becomes rubbery, and exhibits difficulty to evert (Fig. 7).

Elliptical rima oris: In oral submucous fibrosis, when the lips are involved, the connective tissue and muscle bands in the lips run around the rima oris like a thin band. In severe labial involvement, the opening of the mouth is altered to an elliptical shape (Fig. 8).

Buccal mucosa: In all geographic areas the buccal mucosa is the most commonly involved (98%) site in submucous fibrosis. The affected buccal mucosa becomes coarse



Fig.9. A severe and generalized buccal mucosal involvement in Ernakulam District. Note the fibrous bands(arrow).

and inelastic. In advanced cases, the mucosa becomes tough and leathery, with numerous vertical fibrous bands(Fig. 9). Involvement of the buccal mucosa can be graded as mild,



Fig. 10. Early tongue changes in submucous fibrosis marked by depapillation and blanching.

Moderate, and severe, depending on the extent and prominence of fibrous bands. In some geographic areas, for instance in Maharashtra and Gujarat, the posterior part of the buccal mucosa may be involved to a severe extent, yet leaving the remaining buccal mucosa rather unaffected.

Tongue involvement : The initial change in submucous fibrosis of the tongue is depapillation, usually towards the lateral margins (Fig. 10) . This feature may be accompanied by blanching and other



Fig. 11. Blanching on the ventral surface.

Symptoms. Overall, the tongue is involved in 37% of the cases; however, there is a marked regional variation. For example, in Ernakulam, 55% of the 64 individuals with this condition had tongue involvement, while it was present in only 2% of the 60 individuals with this disease in Bhavnagar District.

Blanching on the tongue : Blanching may involve the ventral surface (Fig. 11) or the entire tongue (Fig. 12).



Fig.12. Involvement of the tongue marked by extensive blanching and depapillation.

The floor of the mouth: When affected, the floor of the mouth is blanched and inelastic (Fig. 13). Overall, this location is involved in 29% of the cases. While 22% of individuals with submucous fibrosis in Emakulam had involvement of the floor of the mouth, none of the submucous fibrosis patients in Bhavnagar, showed this change.

The soft palate: Involvement of the soft palate is marked by fibrotic change and a clear delineation of the soft palate from the hard palate as if a "heavy curtain" is hanging from the hard palate (Fig. 14). Overall, the soft palate is affected in 49% of the cases;

but in some areas in India it is very commonly affected. This observation probably prompted some earlier investigators to speculate that submucous fibrosis started in the soft palate and the posterior part of the oral cavity, and then spread anteriorly. However, later studies showed that such an observation represents a regional variation rather than the general pathogenesis of this condition. For example, soft palate was involved in only 12% of the patients in



Fig. 13. Floor of the mouth involvement in Emakulam. Note the blanching on the ventral surface of the tongue.

Emakulam , while 95% of the patients in Bhavnagar and an equally high proportion of cases in Pune District had involvement of the soft palate.

The uvula : The uvula is affected in about 17% of patients; in Emakulam, it was affected in 8% compared to 55% in Bhavnagar. When involved the uvula is



Fig. 14. Characteristic fibrotic soft palate in submucous fibrosis. Note the clear demarcation of the hard and soft plates.

sunken, and in extreme cases it becomes bud-like (Fig.15). It is hypothesized that the regional variations in the affection of specific intraoral sites are due to differences in the type of areca nut used and the chewing practices prevalent in those regions.

The gingival : When the gingival is affected, it is fibrotic, blanched and devoid of its normal stippled appearance (Fig. 16).

Fig. 15 . Bud-like uvula in submucous fibrosis.

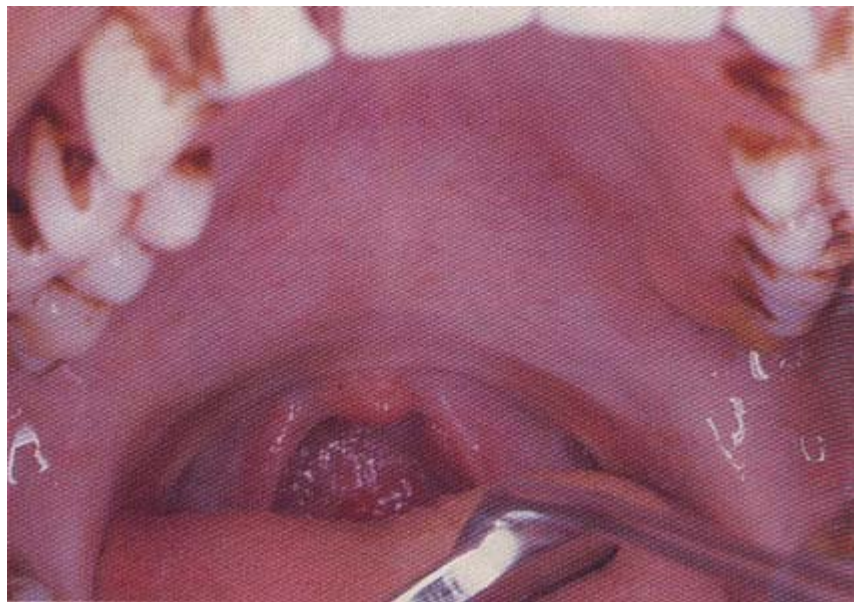




Fig. 16. Gingival involvement in submucous fibrosis. Note the blanching and absence of normal stippled appearance.



Fig. 17. Loss of pigmentation and blanching of the lower labial mucosa in an individual with submucous fibrosis. Note. The blached and fibrotic gingival.

Associated features

Pigmentation changes: A variety of associated features are seen in submucous fibrosis. Of these, hyperpigmentation or loss of pigmentation is very common (Fig. 17). Many a times pigmentation changes on the vermillion border are so striking that this disease can be suspected even before examining the patient.

Vesicle: The presence of vesicles or a history of vesicle formation is reported in 32% of the cases. These vesicles are small (Fig. 18) and subepithelial; they rupture easily because of the masticatory trauma. Often, there is a history of vesiculation following the intake of spicy food, suggesting an allergic reaction to spicy food. Interestingly, certain histologic features of the vesicle also suggest an allergic reaction. Nevertheless, there is no evidence, as yet, to implicate allergic response as the

primary pathogenic mechanism in submucous fibrosis.

Ulceration: Patients with submucous fibrosis often (43%) complain of ulceration (Fig. 19) which is more marked in advanced cases.



Fig. 18. A vesicle (arrow) in the lower labial mucosa in a female who has submucous fibrosis. The patient could not tolerate spicy food. Note the blanching of the lip.



Fig. 19 . Ulcerations on the tongue in a female who has submucous fibrosis. Note the shrunken tongue that is devoid of lingual papillae.

Microscopically, the epithelium is atrophic in this condition, and in advanced cases it is often “ribbon-like”. This possibly renders the

epithelium fragile and vulnerable to ulceration.

Petechiae: Petechiae are small, raised reddish blue-spots that occur in the mucosa in various disorders. These were observed in 22% of the submucous fibrosis patients in Emakulam. Petechiae may be few or many, and they occur most commonly on the tongue (Fig. 20), the labial and the buccal mucosae. Petechiae in submucous fibrosis do not represent a hematologic disorder; they occur due to the loss of connective tissue support to the juxtaepithelial vasculature, leading to their dilatation and the extravasation of blood into the tissue. The petechiae are transient in nature, and no specific treatment is necessary.

Diagnostic pitfalls

Oral submucous fibrosis has a characteristic clinical appearance and there are very few conditions that need to be differentiated from it. One is oral manifestation of scleroderma. Compared



Fig. 20 . Petechiae on the tongue in a female who has submucous fibrosis. Note the extraoral pigmentation changes consisting of hyper- and loss of pigmentation.

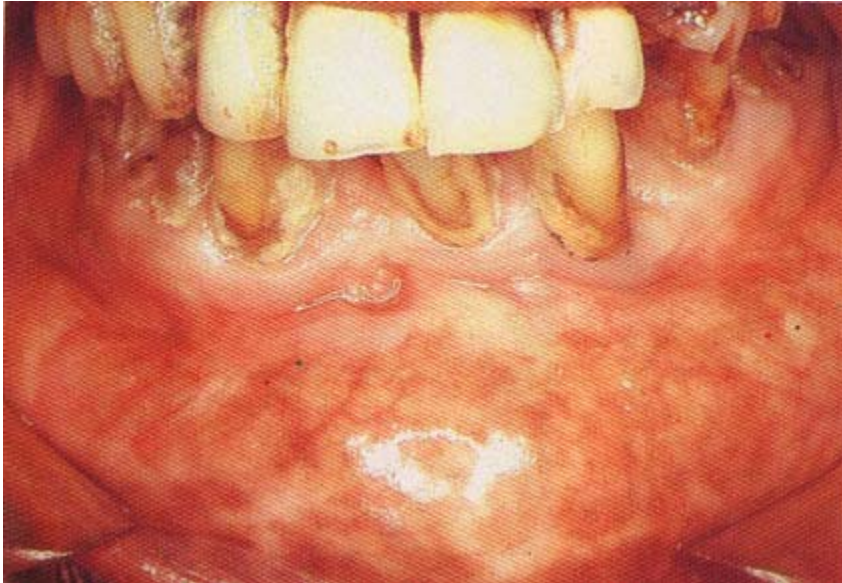


Fig.21. Pigmentation and anemic pallor on the labial mucosa and the gingival in a male who had severe iron deficiency anemia. The patient as treated for anemia, following which the mucosal pallor disappeared.

to submucous fibrosis, however, the occurrence of scleroderma is rare, and rarer still is the oral involvement in scleroderma. More often, pale mucosa, coupled with pigmentation seen in anemic conditions, may be mistaken for blanching in submucous fibrosis.

Pale mucosa in anemia: In severe anemic condition, the oral mucosa is pale (Fig. 21) and hyperpigmented, the tongue is depapillated, and the buccal mucosa is coarse. These features can lead to the misdiagnosis of anemic mucosal pallor as submucous fibrosis, particularly if the criterion of palpable fibrous bands is not followed.

Blanching: Sometimes when blanching is well-circumscribed, i.e., localized, it can be mistaken for a leukoplakia, particularly in the absence of other clinical features of submucous fibrosis (Fig. 22).

Natural history

Unlike precancerous lesions, submucous fibrosis is not known to regress, either



Fig.22. Blanching on the right buccal mucosa without any other feature of submucous fibrosis. In about three years, the blanching extended to other intraoral locations and subsequently fibrous bands developed in the buccal mucosa.

spontaneously, or with the cessation of the areca-nut chewing habit. This condition may either remain stationary or become severe, and also involve additional areas of the oral mucosa. The most serious aspect of this disease is the high risk for the development of oral cancer. As mentioned previously, the epithelium is atrophic in this condition which renders it susceptible to the action of carcinogens. The observations upon which submucous fibrosis is considered precancerous are: (1) higher prevalence of leukoplakia in submucous fibrosis patients (26% versus 1-4% in the general population) (Fig. 23); (2) coexistence of submucous



Fig. 23. An extensive homogenous leukoplakia in the right buccal mucosa of a patient who has submucous fibrosis.

fibrosis and oral cancer (Fig. 24); (3) higher frequency (26%) of epithelial dysplasia; (4) high incidence of malignant transformation (Figs. 25 &26), and (5) the histologic diagnosis of oral cancer in submucous fibrosis without clinical suspicion for it.



Fig. 24. An exophytic cancer on the lateral border (more towards the tip) in a male who has submucous fibrosis. This is a somewhat unusual location for cancer. The tongue was also devoid of its papillae and there was an extensive homogenous leukoplakia on the dorsum.

Submucous fibrosis and coexistent leukoplakia: Leukoplakia is a precancerous ! lesion; its coexistence with submucous fibrosis implies the high risk for oral cancer in submucous fibrosis patients. More frequently, homogeneous and nodular leukoplakias occur in submucous fibrosis (Fig. 23).

Submucous fibrosis and coexistent oral cancer: Not uncommonly (in 5% to 42% of the cases), submucous fibrosis and oral cancer coexist (Fig. 24). As submucous fibrosis is generally a disease of long duration, the presence of oral cancer implies that it is a later development, i.e., a consequence of the malignant transformation of submucous fibrosis.

Malignant transformation: Long-term population based studies have confirmed the precancerous nature of submucous fibrosis. For example, in a 17-year follow-up study in

Ernakulam District, oral cancer developed (Figs. 25 & 26) in 7.6% of submucous fibrosis cases. Another study showed a very high relative risk (397.3) for the development of oral cancer in submucous fibrosis when compared to individuals who had tobacco habits, but did not exhibit any lesions. As mentioned previously, in submucous fibrosis patients, cancer may develop from locations which are otherwise uncommon for cancer, for example, the dorsum and tip of the tongue,



Fig. 25. Submucous fibrosis in a 52-year old female betel-quid chewer. There was a coexistent nodular leukoplakia in the lower labial mucosa and the right buccal mucosa. A biopsy from the leukoplakia showed epithelial dysplasia.

indicating the strong influence of the disease in malignant transformation.

Conclusions

Several therapeutic and surgical methods have been tried in the treatment of submucous fibrosis. Following therapy the oral mucosa should regain and retain its normalcy, and

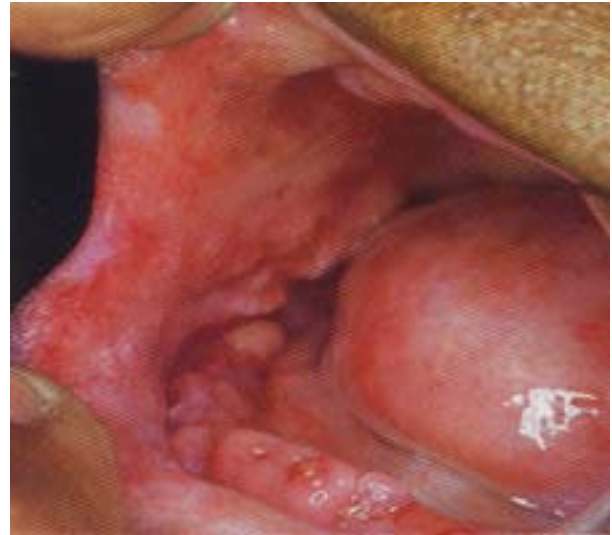


Fig. 26. Four years later, there was an ulceration in the posterior part of the right buccal mucosa in the case shown in Fig. 25 which was microscopically confirmed as a squamous cell carcinoma.

there should be a reduction in the risk for oral cancer. However, no such definitive and widely accepted treatment is currently available for this condition. Some temporary relief from the symptoms and improvement in the oral opening with medicinal treatment such as local injections of cortisone and placentex, has been observed. In view of the lack of availability of curative treatment, and the precancerous nature of this disease, it is essential to follow-up the patients regularly. Furthermore, they must be educated to discontinue the use of areca nut and tobacco in any form, with the aim of preventing further progress of the disease and perhaps reducing the risk of oral cancer. Encouragingly, submucous fibrosis is amenable to primary prevention. Intervention studies have demonstrated a reduction in the development of new cases of submucous fibrosis (incidence cases) when areca-nut chewing habits are discontinued.

