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CLINICAL ASPECTS OF ORAL SUBMUCOUS FIBROSIS

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During the last decade several investigations of a peculiar oral disease mainly observed in India, have been reported. The condition has not yet been described in the dental literature outside of India and different opinions are held on several aspects of the disease. It may, therefore, be helpful to review the literature and add a description of 25 new cases. In subsequent papers histologic features of the disease will be described.

PREVIOUS INVESTIGATIONS

Terminology

In 1952, *Schwartz* described 5 Indian women, from East Africa, with "Atrophia idiopathica (tropica) mucosae oris". From India herself came a report in 1953 by *Joshi*, who coined the term "Submucous fibrosis of the palate and pillars". Other names suggested are "Diffuse oral submucous fibrosis" (*Lal* 1953), "Idiopathic scleroderma of the mouth" (*Su* 1954), "Idiopathic palatal fibrosis" (*Rao* 1962), and "Sclerosing stomatitis" (*Behl* 1962). In the present paper the term of submucous fibrosis (s.f.)

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will be used, because it is widely accepted. The disease may affect several areas of the oral mucosa and pharynx, but affections elsewhere in the body have not been described so far.

Race, sex, and age

No information is available with regard to the overall frequency of s.f. in the Indian population. Examination of 3 large population groups have revealed a higher frequency than expected, viz., about 0.5 per cent (*Pindborg 1964*).

Table 1.

Distribution of oral submucous fibrosis according to geographic location, sex, and age in various investigations.

Investigator	Year	Country	Material	Percentage women	Age range in years
Schwartz	1952	East Africa (Indians)	5	100	?
Lal	1953	India (Madhya Pradesh)	20	?	?
Joshi	1953	India (Bombay)	41	54	10—60
Su	1954	China (Taiwan)	3	0	30—40
Rao & Raju (Lalchand in discussion to Rao & Raju)	1954	India Nepal	7 15	86 ?	18—40 ?
DeSa	1957	India	64	53	10—55
Sharan	1959	India	21	males predominated	12—62
Rao	1962	India (Hyderabad)	46	63	12—64
Sirsat & Khanolkar	1962	India (Bombay)	85	53	10—58
Present investigation	1964	India (Lucknow)	25	60	♀: 22—65 average: 33.7 yrs. ♂: 40—70 average: 53.6 yrs.

Table 1 shows the geographic distribution of the cases of s.f. published so far. The disease is seen in Indians only, except for 3 Chinese men reported by *Su* 1954 and some Europeans living in Hyderabad, mentioned by *Rao* 1962. In a discussion of *Rao & Raju's* paper from 1954 *Lalchand* reports that he saw 15 cases in Nepal during 25 days. No caste or religious group is especially affected. With regard to sex, an equal distribution was found in the largest material published so far (*Sirsat & Khanolkar* 1962) and in *DeSa's* material (1957). A predominance of women has been recorded by *Schwartz* 1952 (5 patients), *Rao & Raju* 1954 (7 patients) and *Rao* 1962 (46 patients). Male predominance was observed by *Sharan* 1959 (21 patients). There seems to be a rather wide age range, although a majority are in the 20 to 40 age group. *Paymaster* 1956 finds, however, that usually younger persons are affected. The disease affects poor as well as well-to-do people.

Symptoms

Prodromal symptoms

The onset of the condition is insidious and is often of two to five years' duration. According to most authors, the first symptom is a burning sensation of the oral mucosa and inability to eat spicy food. A number of patients also complain of "stomatitis" in the early stages.

Later symptoms

After varying periods of time, in some cases a few years after the initial symptoms, the patients complain of stiffening of certain areas of the oral mucosa, leading to inability to protrude the tongue and to whistle or to blow out a candle. Furthermore, fibrosis of the mucosa behind the molars and the pterygo-mandibular raphe causes a trismus. The patients suffer difficulties in swallowing. *Su* (1954) also mentions dryness of the mouth. When the fibrosis reaches the pharynx, referred pain in the ears may be experienced (*Rao* 1962). The same author finds deafness in one third of the patients, due to occlusion of the Eustachian tubes. *DeSa* (1957) mentions a nasal voice as one of the later symptoms in some patients.

Clinical findings

Palate and faucial pillars

These areas of the oral mucosa are ordinarily the first ones affected in s.f. Often the disease begins with stomatitis and occasionally with vesicles on the hard palate and cheek (*Joshi* 1953, *DeSa* 1957, *Sirsat & Khanolkar* 1962, *Pindborg & Singh* 1964). The mucosa then becomes blanched, slightly opaque white, and scar-like formations, consisting of a white network, are seen especially in the lateral parts of the soft palate at the junction of the pillars with the soft palate. The uvula is often reduced in size. On palpation the mucosa feels stiff and inelastic, and the soft palate has reduced mobility. The fibrosis extends into the pillars, which become thick and short. The tonsils are pressed between the fibrosed pillars (*Joshi* 1963). Sometimes the condition spreads to pharynx and down to the pyriform fossae.

Buccal mucosa

In the majority of the patients, the buccal mucosa is also affected. The mucosa is whitish and firmly attached to the underlying tissue. Firm vertical fibrous bands can be felt in the regions opposite the premolars (*Lal* 1953). Sometimes the changes are unilateral.

Tongue

All observers have noted involvement of the tongue, which becomes tied. Thirty of *Rao's* 46 patients demonstrated inability to protrude the tongue, whereas only 9 per cent of *DeSa's* patients exhibited this feature.

Trismus

Two authors (*DeSa* 1957 and *Rao* 1962) have measured the degree of trismus seen in s.f. In contrast to a normal opening of 4.1 cm, *DeSa* found the average opening in s.f. to be 2.6 cm. *Rao* finds that the space between the incisal edges of the upper and lower incisors is reduced to 4—6 mm. *Sirsat* (1958) has reported on deviation of the jaw in opening due to a unilateral involvement of the pterygomandibular raphe.

Laboratory findings

In more than half of his patients *DeSa* (1957) observes an increased blood sedimentation rate. *DeSa* as well as *Sirsat & Khanolkar* (1962) report a marked anemia in patients with s.f., whereas *Rao* 1962 found a microcytic anemia in half of the patients and *Paymaster* (1956) only a moderate anemia. Increased γ -globulin is reported by *DeSa* and *Sirsat & Khanolkar*, whereas *Rao* (1962) finds normal values. All investigators, however, agree that there is an eosinophilia in patients with s.f.

Submucous fibrosis as a precancerous condition

In one third of his material of s.f., *Paymaster* (1956) finds slow-growing squamous cell carcinoma. In contrast, *Sirsat & Khanolkar* (1962) have observed only 6 cases of leukoplakia and 4 cases of carcinoma among 85 patients with s.f.

Etiology

The etiology of s.f. is obscure. The clinical picture of stiffness and immobility of the oral mucosa and the histologic changes in the connective tissue suggest a comparison with the oral involvement in scleroderma, one of the collagen diseases. There are also marked histologic similarities with other connective tissue disorders. In s.f., however, there is neither indication of cutaneous involvement nor visceral spreading.

Suspecting that the pathogenesis of s.f. might lie in the continuous prolonged action of a mild irritant, *Sirsat & Khanolkar* (1960) subjected rat palates to painting with capsaicin. Capsaicin is the active irritant principle of chillies, which makes the Indian food spicy. The experiments showed that in the unimpaired animal capsaicin arouses only a limited connective tissue response. In protein-depleted or vitamin B-deficient animals the response was more widespread and serious.

Another Indian habit, chewing of betel nut, has also been suspected of playing a role in the production of s.f. (*Lal* 1953, *Sharan* 1959). *Sirsat & Khanolkar* (1962 a) tested this by applying arecoline, the most important alkaloid in the betel nut, to the oral mucosa of rats and concluded that arecoline probably plays no significant role in the causation of human s.f.

At present it is not possible to state, whether, if the mild irritant is a causative agent, it acts as an immediate stressor or acts indirectly as an allergen (*Sirsat* 1958).

Treatment

Several procedures have been tried in the treatment of s.f., such as surgical cutting of the fibrotic bands, and/or injection of fibrolysis, gold or vitamins A and E (*Rao* 1962). Only cortisone and its latest purified derivatives have helped. Both *DeSa* (1957) and *Rao* (1962) recommended the combined use of systemically administered corticosteroids and locally injected hydrocortisone. Improvement does not, however, seem to be permanent. In 1953 *Joshi* reported some relief from injections of arseno typhoid and large doses of iodides internally.

OWN INVESTIGATIONS

Material

During an epidemiologic study of oral "white lesions" carried out at the Dental College, Lucknow, 25 patients suffering from submucous fibrosis were subjected to a detailed investigation.

Sex, age, and oral habits

Fifteen were women and 10 were men. The age of the women ranged from 22 to 65 with an average of 33.7 years. For the men, the age range was 40 to 70, with an average of 53.6 years. 18 patients were Hindus and seven were Moslems.

From 24 patients information was obtained as to oral habits. Nine types of habits were noted. Pan* with tobacco: 8 patients, pan with tobacco plus bidi-* or cigarette-smoking: 4; pan with

* Pan is a preparation of betel leaf, betel nut (raw or cured), slaked lime and catachu. This combination is chewed with or without tobacco. The bolus formed by chewing the preparation is either spat out, swallowed or kept in the mouth for hours, sometimes during sleep also. There are differences in the variety of the betel nut, tobacco, and lime used in different regions of India.

** Bidi is an Indian form of a cheap cigarette. In Lucknow, Uttar Pradesh, it is made by rolling between the fingers a rectangular dried piece of Temburni (*diospyros melanoxylon*), also called Tendu leaf, with 0.30 to 0.36 gm of Saurashtra tobacco (from the State of Gujarat) or Nipani tobacco (from the State of Mysore) and finally roped with thread. The length of the bidis varies from 4 to 7.5 cm.

tobacco plus pure tobacco-chewing: 3; pan with tobacco plus pure tobacco-chewing plus bidi-smoking: 2; pan without tobacco: 2; tobacco-chewing plus bidi-smoking: 2; bidi-smoking: 1; pan occasionally: 1; and betel nut-chewing plus cigarettes: 1.

Symptomatology

Six patients experienced symptoms within 1 to 8 months before examination. 19 patients stated to have had symptoms from 1 to 25 years prior to examination.

The most common first symptom seen in 13 out of 25 cases seemed to be a burning sensation in the mouth, often experienced when eating spicy food. Another initial symptom in 8 patients was the occurrence of blisters, especially in the palates, ulcerations or recurrent stomatitis. Other early symptoms were excessive salivation (3 patients), dryness of the mouth (1), referred pain (5), and swelling of the oral mucosa (2).

In the later stages, when the oral mucosa became less movable, the patients complained about difficulties in opening the mouth (9 patients) and about increasing stiffness of the mucosa (2). One patient suffered from dysphagia. In 2 patients no symptoms were reported.

Clinical findings

Vesicles were seen in the buccal mucosa of only one patient. In two others, small superficial erosions were present in the palates.

Pathologic changes were observed in the buccal mucosa of all patients. All patients except two had bilateral lesions. In all patients but one the changes consisted of fibrous strands running in a vertical direction. The fibrosis was sometimes so marked that the cheeks were almost immovable. The mucosa had a blanched, opaque appearance, quite often with scattered red areas and irregular melanin pigmentation (color plate A). The mucosa then took on a marble-like appearance. Two patients exhibited fiery red areas, 10×10 mm, strongly suspicious of malignancy. Biopsy was allowed in one of these patients and it revealed squamous cell carcinoma.

Palate and faucial pillars

In 19 patients, the palates and the anterior faucial pillars were fibrosed, in most cases accompanied by a blanched mucosa. In the majority of patients the fibrosis in the soft palates was easy to recognize, because the changes led to scarlike contractions of the mucosal surfaces (color plate B). The uvulae were very markedly involved by the fibrotic changes and often presented themselves as small fibrous buds. When the patients attempted to move their soft palates, it became obvious that the mobility was markedly reduced.

Lips

The mucosa of the lower lip was affected in 10 patients, whereas the upper labial mucosa was affected in only 3 patients. The changes were the same as those observed in the buccal mucosa (color plate C).

Tongue

The mobility of the tongue was reduced in two patients. Atrophy of most of the dorsal papillae was seen in 5 patients (color plate D), and 5 other patients exhibited a marginal atrophy. Sometimes the atrophic areas had a blanched appearance.

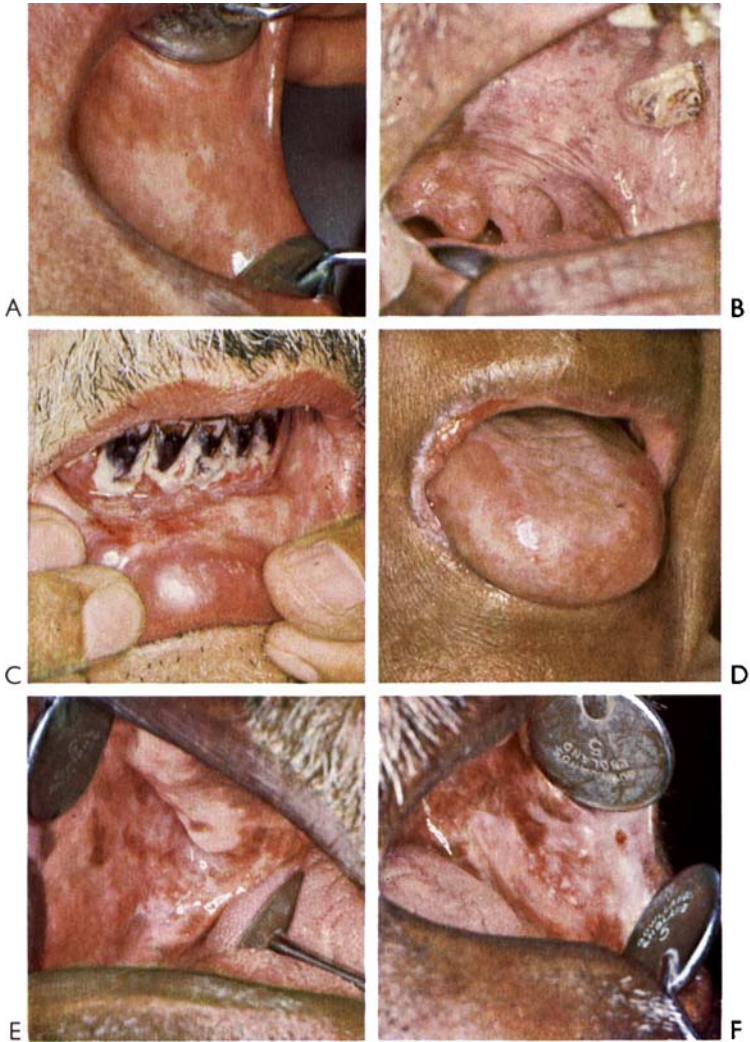
Leukoplakia

In 7 patients leukoplakias were found in areas of fibrosis (color plate E and F), in one a papilloma (which, histologically, turned out to be a carcinoma) had developed in the leukoplakia. In 3 patients the leukoplakias occurred simultaneously with red areas.

Trismus

In order to evaluate the difficulties in mouth opening, the distances between the incisal edges of the upper and lower central incisors and between the cusps of the first premolars were measured. In 4 men the average opening in the incisor region was 2.9 cm and in the premolar region 2.7 cm. In 13 women the corresponding values were 3.2 cm and 2.6 cm. In the most severe case the openings were reduced to 0.6 and 0.5 cm. The values in 10 normal men in the same age group were 4.9 cm and 4.2 cm and in normal women 4.3 cm and 3.7 cm.

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Oral manifestations in submucous fibrosis

- A. Blanched area in left cheek. B. Scarlike contractions in soft palate.
- C. Blanched areas and scarlike contractions in lower lip. D. Atrophy of tongue papillae. E. Loss of pigment and leukoplakia in right cheek.
- F. Blanched area and scattered leukoplakias in erythematous area.

Laboratory findings

In twenty patients erythrocyte sedimentation rate, hemoglobin, and differential leucocyte count were determined. γ -globulin estimations were made in 6 patients. In 17 patients the sedimentation rate was raised; in 7 there was a mild anemia (hemoglobin 10 to 12 gms %), and in one a moderately severe anemia (hemoglobin 8.5 gms %). The differential leucocyte count revealed neutropenia in 7 patients and a slight increase in eosinophils in 3 patients. The γ -globulin in all 6 patients was within the normal range for East-Indians as reported by *Kumar et alii* (1959).

DISCUSSION

In the present material, there were slightly more women (60 per cent) than men. This is in accordance with most of the previous investigations. The age range also agrees with findings in other reports. Men seem to be affected later in life than women. There seems to be no preference with regard to religion.

The presence of oral habits poses some interesting questions as to the etiology of s.f. Because of the occurrence of the disease in betel-chewing areas, this habit has been assigned some etiologic significance, although *Sirsat & Khanolkar* (1962 a) on the basis of negative results in rat experiments have denied this possibility.

The present investigation confirms the opinion that s.f. has an insidious onset. It is extremely difficult to obtain reliable information as to the exact nature of the initial symptoms. Descriptions like "sore mouth", "inflammation of the mouth", and "ulcerations" may very well refer to the occurrence of vesicles which had remained intact for short periods of time due to the moist environment and frequent traumata.

In our study the clinical signs seem to differ from those in other reports in the following respects, (1) among 25 patients only 2 had restricted tongue movements, (2) the presence of papillary atrophy of the tongue in 10 out of 25 patients, and (3) we found the marblelike appearance of the buccal mucosa of great diagnostic help. The changes in color are due to variations

in fibrosis and thickness of the epithelium. (For details see *Pindborg et alii* 1965 b).

Leukoplakia was found in 7 of the 25 patients. The overall frequency of leukoplakia among the patients seeking the admission clinic at the Dental College, Lucknow, is 3.8 per cent (*Pindborg et alii* 1965 a). Thus, it seems likely that the s.f. predisposes to leukoplakia. Whether s.f. is a precancerous condition cannot be decided upon through the present investigation. There was, however, clinical suspicion of malignancy in 2 patients, and there was one proven case of squamous cell carcinoma.

The hematologic investigations in our series demonstrated an increased erythrocyte sedimentation rate and a mild neutropenia. Anemia was present in about 40% of the patients. In contrast to the findings by *DeSa* (1957), *Rao* (1963), and *Sirsat & Khanolkar* (1962) a peripheral eosinophilia was not significant in our series.

SUMMARY

The literature on oral submucous fibrosis is reviewed and 25 new cases are presented. The disease occurs almost exclusively among Indians. Women are affected slightly more often than men and apparently at an earlier age. The onset of the disease is insidious. Initial symptoms are burning sensation of the mouth and occurrence of vesicles. Later, the oral mucosa, especially in the cheek, the soft palate, the anterior faucial pillars, and the lower lip assumes a blanched appearance. The mucosa stiffens and fibrous bands develop. The tongue may present atrophy of the papillae. In 7 patients there was a concomitant leukoplakia. Submucous fibrosis may predispose to development of leukoplakia. A restriction of mandibular movements was found.

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RÉSUMÉ

ASPECTS CLINIQUES DE LA FIBROSE SOUS-MUQUEUSE DE LA CAVITÉ BUCCALE

Les auteurs passent en revue la littérature sur la fibrose sous-muqueuse de la cavité buccale et présentent 25 cas nouveaux. Cette affection apparaît presque exclusivement chez les Indiens. Elle atteint un peu plus souvent les femmes que les hommes, et, semble-t-il, à un âge moins avancé. Le début de la maladie est insidieux. Les symptômes initiaux sont des sensations de brûlure de la bouche et la présence de vésicules. Ensuite, la muqueuse buccale, particulièrement sur les joues, le voile du palais, les piliers antérieurs du voile et la lèvre inférieure, prend une apparence décolorée. La muqueuse perd sa souplesse et des bandes fibreuses se développent. La langue peut présenter une atrophie des papilles. Chez 7 des patients, il existait en même temps une leucoplasie. La fibrose sous-muqueuse peut prédisposer au développement de la leucoplasie. Une limitation des mouvements de la mandibule a été constatée.

ZUSAMMENFASSUNG

KLINISCHE GESICHTSPUNKTE HINSICHTLICH DER SUBMUKÖSEN ORALEN FIBROSE

Die Litteratur über submuköse orale Fibrose ist durchgesehen und 25 neue Fälle sind beschrieben worden. Die Krankheit kommt fast ausschliesslich bei Indern vor. Frauen sind öfter als Männer von ihr befallen und anscheinend im früheren Alter. Der Beginn der Krankheit ist schleichend. Initialsymptome sind eine brennende Empfindung im Munde und das Auftreten von Bläschen. Später bekommen die Schleimhäute insbesondere der Wangen, des weichen Gaumens, der vorderen Gaumenbögen und der Unterlippe ein weissliches Aussehen, fibröse Bänder entwickeln sich, und die Mucosa wird steif. An der Zunge findet man Atrophie der Papillen. In einigen Fällen wurde eine Einschränkung der Bewegungen des Unterkiefers festgestellt. Bei 7 Patienten bestand gleichzeitig eine Leukoplakie. Submuköse Fibrose prädisponiert zu einer Leukoplakie.

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