

ORAL SUBMUCOUS FIBROSIS — AN ALTERNATIVE HYPOTHESIS AS TO ITS CAUSES

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SUMMARY

Submucous fibrosis (SMF) an important precancerous condition occurs almost exclusively in Indians but cases have been reported from several countries throughout the world. The causes of SMF are unknown and there is no known treatment for it. Chillies, tobacco use, vitamin deficiencies and betel quid chewing have been implicated. Ramanathan is of the view that SMF seems to be the Asian version of sideropenic dysphagia. He suggests that SMF appears to be an altered oral mucosa following a prolonged period of chronic deficiency of iron and/or vitamin B complex especially folic acid. This changed state of the oral mucosa subsequently appears to develop more easily a hypersensitivity to oral irritants such as spices especially chillies and to the betel quid. He provides biochemical data as well as quotes several studies to support his hypothesis.

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INTRODUCTION

Although oral submucous fibrosis (SMF) has been present most probably for centuries it was not described in the medical literature until 1952 when Schwartz described five Indian women from East Africa. Both Joshi (1953) and Lal (1953) suggested the name SMF and this terminology is currently used although a more precise description would be juxta-epithelial fibrosis. SMF occurs almost exclusively in Indians but cases have been reported from several countries throughout the world. It is estimated that no less than two million cases of SMF are present in India alone (Pindborg and Sirsat, 1966).

SMF is defined as a chronic disease affecting the oral mucosa. The presence of palpable fibrous bands in the oral mucosa is the most outstanding feature and the most reliable sign of SMF. Diffuse blanching of the oral mucosa and especially the soft palate may be another characteristic sign. In the later stages the oral mucosa becomes stiff, causing difficulty in opening the mouth. Very often the tongue papillae disappear and the surface of the tongue appears smooth, shiny and bald. Burning sensation and inability to eat chillies and/or spicy foods are the earliest symptoms for which patients seek treatment.

The precancerous nature of SMF has been emphasized by several authors - Paymaster (1956); Pindborg and Zachariah (1965); Ramanathan *et al*, 1975 and Shiau and Kwan (1979). There is no known treatment for this condition. SMF is also challenging to manage for quite often leukoplakia supervenes and multiple oral carcinomas develop. Often there seems to be a wide field of cancerization in SMF.

CAUSES

The causes of SMF are also unknown. Sirsat and Khanolkar (1960) and Pindborg and Sirsat (1966) suggested that it may be due to hypersensitivity to chillies. Wahi *et al* (1966) were of the opinion that SMF was the result of tobacco use and vitamin deficiencies. Shear *et al* (1967) strongly implicated betel-nut chewing with SMF. Shiau and Kwan (1979) also stated that SMF was highly correlated with the habit of betel-nut chewing. Their studies showed that tobacco, pungent and spicy foods containing chillies and alcohol were not important etiologic factors. Ramanathan (1979) had expressed the view that SMF seemed to be the Asian version of sideropenic dysphagia (Plummer-Vinson syndrome; Paterson - Kelly syndrome) seen in the Caucasians. In fact he stated that these two conditions were no more than two different spectra of one broad and common entity just like the obverse and reverse of one and the same coin. As suggested earlier (Ramanathan *et al*, 1975) Ramanathan was of the view that Behcet's syndrome and the recurrent aphthous stomatitis major and minor groups again appeared to be different spectra of this one broad group of related families sharing some etiological factors in common. He considered the latter conditions to be probably progressively milder clinical expressions. Wray *et al* (1975), Sapiro (1977) and Wray *et al* (1978) have demonstrated iron, folic acid and vitamin B12 deficiencies in patients with recurrent aphthous stomatitis. Vitamin deficiencies and anaemia have also been reported in SMF (Wahi *et al*, 1966; Lemmer and Shear, 1967; Hamner *et al*, 1974 and Barnes and Duke 1975). Therefore in all the above stated clinical conditions iron deficiency and vitamin B complex deficiency appear to be important causative factors.

ALTERNATIVE HYPOTHESIS

Ramanathan (1979) furthermore suggested that

SMF appeared to be an altered oral mucosa following a prolonged period of chronic deficiency of iron and/or vitamin B complex especially folic acid. This changed state of the oral mucosa subsequently appeared to develop more easily a hypersensitivity to oral irritants such as spices, especially chillies and to the betel-quid which usually consists of the betel leaf, betel-nut, lime, tobacco, 'Katta Kambu' (gambir) and a few other spices.

Full blood picture examinations of 13 patients with SMF studies in our department so far revealed that 10 patients (77 percent) had some abnormal feature such as anisopoikilocytosis, evidence of iron deficiency anaemia and eosinophilia. Of 8 patients screened 5 patients (63 percent) showed a depressed serum iron level below the normal values. Of 6 patients examined all demonstrated a serum folic acid (folate) deficiency. It may be worth noting that we have not been able to demonstrate vitamin B12 deficiency in the patients we have studied so far.

Most of the patients with SMF seen by us are Indians who belong to the lower socio-economic groups. In them nutritional deficiency states are not uncommon. The Indian method of cooking meals moreover encourages folate deficiency by allowing food folate to be highly susceptible to oxidative destruction by cooking. The normal total body folate stores are in the range of 5 to 10 mg. If the meals taken daily are grossly inadequate in both vitamin B12 and folate, the patient suffers from a relatively greater deficiency of the latter because body folate stores last only a little over a month whereas body vitamin B12 stores last for several years. Moreover of the three major racial groups in Peninsular Malaysia, alcoholism seems to be the biggest social problem among the Indians. Most alcoholics, with or without overt cirrhosis, have folate deficiency because of their nutritionally inadequate diets. Additionally alcohol directly suppresses hematopoiesis in part by blocking folate metabolism (Goodman and Gilman, 1970).

Recently Butterworth (1981) had demonstrated that reversing the low-normal folate levels that can accompany oral contraceptive use may reduce the risk of developing cervical cancer. Preliminary results in 47 women showed a decrease in the presence of cervical intraepithelial neoplasias (CIN) in women taking folate with complete regression in seven. There were no changes in those taking the

placebo. Furthermore folate seemed to reduce the progression of CIN: four of them taking placebo and none of the folate-treated women showed evidence of carcinoma in situ. Butterworth further stressed that other causes of folate deficiency such as poor diet could also cause abnormal PAP smears with cells that might appear to be premalignant. The epithelium of the uterus and the oral mucosa are interrelated and share some features in common. If folate deficiency could promote precancerous changes in the cervix then why could it not do the same in the mouth?

Sirsat and Khanolkar (1960) subjected rat palates to painting with capsaicin. Capsaicin is the active irritant principle of chillies (*Capsicum annum*), which is used to spice Indian food. These experiments showed that capsaicin arouses only a limited connective tissue response in the unimpaired animal. However in protein-depleted or vitamin B-deficient rats the response was much more widespread and severe. This experimental study demonstrated two aspects as to the causes of SMF. Up-to-now however most of the studies on SMF have emphasized only one aspect i.e the oral irritants such as the chillies and the betel quid. An equally important second aspect which needs to be reemphasized is the preconditioned oral mucosa following a prolonged period of chronic deficiency of iron and/or vitamin B complex. Like the seed and the soil theory both aspects of oral irritants and the altered oral mucosa following nutritional deficiency states need to be equally emphasized to try to explain the causes of SMF from the evidence available so far. Thus there is a need to carry-out blood chemical studies of larger samples of patients with SMF to test the alternative hypothesis that SMF seems to be the Asian version of sideropenic dysphagia.

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