Oral Submucous Fibrosis: A Review

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Introduction

Oral submucous fibrosis was first described in 600 B.C, by Sushruta a well-known expert on Indian Medicine. He described in his classification of mouth and throat maladies a condition called "Vidari" which is similar to oral submucous fibrosis. [1]

J. Schwartz (1952) described a fibrosing condition in the mouth of five female patients from East Africa for which he coined the term "Atrophia idiopathica mucosae oris". Later it was termed oral submucous fibrosis (OSMF).[2] Other names are "Submucous fibrosis of the palate and faucial pillars"[3], "Idiopathic scleroderma of the mouth"[4].

J.J Pindborg and Satyarati M. Sirsat (1966)[5] defined oral submucous fibrosis as an "insidious, chronic disease affecting any part of the oral cavity and sometimes pharynx. Although occasionally preceded by and/ or associated with vesicle formation, it is always associated with a juxta-epithelial inflammatory reaction followed by fibroelastic change of the lamina propria, with epithelial atrophy leading to stiffness of oral mucosa and causing trismus and inability to eat".

OSMF -A Premalignant Condition

The precancerous nature of OSMF was first reported by J.C Paymaster in 650 patients with oral submucous fibrosis in Bombay; he described the development of slow growing squamous cell carcinoma in one third of the patients with oral submucous fibrosis. [10] Higher incidence of leukoplakia was reported in 26.9% of 101 submucous fibrosis patients from North India in contrast to 3.0% of 19,899 patients without submucous fibrosis.[11]

Pindborg et al[12] reviewed 100 cases of oral cancer in South India and found oral submucous fibrosis in 40% of oral cancer patients admitted in the Cancer Institute of Trivandrum. Gupta PC et al[5] reported a malignant transformation in 2.3% patients with oral submucous fibrosis in a 10-year follow-up study in Ernakulam district, Kerala. 4.5% malignant transformation rate was reported by Pindborg et al in a 15 year follow-up study utilizing the material from the 10-year follow-up study of the Basic Dental Research Unit of Tata Institute of Fundamental Research, Bombay and additional material from the same area. In a 17 year follow-up study Murti et al[13] reported a malignant transformation rate of 7.6%. Oral cancer developed 3-16 years after the diagnosis of submucous fibrosis with average age of 64.6 years.

Epidemiology

Several authors have conducted epidemiologic surveys in different parts of India to find out the prevalence of oral submucous fibrosis. Pindborg et al[11] conducted epidemiologic surveys in Bombay and Lucknow, and reported percentage prevalence of 0.50 and 0.51 respectively. In a large scale epidemiologic survey the prevalence of submucous fibrosis was studied in Srikakulam, Ernakulum and Bhavnagar districts. The prevalence of submucous fibrosis was found to be 0.36%, 0.16% and 0.04% respectively.[5]

In an epidemiological assessment of oral submucous fibrosis among Indian villagers Pindborg et al[14] found a percentage prevalence of 0.2 in Gujarat, 0.4 in Kerala, 0.04 in Andhra Pradesh and 0 to 0.07 in Bihar. 0.4% prevalence of oral submucous fibrosis was reported in an epidemiological assessment in Kerala, South India.[15] In a hospital based prevalence study of oral submucous fibrosis in Aligarh, N. Afroz et al[16] reported a prevalence rate of 3.5 per 1000 patients. 0.55% prevalence of oral submucous fibrosis was reported in Chennai.[17]

A hospital based epidemiologic survey in Wardha, Maharashtra recorded 0.93% prevalence of oral submucous fibrosis.[18] In a hospital based prevalence study in patients attending a dental college V. K. Hazarey et al[19] reported a prevalence range of oral submucous fibrosis from 2.42 in 2000 to 6.42 per 1000 persons per year in 2004 in Nagpur, Maharashtra.[19]

In several studies conducted in different parts of India increased prevalence of oral submucous fibrosis was reported in males as compared to females. Most of the cases were recorded in 2nd to 4th decade of life[11,16,17,18,19]

Etiopathogenesis

A multifactorial pathogenesis has been implicated in the development of oral submucous fibrosis, but various studies conducted in India suggested betel nut product with or without tobacco is responsible for oral submucous fibrosis, but now betel nut specific nitrosamines have been identified which are responsible for the premalignant and malignant oral mucosal lesions/conditions.[20,21]

Areca Nut

Areca nut is chemically composed of carbohydrates: 47-85%, tannins: 11-26%, protein: 4.9-8.3%, areca specific alkaloids: 0.15 to 0.67%. The major alkaloid is arecoline; and there are several minor alkaloids, namely arecadine, arecolidine and guvacine. Areca nut also contains arecoline-derived genotoxic agents. One of these, 3-(methylnitrosamino)-propionitrile (MNPN), is a strong carcinogen and is formed by N-nitrosation of arecoline.[22] It is generally seen that areca nut is chewed by large number of population with betel leaf, lime, tobacco etc. during chewing of these mixtures, the methyl esters of arecoline and guvacoline are hydrolyzed by slaked lime to their corresponding acids arecadine and guvacine.[23]

To find out the role of betel nut in the production of oral submucous fibrosis Sirsat and Khanolkar[24,25] applied arecoline, the most important alkaloid in the betel nut, to the oral mucosae of rats and concluded that arecoline probably plays no significant role in the causation of human submucous fibrosis. J. P. Caniff et al[26] evaluated 44 patients of oral submucous fibrosis and concluded high degree of association of the disease with the habit of chewing betel nuts. Tissue culture experiments show that alkaloids in the nut can stimulate collagen synthesis and proliferation in buccal mucosal fibroblasts. Tannins, which are also present in the betel nut, are able to increase the resistance of collagen to

degradation, and this may further enhance the fibrosis.

Nutritional deficiency

Deficiency of various vitamins like vitamin A, vitamin B, ascorbic acid, vitamin E, beta-carotene and minerals like iron, zinc, copper have been found to predispose to the development of oral submucosis fibrosis. Of all these vitamins and minerals beta carotene and chronic iron deficiency have been strongly correlated with development of oral submucosis fibrosis.[18,27,28,29,30]

Decreased level of superoxide dismutase has been reported in oral submucous fibrosis patients. The deficiency of free radical scavenging enzymes like superoxide dismutase exposes the tissues to oxidative damage.[31,32]

Autoimmunity

Detection of raised frequencies of HLA-A10, A24, DR3, DR7, B7 , DDRB1-11 and DRB3 0202/3and haplotypic pairs of A10/DR3, B8/DR3 and A10/B8 and high incidence of anti-nuclear antibodies and auto antibodies in oral sub mucous fibrosis patients supports an autoimmune etiology for oral submucous fibrosis.[33,34]Higher levels of serum immunoglobulins (IgG, IgA and IgM) and circulating immune complexes were also detected in oral submucous fibrosis patients.[35,36]

Genetic Susceptibility

Increased production of allele TNF2**,** higher phenotype frequency of allele A6 of major histocompatibility complex class I chain related gene A has been reported in oral submucous fibrosis.[37,38]

Oral submucous fibrosis is characterized by dysregulation of collagen metabolism; enzymes such as collagenases and lysyl oxidase together with cytokines (TGF-β) contribute to genetic modulation during the progression of disease. Collagen-related genes play an important role in the homeostasis of collagen in the body. These collagen related genes are altered due to ingredients of betel-quid.[39]

Other Predisposing Factors

Chillies

Evidence in favor of chillies as an irritative factor causing oral submucous fibrois was supported by Sirsat S.M and Khanolkar V.R[40,41] they diagnosed cases of oral submucous fibrosis in countries such as Ceylon, Nepal, Thailand and South Vietnam where chillies are commonly used in the diet. Further positive evidence in favor of this hypothesis is seen in the fact that, on eating of chillies, vesicles appear on the palates of some persons. Support for the theory that chillies are the irritating factor is found in the occurrence of oral submucous fibrosis among Indians living outside India but maintaining Indian dietary habits (for instance, Indians living in East Africa and in Malaysia).

The inability of patients with oral submucous fibrosis to tolerate food seasoned with chillies has led to the hypothesis that the disease is due to hypersensitivity to capsaicin. Capsaicin is the active ingredient of chillies. It is the vanillylamide of 8-methyl-6 nonenic acid, which is the active irritant of chillies. More basic and clinical research is needed, however, to prove indisputably the involvement of chillies in the causation of oral submucous fibrosis.

Clinical Manifestations

OSMF is an insidious disease and progresses over 2-5 years. The prodomal symptoms includes burning sensation in the mouth on consuming spicy foods, erythematous mucosa, appearance of vesicles and ulcers, melanotic mucosal pigmentation, mucosal petechiae especially on the palate, excessive salivation, defective gustatory sensation and dryness of the mouth.

As the disease progresses the oral mucosa becomes blanched. Dense vertical and circular palpable fibrous bands appear in the buccal mucosa and around the rima oris, resulting in a mottled marblelike appearance of the mucosa. Palate and the faucial pillars are the areas first involved.

Reduction of mouth opening (trismus), stiff and small tongue, blanched and leathery floor of the mouth, fibrotic and depigmented gingiva, rubbery soft palate with decreased mobility, blanched and atrophic tonsils, shrunken bud-like uvula and shrunken cheeks, not commensurate with age or nutritional status.[42]

Treatment

The patient should be properly counseled and strictly discouraged from chewing betel nut preparations. The patients should be explained about the disease and its possible malignant potential. Different treatment strategies for oral submucous fibrosis have been suggested like nutritional support with a diet rich in proteins and calories.[43] Vitamins such as vitamin A, B complex, C, E and other vitamin and minerals are commonly employed in combination with other therapeutic agents.[44]

Topical steroids and systemic glucocorticoids are commonly used in patients with oral submucos fibrosis. Glucocorticoids act as immunosuppressive agents and prevent fibrosis by decreasing fibroblastic proliferation and deposition of collagen.[43] Intralesional injections of interferon gamma and immune milk powder have also been tried in oral submucous fibrosis and the post treatment mouth opening increased.[45,46]

Physiotherapeutic measures such as forceful mouth opening and heat therapy have been tried. Heat in the form of hot rinses, lukewarm water or selective deep heating therapies like short-wave and micro-wave diathermy have provided satisfactory results.[47]

Local drug deliveries in the form of intralesional injections of dexamethasone, collagenase, hyaluronidase and placental extract has been tried and have been found to provide good results in patients with oral submucous fibrosis.[43,48]

Intralesional steroids might improve the mouth opening in mild cases of oral submucous fibrosis, surgery with split thickness skin grafting combined with bilateral temporalis myotomy and coronoidectomy was the only effective treatment for severe cases.[49]

Among the above-mentioned modalities for treatment of oral submucous fibrosis none of them can be considered to be completely effective. Conservative types of treatment are more beneficial in patients with initial changes of oral submucous fibrosis but in severe forms of oral submucous fibrosis conservative approach without surgical intervention do not respond favorably.

References

1. Chari PS. Sushruta and our heritage. Indian J of Plastic Surg .2003; 36:4-13.
2. Schwartz J. Atrophia idiopathica (tropica) mucosae oris. Demonstrated at the Eleventh International Dental Congress, London, 1952 (cited by Sirsat & Khanolkar). Ind. j. med. Sci. 1962; 16:189-197.
3. Joshi SG. Submucous fibrosis of the palate and pillars. Ind J Otolaryngol.1953; 4:1-4.
4. Su-I-P. Idiopathic scleroderma of the mouth. AMA Arch Otolaryngol.1954; 59:330-332.
5. P.C. Gupta, Fali S Mehat, D.K. Dafatary. Incidence rates of oral cancer and natural history of oral precancerous lesions in a 10-year follow-up study of Indian villagers. Community Dent. Oral Epidemiol. 1980; 8:287-333.
6. Lemmer J, Shear M. Oral submucous fibrosis: a possible case in a person of Caucasian descent. Br Dent J. 1967; 122:343-346.
7. Pindborg JJ, Singh B. Formation of vesicles in oral submucous fibrosis. Acta Path. Microbiol. Scand. 1964; 62: 562-566.
8. Sirsat SM, Pindborg JJ. Subepithelial changes in oral submucous fibrosis. Acta Pathol. Microbiol. Scand. 1967; 70:161-173.
9. Wahi PN, Luthra UK, Kapur VL. Submucous fibrosis of the oral cavity: histomorphological studies. Br J Cancer. 1966; 20: 676-687.
10. Paymaster J.C. Cancer of the buccal mucosa; a clinical study of 650 cases in Indian patients. Cancer. 1956; 9:431-435.
11. Pindborg J.J. Frequency of oral submucous fibrosis in North India. Bull. WHO.1965; 32:748-750.
12. J.J. Pindborg and J. Zachariah. Frequency of oral submucous fibrosis among 1000 south Indians with oral cancer. WHO Bulletin. 1965; 32: 750-753.
13. Murti PR, Bhonsle RB, Pindborg JJ. Malignant transformation rate in oral submucous fibrosis over a 17-year period. Community Dent. Oral Epidemiol. 1985; 13: 340-341.
14. Pindborg J.J. et al. Prevalence of oral submucous fibrosis among 50,915 Indian villagers. Br J Cancer. 1968; 22:646-654.
15. R. Rajendran, G. K. Raju, S. M. Nair. Prevalence of oral submucous fibrosis in the high natural radiation belt of Kerala, South India. Bulletin of the World Health Organization.1992; 70 (6): 783-789.
16. N. Afroz, S. A. Hasan, S. Naseem. Oral submucous fibrosis a distressing disease with malignant potential. Indian Journal of Community Medicine. 2006; 31(4): 1-4.
17. Saraswathi TR, Ranganathan K, Shanmugam S et al**.** Prevalence of oral lesions in relation to habits: Cross-sectional study in South India. Ind J Dent Res.2006; 17 (3): 121-125.
18. C. Raina, R. M. Raizada, V. N. Chaturvedi et al. Clinical profile and serum beta-carotene levels in oral submucous fibrosis. Indian Journal of Otolaryngology and Head and Neck Surgery.2005; 57 (3): 191-195.
19. V.K. Hazrey, D. M. Erlewad, K. A. Mundhe et al. Oral submucous fibrosis: study of 1000 cases from central India. J Oral Pathol Med.2007; 34: 12-17.

20. Fali. S Mehta, James E. Hamner III. Tobacco-related oral mucosal lesions & conditions in India. Basic Dental Research Unit Tata Institute of Fundamental Research, Mumbai; 1993:pp90-99.
21. PC Gupta, CS Ray. Epidemiology of betel quid usage. Ann Acad Med Singapore.2004; 33 (Suppl): 31S-36S.
22. International Agency for Research on Cancer. IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans. Vol.37. Tobacco habits other than smoking; betel-quid and areca-nut chewing; and some related nitrosamines. Lyon: IARC, 1985; p.211.
23. Bogdan Prokopczyk, Abraham Rivenson, Peter Bertinato et al. 3-(Methylnitrosamino) propionitrile: occurrence in saliva of betel quid chewers, carcinogenicity, and DNA methylation in F344 rats. Cancer Research 1987; 47:467-71.
24. SM Sirsat, Khanolkar VR. Submucous fibrosis of the palate in diet-preconditioned wistar rats. Induction by local painting of capsaicin-an optical and electron microscope study. Arch Path.1960; 70: 171-179.
25. SM Sirsat, Khanolkar VR.Submucous fibrosis of the palate; induction by local painting of capsaicin in wistar rats treated with deoxycorticosterone acetate-an optical and electron microscope study. Arch. Path.1960; 70: 180-197.
26. J.P. Canniff, W. Harvey and M. Harris .Oral submucous fibrosis: its pathogenesis and management.Br Dent J. 1986; 160: 429- 434.
27. Ramanathan K. Oral submucous fibrosis. An alternative hypothesis as to its causes. Med J Malaysia. 1981; 36:243-245.
28. Rennie JS, Mc Donald DG, Dagg JH. Quantitative analysis of the human buccal epithelium in iron deficiency anemia. J Oral Pathol.1982; 11:39-41.
29. Verghese I, Sugathan CK, Balasubramoniyan G et al. Serum copper and zinc levels in premalignant lesions of oral cavity. Oncology.1987; 44(4):224-227.
30. C.D. Anuradha and C.S. Shyamala Devi. Serum protein, ascorbic acid, iron and tissue collagen in oral submucous fibrosis- a preliminary study. Indian J Med Res [B].1993; 98:147-151.
31. Soma Gupta, M.V.R. Reddy and B.C. Harinath. Role of oxidative stress and antioxidants in aetiopathogenesis and management of oral submucous fibrosis. Indian Journal of Clinical Biochemistry.2004; 19(1): 138-141.
32. Suryakant Metkari B, Tupkari JV, Barpande SR. An estimation of serum malondialdehyde, superoxide dismutase and vitamin A in oral submucous fibrosis. Journal of Oral and Maxillofacial Pathology.2007; 11:23-27.
33. J.P. Canniff, W. Harvey and M. Harris .Oral submucous fibrosis: its pathogenesis and management.Br Dent J. 1986; 160: 429- 434.
34. Saeed B, Haque MF, Meghji S et al. HLA typing in oral submucous fibrosis. J Dent Res. 1997; 76: 1024.
35. Shah N, Kumar R, Shah MK. Immunological studies in oral submucous fibrosis. Indian J Dent Res.1994; 5(3):81-88.
36. Cynthia Jane, A.V. Nerurkar and F.R. Karjodkar. Circulating immune complexes (CIC) as marker for disease progress in oral cancer. Indian Journal of Clinical Biochemistry.2007; 22(2):114-117.
37. C.-J. Chiu, C.-P. Chiang, M.-L. Chang. Association between genetic polymorphism of tumor necrosis factor-α and risk of oral submucous fibrosis, a pre-cancerous condition of oral cancer. J Dent Res 2001; 80:2055-9.
38. Chung-Ji Liu, Yann-Jinn Lee, Kuo-Wei Chang et al. Polymorphism of the MICA gene and risk for oral submucous fibrosis. J Oral Pathol Med.2004; 33:1-6.
39. P Rajalalitha and S. Vali. Molecular pathogenesis of oral submucous fibrosis- collagen metabolic disorder. J Oral Pathol Med.2005; 34: 321-328.
40. SM Sirsat, Khanolkar VR. Submucous fibrosis of the palate in diet-preconditioned wistar rats. Induction by local painting of capsaicin-an optical and electron microscope study. Arch Path.1960; 70: 171-179.
41. SM Sirsat, Khanolkar VR.Submucous fibrosis of the palate; induction by local painting of capsaicin in wistar rats treated with deoxycorticosterone acetate-an optical and electron microscope study. Arch. Path.1960; 70: 180-197.
42. Pindborg JJ. Oral submucous fibrosis: A review. Ann Acad Med Singapore. 1989; 18(5): 603-7.
43. R. Rajendran. Oral submucous fibrosis: etiology, pathogenesis, and future research. Bulletin of World Health Organization. 1994; 72(6): 985-996.
44. Hennekens CH. Micronutrients and cancer prevention. Cancer Det Prev. 1984; 7:147-58.
45. M.F. Haque, S. Meghji, R. Nazir et al. Interferon gamma may reverse oral submucous fibrosis. J Oral Pathol Med. 2001; 30:12-21.
46. Y.S. Tai, B.Y. Liu, J.T. Wang. Oral administration of milk from cows immunized with human intestinal bacteria leads to significant improvements of symptoms and signs in patients with oral submucous fibrosis. J Oral Pathol Med.2001; 30:618-25.
47. Gupta DS, Gupta M, Oswal RN et al. Oral submucous fibrosis: clinical study and management by physiofibrolysis. J Indian Dent. Assoc. 1980; 52:375-378.
48. Kumar. K, Srivastava C.M, Mathur R.M et al. The effect of collagenase on oral submucous fibrosis. J Indian Dent. Assoc. 1980; 52: 243-246.
49. J.N. Khanna and N.N. Andrade. Oral submucous fibrosis: a concept in surgical management. Int J. Oral Maxillofac Surg. 1995. 24; 433-439.

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