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Oral Submucous Fibrosis: A Progressive Debilitating Oral Web Disease

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Abstract- Amongst the list of pre-malignant conditions, Oral Submucous Fibrosis (OSMF) forms one of the most debilitating diseases of the oral cavity. It is predominantly seen among populations using betel quid, indicating areca nut as the most conspicuous agent in the etiological agents. A clear dose-dependent relationship In relation to both the duration and frequency of chewing areca nut was revealed, although other risk factors such as excessive use of chilies and spices and malnutrition were also put forth. Research in some aspects in the background of progressive fibrosis associated with the disease, has allowed to put light onto the mechanisms involved in the malignant transformation to the most prevalent, potentially malignant oral disorder in south Asia. Reduction in matrix metalloproteinases (MMP's) and increased secretion of tissue inhibitors of MMP's play the most significant role in collagen accumulation whilst fibrogenic cytokines, mainly TGF-b over expression leading to increased production of collagen. There is increasing incidence of the disease and subsequent malignant transformation..

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Oral Submucous Fibrosis: A Progressive Debilitating Oral Web Disease

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Abstract- Amongst the list of pre-malignant conditions, Oral Submucous Fibrosis (OSMF) forms one of the most debilitating diseases of the oral cavity. It is predominantly seen among populations using betel quid, indicating areca nut as the most conspicuous agent in the etiological agents. A clear dose-dependent relationship In relation to both the duration and frequency of chewing areca nut was revealed, although other risk factors such as excessive use of chilies and spices and malnutrition were also put forth. Research in some aspects in the background of progressive fibrosis associated with the disease, has allowed to put light onto the mechanisms involved in the malignant transformation to the most prevalent, potentially malignant oral disorder in south Asia. Reduction in matrix metalloproteinases (MMP's) and increased secretion of tissue inhibitors of MMP's play the most significant role in collagen accumulation whilst fibrogenic cytokines, mainly TGF-b over expression leading to increased production of collagen. There is increasing incidence of the disease and subsequent malignant transformation. Hence the article focuses to review the etiology, pathogenesis, clinical features and management of OSMF.

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I. Introduction

On the basis of clinical and histopathological findings, Pindborg defined Oral Submucous Fibrosis as "an insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and or associated with vesicle formation, it is always associated with a juxta epithelial inflammatory reaction followed by a fibro elastic change of the lamina propria with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat".

It is a slow, progressive fibrotic disease causing fibroelastic change and inflammation in the oral mucosa, leading to inability to open the mouth, swallow or speak[1, 2]. This was accredited to the accumulation of inelastic fibrous tissue in the juxta epithelial region of the oral mucosa, along with concomitant muscle degeneration[3]. The most common site to be involved was found to be the buccal mucosa, although other parts of the oral cavity were also found to involve, including the pharynx[4].

These reactions may be the result of direct stimulation from exogenous antigens like Areca alkaloids or changes in the tissue antigenicity that may lead to an autoimmune response.

II. Epidemiology

Most common prevalence was found among the Indians, ranging from 0.2% to 1.2%. A survey revealed an overall prevalence of up to 4% in kerala[5]. Amongst the reported cases 0.5% was found to be in women[6]. The reason for the rapid increase of the disease is reported to be due to an upsurge in the popularity of commercially available areca nut in south asia[7].

III. Etiology and Pathophysiology

The etiology of OSMF is still not fully unwinded. It is considered to be a multifactorial disease. According to Liao, the areca nut in betel quid plays a major role in the pathogenesis of OSMF[8]. There was no significant evidence to relate the habits of smoking or alcohol consumption alone in the pathogenesis of the disease[9, 10]. Arecoline, an active alkaloid found in betel quid, stimulates fibroblasts to increase production of collagen by 150%[11]. Chung-Hung in 2006, studied that arecoline was found to elevate mRNA and protein expression of cystatin C, a non glycosylated basic protein consistently upregulated fibrotic diseases, in a dose dependent manner in persons with OSMF[12].

Yet another hypothesis grips on the fact that, the high copper content of areca nut acts as an initiating factor in OSMF. This was suggested by the fact that, soluble copper levels in oral fluids significantly increases after chewing areca nut for 5-30 minutes[13].

Other factors thought to cause OSMF include iron and vitamin B complex deficiency that derange the repair of inflamed oral mucosa, leading to defective healing and resultant scarring. As a result, the oral mucosa becomes more prone to the effects of areca nut and chilies.

The role of chilies and spices in the list of etiological agents is still a topic of debate among the scientific community. It was shown that the capsaicin in chilies stimulates the widespread palatal fibrosis in rats[14]. However, the incidence of OSMF was lower in Mexico and South America than in India, despite a higher dietary intake of chillies[15].

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Genetics is believed to play a role in OSMF patients, which leads to immune system changes. People without the betel nut chewing and chilly ingestion were reported to have OSMF[16]. Mutations in APC gene and low expression of wild type TP 53 tumor suppressor gene in affected patients, increased the risk of malignant transformation[17].The increase in CD4 cells with HLA-DR in OSMF tissues suggest that lymphocytes are activated and number of langerhans cells increased. The presence of these immunocompetent cells and with increased CD4 to CD8 ratio in OSMF tissue, suggest an ongoing cellular immune response resulting in imbalance of immune regulation and an alteration in local tissue architecture. These reactions can be from the direct stimulation from exogenous antigens or of changes in tissue antigenicity that leads to an autoimmune response[18]. Increased levels of proinflammatory cytokines and reduced antifibrotic interferon gamma (IFN-gamma) in patients with OSMF were demonstrated[19].

IV. Clinical Features

OSMF was found to be predominant in females[16]. The mean age was 43 years. Burning sensation and discomfort in the oral mucosa during mastication was the most common complaint amongst the reported cases. There is associated depapillation of the tongue (Fig: 1). Progressive changes including difficulty in mastication, reduced salivation, dysphasia, pain in the ears and loss of auditory acuity due to stenosis of the pharyngeal end of Eustachian tubes.

In advanced cases, the jaws become inseparable and totally inelastic and plastic and nutrition can be maintained only by pushing the food into mouth. The buccal mucosa is frequently ulcerated and secondarily infected consequent to ischemia and constant pressure of the mucosa against the buccal aspect of the teeth.

Pindborg provided staging criteria for OSMF[20]. He divided the stages according to the clinical presentation of the disease as:

Stage 1: Stomatitis including erythematous mucosa (Fig: 2), vesicles, mucosal ulcers, Melanotic mucosal pigmentation and mucosal petechiae

Stage 2: fibrosis occurs in ruptured vesicles and ulcers as they heal (Fig: 3), which is the hallmark of this stage

Early lesions demonstrate blanching of oral mucosa and older lesions presents with vertical and circular palpable fibrous bands in the buccal mucosa and around the mouth opening or lips, resulting in mottled, marble like appearance(Fig:4) of the mucosa.

This stage is characterized by reduced mouth opening, stiff and small tongue, fibrotic and depigmented gingiva, shrunken bud like uvula.

Stage 3: speech and hearing deficits may occur as a part of the sequel.

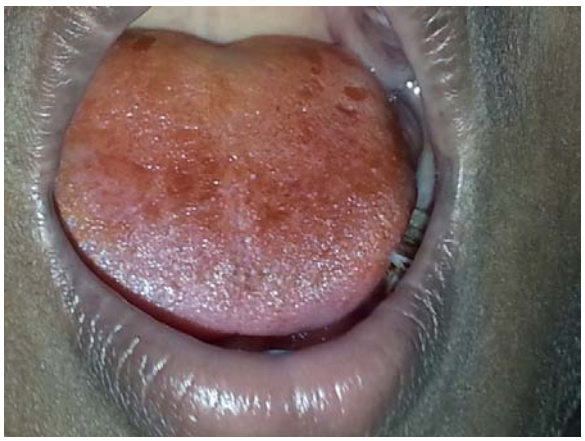
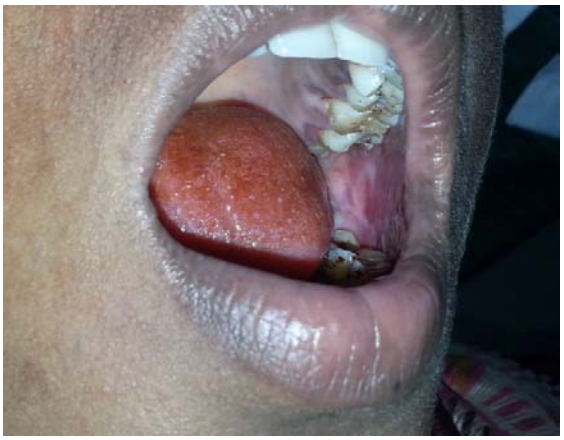


Figure 1



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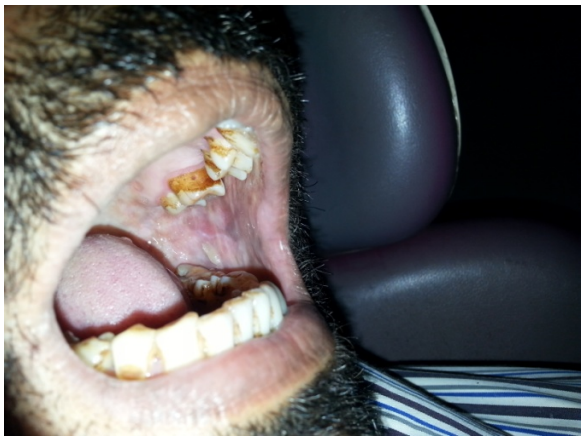

Figure 3

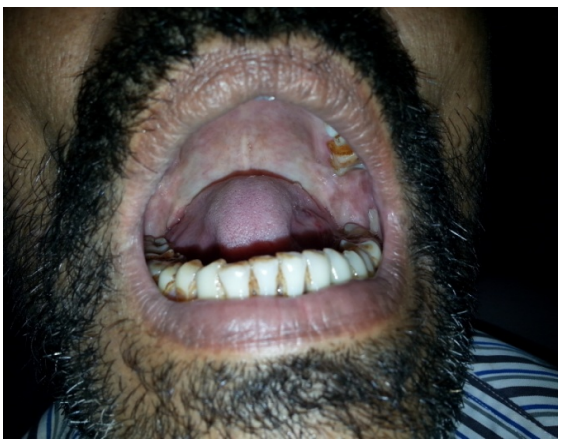

Figure 4

Histological examination reveals severely atrophic epithelium with complete loss of rete ridges. Varying degrees of epithelial atypia may be present. The underlying lamina propria exhibits severe hyalinization, with homogenization of collagen. Cellular elements and blood vessels are greatly reduced[18].

V. Investigations

Clinical presentation of the disease plays an upper hand in the diagnosis phase. Other investigations include complete hemogram, toludine blue test, incisional biopsy and immune fluorescence tests [21].

VI. Management

The earlier the treatment begins, better it is for the patient. The treatment modes depend upon the state of the disease at the time of presentation. If it is detected at a very early stage, cessation of the habit would provide sufficient relief. But moderate to severe stages of OSMF are almost always irreversible. Usually the disease is very resistant to treatment. The proposed treatment regimens aims hinder the progression of the disease process. Submucosal injected steroids and hyaluronidase, placental extracts, oral iron preparations and topical vitamin A and steroids are some the agents that have been used[22]. All of these therapies are usually palliative. Surgical treatment includes simple excision of fibrotic bands, split thickness skin grafting following bilateral temporalis myotomy or coronoidectomy[11]. The use of oral stent as an adjunct to surgery to prevent relapse of the fibrotic bands has also been studied[23]. Other treatment modalities include administration of Antoxid OD for 6-8 weeks, Lycored OD for 6-8 weeks and physiotherapy for improving mouth opening[22].

VII. Malignant Transformation

OSMF is a well recognized potentially malignant disorder of the oral mucosa. Simultaneous occurrence of oral leukoplakia and OSMF is demonstrated to carry a higher risk for malignancy than with OSMF alone which amounts from 4-13%[24].

VIII. Conclusion

The incidence of OSMF is on the rise with the popularity of commercially available betel nut products. It also carries a significant morbidity rate from oral cancer. So it is desirable that OSMF is diagnosed as early as possible. At best, it is palliate the symptoms of OSMF. In palliative care, the patient is the focus of treatment, not the disease. A stepwise approach to OSMF management is advocated, with the level of entry into the treatment algorithm being dictated by the disease severity and response to treatment. Although clinicians strive to achieve lesion resolution and primary outcomes of therapies aims to concentrate on symptom reduction and improvement of quality of life. Intervention studies and public health awareness programme linked with OSMF condition and habits may prove the best way to control disease process at the root level.

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References Références Referencias

1. Zain RB, Ikeda N, Gupta PC et al. oral mucosal lesions associated with betel quid, areca nut and tobacco chewing habits: consensus from a workshop held in Kuala Lampur, Malayasia. November 25-27, 1996. J Oral Pathol Med 1999;28:1-4.
2. Rajendran R. oral submucous fibrosis: etiology, pathogenesis and future research. Bull World Health Org 1994;72(6):985-96.
3. Aziz SR (1997) oral submucous fibrosis: an unusual disease. J N J Dental Association 68: 17-19.
4. Paissat DK, oral submucous fibrosis. Int J Oral Surg 1981 (10) 310-312.
5. Pindborg JJ, Mehta FS. Prevalence of oral submucous fibrosis among Indian villagers. Br J Cancer 1968;22:646-54.
6. Shear M, Lemmer J, Dockrat IS. Oral submucous fibrosis in South African Indians: an epidemiological study. S Afr Med Sci 1967; 32: 41-6.
7. Ekanayaka and Titakaratne, J carcinogene Mutagene 2013, S5: oncogenomics of head and neck.
8. Liao PH. Adenamatoid polyposis coli gene mutation and decreased wild type p53 protein expression in oral submucous fibrosis: a preliminary investigation. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. Aug 2001;92(2):202-7.
9. Ariyawardana A, Athukorala AD, Arulanandam A. Effect of betel chewing, tobacco smoking and alcohol consumption on oral submucous fibrosis: A case-control study in Sri Lanka. J Oral Pathol Med. Apr 2006;35(4):197-201.
10. Ranganathan K, Devi MU, Joshua E, et al. Oral submucous fibrosis: A case control study in Chennai, South India. J Oral Pathol Med. May 2004;33(5):274-7.
11. Caniff JP, Harvey W, Harris M. Oral submucous fibrosis: its pathogenesis and management. Br Dentl 1986; 160: 429-34.
12. Chung-Hung T, Shun-Fa Y, Yu-Chao C. The upregulation of cystatin C in oral submucous fibrosis. Oral Oncol. 2006;24:102-6.
13. Trivedy CR, Warnakulasuriya KA, Peters TJ, et al. Raised tissue copper levels in oral submucous fibrosis. J Oral Pathol Med. Jul 2000;29(6):241-8.
14. Sirsat SM, Khanolkar VR. Submucous fibrosis of the palate in diet preconditioned Wistar rats. Induction by local painting of capsaicin--an optical and

electron microscopic study. Arch Pathol. Aug 1960;70:171-9.
15. Pillai R, Balaram P, Reddiar KS. Pathogenesis of oral submucous fibrosis. Relationship to risk factors associated with oral cancer. Cancer. Apr 15 1992;69(8):2011-20.
16. Seedat HA, van Wyk CW. Betel-nut chewing and submucous fibrosis in Durban. S Afr Med J. Dec 3 1988;74(11):568-71.
17. Liao PH, Lee TL, Yang LC, et al. Adenomatous polyposis coli gene mutation and decreased wild-type p53 protein expression in oral submucous fibrosis: a preliminary investigation. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. Aug 2001;92(2):202-7.
18. Haque MF, Harris M, Meghji S, Speight PM. An immunohistochemical study of oral submucous fibrosis. J Oral Pathol Med. 1997;26(2):75-82.
19. Haque MF, Meghji S, Khitab U, Harris M. Oral submucous fibrosis patients have altered levels of cytokine production. J Oral Pathol Med. Mar 2000;29(3):123-8.
20. Pindborg JJ, Mehta FS, Gupta PC, Daftary DK. Prevalence of oral sub mucous fibrosis among 50915 Indian villagers. BrJ Cancer 1968; 22: 646-54.
21. Sabharwal R et al. Oral Submucous Fibrosis-A review. J Adv Med Dent Scie Res 2013; 1(1): 29-37.
22. Borle RM, Borde SR. management of oral submucous fibrosis: a conservative approach. J Oral Maxillofac Surg 1991; 49(8): 788-91.
23. Le PV, Gornitsky et al. Oral Stent as treatment adjunct for oral submucous fibrosis. Oral Surg Med Oral Pathol 1996;81(2): 148-50.
24. Lian IeB 2013. Progression of precancerous lesions to oral cancer: oral oncol 49: 427-430.