ORAL SUBMUCOUS FIBROSIS

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INTRODUCTION

Oral Submucous fibrosis (OSF) is a slowly, progressive , chronic fibrotic disease of oral cavity & oropharynx characterized by fibroelastic changes & inflammation of the mucosa , leading to progressive inability to open the mouth, swallow or speak.

OSF is characterized as a Pre-cancerous condition which is defined as -A generalized pathological state of the oral mucosa associated with a significantly increased risk of cancer, according to WHO. OSF is a chronic & potentially malignant condition of oral cavity. This condition is first described by Schwartz (1952) as the term " Atrophia Idiopathica Mucosae Oris" . Later in 1953, described as OSF by Dr Joshi from Mumbai on the basis of its histological nature.

The inflammatory response release cytokines and growth factors that promote fibrosis by inducing the proliferation of fibroblasts , upregulating collegen synthesis & down regulating collagenase production. OSF is a chronic and potentially malignant condition of oral cavity.

ETIOLOGY

Primary cause of OSF is the habitual use of betel quid and its constituents which include the nut of areca palm (Areca catechu) , the leaf of the betel pepper(piper betle) , and lime (calcium hydroxide).

OTHER PREDISPOSING FACTORS INCLUDE:

Genetic Susceptibility: It may also be associated with OSF because frequencies of HLA- A10; B7;DR3 are more in OSF patients than normal subjects and PCR (polymerase chain reaction) also demonstrates increased frequencies of HLA-A24,DRB1-11 & DRB3-0202/3 antigens in OSF patients.

Nutrtional Disorders: Like Iron Deficiency

Carcinogens: Like tobacco , Aercoline, flavonoids & tannins.

PATHOGENESIS OF OSF

Some of the different studies that suggest that occurence of OSF may be due to:

- Clonal selection of fibroblasts with a high amount of collagen production during the long term exposure to areca quid ingredients.(By Meghji S,1987)
- Stimulation of fibroblast proliferation & collagen synthesis by areca nut alkaloids (By Harwey,W,1986)
- By fibrogenic cytokines secreted by activated macrophages & T-lymphocytes in the OSF tissues.(Haque MF,2000)
- Deficiency in collagen phagocytosis by OSF fibroblasts. (Tsai CC,1999)
- By production of collagen with a more stable structure (collagen Type 1 trimer) by OSF fibroblasts (KUO MYP ,1987)
- By stabilization of collagen structure by catechin (katha) & tannins from the areca nut (Scutt A,1987)

By an increase in collagen crosslinkage as caused by upregulation of Lysyl oxidase by OSF fibroblasts (MaRH,1995)

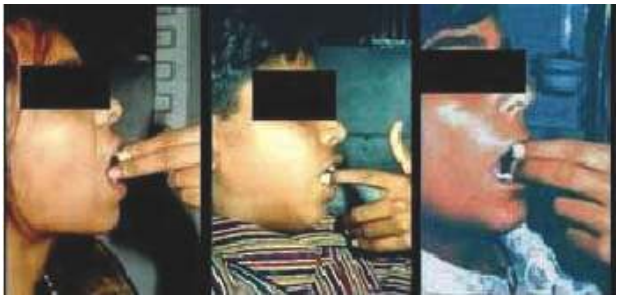
CLINICAL FEATURES

Prodromal symptoms (Early OSF)

- Includes a burning sensation in mouth while taking spicy food
- Ulcerations or recurrent generalized inflammation of oral mucosa
- Appearence of blisters specially on palate
- Defective gustatory sensation
- Dryness of mouth
- Excerbation manifested by small vesicles in cheeks & palate
- Excessive salivation
- Focal vascular dilatations seen as 'petechiae'(It is because of vascular response due to hyper-senstivity of oral mucosa towards some external irritant like areca nut)
- Pain in areas of submucosal bands

Advanced OSF

- With the progression of disease ,oral mucosa blanched , slightly opaque & white fibrous bands appear
- Firstly involved areas are palate & faucial pillars.
- Fibrous bands are seen in vertical direction on buccal mucosa. Density of fibrous bands varies from slightly white area on soft palate causing no symptoms to dense fibrosis causing fixation & shortening of soft palate
- When it involves pterygomandibular raphe that causes degree of difficulty in mouth opening or TRISMUS which is classified as:



STAGE 1 - Mouth opening more than 3cm

STAGE 2 - Mouth opening 2-3cm

STAGE 3 - Mouth opening less than 2cm

- Persistent and recurrent GLOSSITIS & STOMATITIS
- Circular bands are sound around mouth orifice & felt on palpation (seen markedly on lower lip)
- Changes seen in relation to tongue movement & Atrophy of tongue papillae
- Stiffening of mucosal areas causing inability to blow
- If it involves nasopharynx ,nasal voice is a later sign & reffered pain in ear

HISTOPATHOLOGICAL EXAMINATION

For histopathological examination, the biopsy tissue was proceed by paraffin embedding & 2-3 micrometer thick sections are cut & stained by haemotoxylin &eosin(H&E).

OSF is characterized as by a juxtraepithelial inflammatory reaction followed by fibroblastic changes .

According to traditional histopathological grading of OSF is done in FOUR stages:

STAGE 1 - very early OSF

STAGE 2 - early OSF

STAGE 3 - moderatly advanced OSF

STAGE 4 - Advanced OSF

STRUCTURAL & MICROSTRUCTURAL CHANGES

In early stages HYPERPLASIA & in advanced cases ATROPHY associated with an increased tendency for keratizing metaplasia.

High mitotic count in para-keratotic epithelium is seen more common in OSF cases.

Para- keratotic leukoplakia & atrophic epithelium changes predisposes OSF to malignancy.

BIOLOGICAL STUDIES ON INDIVIDUALS & TISSUE FROM OSF

- Deficiency of vitamin B12, folate & Iron can affect the integrity of oral mucosa
- In the OSF cases, there is increased blood ESR, Anaemia & Eosinophilia
- Increase in gammaglobin
- Decrease in serum IRON & Increase in Total Iron binding capacity (TIBC)
- Rise in serum proteins ,mucopolysaccharides & antistreptolysin titre 'o' is seen
- Depression of LDH (lactase hydrogenase) is reported
- Alterations in serum COPPER & ZINC ratio (decrease in zinc content).

GENETIC STUDIES show that the genotoxic effects of betel quid constituents is also effected by chromosomal instability.

Ag NOR Silver binding nucleolar organizer region proteins comprise a simple & reproducible cytological test indicative of proliferative status of cells.

IMMUNOLOGIC STUDIES show there is increase in human leukocytic antigens (HLA) A10,B7,dr3 occured more frequently in OSF

TREATMENT

Treatment of OSF depends on involvement of the disease

AT EARLY STAGE

Elimination of use of (betel quid) areca nut chewing is sufficient . with some Nutritional support like intake of high protein diet & vitamin -B complex supplements.

AT MODERATE STAGE

At this stage we can use both type of DRUG THERAPY- Local & Systemic with PHYSIOTHERAPY

Local Drug Therapy: Local injection of CORTICOSTEROIDS & PLACENTAL EXTRACTS in addition to HYALURONIDASE & COLLAGENASE helps in decreasing collagen formation

Intralesional injection of DEXAMETHASONE SOD. PHOSPHATE(2ml)+1500 I.U of hyaluronidase + xylocaine(0.2cc)+ peripheral vasodilator like NYLINDRIN HYDROCHLORIDE

INJECTABLE PLACENTREX is also used in such cases.

PLACENTREX LOTION- dosage 1-2ml rubbed for 1 min, 3 times daily for 12-16 weeks (DNA 10-15mg ,RNA 5-10mg, tyrosine 0.25-0.35mg ,total protein not<0.65mg, Nitrogen content not<0.08%)

PLACENTREX GEL -(includes extract of 0.1gm of fresh human placenta .total nitrogen not < 0.25% w/w).

Systemic Drug Therapy: Use of immunodulatory drugs like glucocorticoids suppresses the inflammatoryreaction & decrease fibrosis by decreasing fibroblastic activity use of antioxidants like LYCOPENE, Vitamin A & E

Dosage of Lycopene - 2000-5000mcg & should be given with zinc, selenium & vit. A-2500iu Vit.E-25iu & vit.C-50mg.

AT SEVERE STAGE

Surgical involvement is indicated in patients with severe trismus & biopsy revealing dysplastic\neoplastic changes.

SURGICAL modality includes

- Simple excision of fibrous bands
- Split thickness Skin grafting
- Nasolabial flaps & lingual pedicle flaps

Use of KTP-532 LASER release process recently found to increase mouth opening range in patient over a 12 months follow up period.