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Histopathological changes in gingiva in patients with oral submucous fibrosis

ABSTRACT

Objective: To evaluate clinical and histopathological changes in gingiva in patients with oral submucous fibrosis

Methodology: Sample size of 30 and control of three normal gingival specimens were used for the study. Clinical history of current and archival cases was obtained. Individual biopsy of the gingiva was obtained from the patients with oral submucous fibrosis after seeking informed consent. The histological sections were stained by haematoxylin and eosin stain and were viewed under microscope to evaluate the changes in the epithelium and connective tissue of gingiva (if any).

Results: Out of 30 cases in the study, 6 cases (20%) were in very early stage, 6(20%) in early stage, 15(50%) in moderately advanced stage and the remaining 3(10%) were in advanced stage, according to histopathological classification of oral submucous fibrosis.

Conclusions: The present study concludes that gingiva is affected histologically in oral submucous fibrosis in 60% of cases and the findings coincide with those of other oral mucosal sites affected by oral submucous fibrosis. Those affected show changes corresponding to various histological stages ranging from very mild to advance for other mucosal sites.

Keywords: Oral submucous fibrosis, Gingiva, Atrophic epithelium, Hyperplastic epithelium, Loss of stippling

INTRODUCTION

Sushruta, the father of ancient Indian medicine described a condition termed "Vidari" under mouth and throat diseases, characterized by progressive narrowing of mouth and burning sensation, particularly on eating spicy food and depigmentation of oral mucosa {1}. These are characteristic features of oral submucous fibrosis (OSF), till date.

"Atrophia idiopathica (trophica) mucosae" was the first name given to oral submucous fibrosis {1, 2}. The condition was also named as "diffuse oral submucous fibrosis" {3}. Since then it has remained an enigma in spite of innumerable studies over the past five decades. This condition occurs predominantly among Indians and to a much lesser extent in other Asian population. The prevalence rate of oral submucous fibrosis in India is approximately 1.2%. Interestingly, the prevalence and the incidence rates are high in South India where the incidence of oral cancer is also very high {3}. In spite of extensive studies, the pathogenesis and other aspects of oral submucous fibrosis remains unclear till today.

Oral submucous fibrosis is a precancerous condition caused by the use of areca nut in various forms. All areca nut products are associated with OSF, with the risk of being greatest for pan masala (product name). The duration of habit is more significant than frequency of chewing habit {4}. OSF is a chronic condition of oral mucosa and oropharynx with the potential for malignant transformation. Squamous cell carcinoma may occur in 7.6% of cases {5}.

Gingival involvement is characterized by fibrosis, blanching, and loss of normal stippling {6}. A large number of studies have been reported in the literature on mucosal changes in oral submucous fibrosis. However, there have been very few studies on the primary changes in the epithelium and connective tissue of gingiva in patients affected by oral

submucous fibrosis. The aim of this study was to evaluate clinical and histopathological changes in gingival epithelium and connective tissue in oral sub-mucous fibrosis.

MATERIALS AND METHODS

Study samples were obtained from the recalled and fresh cases of oral submucous fibrosis reporting to the Department of Oral Medicine and Radiology. Sample size of 30 and control of three normal gingival specimens were used for the study. Normal gingival tissue was obtained during other oral surgical procedures. This study complied with the Helsinki declaration. The data in this study were collected after the approval of the Institutional Review Board of College of Dental Sciences, Davangere, Karnataka, India, after obtaining informed consent.

Method

Clinical history of current and archival cases was obtained. Individual biopsy of the gingiva was obtained from the patients with oral submucous fibrosis after seeking informed consent. Confirmation of cases was done based on the presence of established clinical signs and symptoms. Clinically OSF is classified into three stages:

Early Stage - Fibrotic bands present, no trismus, and no involvement of tongue.

Established Stage -Trismus present but no gross involvement of tongue.

Advanced Stage - Marked trismus present and gross involvement of tongue {7}.

Clinical information as well as histology of each case was assessed according to pre established parameters (Table I). All the specimens were fixed with 10% NB formalin, and processed for H&E staining after paraffin embedding.

Sections of 5 µm thickness were obtained using soft tissue microtome from paraffin embedded blocks. The histological sections were stained by haematoxylin and eosin stain and were viewed under microscope to evaluate the changes (if any) in the epithelium and connective tissue of gingiva.

RESULTS

The present study was aimed at elucidating the clinical and histopathological changes in gingiva in oral submucous fibrosis patients. For histopathological comparison, three normal healthy gingival specimens were used.

Clinically out of 30 patients, the present study showed loss of stippling in 13 cases (43.3%), gingival recession in 5 cases (16.6%) while the remaining 12 cases (40%) showed both loss of stippling and gingival recession (Graph-1 & Fig-1).

Histologically epithelium showed atrophy in 14 cases (46.6%) (Graph-2 & Fig-2). The epithelium is parakeratinised stratified squamous type with loss of long rete ridge pattern. The thinning of epithelium and loss of rete ridges were due to increased fibrosis in connective tissue. In the connective tissue, blood vessels were dilated in 3 cases and obliterated in 9 cases as compared to normal gingiva specimens. Distribution of chronic inflammatory cells was observed. Increased fibrosis was observed in cases showing atrophic epithelium (Fig-2). 4 cases (13.3%) showed the gingival hyperplasia (Graph-2) (Fig-3).

Out of 30 cases in our study, 6 cases (20%) were in very early stage, 6(20%) in early stage, 15(50%) in moderately advanced stage and the remaining 3(10%) were in advanced stage, according to histopathological classification of OSF.

Categorical data of each of the 30 cases were assessed for severity staging by both clinical and histological gradings. Correlation between clinical and histological findings was done by Kappa measure of agreement, which showed absolute agreement in 50% of the cases.

DISCUSSION

Oral submucous fibrosis is a known premalignant condition predominantly seen among people of Indian origin. Epidemiological studies have suggested the habit of areca quid chewing as a major etiologic factor. Its malignant potential has been exclusively studied for the last three decades but many aspects of etiology and pathogenesis still remain an enigma. Features of OSF are characterized by difficulty in mouth opening (trismus), sinking of cheeks out of proportion to age, stiff and small depapillated tongue, blanched floor of the mouth, fibrotic gingival tissues, stiff soft palate with reduced mobility and shrunken bud like uvula, blanched and atrophic tonsils {8}.

The pathogenesis of this disease is still unclear although numerous studies have suggested that the occurrence of oral submucous fibrosis may be due to increased production and decreased degradation of collagen in the subepithelial connective tissue.

Early study by Sirsat and Pindborg {9}, reported that the biopsy specimen showed the presence of polymorphonuclear leucocytes, eosinophils and a few lymphocytes in the early stages of oral submucous fibrosis

and the presence of lymphocytes and plasma cells predominantly in the advanced stages.

Numerous studies in the past have examined various clinical and histopathological features of OSF, however very little information is available on gingival changes occurring in oral submucous fibrosis. The present study was conducted to evaluate the clinical and histopathological changes in both the epithelium and the connective tissue of the gingiva in patients with oral submucous fibrosis in comparison to normal gingiva.

The total sample size consisted of 33 cases of which 3 were from normal gingiva and used as control while the remaining were from gingiva of clinically diagnosed OSF cases.

In the present study, gingival fibrosis was noted clinically in all the 30 cases, 13 cases showed loss of stippling, 5 cases showed gingival recession and the remaining 12 cases showed both loss of stippling and gingival recession. This finding is in agreement with the earlier study of Pindborg & Sirsat {9} who reported presence of gingival blanching and fibrous bands in OSF patients.

Histologically, a marked atrophy of the gingival epithelium was seen in 14 cases in contrary to 4 cases which showed hyperplastic epithelium. The epithelium in 27 cases showed parakeratinized stratified squamous epithelium, whereas 2 cases showed hyper parakeratinized and 1 case showed orthokeratinized stratified squamous epithelium.

In cases with atrophic epithelium, the connective tissue showed changes like obliteration of blood vessels with extravasated RBC's, chronic inflammatory cell infiltrate and thick collagen bundles arranged in a combination of parallel and haphazard manner to the surface epithelium, whereas in the cases with hyperplastic epithelium, connective tissue showed numerous inflammatory cell infiltrate with scattered RBC's. The cases which showed atrophic epithelium with decrease rete ridge height also showed increased fibrosis. This increased fibrosis could be the causes for the change in the rete ridges.

This finding is in agreement with the previous study done by Pindborg and Sirsat {9} who studied oral submucous fibrosis in Indian population and observed that 90% of the cases showed marked atrophy of the buccal mucosal epithelium. The rete ridges were completely lost; the connective tissue showed juxtaepithelial hyalinization, oedema and thick collagen bundles with completely obliterated or narrowed blood vessels and dense inflammatory cells.

Compared to Pindborg and Sirsat {9} study, which showed atrophy in 90% of the cases, and a study by Pindborg, Chawla, Srivastava and Gupta {10} which showed epithelial atrophy in 97% of the cases with complete disappearance of rete ridges and reduction in the width of the ridges in some cases, the present study showed less than 50% of cases with atrophy. This variation could be due to the sites examined by these authors, which were mainly from non-keratinized mucosa. This may be due to the fact that gingiva is a keratinized tissue and may provide certain resistance to damage delaying the atrophic changes.

Wahi et al {11} found that majority of the cases out of 104 punch biopsies taken from palate (53), buccal mucosa (46), tongue (3) and one each from gingiva and lips showed

hyperplastic epithelium. The present study showed only 4 cases of hyperplastic epithelium. This variation could be explained by the inclusion of nonkeratinised mucosae in the study by Wahi et al and the differences in the clinical stages of the cases included in the studies.

CONCLUSION

The present study concludes that gingiva is affected histologically in oral submucous fibrosis in 60% of the cases and the findings coincide with those of other oral mucosal

sites affected by oral submucous fibrosis. Those affected show changes corresponding to various histological stages ranging from very mild to advance for other mucosal sites. The appearance of the typical changes seen in our study associated with OSF in addition to the fixed nature of gingiva makes it an excellent candidate for diagnostic mucosal biopsies in OSF. However to establish these further studies, correlating the clinical and histopathological grading of the gingiva along with any other mucosal site will be needed.

Table I: Clinical and histological parameters for analysis of the cases

Clinical	Histological
Loss of stippling Gingival recession	Epithelial thickness Epithelial connective tissue interface Connective tissue in relation to fibrosis, blood vessels and inflammatory cells

Fig 1: Loss of stippling and gingival recession



Fig 2: Atrophic gingival epithelium

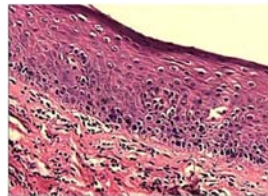
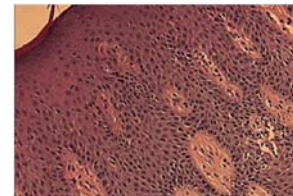
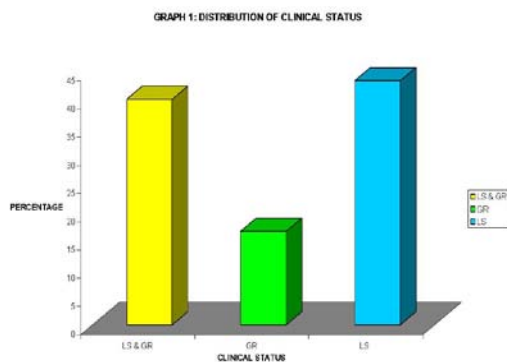


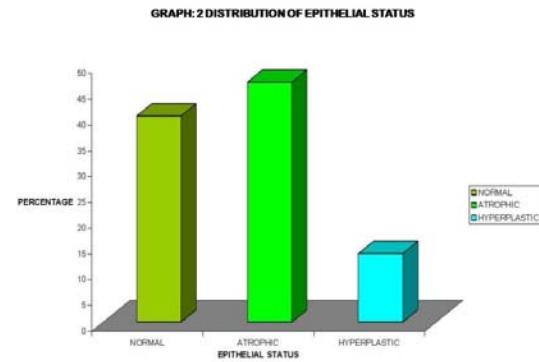
Fig 3: Hyperplastic gingival epithelium



Graph 1: Clinical status of gingiva (LS= Loss of stippling, GR= Gingival recession)



Graph 2: Distribution of epithelial status (Percentage of normal, atrophic and hyperplastic epithelium)



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