International Journal of Research in Health and Allied Sciences

Journal home page:www.ijrhas.com

Official Publication of "*Society for Scientific Research and Studies*" [Regd.]

ISSN 2455-7803 Index Copernicus value 2016 = 68.10

Original Article

Expression of Myofibroblasts in Oral Submucous Fibrosis: An Immunohistochemical Study

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***ABSTRACT*:**

Background: Oral submucous fibrosis (OSMF) is a chronic debilitating disease of the oral cavity. Recent evidence appreciates the notion that the transformation of fibroblast to myofibroblasts is essential for the cells to perform these functions. Hence; we planned the present study to evaluate the expression of myofibroblasts in oral squamous cell carcinoma specimens.**Materials & methods:** A retrospective study was done on archival specimen of 20 oral submucous fibrosis (OSMF) and 20 cases of normal oral mucosa (taken as normal control). Immunostaining was assessed by the evaluation of the staining intensity and percentage of α-SMA-positive cells. All the results were analyzed by SPSS software.**Results:** We observed that expression of α- SMA was significantly higher in OSMF specimens in comparison to normal control.**Conclusion:** Myofibroblasts play a definite role in the pathogenesis of OSMF.

Key words:α- Smooth muscle actin, Myofibroblasts, Oral Submucous fibrosis

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This article may be cited as: Singh J, Singh S.Expression of myofibroblasts in oral submucous fibrosis: An immunohistochemical study. Int J Res Health Allied Sci 2018; 4(1):105-107.

INTRODUCTION

Oral submucous fibrosis (OSMF) is a chronic debilitating disease of the oral cavity. Although the pathogenesis of the disease is not clearly understood; epidemiological data and evidence strongly suggest an association between areca nut and oral OSMF.[1, 2] Fibrosis is often considered as a wound-healing process that has gone out of control which initially is beneficial but becomes pathogenic if it remains unchecked and will result in extracellular matrix (ECM) remodeling and formation of permanent scar tissue. Substantial ECM remodeling and exuberant collagen formation in OSMF has been compared with an excessive scar tissue formation in healing wounds. Fibroblasts are the principal cells involved in wound healing and tissue repair.[3- 5] Recent evidence appreciate the notion that the transformation of fibroblast to myofibroblasts is essential for the cells to perform these functions.[6] Myofibroblasts are a unique group of cells with smooth muscle properties and can be identified by the expression of alpha-smooth muscle actin (α-SMA), and are believed to be primary producers of ECM after injury. Alteration in quantity and functioning myofibroblasts has been implicated in various fibrotic diseases.[7- 9]Hence; we planned the present study to evaluate the expression of myofibroblasts in OSMF specimens.

MATERIALS & METHODS

A retrospective study was done in Jammu region on archival specimen of 20 cases of OSMF and 20 cases of normal oral mucosa (taken as normal control).

This study was based on specimens of histologically diagnosed cases of OSMF obtained from the archives of oral pathology. The tissue sections were stained; one with hematoxylin and eosin (H & E) stain and another with α - SMA antibody by immunohistochemical methods.

Immunostaining was assessed by the evaluation of the staining intensity and percentage of α-SMA-positive cells, according to the method used by Etemad-Moghadam et al. The percentage of immuno-positive cells in the non-inflammatory and non-endothelial stromal cells in the subepithelial connective tissue of OSMF in 4 high power fields (hpf) and average percentage per hpf were calculated. All sections were counted twice to avoid intra-observer variability. All the results were analyzed by SPSS software. Chi- square test and one way ANOVA were used for the evaluation of level of significance. P- value of less than 0.05 was taken as significant.

Table 1: Comparison of staining index in between OSMF group and Normal control group

GROUPS	No. OF SPECIMENS	PERCENTSGE OF MYOFIBROBLASTS SCORE (A)		STAINING INTENSITY SCORE (B)		STAINING INDEX SCORE (I) I = A x B	
		t - value	p - value	t - value	p - value	t – value	p - value
OSMF vs NC	40	14.52	< 0.05	13.25	< 0.05	8.95	< 0.05 (s)

RESULTS

In the present study, we evaluated expression of α- SMA in OSMF specimens and normal control specimens. We observed that expression of α- SMA was significantly higher in OSMF specimens in comparison to normal control.

Figure 1: Negative expression of myofibroblasts in Normal control

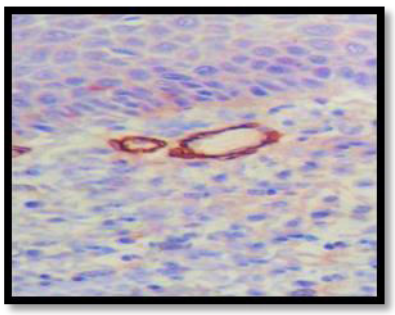
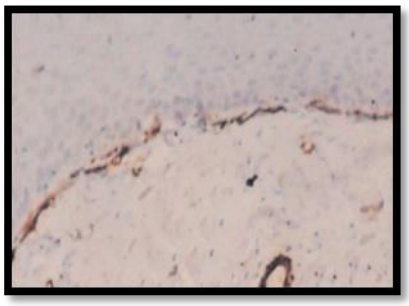


Figure 2: Positive expression of myofibroblasts in OSMF specimen



DISCUSSION

In the present study, observed significant difference while comparing the expression of myofibroblasts in between OSMF specimens and normal control specimens. Kiuchi M et al examined the presence of mast cells and myofibroblasts in 33 denture-induced fibrous hyperplasias (DIFH) compared with 10 healthy gingival tissues. The parameters examined included mast cell numbers, tissue distribution, degranulation, and cell subtypes using immunohistochemistry. On the survey of the origin of myofibroblasts, results showed α – SMA and vimentin positivity indicating these transformed from fibroblasts. These results were the first to show that mast cells and myofibroblasts can be detected in DIFH, indicating important roles of these cells in the pathogenesis of this lesion.[10]

Sridhara SU et al compared the presence of α-SMA and CD34 positive fibroblasts in nonmetastatic and metastatic oral squamous cell carcinoma and to evaluate their role in tumor metastasis. α -SMA positive cases were more in the metastatic group and CD34 positive cases were found to be more in the nonmetastatictumors. They concluded that though difference in the staining pattern was statistically nonsignificant, the inverse relationship between α-SMA and CD34 positive cells is indicative of dynamic nature and the influence of tumor stroma in tumor progression and metastasis.[11]Marangon Junior H et al evaluated the expression of laminin-5 γ2 in OSCC and its association with intensity of tumor budding and density of stromal myofibroblasts. They concluded that, in OSCC, higher laminin-5 γ2 expression is associated with high-intensity tumor budding and with higher density of stromal myofibroblasts, suggesting that this expression is related to the establishment of an invasive phenotype of neoplastic cells and a permissive environment for tumor invasion in this neoplasia.[12]

Lúcio PS et al performed a literature review on the origin of myofibroblasts, their main morphophysiological and immunohistochemical aspects, and to discuss the correlations with oral SCC. A search was made on the pubmed database to select the main papers in the literature in english related to the subject, published between january 1991 and december 2011. Myofibroblasts are an important component of the stroma of oral SCCs, although they are not present in all tumors. Abundant presence of myofibroblasts may be associated with local disease recurrence and decreased patient survival. However, given the relatively limited number of studies on the subject, further research is needed to clarify the molecular mechanisms by which myofibroblasts influence the biological behavior of oral SCC.[13]

Epivatianos A et al detected the presence of myofibroblasts and TGF – β1 in fibrous and ossifying-fibrous epulis and their possible contribution to the collagenous connective tissue formation. The correlation between the myofibroblasts and the degree of inflammatory infiltration was also examined. The data suggested that TGF – β1 and myofibroblasts contribute to the formation of collagenous connective tissue in fibrous epulis and ossifying fibrous epulis. Myofibroblasts were mainly presented in ossifying fibrous epulis than in fibrous epulis. There seemed to be no relationship between the presence of myofibroblasts and the degree of inflammatory infiltration of the lesions.[14]

CONCLUSION

Myofibroblasts play a definite role in the pathogenesis of OSMF. However; future studies are recommended.

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Source of support: Nil **Conflict of interest:** None declared