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Research Article

Collagen : A Double Edged Sword For Oral Cancer

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ABSTRACT

Objectives: The aim of the study was to evaluate the nature, hue, orientation, arrangement of collagen changes in different grades of Oral Squamous Cell Carcinoma (OSCC) and to target our existing treatments more effectively.

Material and Methods: cases of different grades of OSCC were evaluated along with the control group with connective tissue special stains Van Geison and Masson Trichome.

Results: statistical analysis was done to evaluate significant change of collagen fibers between different grades of OSCC. It was highly significant between different grades of OSCC .

Conclusions: The reactive changes in the collagen may alter the biological aggressiveness of oral cancer. Once the exact mechanism of collagen degradation is known, more effective therapies may be created to reduce the degradation of Extracellular matrix (ECM) and basement membrane (BM) inherent in the metastatic process.

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INTRODUCTION

Carcinomas are malignant epithelial tumors in which cells show an atypical arrangement with varying degrees of differentiation. Oral squamous cell carcinoma (OSCC) comprises a bulk of all the oral malignancies and the morbidity rate of this disease is further increased due to a tendency for invasion and metastasis as well as the propensity to develop either second primary tumors or second field tumors¹. There are two discrete independent compartments, the malignant epithelial cells and the stroma in which stromal components are the key factors for provision of nutrition and growth to any tumor as also they act as a barrier for spread of the tumor². Tumor stroma plays a vital role in tumor progression by undergoing dramatic morphological and architectural changes and act as physical Scaffold for influx of inflammatory cells³. Collagen being one of the major component of connective tissue stroma it serves as an effective barrier that tumor cells must break through for local invasion and metastasis, this holds good even for oral squamous cell carcinoma (OSCC) which accounts for approximately ninety four percent of all oral cancers⁴. Collagen is a triple helix structure & rich in basic amino acid, so have strong affinity for acidic dyes. Tumor cell

produces collagenases which has ability to degrade Type-I collagen and helps in invasion and metastasis

AIMS AND OBJECTIVES

- 1.Hue, nature, orientation and arrangement of collagen fibers around tumour islands in various grades of OSCC by using Van-gieson stain and Masson Trichome,
- 2.To compare staining of collagen fibers using van-gieson and masson trichome stain and
- 3.To correlate the hue and spatial distribution of collagen fibers in the progression of OSCC

METHODS AND MATERIAL

Material for the study was retrieved from the Archives of Department of Oral Pathology. Special stains used for the study were Van-Gieson & Masson Trichome. A total of 45 cases of OSCC and 10 cases of normal mucosa will be evaluated. The tissue specimens will be categorized as test group and control group. Only specimens with adequate connective tissue thickness are taken for the study. The sections were further graded according to the World Health Organization grading system, revised in 2005 based on Broders' classification. Categorical data will be analyzed by chi-square test.

RESULT

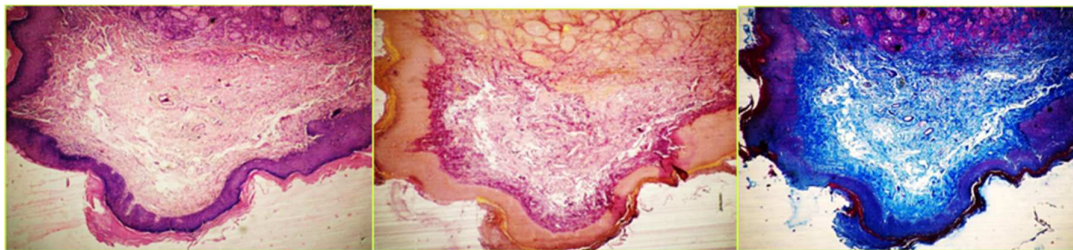


Fig 1; Photomicrograph showing H & E, Van Gieson and Masson Trichome stained section of well differentiated OSCC.

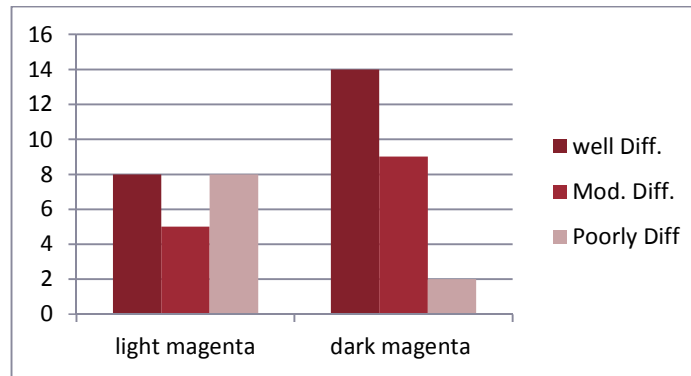


Table – 1: Comparison Of Hue Of Collagen In Different Grades Of Ossc By Van-Gieson Stain

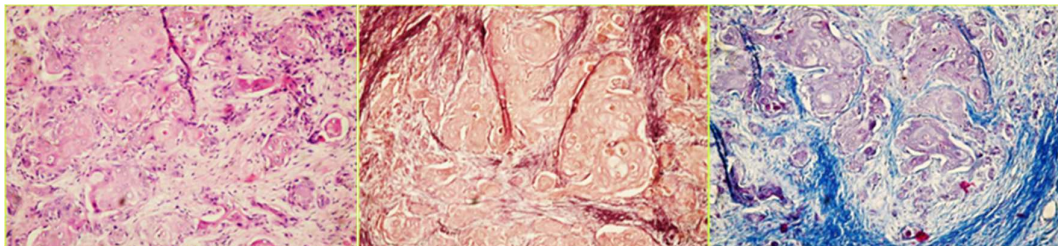


Fig2 : Photomicrograph Showing H & E, Van Gieson And Masson Trichrome Stained Section Of Moderately Differentiated OSCC.

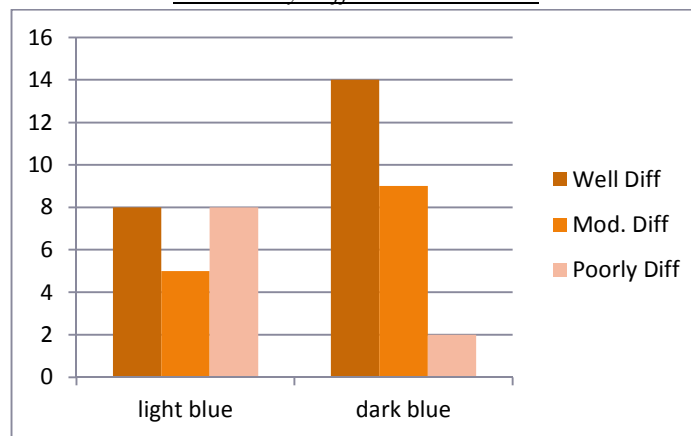


Table -2 : Comparison Of Hue Of Collagen In Different Grades Of Ossc By Masson Trichrome Stain

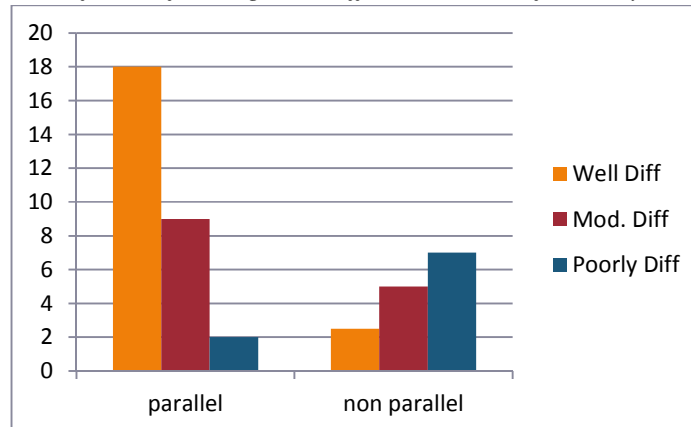


Table – 3: Comparison Of Orientation Of Collagen Fibers In Different Grades Of Scc By Van-Gieson Stain

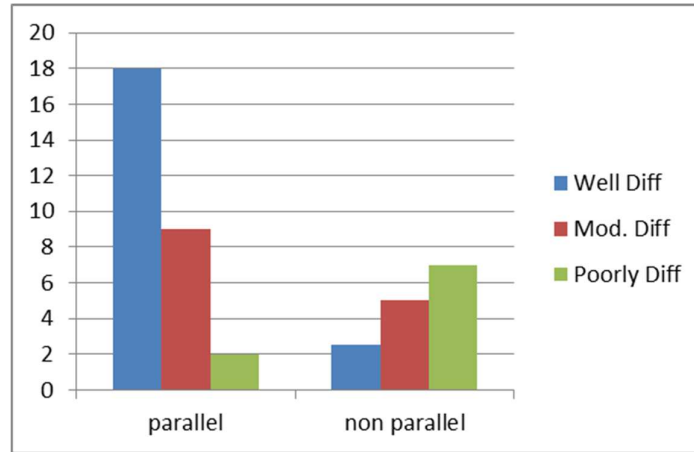


Fig3 ; Phomicrograph showing H & E, Van Giesion and Masson Trichome stained section of poorly differentiated OSCC.

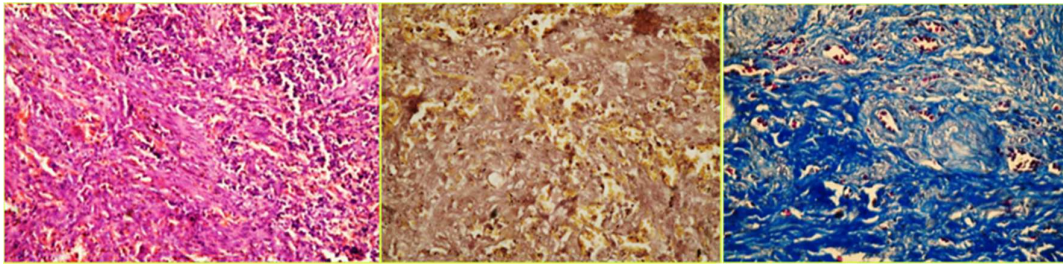


Table -4: Comparison of orientation of collagen fibers in different grades of SCC by Masson Trichome

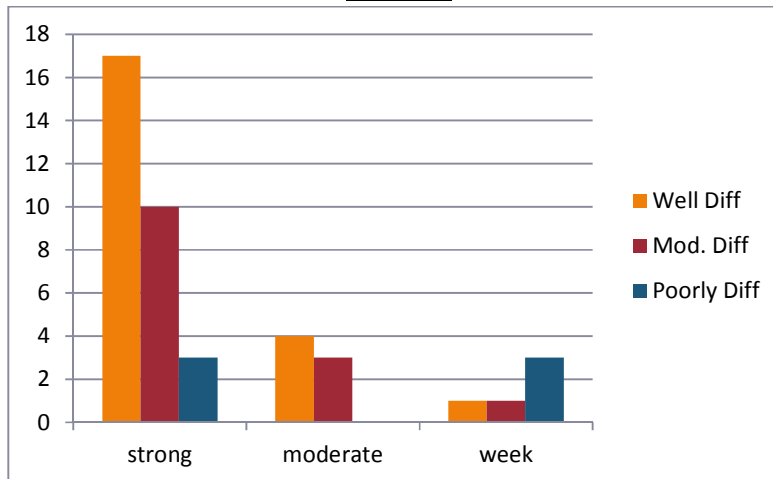


Table -5: Comparison of nature of collagen fibers in different grades of SCC by Van-Gieson stain

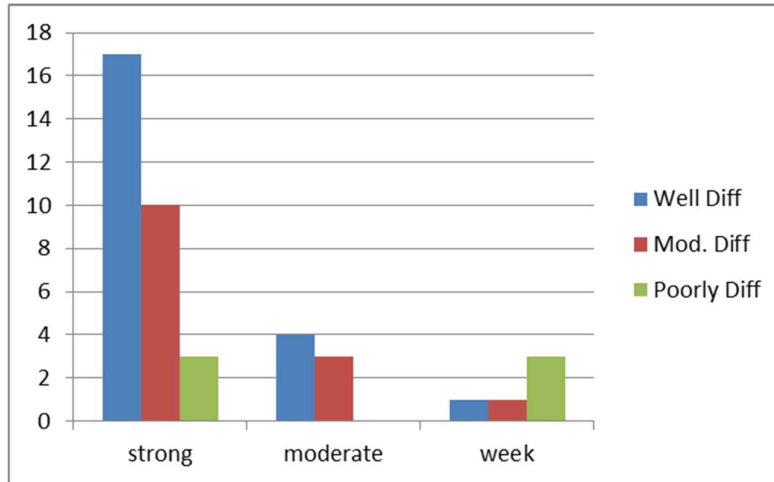


Table 6: Comparison Of Nature Of Collagen Fibers In Different Grades Of SCC By Masson Trichome

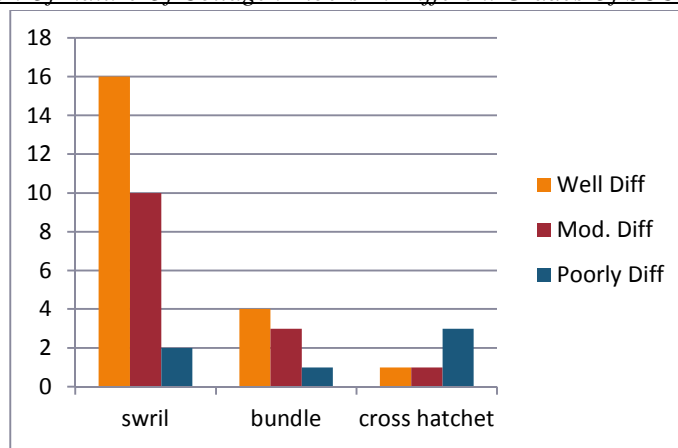


Table 7: Comparison Of Arrangement Of Collagen Fibers In Different Grades Of SCC By Masson Trichome

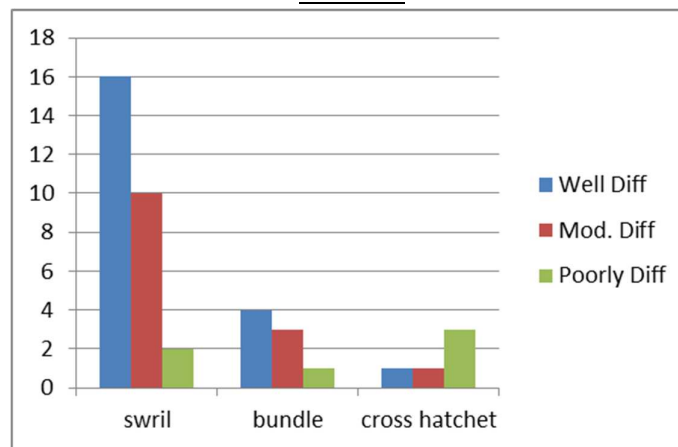


Table 8: Comparison of arrangement of collagen fibers in different grades of SCC by Van-Gieson stain.

In statistical analysis of collagen fibers between various grades of SCC by van-gieson, & masson trichome. Comparison between p value of van-gieson & masson trichome is non-

significant. 14 % of well differentiated OSCC shows dark magenta and blue color(as shown in graph 1,2) because of presence of more collagen fibers. 18 % of OSCC shows parallel

and 4% non parallel orientation (as shown in graph 3,4) because Collagen orient in parallel to normal or hyperplastic epithelium in early stage. 17%, 4%, and 1% of well differentiated OSCC (as shown in graph 4, 5)shows strong moderate and week nature of collagen fibers respectively which depends on way of packing of collagen fibers. 16%, 4%, and 1 % of well differentiated OSCC shows swirl, bundle, and cross hatchet arrangement of collagen fibers respectively. In arrangement of collagen fibers,

advanced stages of OSCC showed mature collagen to immature form.

DISCUSSION

Oral epithelial precursor lesions are defined as altered epithelium with an increased likelihood for progression to OSCC. Interaction between tumour cells leads to angiogenesis, inflammatory reactions, failure of basement formation and remodeling of collagen. These are crucial determinant of tumour cells proliferation, transformation, spread & metastasis.

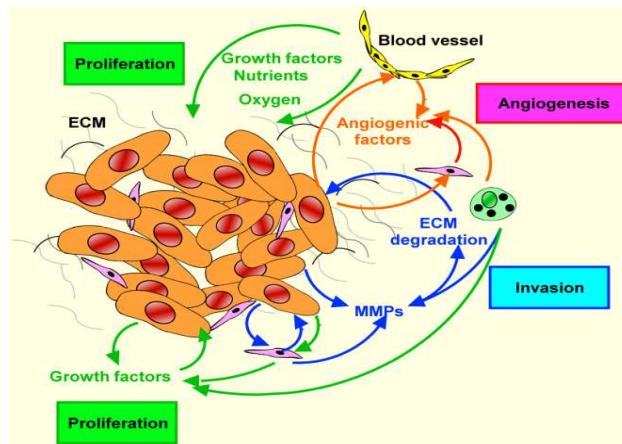


Fig 1: tumor-stromal interactions in HNSCC.

Tumor-stromal crosstalk leads to the overexpression of growth factors sustaining tumor growth, angiogenic factors promoting angiogenesis, and proteolytic enzymes enhancing the degradation of extracellular matrixes. These autocrine and paracrine factors facilitate tumor cell invasion and finally metastasis. (Koontongkaew S)

Colour change is attributed to pathological breakdown in matrix by tumours cells and action of MMPs⁵. Hue of collagen depends on the thickness and their molecular packing⁶. Hue of collagen fiber could be to various growth factors and cytokines that cause proliferation of fibroblasts and ECM resulting in the formation of thick mature collagen⁷. So hue and colour of collagen can be used in the quantitative as well as qualitative analysis and clinical behavior of SCC⁸.

The colors of collagen fibers could be due to various growth factors and cytokines that cause proliferation of fibroblasts and ECM resulting

in the formation of thick mature collagen. As collagen matures, the change in proteoglycans content of fiber causes dehydration of the fibers thereby, increasing the diameter of collagen fibers. Thus, to tight packing of collagen, there was the difference in colors⁹

Collagen orient in parallel to normal or hyperplastic epithelium in early stage but later on progressive change in the fibers orients it in non-parallel to the tumor borders⁸. Hence, orientation of collagen or change in architecture may promote cell invasion by enabling cells to migrate along the collagen fibers. Tumor cells often localize near dense collagen as swirl, bundle & cross hatchet⁸. Expansion (stretching) of the collagen matrix leading to matrix reorganization (possibly assisted by proteolytic cleavage to release collagen fibers) to help facilitate local invasion¹⁰.

Tight packing of collagen presented as strong, moderate & weak. As collage mature there is change in proteoglycans content of fiber causes

dehydration of the fibers that leads to change in proteoglycans content of fiber causes dehydration of the fibers⁵. Decrease in collagen collagen fibres leads to progression towards advanced dysplastic grading.

The present study thus indicate that tumor cells which growing progressively in the host stroma and observable changes were seen in the stroma, in different grades of OSCC's. There was an increased stromal response in poorly differentiated carcinomas, when compared to the other grades. Observable changes in staining reactions of the stromal components reveal an underlying change in the biochemical level. So tumour cells have capacity to induce proliferation of stromal cells and result in tumourogenesis. Study should be conducted further for better treatment strategies and for better drugs penetration.

CONCLUSION

In the present study, it has been observed that collagen changes at juxtaepithelial region & around tumor islands and with increasing grade of the tumor with the use of Van-gieson & Masson Trichome stain. The reactive changes in the collagen may alter the biological aggressiveness of oral cancer and can help for targeting the stroma for various treatment strategies. Li H et.al. also concluded in their study that collagen fibre plays an important role in E.C.M destruction and remodelling. Collagen fibre content in OSCC tissue significantly correlated with tumour differentiation, recurrence and nodal status, which reflects the key role of collagen fibre in carcinogenic process¹¹. Collagen can no longer be considered a static and passive background upon which metastasis take places¹².

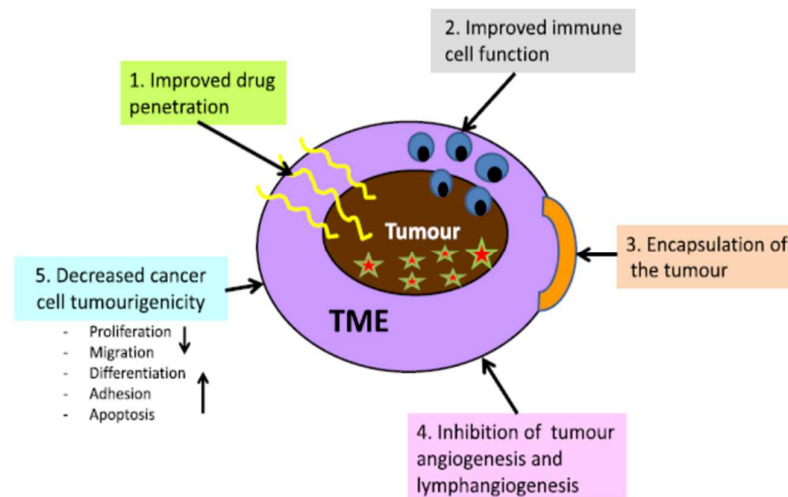


Fig 2; Schematic representation of the desired effects of ECM-based gene therapies in cancer. (Sainio A, Järveläinen H)

Oral squamous cell carcinoma is showing local invasion of the underlying connective tissue in forms of islets and cords of epithelial cells. Interaction between tumor cells and ECM components was essential for tumor growth and onset of cell spreading and subsequent metastatic activity. The stromal tissue in breast cancer has also shown that increase in the collagen content of the ECM increasing mechanical stiffness and transport resistance of the tumor¹³⁻¹⁶

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