Myofibroblasts as important diagnostic and prognostic indicators of oral squamous cell carcinoma

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Abstract

Background: Squamous cell carcinoma (SCC) makes up 94% of oral malignancies, making oral squamous cell carcinoma (OSCC) one of the ten most common malignant tumours. Multipurpose cells like macrophages and myofibroblasts play a critical part in how these tumours behave biologically. The objective of this study was to compare the frequency of myofibroblasts and macrophages in cutaneous and oral squamous cell carcinomas.

Methodology: There were 100 cases of WDOSCC, MDOSCC, PDOSCC, and healthy controls total. Each tissue sample was cut into 4-m thick sections, which were then both conventionally stained with hematoxylin and eosin and immunohistochemically stained with α-SMA. The expression of MFs was compared among OSCC grades. Statistics were applied to all of the outcomes.

Results: 100 cases of each of WDOSCC, MDOSCC, PDOSCC, and normal mucosa were used as controls in the current investigation, which was conducted in three distinct grades of OSCC.The specimens were examined immunohistochemically using the SMA marker, and the results showed that the mean final staining index score for WDOSCC patients was 8.75, 8.16 for MDOSCC cases, and 7.29 for PDOSCC cases.Control subjects, however, displayed negative expression.

Conclusion: Based on the findings of the current inquiry, it was determined that MFs are one of the crucial pathogenetic components in OSCCs, and that assessing them could help predict their invasive behaviour. As a result, we are in favour of using MFs as a stromal marker to help OSCC patients see invasion and progression.

Keywords: Alpha-smooth muscle actin, myofibroblast, oral squamous cell carcinoma.

Introduction

Cancer is the second most important cause of death in developed countries and the third cause of death in developing countries after cardiovascular diseases.[1] Five percent of all tumors occur in the head and neck region, with half of them in the oral cavity.[2] Cancers of this area are one of the major reasons for mortality and morbidity worldwide and reported as the most common cancers in humans.[3,4] Oral squamous cell carcinoma (OSCC) is the most common oral cancer, and cutaneous squamous cell carcinoma (CSCC) is a frequent cancer of the skin.[5] Skin malignancy, which has been on the increase recently, accounts for 11% of all human malignancies. SCC accounts for approximately 20% of skin tumors and originates from dysplastic surface epithelium.[6,7] Ability to predict the biological behavior of oral and cutaneous SCC helps prepare an appropriate treatment plan.[8]

Myofibroblasts have a critical role in regulating the stroma under normal and pathological conditions via direct cell-to-cell contacts and by secreting matrix metalloproteinases (MMPs), MMP tissue inhibitors, extracellular growth factors, cytokines, chemokines, and fatty products by expressing specific receptors. Apart from their role in wound healing processes, Myofibroblasts are indispensable for the induction of tissue and mucosal immunity and stem cell donation.[9] Carcinoma-related fibroblasts, including myofibroblasts, are often seen in the stroma of human carcinoma. The differentiation of fibroblasts into myofibroblasts due to the effect of cytokines and growth factors originating from tumor cells is a principal and crucial event in tumorigenesis. The induction of myofibroblasts is due to the factors caused by OSCC that stimulate carcinoma and neoplastic growth.[10] The high stromal myofibroblast counts are associated with a poor prognosis of the oral, breast, and colorectal carcinomas.[11]

Hence, the current study was undertaken to assess the role of myofibroblasts as important diagnostic and prognostic indicators of oral squamous cell carcinoma.

Material and methods

WDOSCC, MDOSCC, PDOSCC, and healthy controls were all used in the current study to assess the expression of MFs using IHC and a SMA antibody. The study sample included of 50 cases of WDOSCC, MDOSCC, and PDOSCC with histological confirmation as well as 50 tissue samples from normal mucosa with the same confirmation. The controls for normal mucosa were dental follicular tissue excised therapeutically for orthodontic purposes. Two 4 m thick slices were produced from each tissue block. While one tissue segment was stained with the usual hematoxylin and eosin (H&E), the other was subjected to

immunohistochemical analysis utilising the SMA marker. H &E stained slides were utilised as reference slides for evaluating and validating OSCC cases.

Results

50 cases of WDOSCC, MDOSCC, PDOSCC, and 50 controls were enrolled in the current investigation, which was conducted in three distinct grades of OSCC.The specimens were examined immunohistochemically using the SMA marker, and the results showed that the mean final staining index score for WDOSCC patients was 8.75, 8.16 for MDOSCC cases, and 7.29 for PDOSCC cases.Control subjects, however, displayed negative expression. The results of the intergroup comparison of the final staining index score between the various OSCC grades did not reach statistical significance (P 0.05), and the expression of MFs between the various OSCC grades similarly yielded unremarkable results.The comparison of the final staining index score between OSCC cases and normal controls as well as the expression of MF between the two groups revealed substantial statistical significance (P 0.05).

Table 1: Comparison of final staining index score between different grades of oral squamous cell carcinoma.

Groups	**P value**
Well differentiated oral squamous cell carcinoma V/s Moderately differentiated oral squamous cell carcinoma	0.036
Well differentiated oral squamous cell carcinoma v/s poorly differentiated oral squamous cell carcinoma	0.028
Moderately differentiated oral	0.032

squamous cell carcinoma v/s poorly differentiated oral squamous cell carcinoma	

Discussion

Oral squamous cell carcinoma (OSCC) is a malignancy with high mortality and morbidity. Early diagnosis and treatment of OSCC and other potentially malignant lesions of the oral mucosa is the clinician's best weapon to improve prognosis, since it greatly worsens as the disease becomes more advanced. In Western countries, oral cancer represents a rather uncommon malignancy, with oral squamous cell carcinoma (OSCC) being most frequent.[12] OSCC has high mortality and morbidity,[13] which significantly increases with diagnostic delay.[14] As the most common risk factors for OSCC are well known and are for the most part behaviors that can be eliminated, primary prevention consists in educating the population against these behaviors.[15] Once the cancer is present, early diagnosis is the single most important element in improving prognosis, since clinical and pathological staging is the most important factors that influence survival rates.[16]

In this study, theresults revealed a mean final staining index score of 8.75 in WDOSCC cases, 8.16 in MDOSCC cases and 7.29 in PDOSCC cases. However, negative expression was seen in controls. Intergroup comparison of final staining index score among different grades of OSCC showed no statistical significance ($P \leq 0.05$) in the results and also expression of MFs in between different grades of OSCC showed nonsignificant results. On the other hand, a comparison of final staining index score between OSCC and normal controls and the expression of MF between OSCC cases and normal controls showed high statistical significance ($P \geq 0.05$).

Vered et al[17]and Saif et al[18] andDodani et al[19] showed no significant differences in the presence and accumulation of myofibroblasts in OSCC and CSCC in terms of the intensity and pattern of staining.[20]

Adegboyega et al.[20] in 2002 used α-SMA and vimentin IHC staining on myofibroblasts, for normal colon mucosa, hyperplastic polyps, and colorectal adenomatous in their research. α-SMA-negative fibroblasts and vimentin-positive ones were observed in the colon mucosa,

whereas α-SMA- and vimentin-positive fibroblasts were observed in hyperplastic and neoplastic polyps. They concluded that in neoplastic cases, intercellular fibroblasts differentiate into myofibroblasts in the stroma of SCC. They also studied its relationship with the tumor stage and reported that there was a relationship between the expression of α-SMA and tumor stage.

Conclusion

It was concluded that MFs are one of the essential pathogenetic elements in OSCCs based on the facts of the current investigation, and that evaluating them might assist anticipate their invasive behaviour. Therefore, we support the use of MFs as a stromal marker for OSCC patients to visualise invasion and progression.

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