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Assessment of role of mast cells in oral squamous cell carcinoma

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ABSTRACT

Background: Mat cells play a crucial role in homeostasis and inflammation. Recently mast cells have been associated with numerous malignancies like oral squamous cell carcinoma (OSCC).**Aims and Objectives:** To compare mast cell density in normal mucosa and squamous cell carcinoma and to assess the role of mast cells in oral squamous cell carcinoma.**Materials and Methods:** Our retrospective study included 40 specimens, 10 well differentiated OSCC, 10 moderately differentiated OSCC, 10 poorly differentiated OSCC and 10 controls. Mast cell density was determined by toluidine blue staining. Statistical analysis was carried out using Statistical Package for Social Sciences (SPSS) 17.0 version (SPSS Inc., Chicago, IL, USA).**Results:** When compared with controls, mast cells count was a higher in OSCC groups which was a statistically significant ($P < 0.001$). **Conclusion:** Mast cells have a significant role in OSCC.

Keywords: Mast cells, Oral squamous cell carcinoma, Toluidine blue stain

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Introduction

OSCC is a malignant epithelial neoplasm exhibiting squamous differentiation as characterized by the formation of keratin and /or the presence of intercellular bridges. It makes up nearly 95 % of cases [1]. In spite of advancements in the field of cancer diagnosis and availability of latest treatments, survival rates are not satisfactory. This is mainly due to unpredictable behavior of these lesions[2].Mast cells are connective tissue cells that are scattered along the capillaries, characterized by having abundant basophilic granules. Paul Ehrlich in 1878 first described mast cells as "mast zellen" meaning feeding cells in Greek. Mast cells are round, oval or spindle shaped cells measuring approximately 12 microns with 50 to 100 granules in cytoplasm. These cells have a role in inflammation and immunity. Mast cells are usually seen near blood vessels and the mediators

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released from them have been implicated in promoting angiogenesis. Hence, accumulation of mast cells appears to potentiate vessel growth [3,4].Studies have shown that OSCC is associated with chronic inflammation, immune reaction and angiogenesis with the progression of dysplastic changes. Hence, there is a need to assess the role of mast cells in OSCC[1-3].Our study was carried out to compare mast cell density in normal mucosa and squamous cell carcinoma and to assess the role of mast cells in oral squamous cell carcinoma.

Materials and Methods

Our retrospective study included 40 specimens, 10 well differentiated OSCC (WDOSCC), 10 moderately differentiated OSCC (MDOSCC), 10 poorly differentiated OSCC (PDOSCC) and 10 controls. The OSCC blocks were retrieved from the archives of oral pathology department. As control, normal oral mucosa specimens were used.4 micron thickness sections were prepared from each block. Each section was stained with toluidine blue staining for the identification of mast cells. The acidified toluidine blue technique was used as it gives rapid crisp staining of mast cells. The tissue sections were dewaxed in xylene and rehydrated

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in descending grades of alcohol, transferred to potassium permanganate solution for 2 minutes. Then slides were rinsed in distilled water, and then transferrred to potassium metabisulphate solution for 1 minute or until section appears white. Later the slides were washed in tap water for 3 minutes, rinsed in distilled water. Then were stained with toluidine blue for 5 minutes and rinsed in distilled water, cleared in xylene and mounted. Mast cells stained purple and nuclei blue. Both intact and degranulated mast cells were identified by the structure of purple colored granules. These were scattered throughout the connective tissue, with some mast cells near to or adhered to the vessels. Only mast cells found in the hot spot areas were counted (**Fig 1 and 2**).
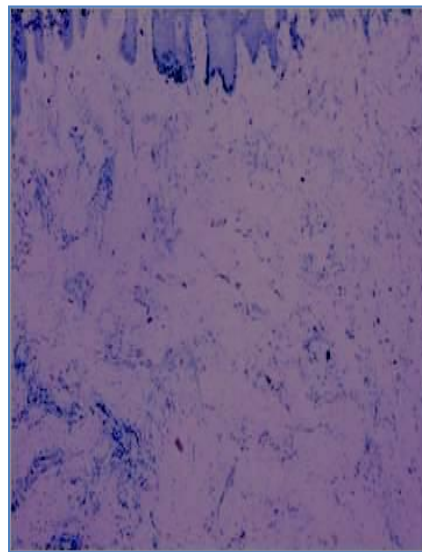

Fig 1: Toluidine blue staining for mast cells in normal tissue (10x)
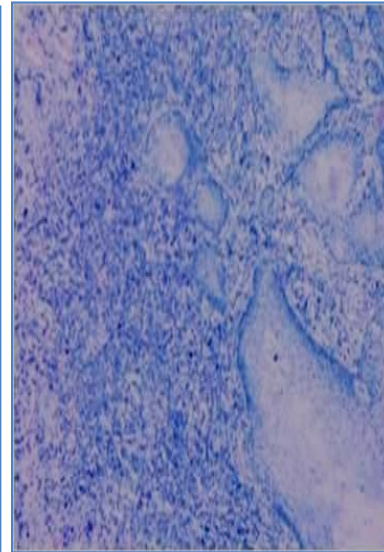
Fig 2: Toluidine blue staining for mast cells in OSCC

Results

We found the mean mast cell Density (MCD) in normal was 26.12 with Standard deviation of 3.14. MCD in WDOSCC, MDOSCC and PDOSCC was 44.65±6.17, 56.83±5.48 and 78.65±9.73 respectively. There was an increase in mean MCD from normal to PDOSCC progressively (**Graph 1**).
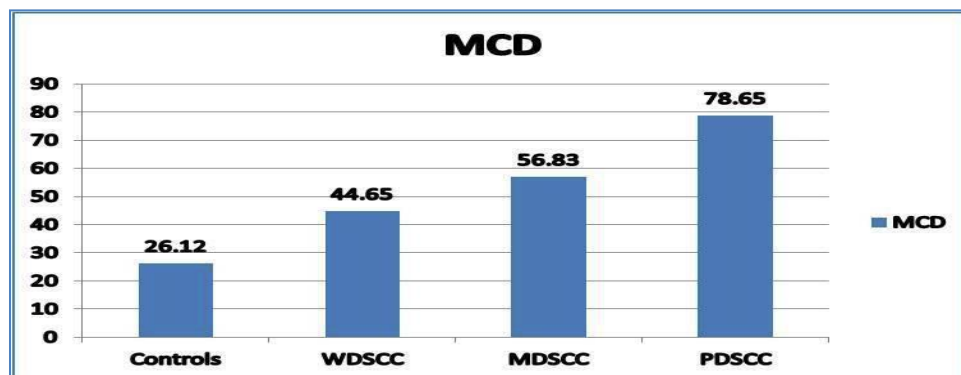
Graph 1: showing MCD in controls and grades of OSCC

When one way ANOVA was applied for MCD, all the groups showed highly statistically significant differences (p<0.001).

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Discussion

Various mechanisms have been proposed to explain the tumorigenic effect of mast cells. They are degradation of extracellular matrix, angiogenesis, mitogenesis and immunosupression. Of all these proposed mechanisms, angiogenesis seems to play a major role in tumor growth[5,6].Angiogenic regulation in carcinogenesis is biphasic. In earlier stages, mast cells degranulate and in turn activate dermal fibroblasts which increase angiogenesis. mast cells were shown to activate progelatinase B, a matrix metalloproteinase which has role in both extracellular remodeling and regulation of angiogenesis. Angogenic activators are released by the mast cells, which further intensify angiogenesis. Due to all these actions, mast cells have vital role in the early stages of cancer progression and hence increased number of mast cells are observed [7, 8].Angiogenesis has been reported in many premalignant lesions like leukoplakias and in cancers of breast, colon and also in OSCC[7-9].Experiments on mice have shown tumor angiogenesis and tumor growth to be less in mast cell deficient mice when compared with mice with normal mast cell numbers. Studies have also shown that mast cells do induce neovascularization through the carcinogenesis of squamous cells [9,10]. These findings are consistent with our results. However some studies have shown contrast reports. **Juma O.Alkhabuli** (**2006**), observed an increase in the number of mast cells in WDOSCC as compared to their low number in PDOSCC[11].Even though several studies have established the presence and implication of mast cells in carcinomas, their mediated angiogenesis is intricate and not totally understood. In agreement with the literature, our study also showed a high mast cell count in OSCC than in control tissue indicating their supportive role in tumor progression and metastasis[12-16].Hence, we suggest to carry out studies on a much larger sample and using antibodies to identify the subtypes of mast cells to establish the exact role of mast cells and their role in tumor progression.

Conclusion

Our study showed that there is a definitive rise in mast cell count in OSCC when compared with normal controls. We also found the increase in mast cells progressing from WDSSC to MDSCC to PDSCC. Hence we substantiate the fact that mast cells have a significant role in angiogenesis and tumorogenesis.

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