



ROLE OF MAST CELLS IN ORAL LEUKOPLAKIA, ORAL SUBMUCOUS FIBROSIS & ORAL SQUAMOUS CELL CARCINOMA-A QUANTITATIVE STUDY

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Conflicts of Interest: Nil

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Abstract:

Mast cells are immune cells that accumulate in the tumors and their microenvironment during disease progression. Mast cells are armed with a wide array of receptors that sense environment modifications and, upon stimulation they are able to secrete several biologically active factors involved in the modulation of tumor growth. For example, mast cells are able to secrete pro-angiogenic and growth factors but also pro- and anti-inflammatory mediators. Here we review that mast cells has a role in pathogenic surveillance, impact on biological factors and also act as gatekeepers in the microvasculature in the oral cavity. Moreover, the degrees of mast cell count in OSMF, Oral leukoplakia and Oral Squamous Cell Carcinoma. The purpose of the current study was to examine the histological progression from normal oral tissues through premalignant condition like OSMF, premalignant lesion like leukoplakia to OSCC.

Keywords: Mast cells, Oral Submucous Fibrosis, Oral Leukoplakia, Oral Squamous Cell Carcinoma

INTRODUCTION

A mast cell (mastocyte) is a resident cell of areolar connective tissue (loose connective tissue) that contains many granules rich in histamine and heparin. Mast cells are relatively small cells, which are round or oval in shape, having a diameter of about 12- 15µm. Their numerous cytoplasmic granules frequently obscure the small, round nucleus. Ehrlich further discovered that mast cell with basophilic granules which appeared to originate in the bone marrow and stated that mast cells are tissue basophils and basophils were blood mast cells. Mast cells develops at different stages of embryonic

development in different organs. So it is difficult to assess the embryology of mast cells. In human embryo no mast cells could be demonstrated between 15th to 60th days of intra uterine life.¹ A typical mast cell has a mean diameter of almost 8-15µm. The mast cells are irregular in outline with clear cut cytoplasmic processes extending from them. The cytoplasm is packed with granules and show very few small mitochondria. Mast cells arise from bone marrow-derived precursors that circulate in the blood and become differentiated after entering tissues.⁴ There are three types of mast cell population are seen. They may be classified as:

a. Cells deeper in connective tissue are round/oval in shape and are dark purple in colour and the nucleus is not visible due to granules present in them. Therefore they are named as “Intact Cells”.

b. In the superficial layer, the cell borders are not defined & the nucleus is only partially appreciable. These cells are called as “Spreading cells”.

c. The cells that are found in the infiltrate have a blue coloured nucleus and are well defined.²

The staining characteristics that can be performed for identification of mast cells are Haematoxylin and Eosin. On staining the granules stain less brightly than those of an eosinophilic leucocyte. Nucleus is ovoid and not lobulated usually. The cytoplasm of the cells is generally pink, the nucleus is purplish or blue and the cytoplasmic granules are dark blue or even blackish.

Aim & Objectives:

The aim of this study is to histologically evaluate the number of mast cells in tissue sections of oral leukoplakia, oral submucous fibrosis and oral squamous cell carcinoma.

Materials & Methods:

17 archival biopsy specimens were taken from Dept. of Oral and Maxillofacial Pathology, I.T.S Dental college and hospital and research centre, Greater Noida. Samples include:

- (a) 5 biopsies of oral leukoplakia
- (b) 5 biopsies of OSMF
- (c) 2 biopsies of normal mucosa
- (d) 5 biopsies of OSCC

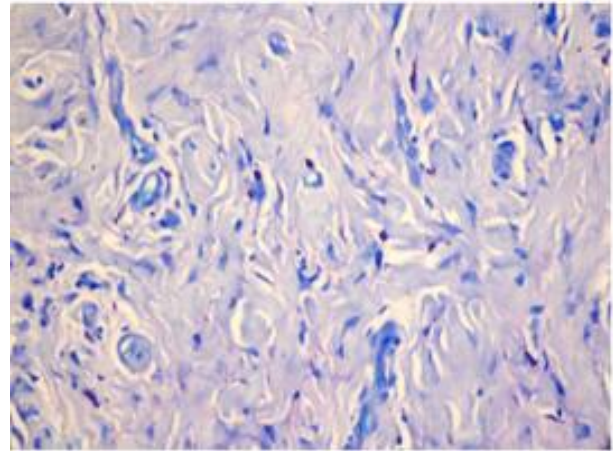
Methods include:

- ✓ All the above tissue sections were stained with H&E to confirm the diagnosis & 1% toluidine blue to study the mast cell.
- ✓ Toluidine blue stains mast cell granules purplish red and nuclei sky blue in colour.
- ✓ Mast cells were counted manually in 20 high-power fields under a magnification of 40x in a stepladder fashion.
- ✓ Mast cells were expressed as an average number of mast cells per 20 high power fields.

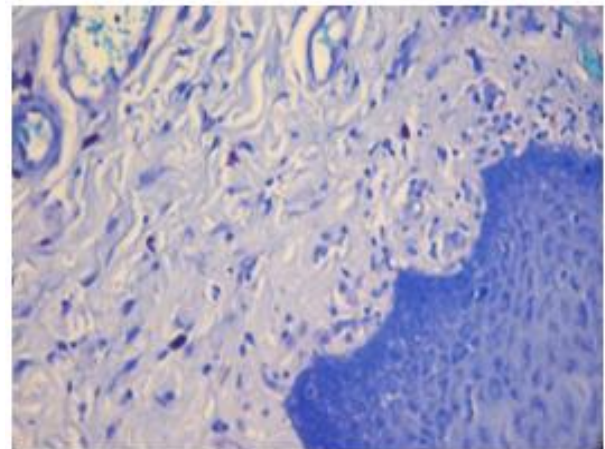
On staining with H&E and 1% toluidine blue as a counter stain, the same slides were viewed under

light microscope. Microphotograph were done with each slide i.e- OSMF, Leukoplakia and OSCC.

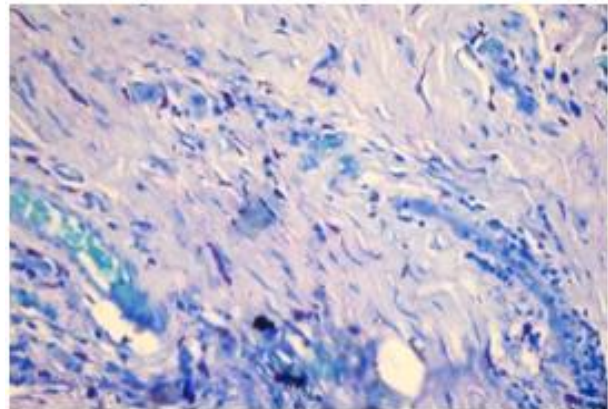
The slides were viewed under 40X magnification.



Microphotograph showing mast cells stained with 1% toluidine blue in 40x magnification in **OSMF**



Microphotograph showing mast cells stained with 1% toluidine blue in 40x magnification in **ORAL LEUKOPLAKIA**



Microphotograph showing mast cells stained with 1% toluidine blue in 40x magnification in **ORAL SQUAMOUS CELL CARCINOMA**

Results:

Results showed that mast cells were found more in OSMF > Oral Leukoplakia > Oral Squamous Cell Carcinoma.

Mast Cell Analysis:

OSMF	---- 33.8/20 HPF
Oral Leukoplakia	---- 28.5/20 HPF
Oral Squamous Cell Carcinoma	---- 20/20 HPF
Normal	---- 7/20 HPF

Thereby, from this above mentioned analysis **OSMF** showed increase number of mast cell count. Followed by **Oral Leukoplakia** showed average increase number of mast cell count. Least number of mast cell count is found in **Oral Squamous Cell Carcinoma**.

Discussion:

Mast cells are fascinating, multifunctional, bone marrow derived, tissue-dwelling cells. They can be activated to degranulate in minutes.³ Mast cells are bone marrow derived, highly granulated cells, which are an important source of several proangiogenic and angiogenic factors, such as histamin and heparin, chymase, bFGF (FGF-2), VEGF .¹⁰In the present study, results suggest that there is significant evidence on the increase in the number of mast cells in case of OSMF. This is similar to a study described by Sabrinath et al in their study where he showed a definite increase in the mast cell density in different grades of OSMF. The pathogenesis behind this are the mast cells that release Histamine, ECF, IL-5, IL-1 and Tryptase which in turn causes various other complications like Submucosal Oedema, Inflammatory Cell Infiltrate, Increases Proliferation, Increases Fibroblastic Response, Increases Fibrosis.⁶

In this study, there is mild increase in number of mast cells in Oral Leukoplakia. This is similar to a study by Rakesh et al where he obtained a statistically significant rise of mast cells in leukoplakia. These mast cells activates and releases (a) IL-1 that leads to increase epithelial proliferation and (b) Histamine release that increases mucosal permeability and facilitates increased access for the antigen to the connective tissue. It has been shown that on degranulating, these mast cells release a range of both preformed

and newly synthesized cytokines and chemokines. These cytokines act by different mechanisms to maintain the OLP lesion.⁷Also it may be due to the decrease in MC numbers in pre-malignant and malignant oral lesions may be related to the migration failure of these cells, possibly reflecting an important modification in the microenvironment during tumor initiation and progression.⁵

In this study, there is significant decrease in number of mast cells in OSCC. This is similar to a study by Anak Iamaroon et al, Elpek et al, increase in mast cell count in SCC in their studies and concluded that they have a role in angiogenesis and hence might be responsible of the aggressive behavior of these lesions. Mast cells activate mast cell release which in turn causes vasoproliferation & increases the half life of fibroblast growth factor which is a potent angiogenic substance that promote tumor angiogenesis/local tumor invasion.⁸

On the other hand, it is said that mast cells are considerably low due to failure in migration of cells and this is possibly due to modification in tumor microenvironment. This is in accordance to a study by Helenesa Helena et al.⁹

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