Mast cells are mobile, granule containing, bone marrow derived secretory cells, also known as mastocyte or labrocyte. Mast cells are regarded as one of the important cells of the immune system. Mast cells have been studied for decades due to their prominent role in normal homeostasis and various pathologies. Although mast cells were discovered over 100 years ago, for the majority of time their function was linked to allergy and allergic disease with few other roles in health and disease. Nowadays the diversity of roles is proposed in the pathogenesis of various oral pathologic lesions, including oral premalignant and malignant lesions. This article reviews the role of the mast cells in oral premalignant and malignant lesions.

**KEYWORDS:** Mast cells, Oral premalignant lesions, Oral malignant lesions.

**INTRODUCTION**

Paul Ehrlich first described mast cells as ‘mastzellen’- a well fed cells in 1878 based on their unique staining characteristics and their large granule content. They are bone marrow
derived, mobile, granule containing cells that are found in most of the environments, including that of oral cavity.\(^1,2\)

Various research studies were carried out to study the role of mast cells in health and disease conditions, with initial speculations that these cells with their large granules were present to ‘nourish’ the surrounding tissue.\(^2\)

Usually the number of tissue mast cells in healthy individuals is stable, but this homeostasis is disturbed by a number of pathophysiologic conditions, like inflammation, allergic diseases and other lesions.\(^3\)

Now, various studies were done to study the role of mast cells in oral lesions, including oral premalignant and malignant lesions like leukoplakia, oral submucous fibrosis, oral lichen planus, oral squamous cell carcinoma.\(^4\)

**Morphology of mast cells**
Mast cells are large mononuclear cells with cytoplasmic granules, which exhibit various chemical and histochemical characteristics of acid mucopolysaccharides. The cytoplasmic granules of mast cells show a fine granular and a lamellar structure. Depending on the density of the surrounding tissues mast cells may assume various shapes; like flat, spherical, spindle-shaped, stellate, or almost filiform.\(^5\)

Mast cells are preferentially distributed about the microvascular bed, close to the basement membranes of vascular endothelial cells and nerves in tissues such as oral mucosa and skin. At the light microscope level, the secretory granules of mast cells give a characteristic metachromatic staining pattern with toluidine blue.\(^1\)

**Role of mast cells**
Mast cells display variety of roles in extracellular matrix degradation, angiogenesis and innate and acquired immune responses, due to their ability to release a range of pre-formed mediators, including cytokines, vasoactive amines, and enzymes on activation. Mast cells have been studied since decades due to their prominent role in normal homeostasis and also in various pathologies.\(^1\)

Mast cells have ability to release various pro-inflammatory, immunoregulatory and angiogenic molecules through different stimulation pathways. Also the activation of mast
cells has been proved to have many biological consequences including mitogenesis, extracellular matrix degradation, angiogenesis, and augmentation of microvascular hyperpermeability and recruitment of inflammatory cells including macrophages.⁶

**Mast cells in oral premalignant lesions**

Numerous studies were done to understand the role of mast cells in oral premalignant lesions and conditions. Rakesh S et al (2012) had done study to assess total and degranulated mast cell counts in patients with oral leukoplakia in subepithelial, intermediate and deeper zones. Mean mast cell count was observed to be higher in oral leukoplakia as compared to normal buccal mucosa. Also, significant difference was found in degranulated mast cell count in leukoplakia and normal buccal mucosa. IL-1 may cause increased epithelial proliferation and histamine causes increased mucosal permeability facilitating increased access to the antigen to connective tissue.⁴

Mast cells role in angiogenesis and inflammation, brought about by the release of their mediators, may play an important role in transformation of oral leukoplakia into invasive carcinoma.⁴

Biviji AT (1973) observed similar findings in leukoplakia and concluded that active agents in mast cells might contribute to inflammatory reaction seen in leukoplakia. These stimulated mast cells may release interleukin-1, which causes increased epithelial proliferation that is observed in oral leukoplakia.⁷

The mast cell hyperplasia could also attribute to some of the signs and symptoms of oral submucous fibrosis. Mast cell mediators like prostaglandins and leukotrienes are potent secretagogues for the serous and mucous cells. This could attribute to increased salivation seen in oral submucous fibrosis. The effect of chemical mediators can explain the histopathological changes seen in oral submucous fibrosis. Histamine could probably attribute to submucosal edema seen in early stages of oral submucous fibrosis.⁷

Oral lichen planus is a chronic oral mucosal disease characterized by hyperkeratosis and basal cell destruction associated with a band-like infiltrate of T lymphocytes and an increased density of mast cells.⁸

Mast cells may respond in two ways in oral lichen planus. They may act as nonprofessional antigen presentation cells and present antigen to T cells in a MHC class I or MHC class II
restricted and co-stimulatory molecule-dependent fashion. The resultant T cell activation would activate mast cells, leading to both degranulation and cytokine release. Secondly, chemokines could induce a calcium flux that would cause direct degranulation of mast cells, with the resulting release of cytokines (TNF-a) that would stimulate T cells (via by TNF receptor II) to secrete cytokines or chemokines.[8] Mast Cells distribution in the different levels could also indicate their roles at different stages of oral lichen planus.[9]

Mast cells in oral malignancy

The presence of mast cells in the periphery of the tumor was first reported by Westple et al in 1981 and then confirmed by several investigators.[10] Enhanced mast cell accumulation in tumors is associated with poor prognosis in a variety of tumors, indicating a biological role for mast cells in tumor progression.[2]

Mast cells were found at areas of dense vascularization (called as “hot spots”), around the tumor margins and near sites of new capillary formation.[6] Mast cells are bone marrow derived, highly granulated cells, which are an important source of several proangiogenic and angiogenic factors, such as histamine and heparin, chymase, bFGF (FGF-2) and VEGF. Also factors secreted by mast cells, such histamine, heparin, VEGF, bFGF, and tryptase, have been shown to exert an activity on the migration and/or proliferation of endothelial cells.[6]

It is well-known that neoangiogenesis is required for the growth and spread of tumors. Increased angiogenesis has been associated with neoplastic progression, metastasis and outcome in several studies and in a number of malignancies. Recent data suggest that the accumulation of mast cells around the tumor margins and their release of potent pro-angiogenic and angiogenic factors may represent a tumor-host interaction which probably favors tumor progression.[5,6] Mast cells can indirectly promote tumor growth through the degradation of the extracellular matrix.[11]

CONCLUSION

Mast cells have regulatory role in the angiogenesis and inflammation, brought about by the release of their mediators, can play an important role in the transformation of oral premalignant lesions into malignant lesion and also in the progression of the malignancy.
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