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REVIEW ARTICLE **OPEN ACCESS**

Mast Cells and Its Mediators: A Review Article

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ABSTRACT
Mast cells have been the object of investigation for almost a century. They are widely regarded as important effector cells in immune responses. Mast cells can represent a critical component of host defense in natural immunity. They originate from bone marrow and migrate to the peripheral tissues. They are normally distributed throughout the connective tissue and they are known for their role in inflammatory processes. In this brief review, we will consider certain aspects of mast cell biology and its various mediators.
***KEYWORDS**: Toluidine blue, Oral Squamous Cell Carcinoma, Mast cells, Oral Dysplasia*

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INTRODUCTION

Paul Ehrlich in 1877 discovered a granular cell of loose connective tissue and named it as "Mastzellan" a well fed cell [1]. Mast cells are the major immunoeffector cells of the mesenchyme and are multifunctional cells manufactured to play a central role in acquired and innate immunity [2]. They have a diameter of about 12 microns, are heterogenous in shape (round, oval or spindle- shaped) and are packed with 50-100 granules and have a life span of weeks to months. These cells release preformed secretory mediators like histamine, heparin, tryptase, lipid derived mediators like leukotrienes, pro-inflammatory cytokines and immunomodulatory cytokines [3].

Mast cells play a role in various processes like wound healing, chronic inflammation, keloid formation, pulmonary fibrosis and angiogenesis [4]. Increased angiogenesis has been correlated with progression of neoplasm and in several malignancies. The accumulation of mast cells is estimated by counting the mast cell density [5].Mast cells originate from bone marrow and migrate to the peripheral tissues where they mature in-situ [6]. Mast cell adhesion to the extracellular matrix is crucial for homing of precursor mast cells to injured tissues and their movement from the vascular to the extravascular compartment of oral mucosa after words. This potential communication between the mast cell and basement membrane laminin is able to induce a number of biological responses [7].

MAST CELLS

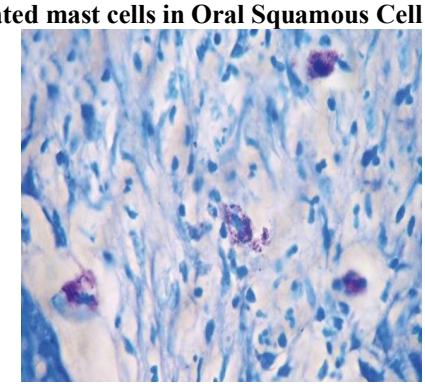
Mast cells are granule-containing secretory cells which are present in mucosal and connective tissue environments. In oral mucosa and skin, mast cells are distributed preferentially about the microvascular bed, being in close proximity to the basement membranes of blood vascular endothelial cells and nerves [8]. This localization of mast cells has been shown to result from their interaction with the laminin component of neural and vascular basement membranes via the CD49f (α6/β1) integrin, which serves as a specific laminin receptor [9].

These cells play an important protective role as well as being intimately involved in wound healing and defense against pathogens. They are large spherical or elliptical mononuclear cells. They resemble circulating basophils in containing large number of cytoplasmic granules containing pharmacologically active mediators and IgEFc receptors [10].

Ultrastructurally, the granules in mast cells of the oral mucosa and skin have a complex form, with amorphous regions located next to crystalline regions. Immuno-electron microscopy has confirmed that the key mediators of chymase, tryptase, TNF, and cathepsin G are packaged separately within the granules [11].

Mast cells stain with basic dyes like toluidine blue (Fig.1) methylene blue and alcian blue. The stained granules often acquire a color that is different from that of native dye, they are referred to as metachromatic dyes. Tryptase is considered a specific mast cell marker.

Fig. 1. Degranulated mast cells in Oral Squamous Cell carcinoma (×100)



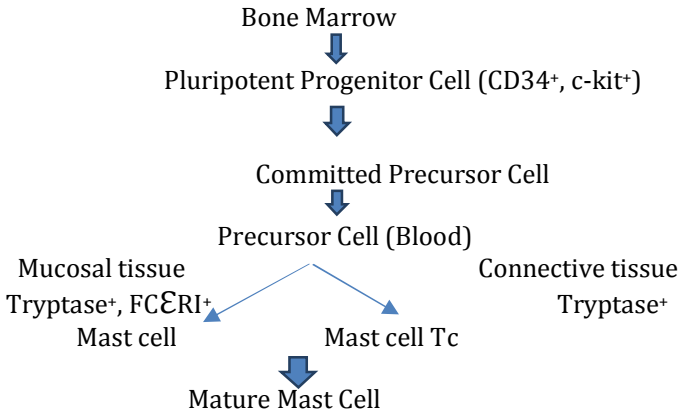
HISTORY

Mast cells were first described by Paul Ehrlich in 1878 on the basis of their unique staining characteristics and large granules and he named them "mastzellan," meaning 'feeding-cells". Elie Metchnikoff (1892) was probably the first to suggest that mast cells led a phagocytic function and might thereby contribute to host defense. Malaviya R (1996) showed that mast cells can represent a central component of host defense against bacterial infection and the recruitment of circulating leukocytes with bactericidal properties that is dependent on mast cells, is one important element of this process [12].

ORIGIN AND DISTRIBUTION

Mast cells originate from pluripotential hematopoietic cells in the bone marrow, undergo part of their differentiation in this site, then enter the circulation and complete their differentiation in peripheral mucosal or connective tissue (CT) microenvironments rich in fibroblasts and other mesenchymal element (Fig. 3). One hallmark in mast cell development is that c-kit (CD117), the receptor of stem cell factor (SCF), is expressed by mast cells and their progenitors, including the pluripotent progenitors of mast cells, committed mast cell progenitors, immature mast cells and mature tissue mast cells. SCF promotes the proliferation of mast cell progenitors, immature or mature mast cells and alters mast cell phenotype and mediator contents.

Fig. 3. Mast cells originate from pluripotential hematopoietic cells



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MAST CELL HETEROGENEITY

Mast cells in different anatomical sites, and even in a single site, can have substantial differences in mediator content, sensitivity to agents that induce activation and mediator release and responses to pharmacologic agents.

Such heterogeneity is regulated by many factors, including certain cytokines, which influence the cell's stage of maturation, differentiation, proliferation and other characteristics. The CT phenotype contains both tryptase and chymase (MC_{TC}), while the mucosal phenotype contains only tryptase (MC_T). Mast cells can phagocytize diverse particles, take up antigens and expresses a number of receptors, particularly MHC class I and II antigens, ICAM-1 and -3, CD43, CD80, CD86 and CD40L, which allow them to interact with T and B lymphocytes.

MEDIATORS

The range of both preformed and newly synthesized cytokines and chemokines (Table-1) from mast cells which may regulate immune responses and activate T cells.

TABLE 1- Various mediators in mast cell

MEDIATORS	PATHOPHYSIOLOGIC EFFECTS
I) Presorted	
1. Chemokines	
IL-8, MCP-1, MCP-3, MCP-4, RANTES	Chemoattraction and tissue infiltration of leukocytes.
2. Biogenic amines	
Histamine	Vasodilation, angiogenesis, mitogenesis, pain
5-Hydroxytryptamine (5-HT, serotonin)	Vasoconstriction, pain.
3. Enzymes	
Arylsulfatases	Lipid/proteoglycan hydrolysis.
Chymase	Tissue damage, pain, angiotensin II synthesis.
Phospholipases	Arachidonic acid generation.
Tryptase	Tissue damage, activation of PAR, inflammation, pain.
Carboxypeptidases A	Peptide processing.
Kinogenases	Synthesis of vasodilatory kinins, pain.
4. Peptides	
Endorphin	Analgesia.
Kinins (bradykinin)	Inflammation, pain, vasodilation.
Corticotropin-releasing hormone (CRH)	Inflammation, vasodilation.
Endothelin	Sepsis.
Somatostatin (SRIF)	Anti-inflammatory action.
Substance P (SP)	Inflammation, pain.
Vasoactive intestinal peptide (VIP)	Vasodilation.
Urocortin	Inflammation, vasodilation.
Vascular endothelial growth factor (VEGF)	Neovascularization, vasodilation.
5. Proteoglycan	
Heparin	Angiogenesis, nerve growth factor stabilization.
Chondroitin sulfate	Cartilage synthesis, anti-inflammatory action.
Hyaluronic acid	Connective tissue, nerve growth factor stabilization.
II) De novo synthesized	
6. Cytokines	
INF-γ, MIF, TNF-α	Inflammation, proliferation of leukocyte /activation.
Interleukins(IL)-1,2,3,4,5,6,9.10,13,16	Inflammation, leukocyte migration, pain.
7. Growth factors	
CSF, GM-CSF, b-FGF, NGF, VEGF	Growth of a variety of cells.
8. Phospholipid metabolites	
Platelet activating factor (PAF)	Platelet activation, vasodilation.
Prostaglandin D_2 (PGD_2)	Bronchoconstriction, pain.
LeukotrieneC_4 (LTC_4)	Vasoconstriction, pain.
Leukotriene B_4 (LTB_4)	Leukocyte chemotaxis.
Nitric oxide (NO)	Vasodilation.

ABBREVIATIONS: TNF-α: tumor necrosis factor-α; INFγ: Interferon-γ; MIF: macrophage inflammatory factor; GM-CSF: granulocyte monocyte-colony stimulating factor; β-FGF: fibroblast growth factor; NGF: nerve growth factor; SCF: stem cell factor; VEGF: vascular endothelial growth factor.

CONCLUSION

Mast cells are multi-tasking cells having both pro-inflammatory and anti-inflammatory effects. They are well known for their involvement in allergic and anaphylactic reactions but can no longer be regarded simply as cells that initiate acute reactions through the release of rapidly metabolites mediators such as histamine and products of AA oxidation. It is so because in the recent times their actions in various diseases have been investigated and have divulged many new facts owing to the plethora of cytokines secreted at different times under different conditions. Related aspects of the mast cells with their actions in some common oral lesions have to be understood in order to explore possibility of treatment modality options involving mast cells.

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