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Role of Mast Cells in Oral-Diseases: A Concise Update

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ABSTRACT

Mast cells are granular cells and native of connective-tissue. They mostly associates with type-1 allergic reactions. Despite their link with multiple kind of allergic reactions, these mast-cells are also related with numerous pathognomic conditions of oral- cavity. Mast cells are usually acts after stimulated by allergic or any pathologic condition, by secreting cytokines or other mediators. Number of mast-cells in normal physiological condition and other pathologic condition is quite important, due to their significance in severity of disease-process. Hence, this review summarizes the relationship of mast-cells among normal physiological condition and different pathologic conditions of oral-cavity.

Aim of this review is to concise the role of mast cells in different pathognomic condition which further assists in better management of these pathologic conditions.

Keywords: Mast cells, Cytokines, Leukoplakia. Lichen planus, Odontogenic cyst

INTRODUCTION

Mast cells are large connective-tissue cell. They are initially mentioned by Paul Ehrlich in 1877.[1]These cells are the locally found in loose connective tissue [2] as granular cell and have been a key- role in various physiological processes like wound healing, chronic inflammation, keloid formation, pulmonary fibrosis and angiogenesis.[3] Originate of mast cells are from bone marrow, after that, they migrate to the peripheral tissues while maturing.[4] Mast cells are granular secretory cells which are evident in both in mucosal as well as in connective tissue . In oral mucosa and skin, mast cells are dispersed usually proximal to the microvascular bed, close to the basement membranes of endothelial cells and nerves.[5].[6]

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Ultra-Structure of Mast Cells

Mast cells have multiple granules- as they are principally secreting cells. Shape of these cells are large spherical or oval mononuclear cells. Nucleus small as compared to the cell and while histological preparations, they are usually masked by the large number of granules in the cytoplasm.[7]Ultrastructurally, the granules in mast cells forms complex-structures with amorphous regions located next to crystalline regions. In brief, they are mobile, bone marrow derived and normally contain 80-300 granules.[8] Under light microscope mast cells gives a peculiar metachromatic staining pattern with toluidine blue.[9],[10]

Different types of Mast cell-

Ultra-structurally Mast-cells are of three different types. As mentioned earlier, these cells are native of connective-tissue. In connective-tissue, mast cells are usually found in superficial as well as in deeper connective tissue. Mast cells which belong to deeper connective tissue have sharp, defined borders and have circular or oval in shape. These cells are extremely granular. On the contrary, mast cells which belongs to superficial area have diffused and irregular borders with lesser granules. These cells are usually found proximal to blood-vessels. Third type of mast cells are those, which seen in inflammatory conditions and evident as degranulated.and on staining with metachromatic dyes, they appeared with pinkish violet hue.[11]

Distribution of Mast Cells in Oral Tissues

Mast cells are the locally found in the connective tissue[2]Mast cells originate from bone marrow and migrate to the peripheral tissues where they mature in-situ.[4]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.[5]Distribution of the mast cells are in such a way ,so that its cell products available to fibroblasts and other cells of the connective tissue, vascular endothelial cells ,surface or glandular epithelial cells, nerves, and respiratory, gastrointestinal and genitourinary smooth-muscle cells[13].

Mediators of Mast Cells [10]

1.Mediators which acts through their granules are seriene protease-tryptase, chymase, cytokine, TNF-a

2.Mediators which perform through activation of mast cells- IL-1, IL-3, IL-4, IL-5, IL-6, IL-8, IL-11, RANTES, Leukotrienes

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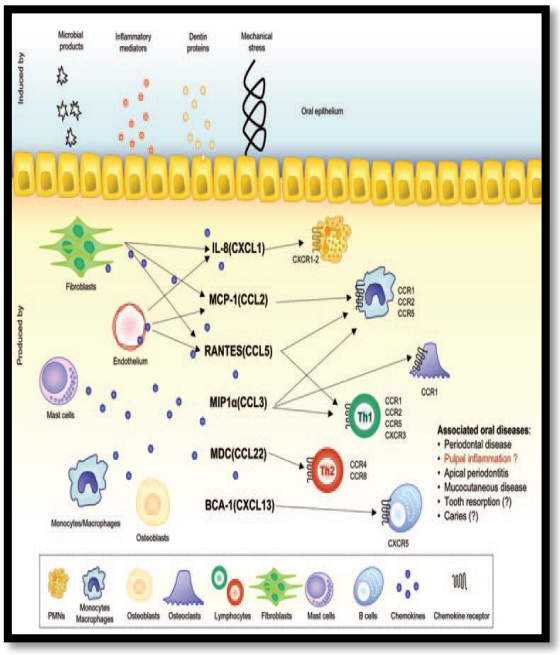

Figure;1 Chemokines and chemokine receptor in oral tissue[11].

Research on the role of MCs in allergic reactions, anaphylactic reactions, autoimmune reaction and reproductive disorders has been done and given in the medical literature as well. However, its role in etiopathogenesis of oral pathologies is under various researches . Hence, the present review article is aimed to explore the role of MCs in initiation and progression of oral pathologies[1]

Mast Cells in Normal Oral Mucosa[1]

The mast cell count in normal oral mucous-membrane has been found to be 25.50/sq.mm and 12.2/microscopic field at 400X using Toluidine blue stain and 41.67 ± 15.38 cells/sq.mm. MCs count has been found to be variable and different in most oral pathological conditions. Some of the studies related to the common oral conditions are as follows:

Gingival and periodontal disease

Mast cells operate at all levels in the various outcomes of gingival and periodontal infection. They plays an important role in the first line of defence against infection. Usually normal gingiva generally have more mast cells per tissue unit rather than the moderately inflamed tissue. Adjacent to the tooth- regions have more mast cells as reaction to an enzymatic degranulation as reaction against by products elaborated by the gingival bacterial plaque or possibly by local antigen-antibody interactions. This ultimately proves that, products released due to degranulation may act as mediators[14].
[Figure;2]

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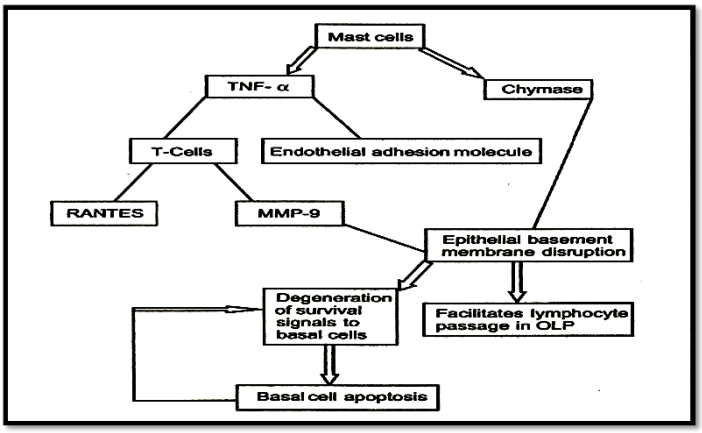

Figure;2 Potential outcomes of gingival and periodontal infection[15].

Hence, immune reaction plays a vital role in tissue repair or periodontal disease .It also depends on multiple well-defined variables related to the potential pathogenicity (virulence) of the indigenous microbiota accumulating in dental plaque, immunological factors such as cytokines.). In this situation, chemokines, found in both gingival tissue and crevicular fluid, are thought to play important roles in the immunopathogenesis of periodontal disease.

Pulpitis and periapical lesion

The advancement of pulpal inflammation to the periapical region and micro-organism colonization of the root canal initiate innate and adaptive immune responses which evokes to periapical alveolar bone destruction and periapical lesion formation. Numerous studies also shown characterization of inflammatory cell infiltrate in dental periapical lesions .

Odontogenic cysts

Mast cells are present widespread in the connective tissue wall of almost all cyst types, particularly proximal to the epithelium. Because of inflammatory response, degranulating of mast cells occurs and release heparin and hydrolytic enzymes which enhanced the breakdown of glycosaminoglycans and proteoglycans. Mast cells are used to be present in sufficient numbers in odontogenic keratocyst as well as in the walls of dentigerous and radicular cysts. These released components diffuse into the luminal fluid and contribute to the osmotic pressure. Also mast cells have also been suggested to initiate collagenolytic activity, facilitate transudation of serum proteins into the luminal fluid and also promote bone resorption and remodeling to accommodate the growing cyst.[16]

Role of mast cells in increasing the hydrostatic pressure of cystic luminal fluid

The increase in osmotic pressure could be in three ways as follows:

1. By direct release of heparin into luminal fluid
2. By release of hydrolytic enzymes which could degrade capsular extracellular matrix (ECM) components, thereby facilitating their passage into the fluid

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3. By the action of histamine on smooth muscle contraction and vascular permeability, encouraging transudation of serum proteins. [17]

Leukoplakia

The mast cells might responsible to inflammatory reaction in leukoplakia. Interleukin-1 released by these stimulated mast cells, which causes enhancement in epithelial proliferation evident in leukoplakia. In oral leukoplakia as comparison to normal oral mucosa average number of mast cells increased. Degranulated Mast cell increased in oral leukoplakia

Table 1:.Depicting, Mediators of Mast cells exert possible impact, which gives rise to oral leukoplakia[2]

Mast cell mediators & their effects	Histopathological features	Clinical features
Interleukin-1 and TNF • Increased epithelial proliferation	Increased thickness of the epithelium	White patch or a plaque
Histamine • Increase transport through epithelial membrane • Number of T-cells increase due to immunogen	Increased mucosal permeability despite hyperkeratosis	Long-standing of the lesion
Heparin • Neovascularization occurs and subsequently increase	Increased vascularity of the stroma and ulceration	Erosive leukoplakia

Oral submucous fibrosis

Interleukin-5 causes increased proliferation and differentiation of eosinophils. Interleukin-1 from the mast cells could cause increased fibroblastic response and mast cell derived tryptase

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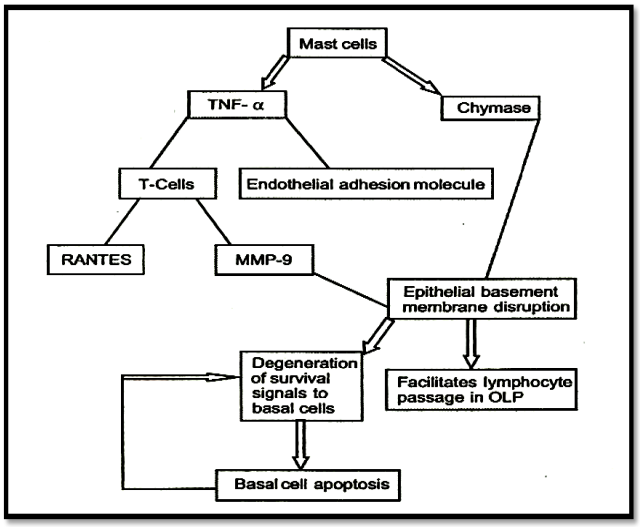
causes increased production of type-I collagen and fibronectin thereby attributing to increased fibrosis. abundant mast cells in grade I and grade II OSMF as compared to normal buccal mucosa.[2]

Oral lichen planus

It has been proved that mast cell degranulation as a result to release of neuropeptides is a major event in the pathogenesis of oral LP (Fig. 3). The most superficial region of lamina propria is the highest number of interactions of nerves with mast cells. Mast cells may be responsible to the development of a specific T-lymphocyte, in the induction phase of inflammation in conditions like LP. In the connective tissue they placed in a perivascular location with dendritic antigen presenting cells, and produce cytokines, which might be



equally important as the expression of accessory molecules on their cell surface.[104]

Figure;3 ***Overall effect of mast cells in pathogenesis of OLP.[2]***

Quantitative studies shown that the number of mast cells associated with the laminin of vascular basement membranes was higher twice or thrice , in the superficial and deep layers in OLP as comparision with normal buccal mucosa.[18]

Squamous cell carcinoma

Head and neck squamous cell carcinoma of is a common pathology with greater mortality and morbidity. Although the way by which, mast cells (host local immunity) contribute to the behaviour of the disease is unclear, but in-vivo studies proved,sequential infiltration of mast cells with degranulation in squamous cell carcinoma. Also angiogenic factors including VEGF, bFGF and platelet derived growth factors have been also play a major role in mast cell migration.[19]

Hypoxia might evoke tumor cells to release angiogenic factors which chemoattract the mast cells to migration into the hypoxic areas of the tumor and then the mast cells release

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angiogenic factors that stimulate the infiltration of more mast cells. Both heparin and tryptase are potent angiogenic factors Fibroblastic growth factor is a potent angiogenic substance which promotes angiogenesis and facilitates local tumour invasion. [2]The mast cell and microvascular counts evidently higher in oral SCC than in hyperkeratosis and normal oral mucosa.[20]

CONCLUSION

From the results of these research works, it may be concluded that though Mast cells functioning as Défense cells under normal conditions, they may plays an important and essential role in disease progression. Further research studies on mast cells needed in near future ,so that it may increase information on their role in pathogenesis of various oral pathologies.

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