Oral Inflammatory Lesions and Presence of Mast Cells: A Pilot Study

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Abstract: **Background:** Mast cells promote inflammation by releasing pro-inflammatory mediators and bring about angiogenesis, degeneration of the extracellular matrix, and tissue remodeling. The aim of this study was to quantify the number of mast cells in oral inflammatory lesions of the oral cavity and to compare these two number of mast cells in normal gingival tissues and to correlate their presence with the state of connective tissue changes in these lesions and probably suggest a role for mast cells in these lesions. **Materials and Methods:** Reactive hyperplasias namely pyogenic granuloma (PG), peripheral ossifying fibroma (POF) and peripheral giant cell granuloma (PGCG) were considered for this study. 15 cases seen in the gingiva were selected for each category and stained with 1% toluidine blue for mast cells. **Results:** In this study, mast cell count was highest in peripheral ossifying fibroma (POF) followed by cases of pyogenic granuloma (PG) and peripheral giant cell granuloma (PGCG). **Conclusion:** The number of mast cells was more numerous in POF suggesting that mast cell activation is a characteristic feature of chronic inflammation, a condition that may lead to fibrosis as a result of increased collagen synthesis by fibroblasts.

**Keywords:** Mast cells, oral inflammatory lesions, inflammation

1. Introduction

Mast cells are granular, monocytic appearing cells which can stain metachromatically.¹ Mast cells arise from multipotent CD 34+ precursor in the bone marrow and circulate in the peripheral blood. After migrating into tissues, these immature mast cells assume their typical granular morphology. Mast cells are normally distributed throughout connective tissues, where they may be especially numerous beneath the epithelial surfaces of the skin, in the respiratory system, in the gastrointestinal and genitourinary tracts, adjacent to blood or lymphatic vessels, and near or within peripheral nerves. Human mast cells range from 5 to 15 µm in diameter and in histologic sections they often appear ovoid, tadpole, or spindle shaped cells. The most significant feature of mast cells is their cytoplasmic granules that vary in size from 0.2 to 0.5 µm diameter.²

Along the walls of blood vessels, they are precursors of heparin and histamine.³ Moreover, mast cells also express leukotrienes, prostanooids, proteases, cytokines, and chemokines that attract neutrophils to the site of infection and thus stimulate host defence mechanism.⁴⁻⁵

Mast cell mediators like tryptase, tumor necrosis factor (TNF-α), interleukin-4 (IL-4) can increase fibroblast proliferation and also act as chemotacric factor for polymorphonuclear leucocytes. Other factors like heparin, fibroblast growth factor, and vascular endothelial growth factor (VEGF) can induce endothelial cell migration and new vessel formation.⁶ The role of mast cells in bringing about neo-angiogenesis has been studied in oral squamous cell carcinomas and a positive relation has been shown.⁷ There is also evidence that these cells, by regulating angiogenesis, can influence growth and progression in human cancers.⁸ On the contrary, an inverse relationship has also been observed between the number of mast cells and the amount of tumor tissue.⁹

In the oral cavity mast cells modulate the pathogenesis of apical periodontitis and may be responsible for stimulating the formation of granuloma with the resorption of underlying bone.¹⁰ Pyogenic granuloma, inflammatory hyperplasias and granulation tissue are some of the more commonly encountered reactive lesions in the oral cavity. Histopathology of these lesions usually consists of neo-vascularization and inflammation depending on the stage of the lesion. Since mast cells contain cytokines that can bring about these actions, their presence in these lesions might help us to have a better understanding of the pathogenesis behind these lesions. Previous studies have shown a direct correlation between mast cells and the state of vascularity and inflammation.¹¹

This study aimed at determining the average mast cell count in oral reactive lesions and compare it with the average count of mast cells in normal oral mucosa.

2. Materials and Method

The cases for inclusion in this study were categorized as PG, POF and PGCG. Clinical data regarding age, gender, location of the lesions were obtained for each case from the patient records. After reviewing the histological slides, serial sections of 5-micron thickness were made from paraffin embedded tissue blocks of 15 active inflammatory lesions and stained with 1% toluidine blue for mast cells. As controls, 5 clinically normal oral mucosa tissue specimens were obtained from those who had surgical removal of impacted tooth and stained for comparative analysis of mast cells with the reactive lesions.
Mast cells were counted in 10 high power fields (X400) where the highest number of mast cells was seen. The degranulated mast cells were not taken into account as these cells lose their characteristic features after degranulation and are difficult to be counted histologically.

3. Results

It has been observed that mast cell distribution was seen in all the 15 cases of inflammatory lesions. In microscopic sections stained with toluidine blue, mast cells were most often located in lamina propria, particularly around blood vessels and appeared as purple and granular mononuclear cells in all the study groups. The mean total number of mast cells was 48.96 ± 10.23 in PG, 73.14 ± 15.53 in POF 21.65 ± 4.56 in PGCG and 6.34 ± 1.32 in normal oral gingival mucosa specimens (Table 1).

<table>
<thead>
<tr>
<th>Mast Cell Count</th>
<th>MEAN ± SD</th>
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<tbody>
<tr>
<td>Normal Gingiva</td>
<td>6.34 ± 1.32</td>
</tr>
<tr>
<td>POF</td>
<td>73.14 ± 15.53</td>
</tr>
<tr>
<td>PG</td>
<td>48.96 ± 10.23</td>
</tr>
<tr>
<td>PGCG</td>
<td>21.65 ± 4.56</td>
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</tbody>
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4. Discussion

Mast cells are mobile, bone-marrow derived, granule containing immune cells that are found in all connective tissue and mucosal environments, and in the peripheral and central nervous systems. Following activation by immunologic or non-immunologic stimuli, mast cells release via their granules a range of pre-formed mediators, including cytokines, vasoactive amines, and enzymes. At the light microscope level, the secretory granules of mast cells give a characteristic metachromatic staining pattern with toluidine blue. Typical histological sections stained with toluidine blue give the impression that mast cells are rounded; however, when they are examined by transmission electron microscopy or immunohistochemistry, a more stellate or dendritic character is seen. Mast cells are found in all tissues of the oral cavity, including the dental pulp.8

The mast cell forms the first step in the mechanism of neo-vascularization and further inflammatory reactions. Degranulation of mast cell activates endothelium through TNF - dependent mechanism which may be critical to the elicitation phase of inflammation.11 Therefore, it is more important to know the role of mast cells and their contents in any stage of controlling inflammation and subsequent reactions. They are characterized by the surface expression of the high affinity immunoglobulin E receptor and localization at tissue sites adjacent to the microvasculature and at mucosal and epithelial surfaces. This localization of mast cells in both normal and inflamed sites results from their interaction with the laminin component of neural and vascular basement membranes via α6/β1 integrin that serves as a specific laminin receptor.12

Volumes of previous literature have evolved pertaining to the role of mast cells in the development of inflammation in the oral mucosa and dental pulp especially in early vasoinductive events and in the transforming stage from acute to chronic inflammation.8 Mast cells exert their influence locally and systemically by releasing a variety of potent mediators through degranulation. Many of these mediators are stored within cytoplasmic granules (preformed mediators) while others are produced at the time of mast cell stimulation. They have been recognized as a source of a number of cytokines. While the importance and role of mast cells derived cytokines in disease is uncertain, it is conceivable that they may play a significant role in both physiologic and pathologic conditions.13

In the present study, mast cells were found to increase and degranulate in POF followed by PG and PGCG.

The findings in this study were in agreement to the study done by Reddy V et al.14 Mast cells have got variable mediators within their granules. Once the mast cells are stimulated they degranulate and bring about required biological action. Therefore, it is only resonate to presume that the predominance of mast cell under degranulation would take place in a stage much before the active stimulation of angiogenesis and subsequent inflammatory reaction. The early stage could be defined as pre-inflammatory stage before the active vascularity and inflammatory cells are increased. Hence, it can be assumed that the pre-inflammatory stage could be the ideal period for intervening with mast cell action during the treatment process.

5. Conclusion

The number of mast cells were more numerous in POF followed by PG, suggesting that mast cell activation is a characteristic feature of chronic inflammation, a condition that may lead to fibrosis as a result of increased collagen synthesis by fibroblasts

6. Source of Funding

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References

in inflamed gingiva from patients with HIV infection. AIDS 2002; 16: 235-43.


