Mast Cell Stabilizers in Persistent Non-Specific Gingival Hyperplasia

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Gingival hyperplasia is one of the most common pathology of the gingiva. Idiopathic gingival enlargement is diagnosed when no etiology can be identified. Few cases of gingival enlargement are associated with abnormal increase in mast cells. This is a case report of a persistent gingival enlargement which regressed after administration of mast cell stabilizer.

In idiopathic gingival enlargement no etiology can be identified and the diagnosis of this disease is by exclusion when no other known causative factor can be identified.[1] Mast cells are present in all tissues of the oral cavity and are the normal components of the connective tissues. Its number is closely related with the degree of inflammation and was found to be increased on inflamed tissues when compared to healthy tissues.[2]

In periodontal disease associated gingival hyperplasia, mast cell numbers are increased and most probably play a role in the destructive events as well as in the defense mechanism of periodontal disease via secretion of cytokines and cellular migration and healing processes.[3]

The mast cells are large spherical or elliptical mononuclear cells with small nuclei as compared to the size of the cell and in histological preparations they are frequently found with the large number of granules in the cytoplasm.[4] Mast cells can be found in a wide variety of tissues, including the skin, sub mucosa or connective tissues of various organs, and mucosal epithelial tissues. They resemble circulating basophils in containing large number of cytoplasmic granules containing pharmacologically active mediators and IgEFc receptors.[5] Mast cells play an important protective role as well as being intimately involved in wound healing and defense against pathogens.[4]

CASE REPORT

A 25 year-old male presented with the complaint of poor aesthetics due to gingival overgrowth. There were no other significant medical findings. His past medical and dental history was not found to be significant. He gave no positive history of medication. There was no family history of hereditary gingival overgrowth.

He presented with a slowly progressive fibrous enlargement of the maxillary and mandibular gingiva. Characteristically, this massive gingival enlargement appeared to cover almost full 1/3rd of the tooth crown surfaces and displace the teeth in the posterior tooth region. He gave the history of being asymptomatic since 10-12 years back, since then he demonstrated with the generalized swelling in his maxillary and mandibular gums which gradually increased with duration.

In Fig.1, the clinical examination of the enlarged gingival tissue was pink in color with certain areas of erythema, firm and resilient in consistency, fibrous and non-tender to touch with a tendency to bleed easily. Local factors in the form of plaque and soft debris had developed in response to gingival overgrowth. Hematological examination did not reveal any abnormality.

Nevertheless, the hyperplasia involved the gingival margin with extension to the inter-dental papilla. The lesion involved the inter-proximal spaces,

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and became so extensive that the teeth were displaced and their crowns covered.

The histopathological view, Fig.4, was characterized with parakeratinized stratified squamous epithelium which was hyperplastic in few areas with long and slender rete ridges. The connective tissue was dense and fibrocellular with focal areas showing thick collagen bundles exhibiting wavy pattern. Fibroblasts were plump and active. Numerous blood vessels were evident, few of which were dilated and few engorged with plump endothelial lining. The inflammatory cell infiltrate was mainly plasmalymphocytic along with increased number of mast cells and macrophages.

The histopathological features corroborated with the clinical findings consistent with idiopathic gingival enlargement. In view of the clinical presentation patient was taken up for scaling and root planning with gingivectomy procedures. A period of 3 months was allowed to evaluate the healing of gingival tissue. On re-evaluation Fig.2, recurrence of the gingival enlargement was observed. In view of the difficulties in mastication, speech and the esthetic effects on the patient an interdisciplinary approach involving mast cell suppressants and periodontal maintenance was adopted in this case. Mast cell stabilizers like sodium cromoglycate were used for the treatment of gingival enlargement.

On re-evaluation, Fig.3, after 9 months of follow up, with the use of sodium-cromoglycate as a mast cell stabilizer showed significant anti-inflammatory activities and no adverse effects were evident. Mast cell stabilizers have also shown a beneficial effect in the form of host modulating drugs in the treatment of idiopathic gingival enlargement.

DISCUSSION

In idiopathic gingival enlargement no etiology can be identified and the diagnosis of this disease is by exclusion when no other known causative factor can be identified.[1] A definitive diagnosis of idiopathic gingival enlargement can be arrived upon by a thorough medical, dental and family history along with histopathological examination of gingival tissue. Very few cases which were similar in nature have been treated by interdisciplinary approach to date as reported in the literature.[6]We report a case of idiopathic gingival fibromatosis which was diagnosed based on history, clinical findings and biopsy.

Idiopathic gingival enlargement is a slowly progressive disease involving excessive collagen deposition.[7,8,9]The enlarged gingiva is usually of normal pink color. The enlargement may be generalized and severity may vary from mild involvement of few teeth to severe involvement of all the teeth.[5]

It has been suggested that the gingival bacterial plaque or possibly by local antigen/antibody interactions, (Bloch & Angevine 1970, Ishizaka & Tomioka 1972) various products like degranulation products of mast cells are elaborated.[10]

Experiments indicate that the bacteria Porhyromonas gingivalis is widely recognized as a major pathogen of gingivitis and periodontitis and it plays a significant role in activation of mast cells to generate and release proinflammatory mediators that are most probably involved in the emergency of inflammatory processes evolved in response to P. gingivalis infection.[11]

It was demonstrated by Uvnas (1964) and others that a variety of stimuli (mechanical, chemical and physical) can affect mast cell degranulation. Biochemical reactions which occur in periodontal disease can induce mast cell degranulation.[12] Various diffusible products elaborated by gingival bacteria (Schultz-Haudt 1963) cause degranulation of mast cells in gingival tissues.[13] Toxins and enzymes of bacterial origin, primary factors in the etiology of periodontal disease, are capable of producing degranulation (Uvnas 1964, Asboe-Hansen 1964, Nosal, Rye, Raskona 1972). Dextrans produced by gram positive organisms and thought to play a role in bacterial plaque formation (Socransky 1970), can produce mast cell disruption (Rowley & Benditt 1956).[14]

The mast cells participate in both acute and persistent inflammatory reactions. Many of these cytokines promote neutrophil aggregation, eosinophil aggregation, T-lymphocyte stimulation, which in turn stimulates B-lymphocytes, acts on endothelial cells, platelets by stimulating platelet activating factor, and directly or indirectly the mast cells leads to inflammation.[4]

Vasoactive components such as histamine or proteases released by degranulation may then act as mediators during the progress of the inflammatory process or perhaps contribute to the local resistance against injury. It has been proposed that a very intimate relationship exists between the mast cell and the gingival defense mechanisms and that even before mast cells are among the first cells to get involved in periodontal inflammation.[15]

In cases of gingival inflammation, gingival connective tissue demonstrates increased degranulated mast cells and mast cells transcribe TNF, interleukin and interferon. A central feature of periodontitis is the remodeling of connective tissue that leads to a net loss of local soft tissues, bone and periodontal ligament attachment apparatus. Mediators produced as a part of host response that contribute to tissue destruction include proteinases, cytokines, TNF, IL-1, IL-6 (some of which are secreted by mast cells).[16]

Since mast cell numbers have been shown to be increased in cases of gingivitis and periodontal disease, mast cell stabilizers like sodium-cromoglycate and nedocromil sodium have been used for the treatment and prevention of periodontal disease without any significant adverse effects and also the fact that drugs like sodium-cromoglycate show significant anti-inflammatory activities, it would be beneficial to use mast cell stabilizers as host modulating drugs.

CONCLUSION

Mast cells have shown a lot of significance in the recent years reflecting a vast number of chemical mediators that are released with wide range of actions in many of the disease processes. The anti-mast cell therapy may provide an adjunct to the existing treatment modalities in the future prospect.

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Fig. 1 Initial clinical presentation



Fig. 2 Recurrence of gingival enlargement after 3 months of oral prophylaxis and gingivectomy

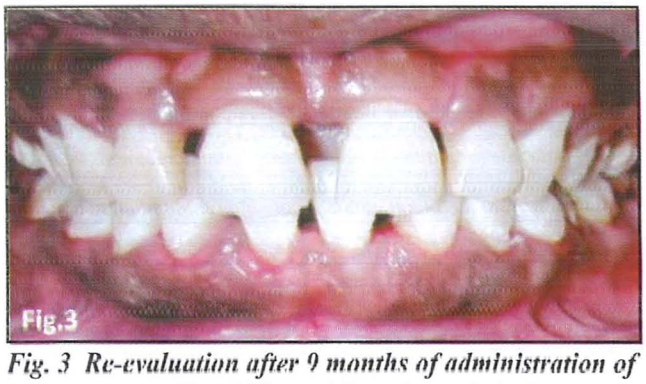


Fig. 3 Re-evaluation after 9 months of administration of mast cell stabilizer with oral prophylaxis

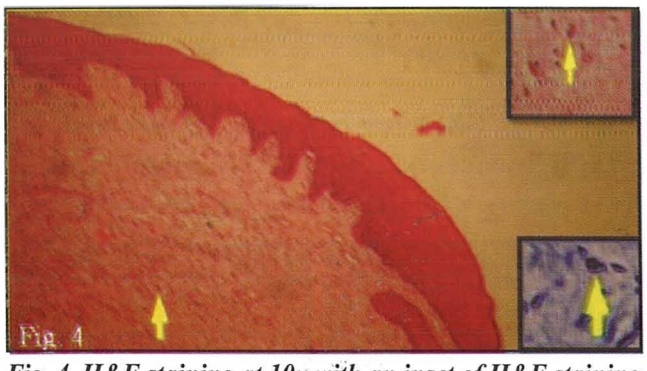


Fig. 4 H&E staining at 10x with an inset of H&E staining and toluidine blue at 40x, arrow- demonstrating mast cells

vascular injury produced by agents which damage mast cells in rats. J. Exp. Med. **103:**334-412.

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