Reactive Hyperplastic Lesions of Oral Cavity: A Review of Literature

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ABSTRACT
Oral mucosa has the potential to give rise to reactive lesions that are non-neoplastic in nature. A wide variety of lesions differing from developmental to neoplastic type can be elicited. Lesions that arise in response to chronic irritation to the oral mucosa are referred to as reactive lesions. Agents like calculus, sharp cuspal tips, overhanging dental restorations, masochistic habits, ill-fitting prosthesis and appliances, and food impactions are the most common etiological factors. These lesions simulate each other in their clinical behavior. Therefore, it is of utmost importance to clinically correlate these lesions with histopathological features to avoid misdiagnosis of the conditions. The most commonly found lesions are traumatic fibroma (TF), pyogenic granuloma (PG), pregnancy tumor (PT), and peripheral giant cell granuloma (PGCG).

Keywords: Epulis fissuratum, Peripheral giant cell granuloma, Pyogenic granuloma, Traumatic fibroma.

INTRODUCTION
Oral cavity is constantly being exposed to many stimuli which can irritate the oral mucosa leading to a variety of hyperplastic reactions. Reactive hyperplastic lesions (also called RHLs) are tumorlike hyperplasia produced in response to chronic irritation or trauma. These hyperplastic lesions simulate non-neoplastic proliferations. The goal for the treatment of these conditions is the elimination of the stimulating agents followed by proper dental therapy. Clinically, the reactive lesions can be classified as traumatic fibroma (TF), pyogenic granuloma (PG), PT, and epulis fissuratum (EF). The histologic classification of RHL is angiomatous proliferation of a vascular type of connective tissue. The most common reactive hyperplastic lesions that are encountered in the day-to-day clinical practice are as follows: traumatic fibroma (TF), pyogenic granuloma (PG), pregnancy tumor (PT), peripheral giant cell granuloma, and epulis fissuratum (EF). All these lesions intermingle with each other in their clinical appearances, but the final diagnosis depends on their histopathological features. According to Eversole and Rovin, the different histological entities of inflammatory hyperplasias may be due to the response of connective tissue to varying intensities of mucosal irritation, which is very similar to neoplastic proliferation. The clinical behavior of RHLs pose a challenge in the differential diagnosis of the lesions, as it may vary in different population depending on the variations in the environmental factors and lifestyles.1–3 This paper explains the distinguishing clinical and histopathological features and the management of some of most commonly encountered reactive hyperplastic lesions.

Pyogenic Granuloma

Introduction
Pyogenic granuloma, also known as acquired lobular capillary hemangioma, is a solitary benign vascular tumor of the skin or mucosa. It commonly affects children and young adults, sometimes pregnant women and rarely elderly individuals.4

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• Factors like trauma, primary tooth injuries, chronic irritation, hormones, drugs, gingival inflammation, chronic irritation due to exfoliation of primary teeth, defective fillings in the region of tumor, food impaction, and toothbrush trauma contribute toward the development of the lesion.
• Cytokines like bFGF, which is a heparin binding angiogenic protein, is found to be highly mitogenic for capillary endothelial cells thereby inducing angiogenesis.
• Hormonal influence in females triggers the formation of pg as estrogen and progesterone acts on gingiva as the target organ.
• Vascular morphogenesis factors like angiopoietin-1, angiopoietin-2, ephrinb2, and ephrinb4 are upregulated in pyogenic granuloma.4–7

Clinical Features
Oral pyogenic granuloma has an increased predilection for females in the second to fifth decades of life. It is found most commonly on the gingiva followed by the lips, tongue, buccal mucosa, and hard plate. Less commonly involved sites are palate, mucobuccal fold, and the frenum. PG presents an array of clinical appearances presenting from a sessile mass to an elevated lesion. They appear as soft, painless, and deep red to reddish-purple nodules which are characteristically ulcerated depending upon the chronicity of the lesion.

Another distinguishing terminology is the occurrence of pyogenic granuloma in pregnant women, which is referred to as pregnancy tumor or pyogenic gravidarium. It develops in the third trimester and may extend till the seventh month of pregnancy. The development of the lesion during pregnancy is due to the elevated levels of estrogen. The pyogenic granuloma presents as a solitary lesion. Satellite lesions do not multiply commonly. Appearance of new lesions around the site of recently treated lesions is an indication of recurrence.2,7

Differential Diagnosis
Peripheral giant cell granuloma, POF, fibroma, peripheral odontogenic fibroma, hemangioma, conventional granulation tissue, hyperplastic gingival inflammation, Kaposi’s sarcoma, bacillary angiomatosis, angiosarcoma, and non-Hodgkin’s lymphoma.4,6,8,9

Histology
The histological appearance of pyogenic granuloma is distinguishing in nature. The lesion has characteristic appearances like (i) the cellular phase, (ii) capillary phase/vascular phase, and (iii) involutionary phase.

Pyogenic granuloma is also of two types, namely, lobular capillary hemangioma (LCH) and nonlobular capillary hemangioma (non-LCH).

Numerous endothelium-lined vascular spaces with neoangiogenesis endothelial proliferation with inflammatory cell infiltrates are the characteristic features of pyogenic granuloma. Lobular aggregates of proliferating blood vessels is the feature of Ich whereas the non-Ich type has high vascular proliferation resembling granulation tissue.2,3,9

Management
The treatment modalities for PG includes excisional surgery, Nd:YAG laser, flash lamp pulsed dye laser, cryosurgery, intralesional injection of ethanol or a corticosteroid, and sodium tetradecyl sulfate sclerotherapy.

• The most commonly used technique is surgical excision of the lesion with wide and negative margins. However, incomplete excision results in recurrence of the lesion and also increased postoperative pain and edema.
• Lasers are the newer techniques available with the advantages of minimal intra and postoperative bleeding and pain; moreover aesthetic benefits are higher.
• Cryosurgery electric scalpel helps in the complete resolution of PG.
• Local injection of ethanol is an alternative therapy for PG.
• Corticosteroids increases the response of the lesion in the vascular bed to vasoconstricting agents.
• Sclerosing agents used in management includes intralesional injection of 3% sodium tetradecyl/sulfate.
• The advantages of this procedure are minimal discomfort to the patient, no or less blood loss, less technique sensitive, and above all is economical.
• Local anesthesia or postoperative dressing is not required or any specific care.9,10

Traumatic Fibroma
Introduction
Fibroma is a benign neoplasm of fibroblastic origin. It is reactive in nature and is a hyperplasia of fibrous connective tissue in response to local irritation. Fibroma is the healed end product of the inflammatory hyperplastic lesion which may occur at any age from any soft-tissue site, tongue, gingiva, and buccal mucosa being the most common.1,2,11

Synonyms
Fibroma, focal fibrous hyperplasia, peripheral fibroma, peripheral ossifying fibroma fibroid epulis (old term), fibroepithelial polyp.

History
Fibroma is a rare intraoral benign neoplasm of fibroblastic origin. Fibromas of oral cavity are reactive hyperplasia of fibrous connective tissue in response to irritants.

• Contradictions exist regarding the presence of true benign neoplasm composed of fibroblasts.
• The histological criteria of a true fibroma were proposed by Barker and Lucas.12,13

Etiology
Irritational fibroma, as the name suggests, has an etiology, that is, a source of irritation. Common irritants are fractured or sharp restorations, sharp cuspal tips, ill-fitting prosthesis, and food impactions.

Clinical Features
The most common location is the buccal mucosa along the occlusal plane. Continuous irritation can result in hyperkeratosis giving it a white appearance. It is also found on the labial mucosa, tongue, and gingiva.14 Most fibromas are sessile, but some are pedunculated though. The lesion typically appears as a smooth surfaced pink nodule simulating the mucosa which may vary on racial discrimination. The size of the fibroma ranges from a few
millimeters to not more than 1.5 cm. Irritation fibromas are usually asymptomatic, unless secondarily ulcerated. Being common in the fourth to sixth decades of life, there is a slightly higher predilection for females.

**Differential Diagnosis**

Hyperplastic fibro-keratinocytic, peripheral giant cell granuloma, peripheral ossifying fibroma, and pyogenic granuloma.

**Histology**

The pattern of arrangement of collagen bundles is unique. A radiating and circular pattern of collagen bundles can be seen. However, it has been hypothesized from various studies that, in areas of a greater degree of trauma, a radiating pattern of collagen is seen whereas in minor traumatic areas a circular pattern is observed.

**Management**

Like any other reactive lesion, traumatic fibroma also has multiple treatment modalities which include both surgical and nonsurgical techniques.

Scalpel Surgery: Surgical enucleation with a scalpel is the most widely used form of treatment, which is the complete removal of the lesion with safety margins during the surgical procedure. The drawbacks of conventional scalpel surgery include intraoperative bleeding management, the need for suturing, and the risk of postoperative edema.

Electrosurgery is an invasive procedure due to the excessive generation of heat with the potential for scarring.

Cryosurgery is the use of liquid nitrogen to destroy tissue by rapid freezing. It is a time-consuming procedure and is contraindicated in patients with cold intolerance.

The removal of an irritation fibroma can be most efficiently performed with the CO2 laser because of its inherent advantages, of hemostasis, diminished postoperative edema, uneventful healing, and decreased scarring.

The Nd:YAG laser of 1,064-nm wavelength is an efficient coagulator but a poor scalpel, as it is highly scattered and weakly absorbed by the soft tissue.

To enhance its cutting efficiency, the low absorption of the Nd:YAG wavelength is attenuated by the use of very high peak power.

**Epulis Fissuratum**

**Introduction**

A poorly fitted prosthesis gives rise to a variety of problems like pain, discomfort in mastication, and speech. Epulis fissuratum refers to reactive tissue response to excessive mechanical pressure from an ill-fitting prosthesis.

**Synonyms**

Inflammatory fibrous hyperplasia, denture-induced fibrous inflammatory hyperplasia, denture injury tumor, denture epulis, denture induced granuloma, granuloma fissuratum.
Peripheral Giant Cell Granuloma

Introduction
PGCG is a common non-neoplastic reactive hyperplastic lesion of the oral cavity which is defined and demarcated by its varied histological appearances. PGCG is a relatively common lesion. However, the etiology, growth potential, biological behavior, histogenesis of its cells and its treatment have always been ambiguous. The lesion is known for its notorious behavior and its high recurrence rate.

Synonyms
Giant cell epulis, peripheral giant cell tumor, and reparative giant cell granuloma.

Historical Background
PGCG could be either peripheral or central giant cell reparative granuloma. Giant cell granulomas occurring within the bone are called central giant cell granuloma (CGCG) and those occurring on edentulous alveolar processes or gingivae are called PGCG.

Etiopathogenesis
The most common predisposing factor is the presence of local irritants and poor oral hygiene. The lesion arises from the periodontal ligament membrane. The periodontal ligament responds intensely to the local irritants which is severe with PGCG than any other reactive lesions.

- Chronic irritants like improper restorations, food impaction, and calculus are the common causative agents.
- Extractions: Post-extraction healing sockets are also one of the instigating agents of the lesion.
- Xerostomia: Decreased salivary flow leads to alteration in physiological functions of saliva exposing the oral mucosa to constant irritation, which inadvertently leads to hyperplastic lesion.
- Hormonal influence: PGCG is pregnancy mediated rather than being “pregnancy dependent.” It is due to the immunosuppressive action of hormones along with hyper responsiveness of the gingiva to these hormones.

Clinical Features
PGCG occurs in any age. It is more prevalent in females of fourth to sixth decades of life. Mandible is more prevalent than maxilla. It appears as painless, soft, nodular mass, usually red to reddish-blue in color. The typical bluish red hue is the characteristic of the PGCG. A secondarily infected lesion has a ‘yellow zone’ caused due to the aggregation of a fibrin clot at the ulcer site.

The size of the lesion ranges from papules to lesions more than 40 mm. The chronicity of the irritants also determines the size of the lesion. Compromised oral health and hygiene, ill-fitting dentures, and xerostomia are the common triggering factors.

Histopathology
PGCG has a characteristic histopathological appearance. Numerous multinucleated giant cells with proliferating fibroblasts in fibrocellular stroma are the hallmark of the lesion. The fibroblasts appear plumply spindles whereas the giant cells are multimorphological. Two types of giant cells are present, namely, type I and type II wherein type I cells are more numerous than type II.

Differential Diagnosis
Pyogenic granuloma, hemangioma, CGCG, POF and metastatic carcinomas.

Management
The treatment of PGCG includes excision of the growth down to the periosteum with scalpel, electrocautery, or lasers and also eliminating any local irritating factors associated with it.

Lasers are a good option to perform excision as they provide excellent hemostasis, bactericidal effect, precision, short healing time, better postoperative pain perception, and less discomfort to the patient.

Recurrence and Prognosis
The prognosis of reactive hyperplastic lesions depends upon the accuracy of elimination of the etiological factors and the type of treatment modality. However, from the previous studies, it is being interpreted that the recurrence rate varies between 2 and 28% with increased prevalence for pyogenic granuloma and least for peripheral giant cell granuloma.

Conclusion
Hence we may conclude that reactive lesions of oral cavity has varying clinical appearances which may simulate multiple lesions. However, a complete clinical examination correlated with the histopathological features is required for the proper diagnosis. Moreover, the choice of the treatment modality also contributes to the prognosis of the lesion.

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