ABSTRACT
Oral cavity, when subjected to various forms of chronic insults or microtrauma, often results in a hyperplastic lesion, commonly referred to as inflammatory reactive hyperplasia. This category includes various lesions such as peripheral fibroma, peripheral ossifying/cementifying fibroma, pyogenic granuloma, and peripheral giant cell granuloma. They are primarily seen to develop in close proximity to the source of chronic irritant and have a close resemblance in terms of biological behavior and clinical presentation. Histopathologically, they display a common feature of hyperplastic fibrous tissue, but also have some variations like the presence of giant cells or aggregate of calcified mass depending on the histogenesis of the lesion. They were the most common tumor-like lesions to be seen in the oral cavity, familiarity with these lesions are of utmost importance. The present article portrays a series of 5 cases of different clinical forms of reactive hyperplasia with a brief literature review. The current manuscript is presented with an aim to enhance the knowledge about hyperplastic lesions.

Keywords: Oral inflammatory hyperplasia, Irritation fibroma, Pyogenic granuloma, Peripheral giant cell granuloma, Peripheral ossifying fibroma

INTRODUCTION
Oral inflammatory hyperplastic (IH) lesions, traditionally referred to as “Epulides”, are considered to be the most commonly occurring mucosal lesion. They are considered as an over exuberant reparative response of the tissues, wherein an increase in a number of the constituent cells is seen, in response to the local irritants [1].

The traumatic irritants come from a wide range, including calculi, overhanging margins of restoration, foreign bodies, chronic biting, overextended boarders of the appliance and sharp spicules [2]. Regardless of the type of irritant, the pathogenesis remains the same. Any of these chemomechanical insults when subjected to oral mucosa for an extended period of time, it initiates a chronic inflammatory process, which in turn stimulates the production of granulation tissue. This hyperplastic tissue, depending on the histopathological picture showing predominant cell type, are clinically identified as irritation fibroma, pyogenic granuloma, peripheral giant cell granuloma or cemento-ossifying fibroma. Similar reactive lesions, usually associated with ill-fitted denture include epulis fissuratum, inflammatory papillary hyperplasia and inflammatory fibrous hyperplasia [3].

This series of cases includes the clinical presentation of the fibrous, vascular and giant cell type of reactive lesions.

CASE SERIES

Irritation Fibroma

Case 1: A 45-year old female patient, presented with a painless, small growth in her lower labial mucosa which showed a gradual increase in size over 4 months. Intraoral examination revealed a sessile, smooth surfaced growth with few areas of ulceration. It seems that the upper central incisors had been a constant source of trauma in the area of growth, which has caused few sites of ulceration on the swelling as well. It was mild tender and firm on palpation (Figure 1a).
Considering the obvious of the source of chronic trauma in the near proximity of growth and firm nature of slow-growing swelling, a provisional diagnosis of irritation/traumatic fibroma was given. The lesion was surgically excised and tissue underwent a histopathological examination. It showed stratified orthokeratinized epithelium of varying degree. Underlying connective tissue showed a thick fibrous stroma with mild chronic inflammatory cells (Figure 1b).

Figure 1 a: Intraoral clinical view of lesion: a smooth surfaced enlargement in the lower labial mucosa; b: Histopathological picture demonstrating parakeratinized stratified squamous

Epulis Fissuratum

Case 2: A 50-year old female patient, reported with discomfort in using her lower denture for the past 6-months. She was completely edentulous and got her complete denture fabricated 2 years back. On questioning, her medical history was non-contributory.

On clinical examination, a well-defined, pedunculated swelling with the lobulated surface was seen in the lower vestibular region, with mandibular denture flange covering it completely. The swelling was approximately 3 cm × 4 cm in size, with a fissure on its surface coinciding with the denture flange. The mucosa was slightly erythematous and firm on palpation (Figure 2a).

Considering the site and benign nature of growth, the provisional diagnosis of epulis fissuratum was made. The surgical excision was performed and the sample was sent for histopathological examination. It showed hyperplastic epithelium as well as fibrous connective tissue and moderate inflammation (Figure 2b). The patient was referred to the Department of Prosthodontics for the fabrication of a new denture. Complete resolution of the lesion without any recurrence was observed on 3-months follow-up.

Pyogenic Granuloma

Case 3: A 40-year-old female presented with a well-defined growth on her buccal aspect of maxillary gingival extended
from 22 to 23 region for the past 5-months. On further questioning, she informed about the asymptomatic and slow-growth nature of the swelling. Clinical examination revealed a smooth, bright red colored, sessile overgrowth with bleeding on probing. It was soft and non-tender on palpation (Figure 3a).

Intraoral periapical radiograph did not reveal any abnormalities like cortical plate erosion. Surgical excision was performed. Histopathological examination revealed, a highly vascular tissue lined by surface epithelium. Plenty of endothelium-lined blood vessels filled with RBCs were found in connective tissue. The final diagnosis of pyogenic granuloma was established (Figure 3b). Recurrence of the lesion was not reported on 1-year follow up.

**Figure 3 a:** A bright red colored growth was seen in left maxillary gingival margin extending from 22 to 23 region; **b:** Photomicrograph showing numerous red blood cells engorged blood vessels in fibrous connective tissue

**Peripheral Giant Cell Granuloma**

**Case 4:** A 25-year male patient reported with a 5-month old, slow-growing lump on his buccal aspect of maxillary gingiva, extending from 13 to 15 region. Since 5 days, the growth had become symptomatic with the onset of pain, followed by a spontaneous pus discharge.

Clinical examination revealed an erythematous, pedunculated overgrowth with the lobulated surface. It was tender and firm in consistency. Pus discharge was appreciated with digital pressure. Right maxillary canine exhibited grade III mobility with positive tender on percussion (Figure 4a).

Cone beam CT revealed a well-defined, non-corticated, homogenous radiolucent lesion with complete erosion of buccal cortical plate alone, sparing palatal cortical plate (Figure 4b). The floating tooth-like appearance was evident in a periapical view (Figure 4c).

Considering the clinical and radiographic findings, the diagnosis of a secondarily infected peripheral aggressive lesion was given. Incisional biopsy shows multinucleated giant cell proliferation within a background of mesenchymal cells. Acute and chronic inflammatory cells were also present. A zone of dense fibrous connective tissue separates giant cell proliferation from the mucosal surface (Figure 4d). Based on histopathology, the final diagnosis of peripheral giant cell granuloma was made. The excision biopsy was performed. No signs of recurrence of the lesion have been observed during the follow-up.
Figure 4 A: Clinically, single well defined, pedunculated swelling seen in attached gingiva of right maxillary canine-premolar region; B: Axial section of cone beam CT image showing resorption of buccal cortical plate; C: Intraoral periapical view showing mesial and distal bone resorption of tooth No. 13; D: Histopathologic section showing hyperplastic granulation tissue with multinucleated giant cells

Peripheral Ossifying Fibroma

Case 5: A 21-year old male patient reported with a chief complaint of a mass of slow progressive nature in the buccal aspect of 11 to 12 region since 6-months. The swelling was otherwise asymptomatic and his medical history was non-contributory.

Intra-oral examination revealed sessile, solitary, smooth surfaced and roughly oval-shaped growth seen on the labial gingival. The growth was approximately 1.5 cm × 2 cm in size with reddish pink colored overlying mucosa. On palpation, it was non-tender and firm in consistency (Figure 5a).

Clinically, the differential diagnosis included peripheral ossifying fibroma, peripheral giant cell granuloma, and pyogenic granuloma. The surgical intervention was carried out considering a peripheral benign lesion. The histopathological picture revealed parakeratinized stratified epithelium with fibrocellular stroma exhibiting thick bundles of collagen fibers interspersed with plump fibroblasts. The focally mineralized component was noted and thus the final diagnosis of peripheral ossifying fibroma was made (Figure 5b). Fortunately, no recurrence was noted in this case.

Figure 5 A: Clinical image showing growth in interdental gingival, extending from 11 to 12 region; B: Photomicrograph depicting parakeratinized stratified squamous epithelium covering a fibrocellular connective stroma with discrete calcifications
DISCUSSION

Reactive hyperplastic lesions, also been referred to as Focal reactive overgrowths (FROGs’), are known to occur as an oral tissue’s adaptive response to a low-grade chronic irritation. This group of the lesion has many things in common like clinical picture and treatment; whereas histopathology varies to a level where a specific cell constituent seems to dominate the picture. Literature suggests a potential relationship between variations of connective response to the serum levels of female endocrine hormones [4].

Being reactive lesion, identification and elimination of traumatic factor are considered to be the most vital segment of treatment. It will not only help in arresting the disease process but also makes a significant reduction in the size of the lesion. The surgical excision becomes easy or sometimes the need is eliminated. Although the recurrence uncommon, it is still important to keep following up the patient for a considerable amount of time [5].

Fibrous Hyperplasia

They are also known as irritation or traumatic fibroma. However, they are considered as the healed end product of inflammatory hyperplastic lesions, where there is an aggregate of scar tissue is seen covered by stratified epithelium [6].

Often, these lesions are sessile with smooth contour with pale pink color. The commonest location for these lesions is reported to be buccal mucosa and gingiva. Treatment of these lesions includes removal of ethological factor followed by excision biopsy [7]. Giant cell fibroma is an important differential diagnosis in addition to the benign mesenchymal tumor. The presence of multinucleated giant cell will the differentiating feature from the traumatic fibroma.

Pyogenic Granuloma

The terminology “pyogenic” is a misnomer, as the early clinicians considered the ulcerated and necrotic picture as a pathognomonic feature of it. But in fact, this appearance is an outcome of trauma to the lesion, with later getting contaminated with oral flora and fluids. It is shown predominantly affecting the females especially during the periods of puberty or pregnancy, during which hormonal levels have wide fluctuations [1]. The most common location by far is the anterior segment of the gingiva, although other sites like buccal mucosa and alveolar mucosa have been reported. They are reported to have a bright red color and soft in consistency, primarily by virtue of abundant proliferating blood vessels. Predominantly endothelia related tumors like hemangioma and Kaposi sarcoma are considered in differential diagnosis [2].

Peripheral Giant cell granuloma

It is a type of hyperplastic lesion which has multinucleated giant cells, supposedly arise from osteoclast as a result of the reactive response from the periodontal ligament. They are known to arise in the slightly elder age group of 30-70 years with a greater number of women being affected [7].

They are reported to occur on the gingiva and known to cause a compression of the labial cortical plate, which is referred to as “cuffing type of bone resorption”. Considering a little aggressive behavior and middle age of occurrence, malignant connective tissue tumors and metastatic tumors of the jaws are generally considered as differential diagnosis [8].

Peripheral Ossifying Fibroma

When peripheral fibroma is seen with calcified deposits resembling cementum or osteocementum scattered in the background of fibrous connective tissue, it is referred to as a peripheral cemento-ossifying fibroma or peripheral ossifying fibroma. Such lesions will display radiopaque foci on the radiograph, provided there is significant calcification [9].

They are known to occur predominantly in female compared to male, between the age of 25-40 years. It usually involves interdental papillae with sometimes causing separation of the adjacent teeth and minimal bone resorption [10].

With the signs of bone resorption, malignant lesions like osteogenic sarcoma and chondrosarcoma should be considered in the differential diagnosis. A band like the asymmetrical widening of the periodontal ligament of the involved teeth will be a suggestive finding of these malignant lesions [6].

CONCLUSION

Peripheral hyperplastic lesions are the most common soft-tissue swellings of the mouth. They are not neoplasm but hyperplastic swellings that develop in sites subject to chronic low-grade injury. Though different entities are seen in
this category, they all share a common clinical presentation and biological behavior. Identification and removal of the etiological factor remain the most crucial aspect of the treatment in addition to the surgical excision.

DECLARATIONS

Conflict of Interest
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES


