Assessment of reactive gingival lesions of oral cavity: A histopathological study

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INTRODUCTION

Growth of the gingival tissues are widespread and frequently result from underlying systemic disease, drug-induced stimulus, dental plaque and local iatrogenic factors. These lesions are majorly reactive and demonstrate tumor-like hyperplasia. These proliferations are painless pedunculated or sessile masses in dissimilar colors, Background: In the literature, many studies were attempted to analyze the distribution of oral reactive lesions in terms of age, gender and location. However, very few studies have focused on the detailed histopathological features of these reactive lesions of oral cavity. Thus, the purpose of this paper is to document the occurrence, distribution and various histopathological features of reactive gingival lesions. Materials and Methods: This study is a retrospective archival review of reactive gingival lesions of oral cavity such as irritational fibroma (IF), inflammatory gingival hyperplasia (IGF), pyogenic granuloma (PG), peripheral giant cell granuloma (PGCG) and peripheral ossifying fibroma involving gingival tissues. All the cases were histopathologically reviewed on some microscopical parameters according to the criteria given by Peralles et al. Results: Regarding epithelial morphology, atrophy, ulceration and hyperplasia were found predominantly in PG. Connective tissue was predominantly dense in IGF and IF with fibroblastic proliferation; whereas loose connective tissue was seen in PG. Vascular proliferation, especially capillary, was commonly present in PG and inflammatory gingival hyperplasia (IGH). Inflammatory cell infiltrate was intense in both PG and IGH. Mineralization showed a marked affinity for peripheral cement-ossifying fibroma, and bone/bone-like areas were found in about ten cases of them. The Foreign body type of multinucleated giant cells was found exclusively on PGCG. Conclusion: Despite their clinical similarities, the findings of this study reports that all reactive gingival lesions show some differences in age, type, location, duration and histopathological features. Nevertheless, the differing histological pictures are a range of a single lesion in diverse stages of maturation. Essential in the treatment of reactive lesions is the total removal of the lesion with local irritants such as defective restorations or calculus formation.

Keywords: Gingival reactive lesions, histopathology, inflammatory gingival hyperplasia, irritational fibroma, peripheral giant cell granuloma, peripheral ossifying fibroma, pyogenic granuloma

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beginning from light pink to red. The outside appearance is changeable from nonulcerated flat to ulcerated mass. Lesion dimension varies from hardly any millimeters to several centimeters.\textsuperscript{1,2}

Epulis is a conventional clinical name given for gingival reactive proliferations. Pyogenic granuloma (PG), irritation fibroma, peripheral ossifying fibroma (POF), peripheral giant cell granuloma (PGCG) and inflammatory gingival hyperplasia (IGF) are the frequent reactive lesions of the oral cavity.\textsuperscript{3}

The clinical features of these reactive lesions of gingiva appear to reflect the various stages of development since in the early stages they appear red, raw with ulcerated surfaces and bleed on slight touch or spontaneously, while in the late stages, they appear as firm, mature and avascular fibrous growths which may be pedunculated or leaf-like in shape or as sessile.\textsuperscript{4}

Histopathologically, there is also a wide spectrum of changes changeable from chronically, well-off cellular granulation tissues to moderately noninflamed, avascular masses of collagen.

It is probable to make a diagnosis of reactive proliferations as particular entities based mainly on their histopathological features which can be alienated into vascular and fibrous types. Other histological components that can be seen are small vessels hyperplasia, calcified material, inflammatory cell infiltrate and multinucleated giant cells.\textsuperscript{4,5}

In the literature, many studies were attempted to analyze the distribution data of oral reactive lesions in terms of gender, age and location of oral reactive gingival lesions. Although exceptionally any studies have focused on the thorough histopathological features of these reactive lesions of the oral cavity.\textsuperscript{6} Thus, the aim of this paper is to document the occurrence, distribution and various histopathological features of reactive gingival lesions at a teaching hospital in Raichur.

**MATERIALS AND METHODS**

This study is a retrospective archival review of reactive gingival lesions of oral cavity obtained from Department of Oral Pathology, Navodaya Dental College, Raichur, and Karnataka, India from 2006 to 2015. This study comprises a group of epithelial and fibrous connective tissue lesions that commonly occur in the oral mucosa as a result of the injury. The cases for inclusion in this study were those categorized as IGF, irritation fibroma (IF), PG, POF and PGCG involving gingival tissues of both maxillary and mandible.

Clinical information concerning gender, age and location were obtained from the patient’s reports for each case. Unfinished registered reports and missed pathologic slides were disqualified from the study.

All the gingival lesions were histopathologically analyzed on hematoxylin and eosin staining, and final analysis was grouped in one of the four previously mentioned lesions. For detailed histopathological diagnosis, some microscopical parameters were analyzed according to the criteria given by Peralles et al.:\textsuperscript{6}

- Pattern of the gingival lining epithelium – subdivided in normal, atrophic (thin epithelium with <5 cell layers), hyperplastic (epithelium with more than 15–20 cell layers), or absent (areas of ulceration)
- Type of connective tissue loose or dense; as well as the presence of fibroblastic proliferation dispersed in the connective tissue
- Presence of vascular proliferation – presence of abundant capillary or cavernous vascular proliferations in the connective tissue
- Distribution of inflammatory infiltrate
  - Mild: When distributed in focal areas, especially on the subepithelial area
  - Intense: When dispersed all over and deep into the connective tissue
- Type of inflammatory infiltrate predominantly acute, chronic or both
- Presence of mineralized material – foci of bone and/or cementum
- Presence of foreign body multinucleated giant cells.

Data were analyzed using SPSS Inc. Released 2007. SPSS for Windows, Version 16.0. Chicago, SPSS Inc; and presented in descriptive and tabular forms.

**RESULTS**

IGF was the most prevalent lesion ($n = 268, 58\%$). It was followed by PG ($n = 127, 27.6\%$), irritation fibroma ($n = 44, 10\%$), POF ($n = 18, 4\%$) and PGCG ($n = 2, 0.4\%$).

**Age**

The age ranged from 8 to 63 years, with a mean age of 40.5 years. PG, IF and IGF were more frequent in the fourth decade, whereas PGCG and POF were more common in the third decade. Table 1 shows the frequency of reactive gingival lesions in different ages.
Gender
Seventy-three (16%) cases occurred in males whereas 387 (84%) cases occurred in females. Male to female ratio was 1:3. All the reactive gingival lesions were more common in females. Table 2 shows the distribution of reactive gingival lesions in different genders.

Anatomic location
The analysis of site of the lesions showed that the anterior portion of the maxillary and mandibular gingiva was affected in 42% and 38% of the cases, respectively. This was followed by lower posterior (13%) and upper posterior (7%). Table 3 shows the frequency of reactive gingival lesions in different anatomic locations.

Histopathological analysis
Histopathological parameters such as epithelium, connective tissue, type and intensity of inflammatory cell infiltrate, vascular proliferation, presence of mineralization and multinucleated giant cells were evaluated.

Table 1: Distribution of reactive gingival lesions of oral cavity by different ages

| Reactive gingival lesions | Age (years) | Total (%) |
|--------------------------|-------------|-----------|
|                          | Mean | Range |      |
| PG                       | 33.3 | 8-60  | 127 (27.6) |
| IF                       | 37.3 | 9-85  | 45 (10) |
| IGF                      | 34.5 | 10-63 | 268 (58) |
| POF                      | 21.8 | 15-48 | 18 (4) |
| PGCG                     | 30   | 20-40 | 2 (0.4) |
| Total                    | 40.5 | 8-63  | 460 |

IF: Irritative fibroma, POF: Peripheral ossifying fibroma, IGF: Inflammatory gingival hyperplasia, PG: Pyogenic granuloma, PGCG: Peripheral giant cell granuloma

Table 2: Distribution of reactive lesions of oral cavity by gender

| Reactive gingival lesions | Males | Females |
|--------------------------|-------|---------|
| PG                       | 9     | 118     |
| IF                       | 14    | 31      |
| IGF                      | 48    | 220     |
| POF                      | 2     | 16      |
| PGCG                     | 0     | 2       |
| Total ( % )              | 73 (16) | 387 (84) |

IF: Irritative fibroma, POF: Peripheral ossifying fibroma, IGF: Inflammatory gingival hyperplasia, PG: Pyogenic granuloma, PGCG: Peripheral giant cell granuloma

Table 3: Distribution of reactive gingival lesions of oral cavity by location

| Reactive gingival lesions | Upper anterior | Lower anterior | Upper posterior | Lower posterior | Total |
|--------------------------|----------------|----------------|-----------------|-----------------|-------|
| PG                       | 60             | 50             | 2               | 15              | 127   |
| IF                       | 10             | 20             | 10              | 5               | 45    |
| IGF                      | 120            | 90             | 20              | 38              | 268   |
| POF                      | 4              | 8              | 2               | 4               | 18    |
| PGCG                     | 1              | 1              | 0               | 0               | 2     |
| Total ( % )              | 195 (42)       | 169 (38)       | 34 (7)          | 62 (13)         | 460   |

IF: Irritative fibroma, POF: Peripheral ossifying fibroma, IGF: Inflammatory gingival hyperplasia, PG: Pyogenic granuloma, PGCG: Peripheral giant cell granuloma

Regarding epithelial morphology, atrophy, ulceration and hyperplasia were found predominantly in PG [Figure 1], and these findings were also present in all other histological types. 55% of reactive gingival lesions showed epithelial hyperplasia followed by 23% of atrophic epithelium. Further epithelial hyperplasia was seen in majority of inflammatory gingival hyperplasia cases [Figure 2 and Table 4].

Connective tissue was predominantly dense (52%) in inflammatory gingival hyperplasia and irritational Fibroma with fibroblastic proliferation [Figure 3a]; where as loose connective tissue was seen in pyogenic granuloma (25%) [Figure 3b]. Fibroblastic proliferation was present almost exclusively in PCOF and PGCG [Table 5].

Inflammatory cell infiltrate was considered intense in 40% of the cases, especially in PG and IGH. Chronic inflammatory infiltrate was found in all cases (100%) and acute infiltrate was particularly common in PG [Figure 5a and b] and IGH (16%) [Table 6].

Vascular proliferation, especially capillary, was commonly present in PG and IGH [Figure 5a]. Mineralization showed marked affinity for PCOF, and bone/ bone-like areas were found in about 10 cases of them [Figure 5b]. Two cases
of PG showed areas of bone formation. In these 2 cases, all other microscopic characteristics together allowed the diagnosis of PG, even with some mineralization foci present in the lesion. However foreign body multinucleated giant cells were found exclusively on PGCG [Figure 5c and Table 7].

**DISCUSSION**

Reactive lesions of gingiva are frequently responses to chronic inflammation caused by a range of forms of low-grade irritations to gingiva such as sharp edges of grossly carious teeth, dental plaque and calculus, ill-fitting dental/oral appliances, faulty dental restorations and food impactions. Apart from local chronic irritations, these lesions emerge to be etiologically associated to systemic factors such as hormonal changes.\[7,8\]

In the pathogenesis of these reactive lesions, a necessary characteristic of chronic inflammation is that the process of inflammation and repair happen concurrently with the ensuing creation of granulation tissue and consequently, most of these lesions symbolize the exuberant creation of granulation tissue in chronic inflammatory reactions.\[4\]

To the finest of our knowledge, there are presently no huge reviews on the occurrence, pattern of distribution and histopathological features of reactive gingival lesions of the oral cavity.

Therefore, this study is an effort to estimate the prevalence and allocation of histopathological parameters of five main reactive gingival lesions from achieves available in Department of Oral Pathology, Navodaya Dental College and Hospital, Raichur, Karnataka, India.

The present study results showed that IGF is the most common reactive gingival lesion, followed by PG, which is in accordance with Zain and Fei and Peralles et al.\[6,9\] Adults in their 3rd–4th decades are the most affected patients, especially females, which is also in accordance with previous reports of Peralles et al. and Effiom et al.\[6,10\]

Most of the studies showed that the anterior regions of the oral cavity are exaggerated more regularly, varying from 38% to 42% of the cases. This can be explained by the fact that according to Peralles et al. anterior regions of oral cavity are more dried than the posterior regions, thus prone to be affected by calculus deposition in the inferior region,

![Figure 2: Epithelial morphology showing hyperplasia in inflammatory gingival hyperplasia (H&E, x20)](image)

![Figure 4: (a) Intense chronic inflammatory cell infiltrate seen in pyogenic granuloma (H&E, x10). (b) Acute infiltrate was particularly common in pyogenic granuloma (H&E, x40)](image)

![Figure 3: (a) Connective tissue is predominantly dense with fibroblastic proliferation in irritational fibroma (H&E, x20). (b) Loose myxoid connective tissue stroma seen in pyogenic granuloma (H&E, x20)](image)

![Figure 5: (a) Vascular proliferation, especially capillary, seen in pyogenic granuloma (H&E, x20). (b) Mineralization of bone/bone-like areas seen in peripheral cement-ossifying fibroma (H&E, x10). (c) Foreign body type of multinucleated giant cells seen exclusively in peripheral giant cell granuloma (H&E, x20)](image)
and the frequent teeth malposition in this area, leading to the difficulty of maintaining hygiene and consequently, plaque control.\[6\]

Table 4: Distribution of type of epithelium in different reactive gingival lesions of oral cavity

| Reactive gingival lesions | Epithelium     | Normal | Atrophic | Hyperplastic | Absent |
|--------------------------|----------------|--------|----------|--------------|--------|
| PG (n=127)               |                | 2      | 20       | 35           | 70     |
| IF (n=45)                |                | 3      | 32       | 2            | 8      |
| IGF (n=268)              |                | 12     | 40       | 212          | 4      |
| POF (n=18)               |                | 2      | 13       | 2            | 1      |
| PGGG (n=2)               |                | 1      | 1        | 0            | 0      |
| Total (%)                |                | 20 (4) | 106 (23) | 251 (55)     | 83 (18) |

IF: Irritation fibroma, POF: Peripheral ossifying fibroma, IGF: Inflammatory gingival hyperplasia, PG: Pyogenic granuloma, PGGG: Peripheral giant cell granuloma

Table 5: Distribution of type of the connective tissue and vascular proliferation in different reactive gingival lesions of oral cavity

| Reactive gingival lesions | Connective tissue | Vascular proliferation | Loose | Dense | Fibroblastic proliferation | Present | Absent |
|--------------------------|-------------------|------------------------|-------|-------|---------------------------|---------|--------|
| PG (n=127)               |                   |                        | 104   | 10    | 13                        | 127     | 0      |
| IF (n=45)                |                   |                        | 2     | 35    | 20                        | 2       | 43     |
| IGF (n=268)              |                   |                        | 20    | 180   | 68                        | 80      | 188    |
| POF (n=18)               |                   |                        | 1     | 12    | 18                        | 6       | 12     |
| PGGG (n=2)               |                   |                        | 0     | 2     | 2                         | 2       | 0      |
| Total (%)                |                   |                        | 127 (25) | 239 (52) | 121 (23) | 217 (47) | 243 (53) |

IF: Irritation fibroma, POF: Peripheral ossifying fibroma, IGF: Inflammatory gingival hyperplasia, PG: Pyogenic granuloma, PGGG: Peripheral giant cell granuloma

Table 6: Distribution of type and intensity of inflammatory cell infiltrate in different reactive gingival lesions of oral cavity

| Reactive gingival lesions | Type of ICI      | Intensity of ICI |
|--------------------------|------------------|-----------------|
|                          | Acute | Chronic | Mild | Intense |
| PG (n=127)               |       | 32      | 127  | 46      | 81     |
| IF (n=45)                |       | 8       | 45   | 36      | 9      |
| IGF (n=268)              |       | 30      | 268  | 185     | 83     |
| POF (n=18)               |       | 3       | 18   | 8       | 10     |
| PGGG (n=2)               |       | 0       | 2    | 1       | 1      |
| Total (%)                |       | 73 (16) | 460 (100) | 276 (60) | 184 (40) |

IC: Inflammatory cell infiltrate, IF: Irritation fibroma, POF: Peripheral ossifying fibroma, IGF: Inflammatory gingival hyperplasia, PG: Pyogenic granuloma, PGGG: Peripheral giant cell granuloma

In our study, the most frequent histopathologically described gingival enlargement was IGF (58%). The average age of occurrence was 34.5 with the range being 10–63 years. Females were frequently affected than males. The most common site affected was upper anterior gingiva followed by lower anterior gingiva. Histopathologically, IGF showed predominantly hyperplastic epithelium with dense connective tissue showing some amount of fibroblastic proliferation with few vascular proliferations. Mild chronic inflammatory cell infiltrate was seen predominantly in IGF with no calcifications or multinucleated giant cells. These findings of IGF are similar to the studies done by Peralles et al., Ramu and Rodrigues.\[6,11\]

The prevalence of PG reported in the present study was 27% of all the reactive gingival lesions with an average age of occurrence being 33.3 and in the range of 8–60 years. Females were commonly affected than males and most common site exaggerated was upper and lower anterior gingiva.

The conditions “pregnancy tumor” and “granuloma gravidarum” are frequently used to explain the incidence of PG during pregnancy. Such lesions commonly begin to develop in the first trimester and their occurrence increases onto the 7th month of pregnancy. The cause for the PG in pregnancy is the raised levels of progesterone and estrogen. The effects of estrogen on periodontal tissues include proliferation of gingival fibroblasts, increased gingival inflammation and reduction of keratinization in the presence of minimal plaque accumulation, while progesterone increases vascular dilatation, thus increasing the permeability of periodontal tissues leading to more endothelial cell proliferation.\[12\] In the present study, histopathologically, PG predominantly showed loose connective tissue stroma, ulcerated epithelium with extensive vascular proliferation and intense chronic inflammatory cell infiltrate. Two cases of PG showed foci of bone in the connective tissue.

Table 7: Distribution of mineralization and multinucleated giant cells in different reactive gingival lesions of oral cavity

| Reactive gingival lesions | Mineralization | Multinucleated giant cells |
|--------------------------|----------------|---------------------------|
|                          | Absent | Cementum/cementum-like | Bone/bone-like | Present | Absent |
| PG (n=127)               | 125    | 0                         | 2             | 0       | 127   |
| IF (n=45)                | 45     | 0                         | 0             | 0       | 45    |
| IGF (n=268)              | 268    | 0                         | 0             | 0       | 268   |
| POF (n=18)               | 8      | 10                        | 0             | 0       | 18    |
| PGGG (n=2)               | 2      | 2                         | 0             | 2       | 0     |
| Total (%)                | 440 (96) | 8 (1)                      | 12 (3)       | 2 (1)   | 458 (99) |

IF: Irritation fibroma, POF: Peripheral ossifying fibroma, IGF: Inflammatory gingival hyperplasia, PG: Pyogenic granuloma, PGGG: Peripheral giant cell granuloma
In the present study, the prevalence of IF was 10% of all the reactive gingival lesions. It was seen most commonly in third decade and in females with most frequent location being lower anterior gingiva. Histopathologically, IF showed atrophic epithelium and dense connective tissue stroma with fibroblastic proliferation. Mild chronic inflammatory cell infiltrates with no mineralization, or multinucleated giant cells were seen. The results were similar to Peralles et al. and Reddy et al.[6,13]

POF constituted 4% of all the reactive gingival lesions with an average of 21 years. Females were more frequently affected and lower anterior gingiva being most commonly involved. Histopathologically, POF showed atrophic epithelium and dense connective tissue stroma with fibroblastic proliferation and minimal vascular proliferation. Intense chronic inflammatory cell infiltrate was seen. Foci of cementum and bone calcifications were seen in all the cases of POF with no multinucleated giant cells. These results were in accordance with Amirchaghmaghi et al. and Kashyap et al.[14,15]

PGCG constitutes only 0.4% of all reactive gingival lesions. PGCG is seen in the third decade, females and prevalent in both upper and lower anterior gingiva seem to be influenced by hormonal stimulus, especially estrogen. PGCG showed normal to atrophic epithelium and dense connective tissue stroma with fibroblastic and extensive vascular proliferation. Both the cases of PGCG showed much foreign body type of multinucleated giant cells in the connective tissue stroma. They appear to initiate from mononuclear macrophage cells. Results were comparable to Naderi et al. and Peralles et al.[2,6]

The management of these reactive gingival lesions includes removal of the causative factors and surgical elimination of the lesion. The most widespread techniques used for removing the lesion are surgical scalpel, carbon dioxide laser and electrical scalpel. Successful treatment involves obtaining a precise diagnosis throughout histopathologic analysis, complete removal of the gingival lesion and addressing the local irritants by means of follow-up care, as well as dental hygiene preservation to stop or take care of recurrence.[16] However, there was no recurrence seen in our study.

CONCLUSION

The reactive gingival lesions depicted in this paper frequently have comparable clinical appearances and have a 3:1 preference for females. Nevertheless, the differing histological pictures are a range of a single lesion in diverse stages of maturation. Regardless of their similarities, the findings of this study report that all reactive gingival lesions show some differences in age, type, location, duration and histological features. Essential in the treatment of reactive gingival lesions is the total removal of the lesion with local irritants such as defective restorations or calculus formation.

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Conflicts of interest
There are no conflicts of interest.

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