Reactive Hyperplastic Lesions of the Oral Cavity: A Retrospective Survey Study and Literature Review

Abstract

**Context:** The reactive lesions are relatively common in the oral cavity because of the frequency with which the tissues are injured. They often result from a known stimulus or injury such as dental plaque, calculus, or foreign material. **Aims:** The aim of this study was to review the clinicopathologic features of reactive hyperplastic lesions (RHLs) of the oral cavity at MIDSR, Dental College and Hospital, Latur, Maharashtra, and to compare these data with those of previously reported studies. **Settings and Design:** The patient case files from the Department of Oral and Maxillofacial Pathology from June 2010 to May 2016 were reviewed for cases of RHLs of the oral cavity. **Subjects and Methods:** Both clinical and histopathological diagnosis of reactive lesions was selected for the study. Data including the type of the lesion, age, gender, and the site involved were collected. **Statistical Analysis Used:** Descriptive statistics was applied to the data and differences in frequencies among groups were evaluated using SPSS (IBM Corporation) software. **Results:** A total of 155 histologically diagnosed cases of RHLs were obtained with a prevalence of 11.7%. The data consist of 56 (36.1%) males and 99 (63.9%) females. The most common lesion clinically was traumatic fibroma (36.5%) and histologically fibrous hyperplasia (37.4%). The reactive lesions clinically presented as either sessile (51%) or pedunculated (49%) lesions. **Conclusions:** The clinical features of reactive hyperplasia among our patients were similar to those reported previously with divergence in some analyzed data. The novelty in our study was the correlation between histopathology and clinical features which were not reported in literature till date.

**Keywords:** Peripheral giant cell granuloma, peripheral ossifying fibroma, pyogenic granuloma, reactive hyperplastic lesions, traumatic fibroma

Introduction

Reactive hyperplastic lesions (RHLs) are tumor-like hyperplasias which show a response to tumor-like nonneoplastic proliferations produced in involvement through chronic irritation or trauma.[1] The proliferative activity of the reactive lesions is considered to be initiated by local irritants. The elimination of local irritants and proper dental replacement may contribute to the reduction of these lesions. Clinically, the reactive lesions can be classified as traumatic fibroma (TF), pyogenic granuloma (PG), pregnancy tumor (PT), and epulis fissuratum (EF).[2] Their histopathological features are quite distinct but considerable overlap still exists in these lesions. Eversole and Rovin speculated that the different histological entities of inflammatory hyperplasia may be due to connective tissue response to varied intensities of mucosal irritation. This response may be influenced by the serum levels of certain endocrine hormones.[3] The histological classification of RHL has been equivocally described in literature. However, Kfir et al. had proposed a histological classification of RHLs as angiomatous hyperplasia (AH), focal fibrous hyperplasia (FFH), peripheral ossifying fibroma (POF), and peripheral giant cell granuloma (PGCG).[4]

The clinical appearance of reactive lesions is very similar to that of neoplastic proliferations. This similarity is a challenging matter for differential diagnosis. Clinical behavior of reactive lesions may vary in different population which reflects the different environmental factors, lifestyles, and racial factors.[5] We conducted this survey as the results of various studies on reactive lesions have inconclusive results. Hence, the aim of the survey is to evaluate the frequency and distribution of oral cavity reactive lesions.

Address for correspondence:
Dr. Varsha Ajit Sangle,
Department of Oral Pathology and Microbiology, MIDSR Dental College, Ambajogai Road, Latur, Maharashtra, India.
E-mail: dr.varshadhas@gmail.com

How to cite this article: Sangle VA, Pooja VK, Holani A, Shah N, Chaudhary M, Khanapure S. Reactive hyperplastic lesions of the oral cavity: A retrospective survey study and literature review. Indian J Dent Res 2018;29:61-6.
Subjects and Methods

The study was retrospective archive review. The records of 155 patients with histopathologic diagnosis of oral cavity reactive lesions were obtained from Oral and Maxillofacial Pathology Department, MIDSR Dental College and Hospital, Latur, from 2010 to 2016. Data including the type of the lesion, age, gender, and the site involved were collected. Incompletely registered records and missed pathologic slides were excluded from the study. The complete medical records which had pathologic slides were included in the study. The lesions were classified into seven groups as PGCG, PG, cemento-ossifying fibroma, EF, irritation fibroma, inflammatory fibrous hyperplasia, and inflammatory papillary hyperplasia. The sites involved were lip, palate, tongue, buccal mucosa, and gingiva. Clinical appearance consists of sessile or pedunculated masses. Correlation between clinical and histopathological features was done. All the lesions were treated by excisional biopsy, and the cause for chronic irritation was eliminated at the time of excision. Microscopic sections were examined by two pathologists. Descriptive statistics was applied to the data and differences in frequencies among groups were evaluated using SPSS (IBM Corporation) software.

Results

A total of 155 cases were diagnosed as RHLs, with a prevalence of 11.7%. The data consisted of 56 (36.1%) males and 99 (63.9%) females [Table 1]. The predominant site of distribution of lesion was in the gingiva (57.4%), followed by the buccal mucosa (28.4%) with the other sites accommodating the remaining percentile [Table 2]. The age ranged from 1st to 7th decades, with a mean occurrence of 2nd -3rd decades [Table 3]. The most common lesion clinically was TF (37.4%), followed by EF (31.6%), PG (22.6%), and PT (8.4%) [Table 4]. The histopathological diagnosis of the above mentioned lesions includes FFH (37.4%), PG (25.2%), inflammatory gingival hyperplasia (IGH) (16.1%), PGCG (12.9%), and POF (8.4%) [Table 5]. The reactive lesions clinically presented as either sessile (51%) or pedunculated (49%) [Table 6] lesions. There was a wide fluctuation in the age distribution of the sample selected in our study henceforth this variable was excluded.

Discussion

In the oral cavity, periodontium can show different types of focal overgrowths. These lesions arise due to overgrowth and proliferation of different components of connective tissue in periodontium, i.e. the fibers, bone, cementum, blood vessel, or any particular type of cell. The lexicon of focal proliferative lesions commonly occurring on gingival tissue includes fibroma, giant cell fibroma, PG, PGCG, and POF. Most of these lesions are reactive chronic inflammatory hyperplasias, with minor trauma or chronic irritation being the etiologic factors.[6]
clinically not easily distinguished. A review of 15,783 oral lesions during a 17.5-year period by Weir et al.[7] in the US found that fibromas, periapical granulomas, mucoceles, and radicular cysts were the most common reactive lesions observed in the oral cavity. It has been shown that 77% of lesions observed in the oral cavity are reactive in nature.[7,8] RHLs represent the most common oral lesions, and reactive gingival lesions rank second in this group of lesions.[9]

In a study carried out by Zarei et al.[10] RHLs were more common in females (male: female ratio was 1:1.4). In addition, in a study carried out by Alkhateeb,[5] the most commonly affected site was gingiva. We also got consistent results as the aforementioned studies, with a female predilection and gingiva being more frequently affected.

According to Perallas et al.[11] the most reactive gingival lesion is FFH (41%) followed by PG (30%), similar to the findings of the present study (37.4% and 31.6%, respectively). Reddy et al.[12] also observed similar results in the north Indian population, they observed FFH in 57.4% cases and PG in 18.7% cases. Ala Aghbali et al.[13] in a study, distributed the reactive lesions according to the prevalence as fibroma being most prevalent followed by giant cell granuloma, PG, POF, and EF. Conflicting to the results obtained in the survey conducted by Ala Aghbali et al.[13] the results of our study showed that the most common lesion encountered clinically was TF followed by PG and EF. The frequency distribution of cases histopathologically in the descending order was FH, AH, IGH, PGCG, and POF.

The four reactive lesions clinically presented as either sessile or pedunculated masses. Many studies suggested that sessile base was the typical clinical feature in RHL.[14] However, it has been shown in one report that most of PGCGs were pedunculated.[15] Interestingly, in our study, sessile bases were predominantly seen in TF; pedunculated were common in PT and PGCG; EF, PG, and POF showed equal predilection.

TF [Figure 1] accounts for the great majority of localized gingival swellings. Neville et al. reported that TF can occur anywhere in the mouth, the most common location is the buccal mucosa along the bite line.[12] In the present study, it was found that gingiva is the most common site for fibroma with equal incidence in lower and upper jaws, this is in accordance with the study by Reddy et al.[12] The term “focal fibrous hyperplasia” implies to localized progressive proliferation of oral mucosa in response to local irritation or local injury.[16] Daley et al.[17] suggested the term “fibroma,” which implies incorrectly, a benign neoplastic proliferation of fibrous connective tissue. In our study, FFH accounted for 37.4% of all cases. FFH was the most common lesion occurring over a wide age range (9–70 years), with a peak incidence in the third to fourth decades. These observations were in agreement with previous studies.[2,3,17] Clinically, the lesion may be round to ovoid, asymptomatic, smooth-surfaced, firm, sessile or pedunculated mass, the diameter of which may vary from 1 to 2 cm. Hard in consistency and pale pink in color, surface may be hyperkeratotic or ulcerated owing to repeated trauma. Histopathologically, the sections showed hyperplastic stratified squamous epithelium which was partly hyperkeratotic and hyperorthokeratotic at some places. Thin, finger-like rete ridges extend into underlying connective tissue stroma which was fibrocellular. Solid nodular mass of dense hyalinized fibrous connective tissue arranged in haphazard fascicles was seen in one of the lesions. A mild-to-moderate chronic inflammatory cell infiltrate was seen at a few sites [Figure 1]. These findings are similar to those reported by Barker and Lucas and Esmeili et al.[9,18] The clinicopathologic diagnosis of fibroma was done in all these lesions.

The second-most common lesion is PG [Figure 2]. PG or angiogranuloma is one of the inflammatory hyperplasias seen in the oral cavity. This term is a misnomer in the real sense because the lesion is unrelated to infection and arises in response to various stimuli such as low-grade local irritation, traumatic injury, or hormonal factors. It predominantly occurs in the second decade of life in young females, possibly because of vascular effects of female hormones. Similar observations were reported by Kfir et al.[19] who suggested that the age incidence and female predilection of PG may reflect the influence of pregnancy on the pathogenesis of the disease. The gradual rise in the development of PG in pregnancy may be due to the increasing levels of estrogen and progesterone that occur as pregnancy progresses. Recently, Daley et al.[17] reported a positive relationship between the incidence of PG and the serum progesterone and estrogen concentrations in pregnant women. It was speculated in this report that the two hormones render the gingival tissue more susceptible to chronic irritation caused by plaque and calculus. Histopathologically, these lesions showed thin parakeratinized stratified squamous epithelium which was atrophic and ulcerated at places. The underlying connective tissue showed delicate fibrocellular stroma with abundant endothelial lined blood capillaries which were...
engorged with red blood cells (RBCs) and dense chronic inflammatory cell infiltrate, chiefly of lymphocytes and plasma cells. Hence, they were diagnosed as PG. These findings are similar to those reported by Neville et al.\(^2\)

PGCG [Figure 3] is a benign hyperplastic lesion caused by chronic local trauma. PGCG is one of the most frequent giant cell lesions of the jaws and originates from the connective tissue of the periosteum or the periodontal membrane. The PGCG is also known as osteoclastoma, peripheral giant cell tumor, reparative giant cell granuloma, giant cell epulis, and giant cell hyperplasia of the oral mucosa.\(^{19}\) The etiology and nature of PGCG still remains undecided. In the past, several hypotheses had been proposed to explain the nature of multinucleated giant cells, including the explanation that they were osteoclasts left from physiological resorption of teeth or reaction to injury to periosteum. There is strong evidence that these cells are osteoclasts as they have been shown to possess receptors for calcitonin and were able to excavate bone \textit{in vitro}.\(^{20}\) There is also a growing body of opinion that giant cells may simply represent a reactionary component of the lesion and are derived through bloodstream from bone marrow mononuclear cells and may be present only in response to an as yet unknown stimulus from the stroma. This concept is based on the results of some more recent studies using cell culture and transplantation.\(^{21}\) in which the giant cells have been found to be short-lived and to disappear early in culture in contrast to the active proliferation of the stromal cells. It manifests clinically by a painless, soft, nodular mass, sessile or pedunculated, usually red to reddish-blue in color, occasionally ulcerated surface and located in the interdental papilla, edentulous alveolar margin or at the marginal gingival level. They are very aggressive lesions with significant growth potential. The high vascularity of these lesions can be understood by their purplish-red color and tendency to bleed. They also tend to penetrate interdentally and erosion of adjacent bone along with separation of adjacent teeth is a common occurrence. The clinical appearance resembles PG of the gingiva, although the PGCG often is more bluish purple compared with the bright red color of a typical PG. The PGCG occurs throughout life, with peak incidence during the mixed dentition years and in the age group of 30–40 years. The mandible is affected slightly more often than the maxilla. Lesions can become large, some attaining 2 cm in size.\(^{22}\) Histologically, PGCG is composed of nodules of multinucleated giant cells in a background of plump ovoid and spindle-shaped mesenchymal cells and extravasated RBCs. The giant cells may contain only a few nuclei or up to several dozen of them. Some of them are large, vesicular nuclei; others demonstrate small, pyknotic nuclei with associated prominent vascularity. Mineralized tissue in the form of woven and/or lamellar bone can be identified in about one-third of these lesions.\(^{19,22}\)

The term POF [Figure 4] was coined by Eversole and Rovin.\(^{14}\) It is a nonneoplastic enlargement of the gingival
tissue and is precipitated by local irritation and minor trauma. As the lesion occurs only on gingiva and is supposed to be derived from periodontal ligaments or interdental papilla, some authorities believed the lesion to be odontogenic in origin. At present, the origin and pathogenesis of the lesion is unknown. However, due to their clinical and histopathologic similarity, it is considered that at least some cases of POF may arise as a result of maturation of a long-standing PG. The mineralized product in POF probably has its origin from cells of periosteum or periodontal ligament. Clinically, the lesion appears as a nodular mass which may be pedunculated or sessile, pink to red in color and surface is usually but not always ulcerated. The peak incidence for the POF is third decade followed by a definite decline, which is concurrent with present study. Histopathologically, the lesion shows stratified squamous epithelium covering an exceedingly cellular mass of connective tissue made up of plump fibroblasts, fibrocytes, fibrillar stroma, and areas of mineralization with multinucleated giant cells near them in some cases. The mineralization may consist of bone, cementum-like material, or dystrophic calcifications. The dystrophic calcifications are usually seen in early, ulcerated lesions, whereas the older, mature, nonulcerated lesions show well-formed bone and cementum-like material.

IGH [Figure 5] is a histopathological diagnosis. Enlargements of gingiva may be inflammatory, noninflammatory, or a combination of the two types. Usually, the hyperplasia occurs primarily because of local irritations such as buildup of dental plaque or calculus and mouth breathing leading to poor oral hygiene. A histological examination of gingival overgrowth when shows inflammatory cell infiltration, vascular engorgement, and edema predominately then such type of gingival enlargement is referred to as IGH. When major component is represented by dense fibrous tissue, the lesion is referred to as fibrotic gingival hyperplasia. In our study, the most frequent histopathologically described gingival enlargement was IGH (16.1%). The average age of occurrence was 34.5 with range being 10–63 years. Females are frequently affected than males. The most common site affected was gingiva.

The clinical appearance of reactive lesions is very similar to that of neoplastic proliferations. This similarity is a challenging matter for differential diagnosis. When presented clinically with a gingival lesion, it is important to establish a differential diagnosis. Clinical differentiation is very difficult. Although TF appears as an elevated nodule of normal color with smooth surface whereas POF is of slightly reddened color while PGCG is often dark red, vascular, or hemorrhagic in appearance. Considerable overlap exists among the different histological entities of the RHLs but whether or not they represent the same lesion at different developmental stages as suggested by some authors is debatable. The component of PG may be subsequently replaced partially or completely by fibrous tissue and hence, diagnosed as FFH or a fibroma. The frequent location of the inflammatory hyperplasia on the gingiva appears to support the notion that they are the same lesion at different stages of histological maturation. However, if this is true, then a definite age grouping for the different histological entities should be obvious. The mean ages for various lesions should reflect the progressive development of the lesion through the different histological stages, but this was not the case in our study or any of the previous reports.

**Conclusion**

Differential diagnosis of gingival enlargement requires thorough dental and medical history, careful evaluation of the type, nature and extent of enlargement and identification of etiologic or predisposing factors. Majority of the intraoral localized gingival lesions are slowly progressing, the growth of which is generally limited. Several cases progress for long periods before the patient seeks treatment for them as they are asymptomatic. However, it was observed that patients usually undergo treatment once the lesion becomes visible. The reactive focal fibrous overgrowths arise in response to chronic stimuli and are generally nonneoplastic growths. Proper diagnosis, prevention, management, and treatment of these lesions are of chief importance. Treatment involves removal of the local irritants along with surgical excision of the lesion.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Effiom OA, Adeyemo WL, Soyele OO. Focal reactive lesions of the gingiva: An analysis of 314 cases at a tertiary health institution in Nigeria. Niger Med J 2011;52:35-40.
2. Neville BW, Dam D, Allen CA, Bouguet JE. Oral and Maxillofacial Pathology. 2nd ed. Philadelphia: W.B. Saunders; 2002.
3. Eversole LR, Rovin S. Reactive lesions of the gingiva. J Oral Pathol 1972;1:30-8.
4. Kfir Y, Buchner A, Hansen LS. Reactive lesions of the gingiva. A clinicopathological study of 741 cases. J Periodontol 1980;51:655-61.
5. Hashemi Pour MA, Rad M, Mojtaba A. A survey of soft tissue tumor-like lesions of oral cavity: A clinicopathologic study. Iran J Pathol 2008;3:81-7.
6. Rajendran R, Sivapatnasundharam B. Shafer’s Textbook of Oral Pathology. 6th ed. Noida, India: Elsevier; 2009. p. 128.
7. Weir JC, Davenport WD, Skinner RL. A diagnostic and epidemiologic survey of 15,783 oral lesions. J Am Dent Assoc 1987;115:439-42.
8. Brannon RB, Carr RF, Weir JC. Oral pathology biopsy service at the Louisiana state university school of dentistry: Status report 1995. LDA J 1997;56:7-9.
9. Esmeili T, Lozada-Nur F, Epstein J. Common benign oral soft tissue masses. Dent Clin North Am 2005;49:223-40.
10. Zarei MR, Chamani G, Amanpoor S. Reactive hyperplasia of the oral cavity in Kerman province, Iran: A review of 172 cases. Br J Oral Maxillofac Surg 2007;45:288-92.
11. Perallas PG, Viana AP, Azevedo AL, Pires FR. Gingival and alveolar hyperplastic reactive lesions: Clinicopathological study of 90 cases. Braz J Oral Sci 2006;5:1085-9.
12. Reddy V, Saxena S, Saxena S, Reddy M. Reactive hyperplastic lesions of the oral cavity: A ten year observational study on North Indian population. J Clin Exp Dent 2012;4:e136-40.
13. Ala Aghbali A, Vosough Hosseini S, Harasi B, Janani M, Mahmoudi SM. Reactive hyperplasia of the oral cavity: A survey of 197 cases in Tabriz, Northwest Iran. J Dent Res Dent Clin Dent Prospects 2010;4:87-9.
14. Greenberg MS, Glick M, Ship JA. Burket’s Oral Medicine. 11th ed. Hamilton: BC Decker Inc.; 2008. p. 134.
15. Shadman N, Ebrahim SF, Jafari S, Esfami M. Peripheral giant cell granuloma: A review of 123 cases. Dent Res J (Isfahan) 2009;6:47-50.
16. Mathur LK, Bhalodi AP, Manohar B, Bhattia A, Rai N, Mathur A. Focal fibrous hyperplasia: A case report. Int J Dent Assoc 2010;2:56-7.
17. Daley TD, Wysocki GP, Wysocki PD, Wysocki DM. The major epulides: Clinicopathological correlations. J Can Dent Assoc 1990;56:627-30.
18. Barker D, Lucas R. Localized fibrous overgrowths of the oral mucosa. Br J Oral Surg 1967;5:86-92.
19. Chaparro-Avendaño AV, Berini-Aytés L, Gay-Escoda C. Peripheral giant cell granuloma. A report of five cases and review of the literature. Med Oral Patol Oral Cir Bucal 2005;10:53-7.
20. Chadwick BL, Crawford PJ, Aldred MJ. Massive giant cell epulis in a child with familial cyclic neutropenia. Br Dent J 1989;167:279-81.
21. el-Mofy SK, Osdoby P. Growth behavior and lineage of isolated and cultured cells derived from giant cell granuloma of the mandible. J Oral Pathol 1985;14:539-52.
22. Katsikeris N, Kakarantza-Angelopoulou E, Angelopoulos AP. Peripheral giant cell granuloma. Clinicopathologic study of 224 new cases and review of 956 reported cases. Int J Oral Maxillofac Surg 1988;17:94-9.
23. Fausto KA, Robbins and Cotran Pathologic Basis of Disease. 7th ed. Philadelphia: W.B. Saunders; 2008. p. 775-6.
24. Rajendran R, Sivapathasundharam B. Shafer’s Textbook of Oral Pathology. 7th ed. India: Elsevier; 2007. p. 543-8.
25. Janosi K, Popso R, Ormenisan A, Martha K. Comparative study of hyperplastic lesions of the oral mucosa. Eur Sci J 2013;9:7-15.
26. Auclair PL, Cuenn P, Kratochvil FJ, Slater LJ, Ellis GL. A clinical and histomorphologic comparison of the central giant cell granuloma and the giant cell tumor. Oral Surg Oral Med Oral Pathol 1988;66:197-208.