



DIAGNOSTIC CHALLENGES IN ASSESSMENT OF REACTIVE SOFT TISSUE LESIONS OF ORAL CAVITY

Farhat Kazmi¹, Wajiha Alamgir², Muhammad Mumtaz³

¹Associate Professor/Head Department of Oral Pathology, University College of Dentistry, University of Lahore, Pakistan, ²Assistant Professor Oral Pathology, University College of Dentistry, University of Lahore, Pakistan, ³Associate Professor Oral and Maxillofacial Surgery, University College of Dentistry, University of Lahore, Pakistan.

ABSTRACT

Objective: The study emphasizes on the features which lead to diagnostic complexities of localized reactive hyperplastic lesions (LRHL) in clinical settings thus making histopathological examination imperative for definite diagnosis.

Materials and Methods: A total of 314 patients presenting with reactive hyperplastic lesions in out-patient department of University College of Dentistry from June 2012 to January 2015 were included in the study. After provisional diagnosis, lesions were excised and specimens were submitted for definite histopathological diagnosis. Descriptive statistics and Chi-square test was applied using SPSS version 20.0.

Results: Most common age group was 30-39 years (n=147, 50.6%) with male to female ratio of 1:3. Most affected site was maxillary gingivae (n=140, 49.3%) while poor oral hygiene (n=152, 52.4%) was most frequent aetiological factor. Provisional diagnoses included pyogenic granuloma (PG) with maximum number of cases (n=141, 45%) followed by focal fibrous hyperplasia (FFH) (n=118, 37%), peripheral giant cell granuloma (PGCG) (n= 34, 11%) and peripheral ossifying fibroma (POF) (n=21, 7%). After definite diagnosis, the order of occurrence of LRHL remained the same but the number of cases of each individual lesion carried a significant discrepancy with 157 histopathologically proven cases of PG (50%) followed by FFH (n=111, 36%), PGCG (n=29, 9%) and POF (n=17, 5%) respectively.

Conclusion: Variations in subjective assessment of LRHL could be lessened if histopathological examination is incorporated as a mandatory component in diagnostic protocol. Oral hygiene maintenance may also significantly improve the status of oral health and diminish possible chances of development of pathologies.

Key Words: Hyperplastic lesions, Pyogenic granuloma, Focal fibrous hyperplasia, Peripheral giant cell granuloma, Peripheral ossifying fibroma

INTRODUCTION

A collection of reactive hyperplastic lesions presenting as gingival and mucosal localized overgrowths pose a diagnostic tight spot to clinician due to close imitation in their clinical appearance. In such circumstances, histopathologists provide an aid to clinicians to rule out the possibility of these lesions being malignant in nature and therefore establishing a definite diagnosis.^{1,2}

Chronic trauma subjected to oral cavity can induce inflammation that leads to formation of granulation tissue along with endothelial cells, chronic inflammatory cells and later fibroblasts which proliferate and manifest as an overgrowth called 'Reactive hyperplasia'³. Localized factors which can lead to chronic local traumatization

include; calculus, food impaction, restorations with irregular margins and iatrogenic factors⁴. Underlying systemic disease, drug-induced stimulus or endocrine hormones may also play a contributing role in development of LRHL^{5,6,7}.

Several investigators have classified reactive lesions on histopathological basis as fibrous, vascular or hemorrhagic and giant cell types^{1,2,7-9}. Some others claim that all these entities represent same lesion at different developmental stages^{4,5,7}. Currently, accepted classification of reactive lesions is given by Neville pertaining to four categories: 1. Focal fibrous hyperplasia (FFH) 2. Pyogenic granuloma (PG) 3. Peripheral ossifying fibroma (POF) 4. Peripheral giant cell granuloma (PGCG)^{4,5,7,10}.

Corresponding Author:

Dr. Muhammad Mumtaz, Associate Professor Oral and Maxillofacial Surgery, University College of Dentistry, University of Lahore, 1-km off Raiwind Road Lahore, Pakistan, Mob: 0092-300-4554790, E-mail: mumtazmaxfac@gmail.com

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The prevalence of these lesions as reported in the literature is rather most common with focal fibrous hyperplasia comprising 56-61% followed by pyogenic granuloma (19-27%), peripheral ossifying fibroma (10-18%) and peripheral giant cell granuloma (1.5 – 7%)¹⁰⁻¹².

These LRHL share many similarities on clinical examination that makes physician indecisive in making a definite clinical diagnosis. Table 1 elaborates intimately mimicking clinical features of LRHL of the gingiva.¹³⁻¹⁶

Table 1: Comparison of clinical features of LRHL of oral cavity

Clinical Feature	FFH	PG	POF	PGCG
Age (in decades)	4 th -6 th	1 st -2 nd	2 nd -3 rd	3 rd – 6 th
Gender Predilection	Females > males*	Females > males	Females > males	Females > males
Site of Predilection	Buccal mucosa followed by gingiva	Anterior facial maxillary gingiva	Anterior maxilla exclusively interdental papillae	Mandibular gingiva
Size	Few mm – several cm†	Few mm – several cm	< 2cm	< 2cm□
Color	Pink	Bright red	Red- Pink	Blue-purple
Surface	Smooth	Smooth lobulated	Smooth nodular	Smooth nodular
Ulceration of overlying epithelium	In case of trauma	In case of trauma	In case of trauma	May or may not be
Base of Attachment	Usually sessile	Usually pedunculated	Pedunculated / sessile	Pedunculated / sessile
Bleeding tendency	Low	High	low	High
Recurrence potential	Rare	Frequent	Occasional – 16%	Occasional – 10%

*> Greater than; † mm-millimeters, cm- centimeters ; < Less than

FFH represents the most common localized, reactive proliferation of oral soft tissues in response to injury or local irritation^{13,14} followed by PG representing as an exuberant tissue response^{10,13}. Researchers have divided PG in two types namely lobular capillary hemangioma (LCH type) and non – LCH type which differ in their histological picture¹⁷. LCH type is currently categorized as vascular tumors under the classification scheme of international society for the study of vascular anomalies¹³. Among pregnant females, 5% develop PG which regress after delivery, indicating a definite role of female sex hormones in the etiology of this lesion^{2,17,18}. POF has mostly solitary occurrence, multicentric lesions have also been reported in the literature¹⁸. Current studies refer this lesion as POF (WHO type) and it is recognized separately from POF of gingiva^{7,10}. In 1953, Jaffe proposed the term “giant cell reparative granuloma” to distinguish PGCG from giant cell tumor²⁰. This term was used to show the association of development of this lesion to chronic irritation²¹. Development of POF and PGCG in children has also been reported in the literature^{19,22}.

In present study, emphasis is made on the features which lead to diagnostic complexities of LRHL in clinical settings thus making histopathological examination imperative for definite diagnosis. Moreover, focus is made

on the etiological factors involved in the development of these lesions especially those which are related to oral hygiene status of the patients.

MATERIALS AND METHODS

The study was conducted in Oral Diagnostic, Oral pathology and Oral Surgery department of University College of Dentistry, University of Lahore, Pakistan between June 2012 to March 2014 after approval from the ethical review committee (Approval No. 101/UCD/2012). A total of 314 patients presenting with exophytic hyperplastic lesions were examined in Oral Diagnostic department. Clinical data including age, gender, chief complaint at the time of presentation, etiology, site and size of the lesion, lesion attachment, surface and color was gathered and provisional diagnosis was made after clinical examination.

Further referral was made to Oral Surgery department and biopsy was taken after making written informed consent from the patients. Biopsy specimens were submitted to Oral Pathology department. Microscopic evaluation for definite diagnosis was done by two oral pathologists to minimize the inter-observer bias.

Statistical analysis was done using SPSS software version 20.0. Descriptive statistics were employed to report the findings. Chi-square test was applied for evaluation of differences in frequencies among groups. P- value<0.05 was considered as statistically significant.

RESULTS

After clinical examination of 314 patients presenting with LRHL, provisional diagnoses made included (Figure: 1) pyogenic granuloma with maximum number of (n=141, 45%) followed by focal fibrous hyperplasia which comprised of 118 cases (37%). Peripheral giant cell granuloma with 34 cases (11%) and peripheral ossifying fibroma with 21 cases (7%) were next in the order. The diagnosis was based upon parameters mentioned in the previous section. Among socio- demographic parameters, most common age group was 30-39 years comprising of 157 cases (50%) followed by 20-29 years age group that counted 125 cases (40%)(p=0.000)(Table:2). Females were most commonly affected than males with a count of 241 (77%) yielding a male to female ratio of 1:3 (p=0.000)(Table 2). Most frequently involved site was maxillary gingiva with 155 cases (49%) followed by mandibular gingiva (n=142, 46%) (p=0.000). Majority of the patients presented with the chief complaint of bleeding (n= 132, 39%, p=0.000) followed by pain

(n=122, 39%, p=0.000) and ulceration (n=60, 19%, p=0.000) (Figure: 1). Greater part of the lesions measured <1cm in size (n=260, 83%)(p=0.193) with majority having sessile base (n=224, 71%)(p=0.155). The most common surface appearance (p=0.000) of the lesions was smooth constituting 193 cases (61%) followed by ulcerated surface with 89 cases (28%) (Table 3). Large proportion of lesions were red in color comprising of 197 cases (62%) (p=0.000)(Table: 3). Evaluating the etiology of the lesion, (Figure:2)the greatest number of lesions was associated with poor oral hygiene with 185 cases (59%) while in small proportion of the cases aetiology could not be identified (n=19, 6%)(p=0.000).

Detailed description of data recorded for each individual lesion is shown in Table: 2 and Table: 3.

After excisional biopsy and histopathological review of cases of LRHL, a discrepancy rate of 10% (n=32) was observed between provisional diagnosis based on clinical examination and definite diagnosis which was made after microscopic examination. (Figure: 3). After definite diagnosis, the order of occurrence of LRHL remained the same but the number of cases of each individual lesion carried a significant difference with 157 histopathologically proven cases of PG (50%) followed by FFH (n=111, 36%), PGCG (n=29, 9%) and POF (n=17, 5%) respectively (Figure: 4 – Figure: 7)

Table 2: Frequency of age and gender among LRHL of oral cavity (n= 314)

Socio-Demographic Parameters	Pyogenic Granuloma (n =141)	Focal Fibrous Hyperplasia (n =118)	Peripheral Giant Cell Granuloma (n =34)	Peripheral Ossifying Fibroma (n =21)	Total (n=314)
Age (Years)	20-29	80	19	19	125
	30-39	52	82	12	157
	40-49	9	17	02	30
	50-59	0	0	01	2
Total					314
Gender	Male	0	50	17	73
	Female	141	68	17	241
Total					314

Table 3: Distribution of size, lesion base attachment, surface and colour of lesion among cases of LRHL (n=314)

Clinical Features		Pyogenic Granuloma (n=141)	Focal Fibrous Hyperplasia (n=118)	Peripheral Giant Cell Granuloma (n=34)	Peripheral Ossifying Fibroma (n=21)	Total (n=314)
Size	>1cm	23	24	03	04	54
	< 1cm	118	94	31	17	260
Total						314
Base attachment	Sessile	96	85	29	14	224
	Pedunculated	45	33	05	07	90
Total						314
Surface	Smooth	88	104	0	01	193
	Ulcerative	37	09	28	15	89
	Polypoid	16	05	06	05	32
Total						314
Colour	Pinkish white	37	53	13	14	117
	Red	104	65	21	07	197
Total						314

DISCUSSION

An extensive research of the literature revealed that present study is the first attempt to document shortcomings of clinical evaluation and diagnosis of LRHL of oral cavity. Considerable discrepancy exists between visual assessment and histopathological appraisal of these lesions. Therefore, overlap in clinical appearance of these lesions led to subjective interpretation of histological specimens and their clinical correlation which led to contradictory results. Furthermore, the investigation also focuses on the frequency of different etiological factors associated with development of LRHL of oral cavity.

Patients in of Oral Diagnostic department were provisionally diagnosed for different types of LRHL of oral cavity. The clinical information was based upon patient's demographics such as age, gender, chief presenting complaint and etiological factors as well as diagnostic inspection points; location, size, surface, color and attachment base of the lesion.

Out of total 314 lesions, most prevalent lesion figured out was PG (45%) followed by FFH (37%), PGCG (11%) and POF (7%) respectively. These results were in agreement to those demonstrated by Shahsavari et al as well as to some other studies which showed PG as most commonly occurring entity^{2,7,23}. On contrary, many of the global studies showed FFH as the most commonly found

lesion as well as cases of POF exceeding to those of PGCG³⁻⁵. Striking difference in the results was reported by Naderi et al demonstrating PGCG as most frequently found lesion^{1-7, 20-24}.

Females turned out to be more affected than males with a male to female ratio of 1:3. This finding was concurrent with most of the studies conducted worldwide^{1-5, 7, 23}. Conversely, distribution of oral reactive lesions shown by Naderi et al in males outnumbered to that of in females with male to female ratio of 1.4:1²⁴. In current study, a conspicuous finding is the involvement of only females in cases of PG with no male patient affected by this entity. This finding was in accordance to majority of the studies conducted worldwide but all of them showing considerable involvement of males as well²⁻⁷. On the other hand, in an Iranian study, Aghbali et al showed equal involvement of both genders among cases of PG²⁵. In present study, 30-39 years age group was most commonly affected among all lesions (n=157, 50%). This result was exactly in concordance with that shown by Ramu and Rodrigues who also demonstrated the greatest prevalence of reactive lesions in the same age group⁵. Many other studies depicted the same finding in terms of mean age^{7,24,25}. However, Shahsavari et al reported 4th to 6th decade as more prevalent age group in patients with reactive soft tissue lesions of oral cavity⁹. The difference in the results may be attributed to ethnic or demographic factors as well as differences in lifestyle and oral hygiene

awareness among different populations.

In current study, most frequent site of involvement was maxillary gingiva with 155 cases (49%). The finding was in agreement to many other studies showing the similar site predominance^{2,4,25}. However, Ramu and Rodreigus⁵ as well as Zarei et al⁶ showed a mandibular preponderance in their results. In present study, cases of PG were most commonly found involving maxillary gingiva (n=75, 53%). This finding was concurrent to many wide-reaching studies^{4-8,25}. Only a few researchers like Kashyap et al demonstrated large proportion of cases with PG occurring in anterior mandible⁷. In current research, greater frequency of FFH cases was found involving maxillary gingiva with a count of 61 (52%). Al-Rawi showed the same results in his study while few other studies showed opposing results with preference of mandibular involvement^{2,5,6}. The aforementioned result in enduring study was followed by mandibular involvement (n=40, 34%) and buccal mucosa (n=17, 14%) respectively. In literature, buccal mucosa along bite line is the site which is considered most vulnerable for the development of FFH^{13,16}. In accordance to this concept, Kashyap et al revealed buccal mucosa as the most frequently involved site⁷. At the same time, Buchner et al⁴ and Pour et al⁸ depicted equal involvement of maxilla and mandible with cases of FFH. In present study, cases of PGCG were found more involving mandibular gingiva than maxillary gingiva (n=23, 68%). This result was in agreement to a wide range of studies conducted worldwide^{4-6,8,20}. To our knowledge, till now no single study covering up PGCG revealed mandibular dominance for the lesion. However, Kashyap et al in their findings demonstrated equal occurrence of PGCG in both maxilla and mandible⁷. Site preponderance for POF in current study is same to that of PGCG with majority of cases found in mandible (n=13, 62%). This finding was parallel to various studies²⁻⁵ while some others mentioned opposing results in their studies^{5,6}.

In present study, an enormous percentage of reactive hyperplastic lesions (n=248, 85.5%) measured <1cm in size. This result was in agreement to several other global studies^{2,6}. On contrary, Perallas et al in their research revealed majority of the cases measuring >1cm¹⁵. Likewise, Effiom et al demonstrated a large proportion of the lesions measuring >1cm²³. However, a quite different size range of 8mm to 6cm was showed by Amirchaghmaghi et al in their study²⁶. In enduring study, a major bulk of the localized reactive hyperplastic lesions turned out having sessile base attachment to the underlying bone (n=211, 72.7%). These results were in agreement to those revealed by Amirchaghmaghi et al showing majority of the lesions exhibiting sessile base²⁶. Among different studies which were overviewed in reference to present one, none demonstrated lesions with pedunculated base attachment in majority.

In current study, a major proportion of the lesions had smooth surface (n=188, 64.8%). This was followed by ulcerated surfaced lesions with 79 cases (27.2%) and polypoid lesions with 23 cases (7.9%) respectively. These results were in accordance to those showed by Amirchaghmaghi et al²⁶. In present study, maximum number of cases with PG (n=85, 64.8%) and with FFH (n=102, 91%) exhibited smooth surface. These findings were exactly concurrent with those depicted by Zarei et al⁶. Majority of the cases with PGCG (n=25, 86.2%) and POF (n=13, 72.2%) exhibited ulcerated surface in present study. These explorations too were precisely in agreement to those demonstrated by Zarei et al⁶.

In present study, greater frequency of the lesions displayed red surface hue (n=197, 62%). Among these lesions, majority of cases with PG (n=104, 73%) exhibited red color. This outcome was similar to that demonstrated by Kashyap et al⁷ and Peralles et al¹⁵. The later showed 28 cases of PG with red surface appearance while 14 with pink color. Likewise Peralles et al¹⁵ showed greater proportion of cases with FFH having red surface color, the finding that was consistent with the cases of FFH (n=65, 55%) in present study. Among cases of POF, current study demonstrated greater part displaying pinkish white appearance (n=14, 66.6%). However Peralles et al showed more cases of POF with erythematous surface color¹⁵. In this study majority of the cases with PGCG (n=19, 62%) exhibited red surface color. This finding is quite usual for the lesions diagnosed as PGCG. However, no studies could be found during the work up of present study containing series of PGCG cases expressing clinical data regarding color of lesion. Though in a case reported by Flaitz regarding PGCG in children the lesion was shown to have reddish-purple appearance²².

Among etiological factors poor oral hygiene turned out to be the most frequent factor (n=185, 59%) in current study. These results were in accordance to those reported by Peralles et al¹⁵. This finding is also well reported in many of the world's retrospective literature regarding development of hyperplastic lesions and denoting them as 'reactive' in response to chronic trauma^{5,6,10}. This outcome also signifies the fact of more female involvement by these reactive lesions due to the poor compliance of female patients towards dental care in our part of world³. In present study, most common etiological factor among cases of PG turned out to be pregnancy (n=77, 55%). Ramu and Rodrigues reported an association between incidence of PG and serum concentrations of estrogen and progesterone in pregnant women⁵. It was speculated in few studies that the two hormones render gingival tissue more susceptible to chronic irritation caused by plaque and calculus^{17,18}. In enduring study, poor oral hygiene was also figured out as etiological factor in majority of the cases of FFH (n=85, 72%) and PGCG (n=20, 59%), a finding that is validated in many wide-reaching studies

^{7,14,20}. Conversely, in current study majority of the cases with POF demonstrated trauma as more prevalent etiological factor in this entity (n=13, 62%). However the possible causative factors for POF reported in literature depict a multitude of calculus, plaque, dental appliances, ill-fitting prostheses and microorganisms ¹⁹.

In present study, most common chief complaint explored was bleeding with 132 cases (42%) followed by pain (n=122, 39%) and ulceration (n=60, 19%) respectively. Zarei et al in their study reported an equal prevalence of both bleeding and ulceration among reactive hyperplastic cases⁶. Amirchaghmaghi et al mentioned swelling as chief complaint in majority of cases (76.2%) followed by burning sensation (8%), pain (5.7%) and ulceration (3.3%)²⁶. Observation in present study led to conclusion that ulceration of overlying mucosa causes the exposure of nerve ending present in submucosa later on leads to development of burning sensation. Although this is a little reported finding in the world's widespread literature, but it was presented as a noticeable clinical data in our region.

After histopathological diagnosis, a significant disparity of 5% was seen among cases of PG with 157 (50%) of cases as compared to 141 (45%) which were diagnosed clinically. However an average discrepancy of 2% was seen among cases of FFH (n=111, 36%), PGCG (n=29, 9%) and POF (n=17, 15%). To our knowledge, so far no single study has been done based upon disagreement between clinical and histopathological diagnosis of LRHL. However, Prasanna and Sehwat identified the diagnostic dilemmas of these lesions which mimic diverse groups of distinct pathological processes ²⁷. Moreover, Krahl et al also emphasized the need of scrutinizing these lesions clinically and histologically from potentially malignant and neoplastic lesions²⁸. Histopathological examination must be a mandatory part of clinicopathological evaluation which later on aids in appropriate therapeutic management of these lesions. The need of this practice is important particularly in elderly patients where biopsy and histopathological examination provide more accurate distribution of oral diseases especially when considering premalignant and malignant lesions ²⁹.

CONCLUSION

This investigation submits variations in subjective assessment of LRHL on clinical grounds. This inter-observer variability could be lessened if histopathological examination is incorporated as a mandatory component in diagnostic protocol. Moreover, most common age range encountered in present study is 30-39 years which is crucial for the development of many pathologic processes which bear close resemblance to LRHL. Therefore, a careful diagnostic approach imparts a critical role in

therapeutic management of the patients and elimination of anticipated dento-alveolar complications. Patient education regarding oral hygiene maintenance may also significantly improve the status of oral health and diminish possible chances of development of pathologies.

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Authors contribution

Farhat Kazmi contributed with histopathological review, classification of cases and compilation of results. Wajaha Alamgir made the literature research, reviewed the cases and made the whole writing. Muhammad Mumtaz worked on clinical data and results. Moghees A. Baig guided in making necessary amendments in write up and final review.

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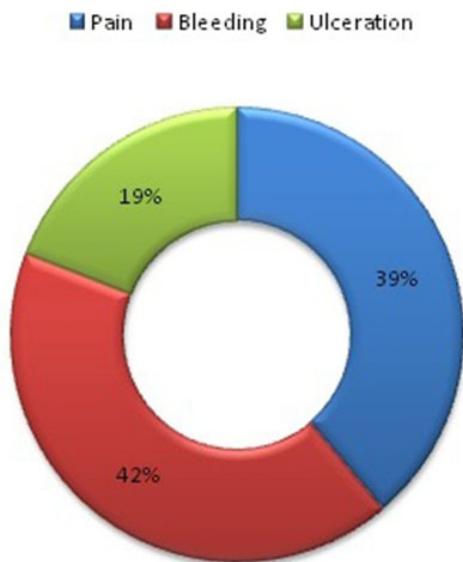


Figure 1: Distribution of chief complaint among cases of localized reactive hyperplastic lesions of oral cavity (n=314)

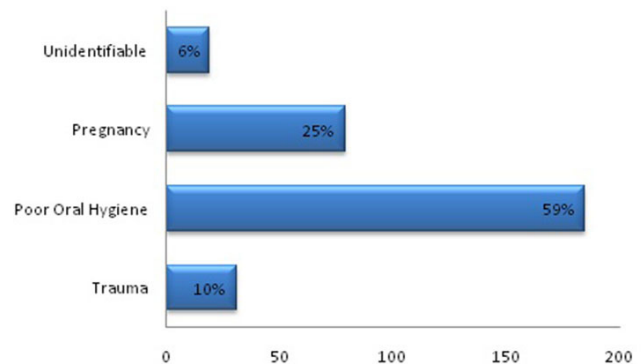


Figure 2: Distribution of aetiological factors among cases of localized reactive hyperplastic lesions of oral cavity (n=314)

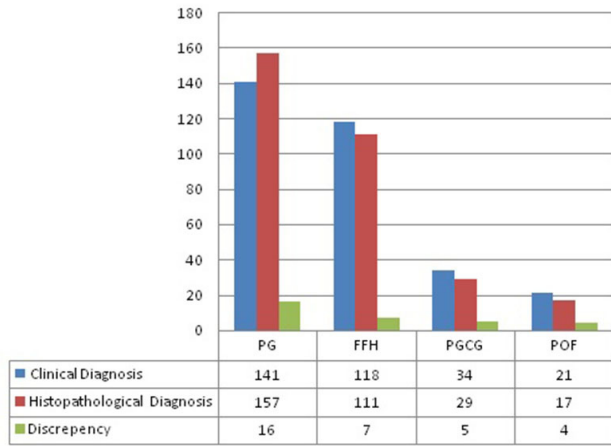


Figure 3: Estimation of discrepancy in clinical and histopathological diagnosis of LRHL (n=314)

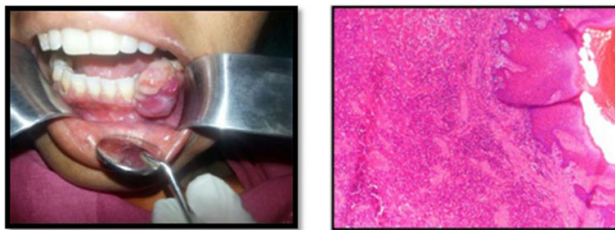


Figure 4: A 28 years non-pregnant female- Lesion clinically diagnosed as FFH turned out to be PG histopathologically)



Figure 5: A 20 years female – Lesion clinically diagnosed as PG turned out to be FFH histopathologically)

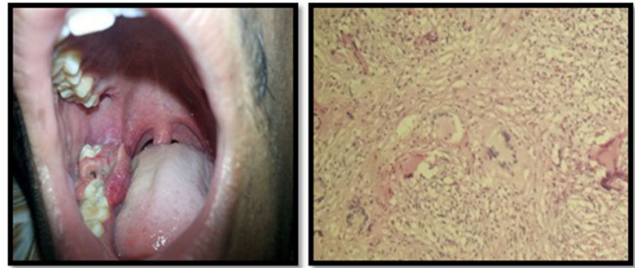


Figure 6: A 36 years male – Lesion clinically diagnosed as PGCG also confirmed histopathologically)



Figure 7: A 30 years female – Lesion clinically diagnosed as PGCG which turned out to be POF histopathologically)