Management of recurrent pyogenic granuloma with platelet-rich fibrin membrane

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Abstract:
Pyogenic granuloma (PG) is an inflammatory hyperplastic lesion of the oral cavity. The most common etiological factors for PG are low-grade local irritation, traumatic injury, or hormonal factors. Clinically, it appears to be smooth or lobulated exophytic lesion. It appears to be erythematous papule and is either pedunculated or has a sessile base. The lesion has shown a recurrence rate of 15.8%. Various treatment modalities have been present in the literature. The present article emphasized the treatment modalities and an effort to treat the recurrence of PG with the use of platelet-rich fibrin (PRF) membrane. This case report presents a 28-year-old female patient who had reported with PG that recurred twice in 2-year period. The lesion appeared to be recurrent with sessile base and was diagnosed clinically and histopathologically as PG. The PG was excised with the conventional scalpel method exposing the underlying bone. The exposed surface was then covered with PRF membrane. At 12-month follow-up period, the patient did not show any further recurrence of the lesion.

Key words:
Conditioned gingival enlargement, pyogenic granuloma, platelet rich fibrin

INTRODUCTION
Inflammatory hyperplasia was used to describe large nodular growths of oral mucosa. Histologically, it represents fibrous and granulation tissue. Clinical fibroma, epulis fissuratum, pulp polyp, palatal papillary hyperplasia, giant cell granuloma, pregnancy epulis, and pyogenic granuloma (PG) fall under the umbrella of fibrous inflammatory hyperplasia. Hullihen in 1844 first presented a report and had termed it as PG. Later, in 1904, Hartzell termed it as granuloma pyogenicum. It is the most common nonneoplastic tumor-like growth of the oral cavity. PG is a reactive tumor which arises in response to various stimuli due to local irritation and traumatic activity of tumor cells and on the rate of cell death. Prevalence of PG is more common in females in the second decade of life, probably due to vascularization effect of estrogen and progesterone. In the oral cavity, 75% of the cases had predilection for the gingiva and it was accounted by calculus or any foreign material. Along with it, stimulant or injury present in the gingival crevice may pave the way for the occurrence of PG, and the irritation of the fibrovascular connective tissue results in exuberant proliferation of a granulation tissue. Other factors that could cause PG are some hormones, certain drugs (e.g., oral contraceptives and isotretinoin), bacteria, and viruses. In addition, deciduous teeth injury, aberrant tooth development, and even tooth eruption have been considered as predisposing factors for PG development. The other predominant sites affected were lips, tongue, buccal mucosa, and hard palate. The known stimuli in the maxillary gingiva are more commonly affected than the mandibular one and the anterior region is more commonly affected than the posterior region. Furthermore, the lesions are more frequently on the facial aspect of gingiva than on the lingual side. Clinically, PG appears smooth or lobulated with sessile or pedunculated base which is usually hemorrhagic and compressible and may develop a dumbbell-shaped mass. It was noted that 66% were sessile in nature and 77% had a pedunculated type of lesion. The lesion usually develops slowly and is asymptomatic. However, in some cases, it may develop fast, reaches its full size, and remains stable. The size ranges from a few millimeters to several centimeters, but it rarely exceeds 2 cm. The differential
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The present article describes a case report of a 28-year-old female patient who had recurrent PG twice in a 2-year period. The patient was followed up for a 12-month period following the conservative excision procedure and placement of platelet-rich fibrin (PRF) membrane to check for the recurrence of the lesion.

CASE REPORT

A 28-year-old female patient came to the Department of Periodontics, Bengaluru, India, with a chief complaint of swelling on the right mandibular front tooth region for 3 weeks. The lesion at the initial stage was of poppy seed in size which gradually increased within 3-week time as a size of dumbbell. The lesion was painless but caused discomfort and often bled on slight provocation. She stated that a similar type of growth in the same area was present for 2 years. The patient’s past history revealed the appearance of the lesion during the third trimester of pregnancy which was excised after parturition. The lesion reappeared in the same area approximately 7 months later following the excision. The lesions were excised by scalpel method as mentioned by the patient, and the histopathological examination was performed for the excised lesion which confirmed the diagnosis of PG. The patient stated that the present recurrence of the lesion occurred after approximately 8 months from the last excision performed.

No relevant medical and family history was reported by the patient. On intraoral examination, the lesion was present around the right labial mandibular anterior tooth region extending from the distal aspect of incisor to the mesial aspect of the canine region. It measured approximately 3 mm × 4 mm in dimension. On visual examination, it appeared reddish pink as observed in Figure 1. It was large and lobulated with a sessile base. On palpation, the lesion was firm and resilient with bleeding on slight provocation. Periodontal examination revealed good plaque index score of <1 as per Silness and Löe in 1964 and mild gingival inflammation as per gingival index score of <1 by Löe and Silness in 1963. Intraoral periapical radiograph showed no horizontal or vertical bone loss in the region as contemplated in Figure 2. The differential diagnosis of peripheral giant cell granuloma, peripheral ossifying fibroma, hemangioma, and hyperplastic gingival inflammation was ruled out based on the recurrence of the lesion and similar growth. Following the previous histological findings and clinical examination, the lesion was diagnosed as a recurrent PG.

The patient was explained about the nature and etiology of the lesion and also the possible reasons for the frequent recurrence of the lesion. Conventional surgical procedure by scalpel method was chosen for the excision of the lesion. A complete excision of the lesion could expose the underlying bone leading to resorption. An autologous PRF membrane was placed on the excised area. A written signed informed consent was taken from the patient before the commencement of the surgical procedure.

The area of interest was anesthetized with local anesthesia with a solution of 2% lignocaine with 1:200,000 adrenaline. A circumferential full-thickness incision was given. The incision extended from the distal aspect of incisor to the mesial aspect of the canine region circumferentially including 2 mm of an adjacent gingival region. Scalpel excision was performed from the base of the lesion exposing the bony surface as observed in Figures 3 and 4. The excised lesion as shown in Figure 5 was then transferred to a bottle of 10% formalin solution and was sent for histopathological evaluation. The denuded bone surface was then covered with PRF membrane. The PRF was prepared as per Choukron et al.’s protocol in 2001 as shown in Figure 6. 10 ml of the patient’s blood was withdrawn from the antecubital vein and was immediately transferred to REMI-4C centrifugation machine within 30 s. It was centrifuged at 2700 rpm for 12 min.

The clot was then squeezed between a sterile gauze, and a PRF membrane was placed into the exposed bone surface. The membrane was further stabilized by suturing it with direct interrupted suture on the mesial and distal aspects as shown in Figure 7. The periodontal dressing was placed. Postoperative instruction was given to the patient and chlorhexidine mouthwash (0.12%) was prescribed to the patient.

The histopathological evaluation showed a large ulcerated area covered with fibrin exudate. The epithelium appeared to be hyperplastic, edematous, and was infiltrated with inflammatory cells. Underneath the epithelium, numerous small endothelial lined channels in the lobular structure were seen, suggestive of perivascular inflammation. The lesion had a fibrous appearance with neutrophils, plasma cells, and lymphocyte inflammatory cell infiltrate. The histopathological slide at ×20 and ×40 magnification confirmed the diagnosis of PG as shown in Figure 8. The patient was recalled at 2-week follow-up period where a complete epithelialization over the denuded bone surface was seen as contemplated in Figure 9. At 12-month follow-up period, recurrence of the lesion was not observed as shown in Figure 10.
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**Figure 1:** Preoperative view of pyogenic granuloma in mandibular anterior tooth region

**Figure 2:** Intraoral radiographic view of mandibular anterior tooth region showing no bone loss

**Figure 3:** Incision given around the lesion by scalpel method

**Figure 4:** Excision of the lesion caused exposure of the underlying bone as encircled

**Figure 5:** Excised lesion

**Figure 6:** Preparation of platelet-rich fibrin membrane

**Figure 7:** Placement of platelet-rich fibrin membrane on the exposed bone surface

**Figure 8:** Histopathological section at ×20 and ×40. (a) Hyperplastic epithelium; (b) dense inflammatory cell infiltrate in the connective tissue; (c) perivascular inflammation
PG is a well-identified inflammatory hyperplastic oral lesion which comprises about 1.85% of all oral pathologies, other than caries and gingivitis. Usually, the lesion is neither symptomatic nor painful, but minor trauma to the growth can induce significant bleeding. It arises due to low-grade local irritation, traumatic injuries, and hormonal fluctuations. PG creates esthetic problem and leads to functional problems with mastication, swallowing, and speaking. The rapid growth of PG is mainly attributed to factors such as inducible nitric oxide synthase, vascular endothelial growth factor (VEGF), basic fibroblast growth factor, and connective tissue growth factor. The present case report describes a lesion which had a history of recurrence twice within 2 years on the same area. The recurrence of the lesion in the present case could be attributed to the most common cause of hormonal changes as the patient gave a history of appearance of the lesion during her third trimester of pregnancy. The persistent influence of increase in estrogen level increases vascular permeability enhancing the acute gingival inflammation and hyperplastic gingival tissues. The lesion reappeared twice after 7–8 months approximately which could be attributed to incomplete excision of the lesion. Various treatment modalities are present in literature for the treatment of PG. The most common method of treatment is by surgical convention. The other treatment modalities for the treatment of PG include the use of laser, cryotherapy, and electrocauterization, which have rendered successful results. In spite of the success of the treatment modalities, it conveys certain advantages and disadvantages of its own. From the bountiful treatments, the laser and electrosurgery have reported injury to the neighboring tissues and delayed wound healing, although bloodless surgical field has shown patient comfort, less pain, and healing without scar formation.

In the present case as the patient had the recurrence of lesion, scalpel method was chosen over the other mentioned techniques. As per Asnaashari et al. in 2014, the reported recurrence rate of lesion following conventional method was 16%. This treatment modality was preferred as the lesion had a sessile base and a history of repeated recurrence. The excision was aimed to completely excise the underlying soft tissue in an attempt to prevent the recurrence of the lesion. The procedure had led to exposure of bone surface. Wilderman in 1964 stated that, following full-thickness incision, the denuded bone results in superficial necrosis at 1–3 days. Osteoclastic resorption reaches a peak at 4–6 days, which thereby declines. This further results in loss of bone of about 1 mm and greater if bone was thin which was mostly seen in anterior mandibular region due to its thin alveolar housing.

To prevent the sequence of events following exposure of the bone surface, PRF membrane was placed. PRF is the activated form of a plasmatic molecule called fibrinogen. The fibrin formed after the centrifugation is transformed into biologic glue which consolidates the initial platelet cluster. It thus forms a protective wall along vascular breaches during coagulation. The fibrin architecture entraps various numbers of leukocytes in the fibrin matrix, allowing an intense slow release of growth factors, and favors the sealing of wound borders and facilitates rapid epithelialization. The use of PRF membrane was also known to release various pro-inflammatory cytokines such as interferon-γ, tumor necrosis factor-α, interleukin (IL)-1β, and IL-6, which helps in T-cell differentiation, and growth factors such as VEGF, platelet-derived growth factor, fibroblast growth factor, transforming growth factor, and insulin growth factor, which acts as an anti-inflammatory agent and promotes faster healing. The PRF membrane has been used as a palatal bandage following harvesting of subepithelial connective tissue graft due to its fibrin meshwork and release of growth factors for a prolonged period of time. The use of PRF membrane has also been successful in gingival recession defects, intrabony defects, furcation defects, and epithelialization following depigmentation procedure. A recent systematic review by Miron et al. in 2017 has proven the immense potential of PRF on wound healing after regenerative therapy for the management of various soft-tissue defects.

The same result in terms of epithelialization and patient comfort was achieved following its placement over the denuded bone surface. At 12-month follow-up period, no recurrence of the lesion was observed. A complete removal of the lesion exposing the underlying bone surface was attributed to the success of the therapy. The use of PRF membrane following excision of recurrent PG also prevented the underlying resorption and an esthetic soft-tissue coverage. However, the treatment of recurrent PG with PRF membrane followed up for 12 months was executed for the first time as per a thorough literature search.
Further research should be done to perform the same in randomized controlled clinical trial design and with statistical evaluation of clinical and esthetic outcome.

**CONCLUSION**

The use of scalpel method for excision of PG is a safe technique with various clinical benefits. The recurrent lesions should be wisely treated with the aim of removing the etiological factors and also not to have a detrimental effect on the underlying and adjacent soft and hard tissues. The autologous biomaterial PRF membrane due to its immense biological activity in wound healing and regeneration has played a pivotal role in the success of the therapy.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that her name and initial will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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