CASE REPORT

Peripheral Ossifying Fibroma: Case Report and a Mini Review

Girish Babu KL[1], Vivek CR[2], Venkatesh Garla[3], Geeta Maruti Doddamani[4], Prakurthi BV[5], Bipin Reddy[6]

1-Professor and Head, Department of Dentistry, Hassan Institute of Medical Sciences, Hassan, Karnataka, India. 2-Senior Lecturer, Department of Orthodontics, The Oxford Dental College, Hospital and Research Centre , Karnataka, India. 3,4- Reader, Department of Orthodontics, The Oxford Dental College, Hospital and Research Centre, Karnataka, India. 5-Senior Lecturer, Department of Oral and Maxillofacial Pathology, The Oxford Dental College, Hospital and Research Centre, Karnataka, India. 6- Reader, Department of Oral and Maxillofacial Surgery, The Oxford Dental College, Hospital and Research Centre, Karnataka.

Correspondence to:
Dr. Girish Babu KL, Professor and Head, Department of Dentistry, Hassan Institute of Medical Sciences, Hassan, Karnataka.
Contact Us: www.ijohmr.com

ABSTRACT

Peripheral ossifying fibroma (POF) is typically a solitary, slow growing, nodular mass, which may be either pedunculated or sessile**.** The size of the POF is usually<1.5 cm in diameter. The cause and pathogenesis of POF is unknown. The aim of this article is to report a case of POF and briefly review the current literature on this condition.

KEYWORDS: Peripheral ossifying fibroma, pedunculated, sessile, peripheral fibroma

INTRODUCTION

Peripheral ossifying fibroma (POF) is typically a solitary, slow growing, nodular mass, which may be either pedunculated or sessile.[1] POF is usually consist of a cellular fibroblastic connective tissue stroma along with the randomly dispersed foci of a mineralized product consisting of either bone, cementum-like tissue or dystrophic calcifications.[2] This may be the reason why in the literature, this pathologic lesion sometimes has been described as an ossifying fibroid epulis, a peripheral fibroma with calcification or a calcifying granuloma. However, in 1982, Gardner recommended that the only term used to describe this lesion should be POF.[3]

The size of the POF is usually<1.5 cm in diameter, but lesion measuring of 6 cm and 9 cm have also been reported. The cause and pathogenesis of POF still remain unknown. Some of the investigators consider it as a neoplastic process, whereas others consider it as a reactive process. In both situations, the lesion is thought to arise from cells of the periodontal ligament. The other possible risk factors associated with POF are trauma or local irritants, (like dental plaque, and calculus) microorganisms, masticatory forces, dental appliances and poor quality of restorations.[4-6]

The aim of this article is to present a case of POF and briefly review the current literature on this condition.

CASE REPORT

A 40 -year-old male patient reported to our clinic with a chief complaint of a soft tissue growth in the upper front teeth region since 12 months. (Figure 1and 2). The swelling was of smaller than peanut size when he noticed for the first time and gradually increased to reach the present size. There was no history of trauma, injury or food impaction to the same region. The medical status was non-contributory, and family history was not

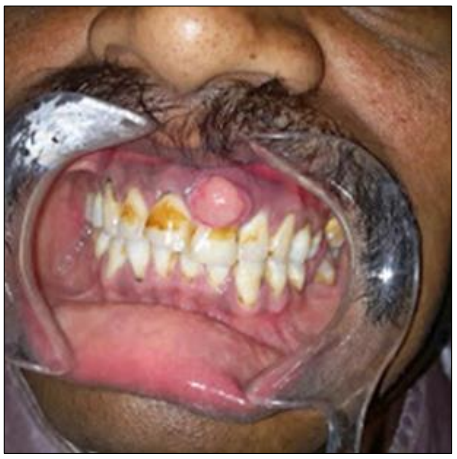

Figure 1: Swelling on gingiva associated with 21 (frontal view)

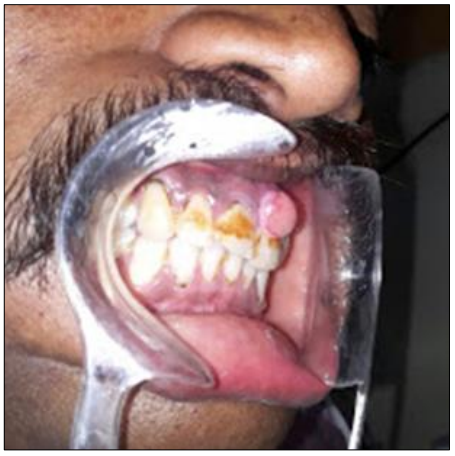

Figure 2: Swelling on gingiva associated with 21 (Side view)

How to cite this article:
Girish Babu KL, Vivek CR, Venkatesh G, Doddamani GM, Prakurthi BV, Reddy B. Peripheral Ossifying Fibroma: Case Report and a Mini Review. Int J Oral Health Med Res 2017;3(6):103-108.

significant. The patient's past dental and medical histories were non-contributory. He denied tobacco and alcohol use. Occasionally, bleeding occurred when he brushed his teeth.

Clinical Examination: Extra-oral examination showed no gross facial asymmetry and no signs of inflammation on the overlying skin. There was no regional lymphadenopathy. On intra-oral examination, there was a soft tissue swelling irt maxillary left central incisor attached to the gingiva of approximately 1 cm × 1.5 cm. The consistency of growth was firm, pedunculated, solitary and pinkish in color with no associated pain. The lesion was not fluctuant or did not blanch with finger pressure. Oral hygiene was considerably poor.

Radiographic Examination: Panoramic and periapical radiographs were obtained. The radiographic examination revealed both incisors with normal periodontal ligament space and periradicular architecture. No findings were seen pertaining to the maxillary exophytic lesion.

Provisional diagnosis: The case was provisionally diagnosed as irritation fibroma, and surgical excision of the same lesion was planned.

Differential diagnosis: Peripheral giant cell granuloma, irritation fibroma, pyogenic granuloma, fibrous hyperplasia and peripheral ossifying fibroma were considered for differential diagnosis

Blood investigations: The patient was advice to undergo complete blood investigation prior to the surgery. All parameters like hemoglobin, bleeding time, clotting time, total and differential leukocyte counts were within normal limits. The patient was negative for human immunodeficiency virus and Australian antigen (hepatitis B surface antigen).

Treatment: After obtaining written informed consent, the growth was completely surgically excised under local anesthesia using an electrocautery device (Figure 3). The excised specimen was sent to histo-pathological laboratoty. Teeth were scaled to remove any local irritants.

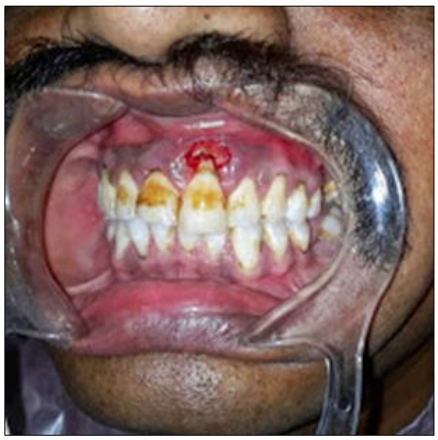

Figure 3: Immediately after surgical removal of the swelling

The patient was given cap. amoxicillin 500 mg every 8 h, for a 5- days postoperative period, and 500 mg of acetaminophen three times daily for 5 days along with mouth rinse (0.2% chlorhexidine gluconate for twice daily).

Microscopic examination: The microscopic examination of the excised tissue revealed a para keratinized stratified squamous epithelium of varying thickness with long thin rete ridges and showed ulceration with fibropurulent exudate in one area. Underlying connective tissue was dense, fibrillar with plump fibroblasts. The connective tissue showed areas of ossification i.e., bony trabaculae with osteocytes entrapped with osteoblastic rimming. Inflammatory cell infiltrate with lymphocytes, and plasma cells were also seen. The microscopic features were suggestive of POF (Figure 4 and 5).

Thus on based on clinical and histopathologic examination, the lesion was diagnosed as POF.

Follow-up: The patient presented for a follow-up examination after a week. The healing in surgical site was well and the patient was asymptomatic. The patient was advised to undergo gingival defect correction and esthetic rehabilitation of his teeth, but he was not willing. The patient was under observation and followed up after 24 months with no recurrence in the lesion. (Figure 6)

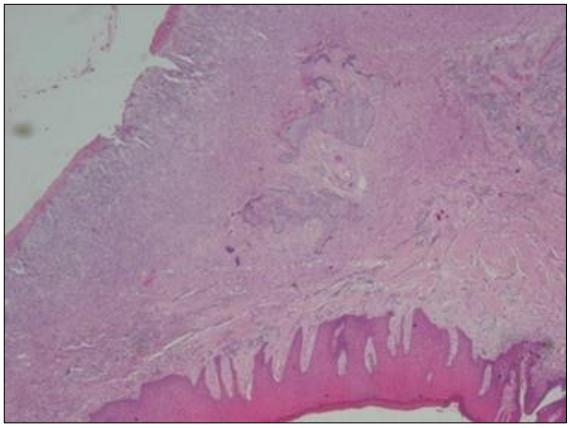

Figure 4: Photomicrograph showing parakeratinized stratified squamous epithelium & underlying connective tissue with bony trabeculae (H & E Stain 2X)

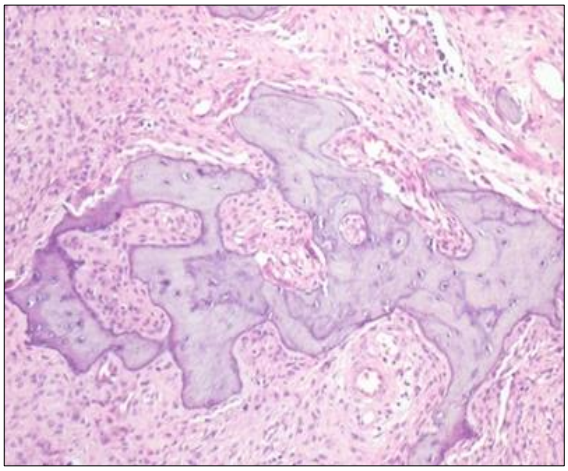

Figure 5: Photomicrograph showing cellular fibrous connective tissue with bony trabaculae and inflammatory cells (H &E Stain, 40X)

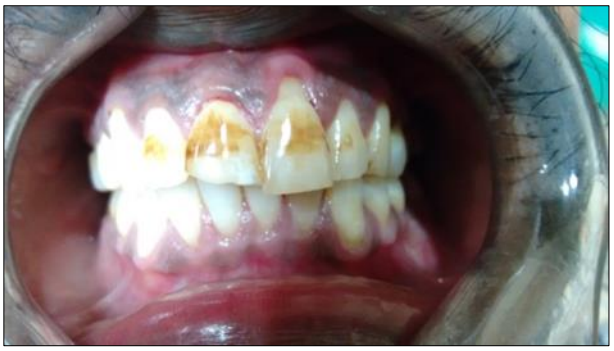

Figure 6: After six month of follow up

MINI -REVIEW OF PERIPHERAL OSSIFYING FIBROMA

Terminologies: POFs have been described in the literature since the 1940s. Earlier many names have been proposed to similar lesions such as epulis,[5] peripheral fibroma with calcifications,[4] peripheral ossifying fibroma[3,4] calcifying fibroblastic granuloma,[7] peripheral cemetifying fibroma,[3] peripheral fibroma with cementogenesis[8] and peripheral cement ossifying fibroma.[9] The use of various names for fibroblastic calcifying gingival lesions indicates that there is much controversy surrounding their classification. Gardner suggested that the peripheral ossifying fibroma and peripheral odontogenic fibroma are two different lesions, the former being a common reactive lesion and the latter a rare lesion.[3] He also suggested that the name peripheral ossifying fibroma should be retained for this lesion. Eversole and Rovin coined the term POF.[4]

Peripheral ossifying fibroma contains bone, cementum and spheroidal calcifications. When bone predominates, 'ossifying' is used; when curvilinear trabeculae or spheroidal calcifications are seen more then the term 'cementifying' has been assigned. When both bone and cementum-like tissues are seen, the lesions have been referred as peripheral cemento-ossifying fibroma.[10] The observation of identical cementum-like tissue in lesions in extra-gnathic sites suggests that this tissue may merely be a normal variant of bone and that dental cementum itself is a specialized form of "bundle-bone". Recently, the term, ossifying fibroma is more appropriate.[10-12]

The term 'peripheral odontogenic fibroma' has also been used to describe peripheral ossifying fibroma. But peripheral odontogenic fibroma has been designated by the World Health Organization (WHO) as rare and extraosseous counterpart of central odontogenic fibroma and histologically presents as a fibroblastic neoplasm containing odontogenic epithelium .[13]

Etiology: The etiology of POF is unclear. Inflammatory hyperplasia originating in the superficial periodontal ligament is considered to be a factor in POF's causation.[2] Orkin and Amaidas suggested that excessive proliferation of mature fibrous connective tissue is a response to gingival injury or gingival irritations.[14] Gingival irritation may be caused by calculus, dental appliances, poor restorations or a foreign body in the gingival sulcus. [2, 15,16]

POFs are believed to arise from gingival fibres of the periodontal ligament as hyperplastic growth of tissue that is unique to the gingival mucosa.[3-5,17] This hypothesis is based on the fact that POFs arise exclusively on the gingiva, the subsequent proximity of the gingiva to the periodontal ligament and presence of oxytalan fibers within the mineralized matrix of the lesions.[8] Supporting this hypothesis is the inverse correlation between age distribution of patients presenting with POF and the number of missing teeth. [2, 13,17] It has also been suggested that the lesion may be caused by fibrosis of the granulation tissue.[18] A study revealed that 73% of the 22 POF cases examined contained a fibrocellular connective tissue stroma surrounding the mineralized mass. The mineralized mass was comprised of woven bone in 50% of the cases, while 18% of the cases showed a combination of lamellar bone and cellular cementum, 18% of the cases comprised only cementum (cellular and acellular), and the remaining 13.6% exhibited a mixture of woven and lamellar bone. This evidence supports the theory that POF develops from the periodontal ligament/periosteum as undifferentiated mesenchymal cells with an inherent proliferative potential to form bone or cementum.[19] In a study of 134 pediatric patients with POF, in only 2 cases POF was closely associated with primary teeth, bringing into question the reactivity of the lesion.[2] The exfoliation of primary teeth and eruption of their successors should result in an increased incidence of periodontal ligament associated reactive lesions.[2,4]

Change in the hormonal levels in the body may play a role. Supporting to this, there is higher incidence of POF among females, increasing occurrence in the second decade and declining incidence after the third decade. [13] However, an immunohistochemical study on 4 female cases of POF did not show estrogen or progesterone receptor positivity.[15] Kumar et al[8] noted the presence of a lesion at an edentulous site in a 49-year-old woman. The POF was also seen at a dentulous site in a 50-year-old female.[20] Shamim et al. [21] and Stablein et al.[22] group POF as a neoplastic lesion. According to Kfir et al[23] and Buchner et al[24] POF is considered as a reactive lesion.

The clinically initially the lesion is asymptomatic, the tumor progress to the point where its size causes pain, functional limitation and cosmetic deformities.[5, 25] The lesion may persist for lonf time depending on the degree of ulceration, discomfort, and interference with function. [5, 24] Cases of tooth migration and bone destruction have been reported, but these are not common.[2, 26]

Prevalence: POF accounts for 3.1% of all oral tumors and 9.6% of gingival lesions [13, 27] It is a fairly common lesion, comprising nearly 3% of oral lesions biopsied in one study,[5] approximately 1%–2% in other studies.[2, 13, 28,] Das and Das also observed similar results, with 1.6% POFs among 2,370 intraoral biopsies.[29] Literature search by Kohli et al revealed 2 cases of POF presenting at birth, diagnosed clinically as congenital epulis.[30] In the

pediatric age group (0–19 years), Cuisia and Brannon reported that only 134 out of 657 diagnosed cases of POF (8% of them being in the first decade).[2] However, Kenney et al. reported 1.9% prevalence in children aged 0 to 9 years.[13] Few studies have shown peak incidence of POF in the fifth decade. [21, 31] Neville et al stated that POF greatly affects adolescents and young adults, with peak prevalence between 10 to 19 years of age. [32]

Approximately 60% of POFs occur in the maxilla.[13,31] They occur more often in the anterior than the posterior area [13,29,31] with 55%–60% presenting in the incisor-cuspid region.[2,4, 31] One of the case showed occurance in the mandibular posterior region.[33] Multicentric POF has been reported very rarely.[8] Kendrick & Waggoner reported a case involving the interdental papilla, between the mandibular left second primary molar and first permanent molar.[18]

The female to male ratio varies from 1.22:1[31]and 1.7:1 [13,24,,28] to 4.3:1.[4] The majority of the lesions occur in the second decade, with a declining incidence in later years.[4,5,13,24,28] In a retrospective study of 431 cases in the Chinese population by Zhang and others,[31] the mean age of incidence of POF was found to be 44 years. POF is more common among whites (71%) people than black (36%) [2] and slightly less common among those of Hispanic origin.[29]

POF may occur at various age, but exhibits a peak incidence between the second and third decade. This condition affects both genders with a higher rate in females. Supporting this findings Cundiff reported prevalence of POF to be between 5 and 25 years, with a peak incidence at 13 years of age. [34]

Clinical Features: Clinically, POF manifests as a pedunculated or a sessile nodular mass, which usually originates in the interdental papilla. POF may appear as a pedunculated nodule, or it may have a broad attachment base.[2, 5, 32] These lesions can be red to pink and its surface may be smooth or irregular; it may be ulcerated or nonulcerated. Studies have reported ulceration in more than 50% of the cases.[2, 24] Ulceration is commonly seen because of its exophytic growth, gingival location and its presence in trauma-prone region.

Although the usual size of the lesion is < 2 cm in diameter,[24, 32] reports range from 0.2–3.0 cm [2, 24] to 4 mm–8 cm [5 35] are reported. Rarely lesions may be as large as 9 cm in diameter. [26] Cases of tooth migration tooth separation, delayed tooth eruption, and bone destruction have been reported, but these are not common. [26]

Radiographic Features: Radiographically, in a most of the cases there is no apparent visible underlying bone involvement. Radioopaque foci of calcification have been reported to be scattered through the central area of the lesion, but not all lesions demonstrate radiographic calcifications.[36] On rare occasions, there appears to be a superficial erosion of bone. [13, 36]

Histological Features: Histologically, the key feature of this lesion is exceedingly cellular mass of connective tissue comprising large number of plump, proliferating fibroblasts intermingled throughout with delicate fibrillar stroma. Buchner et al [24] observed that the mineralized tissues observed in POF can be of three basic types: 1) bone that may be woven, lamellar or trabecular, sometimes surrounded by osteoid, 2) cementumlike material that appears as spherical bodies resembling cementum or large acellular round tooval eosinophilic bodies, which seemed to have coalesced to form islands in various sizes and shapes, 3) dystrophic calcification, which can range from small clusters of minute basophilic granules or tiny globules to large, solid irregular masses. The surface of POF exhibits either an intact or, more frequently, an ulcerated layer of stratified squamous epithelium. On occasion, areas will be found containing multinucleated giant cells that, with the surrounding tissue, bear considerable resemblance to some areas of peripheral giant cell granuloma. [37]

Differential Diagnosis: Frequently, POF shows similar clinical features to other extraosseous lesions. It may be misdiagnosed as pyogenic ganuloma, fibrous dysplasia, peripheral giant cell granuloma, osteoid osteoma, osteoblastoma, low grade osteosarcoma, cementoblastoma, chronic osteomyelitis and sclerosing osteomyelitis of Garre. [25, 38, 39]

In general the pyogenic granuloma presents as a red soft friable nodule that bleeds with minimal manipulation but tooth displacement and resorption of alveolar bone are not observed. Although peripheral giant cell granuloma has features similar to those of PCOF, the latter lacks the blue discoloration commonly associated with peripheral giant cell granuloma and shows flakes of calcification, radiographically as well histologically. Unlike the POF, the peripheral odontogenic fibroma is a real tumourous condition and has an odontogenic epithelium and dysplastic dentine.[21] POF is poorly vascularized and well circumscribed and can be easily removed from the surrounding bone. This is one of the main differences with fibrous dysplasia [25, 39] Despite a preponderance of literature supporting differentiation, some authors continue to argue that the POF (or peripheral cemento-ossifying fibroma) is the peripheral counterpart of the central cemento-ossifying fibroma.[9]

The diagnosis of POF based only on clinical observations can be difficult and histopathological examination of the surgical specimen obtained by excisional biopsy is essential for an accurate diagnosis. Discussion with family members should be tactful to prevent undue distress during the waiting period between differential diagnosis and definitive histopathological diagnosis.

Treatment: Treatment consists of proper surgical intervention that ensures deep excision of the lesion including periosteum. Through scaling and root planning of adjacent teeth and/or removal of other sources of irritants should be accomplished.[2] Walters et al [27] stated

that total excision of the lesion in the maxillary anterior region can result in an unsightly gingival defect unless appropriate efforts are taken to repair the periosteal defects. Various surgical techniques like lateral sliding full thickness or partial thickness flap, subepithelial connective tissue graft or coronally positioned flap may be used to manage this defect and minimize patient esthetic concerns.

Recurrence: Due to the high rate of recurrence, close postoperative monitoring is required in all cases of POF (1)The rate of recurrence has been reported at 8.9%,[5] 9%,[2] 14%,[13] 16% [24] and 20%.[4] Therefore, regular follow-up is required. POF recurs due to 1) incomplete removal of the lesion, 2) failure to eliminate local irritants and 3) difficulty in accessing the lesion during surgical manipulation as a result of the intricate location of the lesion (usually an interdental area). [19] Prognosis is excellent and recurrence is rare if correctly managed. [38, 39]

CONCLUSION

POF is a slowly progressive lesion generally with limited growth. Many cases will progress for long periods before the patient seeks treatment. A slowly growing pink soft tissue nodule in the anterior maxilla should raise suspicion of POF. As the diagnosis of POF based only on clinical features is very difficult, radiographs and histopathological examination are very essential for definitive diagnosis. Treatment consists of surgical excision including periodontal ligament periosteum and scaling of adjacent teeth. Continuous follow-up is required because the recurrence rate is 8%-20% .

REFERENCES

1. Trasad VA, Devarsa GM, Subba Reddy VV, Shashikiran ND. Peripheral ossifying fibroma in the maxillary arch. J Indian Soc Pedod Prev Dent 2011;29:255-9.
2. Cuisia ZE, Brannon RB. Peripheral ossifying fibroma – a clinical evaluation of 134 pediatric cases. Pediatr Dent 2001;23:245-8.
3. Gardner DG. The peripheral odontogenic fibroma: an at-tempt at clarification. Oral Surg Oral Med Oral Pathol 1982; 54: 40-48
4. Eversole LR, Rovin S. Reactive lesions of the gingiva. J Oral Pathol 1972; 1: 30-8
5. Bhaskar SN, Jacoway JR. Peripheral fibroma and peripheral fibroma with calcification: report of 376 cases. J Am Dent Assoc 1966; 73: 1312-1320.
6. Kohli K, Christian A, Howell R. Peripheral ossifying fibroma associated with a neonatal tooth: case report. Pediatr Dent 1998;20:428-9.
7. Lee KW. The fibrous epulis and related lesions. Granuloma pyogenicum, 'Pregnancy tumour', fibro-epithelial polyp and calcifying fibroblastic granuloma. A clinico-pathological study. Periodontics 1968; 6: 277-292
8. Kumar SK, Ram S, Jorgensen MG, Shuler CF, Sedghizadeh PP. Multicentric peripheral ossifying fibroma. J Oral Sci 2006; 48: 239-243.
9. Feller L, Buskin A, Raubenheimer EJ. Cemento-ossifying fibroma: case report and review of the literature. J Int Acad Periodontol 2004; 6: 131-135.
10. Yadav R, Gulati A: Periphearl ossifying fibroma: a case report. J Oral Sci. 2009;51:151-4.
11. MacDonald-Jankowski DS: Fibro-osseous lesions of the face and jaws. Clin Radiol. 2004;59:11-25.
12. Speight PM, Carlos R: Maxillofacial fibro-osseous lesions. Current Diagnostic Pathology, 2006;12(1):1–10
13. Kenney JN, Kaugars GE, Abbey LM. Comparison between the peripheral ossifying fibroma and peripheral odontogenic fibroma. J Oral Maxillofac Surg 1989;47:378-82.
14. Orkin DA, Amaidas VD. Ossifying fibrous epulis—an abbreviated case report. Oral Surg Oral Med Oral Pathol 1984;57:147–8.
15. Gracia de Marcos JA, Gracia de Marcos MJ, Rodriguez SA, Rodrigo JC, Poblet E: Peripheral ossifying fibroma: a clinical and immunohistochemical study of 4 cases. . J Oral Sci. 2010;52: 95-9.
16. Moon WJ, Choi SY, Chung EC, Kwon KH, Chae SW: Peripheral ossifying fibroma in the oral cavity: CT and MR findings. Dentomaxillofac Radiol. 2007;36:180-2.
17. Miller CS, Henry RG, Damm DD. Proliferative mass found in the gingiva. J Am Dent Assoc 1990; 121(4):559–60.
18. Kendrick F, Waggoner WF. Managing a peripheral ossifying fibroma. ASDC J Dent Child 1996; 63: 135-138.
19. Shetty DC, Urs AB, Ahuja P, Sahu A, Manchanda A, Sirohi Y. Mineralized components and their interpretation in the histogenesis of peripheral ossifying fibroma. Indian J Dent Res 2011; 22:56-61.
20. Mishra AK, Bhusari P, Kanteshwari K. Peripheral cemento-ossifying fibroma--a case report. Int J Dent Hyg 2011; 9: 234-237.
21. Shamim T, Varghese VI, Shameena PM, Sudha S. A retrospective analysis of gingival biopsied lesions in South Indian population: 2001–2006. Med Oral Patol Oral Cir Bucal 2008; 13:E414–8.
22. Stablein MJ, Silverglade LB. Comparative analysis of biopsy specimens from gingiva and alveolar mucosa. J Periodontol 1985; 56:671–6.
23. Kfir Y, Buchner A, Hansen LS. Reactive lesions of the gingiva. A clinico-pathological study of 741 cases. J Periodontol 1980; 51:655–61.
24. Buchner A, Hansen LS. The histomorphologic spectrum of peripheral ossifying fibroma. Oral Surg Oral Med Oral Pathol 1987; 63:452–61
25. De Vicente Rodríguez JC, González Méndez S, Santamaría Zuazua J, Rubiales B. Tumores no odontogénicos de los maxilares: clasificación,clínicay diagnóstico. Med Oral 1997; 12: 83-93
26. Poon CK, Kwan PC, Chao SY. Giant peripheral ossifying fi-broma of the maxilla: report of a case. J Oral Maxillofac Surg 1995; 53: 695-698
27. Walters JD, Will JK, Hatfield RD, Cacchillo DA, Raabe DA. Excision and repair of the peripheral ossifying fibroma: a report of 3 cases. J Periodontol 2001;72:939-44.
28. Skinner RL, Davenport WD Jr, Weir JC, Carr RF. A survey of biopsied oral lesions in pediatric dental patients. Pediatr Dent 1986; 8:163–7.
29. Das S, Das AK. A review of pediatric oral biopsies from a surgical pathology service in a dental school. Pediatr Dent 1993; 15:208–11.
30. Kohli K, Christian A, Howell R: Peripheral ossifying fibroma associated with a neonatal tooth: case report. Pediatr Dent 1998;20:428–429.
31. Zhang W, Chen Y, An Z, Geng N, Bao D: Reactive gingival lesions: a retrospective study of 2,439 cases.

Quintessence Int. 2007;38:103-10.
32. Neville BW, Damm DD, Allen CM, Bouquot JE. Oral and Maxillofacial Pathology. 2nd ed. Philadelphia: WB Saunders Co; 2002. p. 451–2.
33. Pal S, Hegde S, Ajila V. The varying clinical presentations of peripheral ossifying fibroma: A report of three cases. Rev Odonto Cienc 2012;27(3):251-255.
34. Cundiff EJ. Peripheral ossifying fibroma: A review of 365 cases. USA: MSD Thesis Indiana University; 1972.
35. Bodner L, Dayan D. Growth potential of peripheral ossifying fibroma. J Clin Periodontol 1987; 14:551–4.
36. Mesquita RA, Orsini SC, Sousa M, de Araújo NS. Proliferative activity in peripheral ossifying fibroma and ossifying fibroma. J Oral Pathol Med 1998; 27: 64-67.
37. Southam JC, Venkataraman BK: Calcification and ossification in epulides in man (excluding giant cell epulides). Archives of Oral Biology, 1973;18:1243-53.
38. Martín-Granizo R, Sanchez-Cuellar A, Falahat F. Cemento-ossifying fibroma of the upper gingivae. Otolaryngol Head Neck Surg 2000; 122: 775.
39. Waldron CA. Fibro-osseous lesions of the jaws. J Oral Maxil-lofac Surg 1993; 51: 828-835.

Source of Support: Nil
Conflict of Interest: Nil