Familial florid cemento-osseous dysplasia: a report of three cases and review of the literature

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Abstract

Familial cases of benign fibro-osseous lesions of the jaws are rare and have been described under numerous terms including familial gigantiform cementoma, multiple cemento-ossifying fibromas, sclerotic cemental masses and familial florid cemento-osseous dysplasia. The synonymous and interchangeable use of these terms to describe distinct entities with overlapping features has resulted in confusion and inaccurate categorisation of these lesions. This study highlights three family members with diffuse fibro-osseous jaw lesions with areas of significant expansion. In the pursuit of finding the best clinicopathological categorisation for the reported cases, familial florid cemento-osseous dysplasia and familial gigantiform cementoma were investigated. The final consensus of these three cases was that of familial florid cemento-osseous dysplasia, and one patient presented with a concurrent "ossifying fibromatoid lesion". A literature review on the above entities was performed in an attempt to provide clarification and delineate distinguishing features of the individual diseases.

Key Words: Developmental bone diseases, Bone dysplasia, Florid cemento-osseous dysplasia, Familial Gigantiform Cementoma, Cemento-ossifying Fibroma

Introduction

Benign fibro-osseous lesions are characterised by the replacement of normal bone by cellular fibrous tissue containing foci of mineralisation. Benign fibro-osseous lesions can be divided into three broad categories, namely, cemento-osseous dysplasia (COD) (dysplastic/reactive), cemento-ossifying fibroma (COF) (neoplastic) and fibrous dysplasia (developmental). A fourth category termed "atypical fibro-osseous lesions" has also been recognised by some authors that describe lesions which do not fit into a specific diagnostic category.[1] Fibro-osseous lesions present with similar histological findings and in some instances overlapping clinical features, causing confusion during clinicopathological categorisation.[2–4] The pathogenesis of these lesions remains unclear, but several theories have been suggested. One theory proposes that COD could be caused by an unusual reaction of the alveolar bone to local factors.[4–7] Defective bone remodelling triggered by local injury or, possibly, an underlying hormonal imbalance has also been postulated.[8] COD is further subclassified based on the extent and distribution of lesions into focal, periapical and florid COD. Focal COD presents with a single lesion predominantly found in black African and East Asian females. A systematic review found that focal COD was associated with extraction sites, supporting the aetiology of an abnormal bony reaction to injury or trauma.[9] Periapical COD presents with multiple lesions restricted to the anterior aspect of the mandible. The lesions are self-limiting and do not exhibit significant growth.[9] In an African

setting periapical COD is prevalent in middle-aged black females, suggesting a genetic predisposition.[8] Florid COD presents with multifocal and multiquadrant involvement of tooth-bearing areas of the jaws.[8,10] Florid COD can occur sporadically or be inherited as familial florid COD.
The objective of this review was to present a family with diffuse fibro-osseous jaw lesions associated with areas of significant expansion. All three family members presented with similar radiographic findings; therefore, hereditary conditions associated with benign fibro-osseous lesions were considered.

Case 1
A 58-year-old black female presented with a chief complaint of pain in the right maxilla that had been present for several months. The patient's medical history revealed hypertension and no other co-morbidities. On examination, we noted facial asymmetry and a protrusive right maxilla. According to the patient, the swelling in the right maxilla had been present for several years, however, she could not recall when the swelling started. Alveolar bone necrosis with extruding bony sequestra was visible at the right posterior maxillary alveolus with associated mobile molar teeth. No active purulent drainage was noted (Figure 1). A panoramic radiograph demonstrated an edentulous mandible and a partially dentate maxilla. The right maxilla contained an irregular mixed radiolucent-radiopaque mass extending from the third molar to the midline, displacing the walls of the maxillary sinus, orbit and nasal cavity. The lesion displayed significant bony expansion. The right maxillary second premolar was impacted and enveloped by the sclerotic mass. Additional radiopaque sclerotic lesions were present in the left posterior maxilla and mandibular corpus (Figure 2). The clinical differential diagnosis of familial gigantiform cementoma (FGC) and familial florid COD with secondary osteomyelitis was considered.

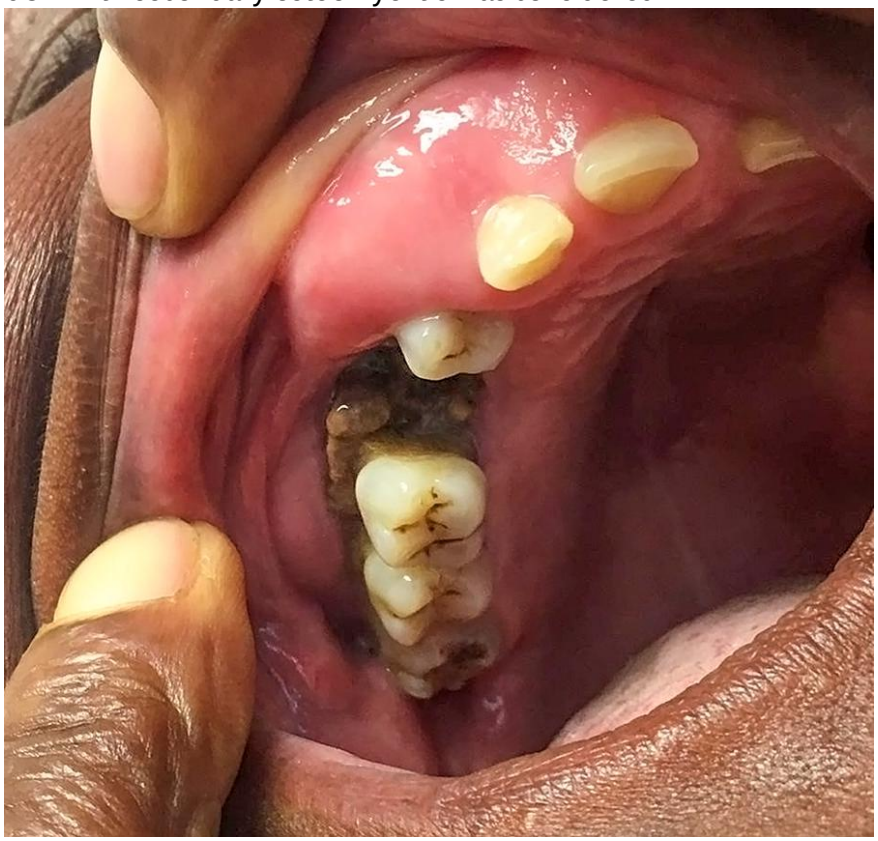

Figure 1. Case1: Intraoral photograph showing maxillary expansion and exposure of necrotic bone.

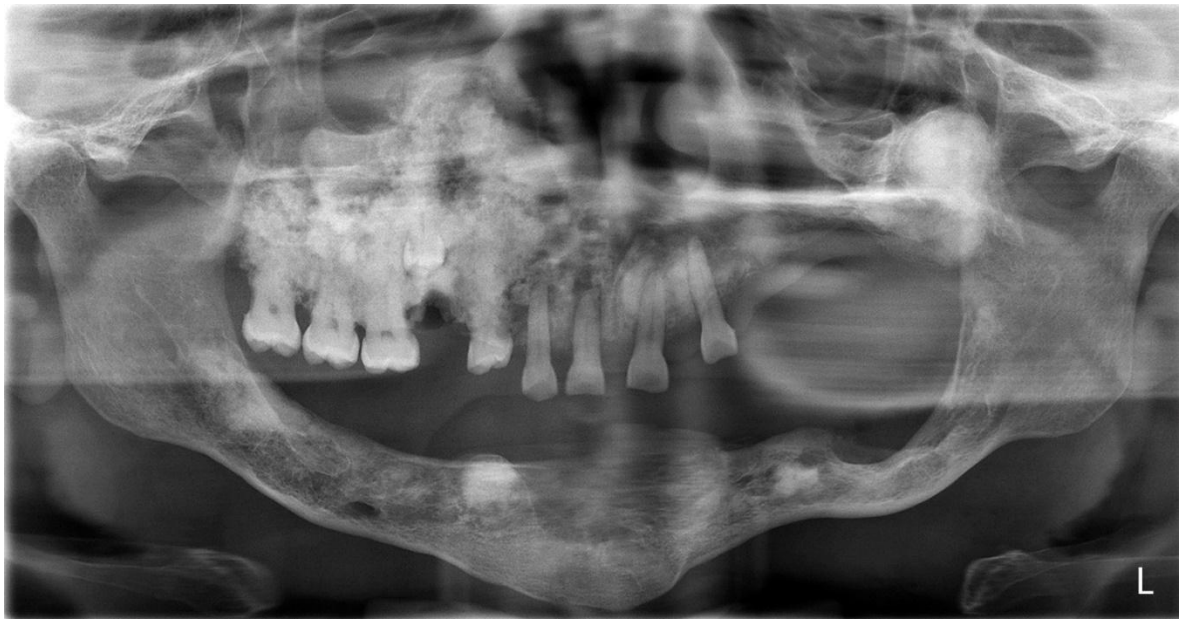

Figure 2. Case 1: Panoramic radiograph showing multifocal mixed radiolucent-radiopaque lesions.

Surgical debridement of the necrotic bone in the right maxilla was done to relieve the patient's symptoms. During the surgical procedure, the mass in the right maxilla was removed in its entirety. The tissue collected during surgery was submitted for histological examination. The specimen consisted of several bony tissue fragments with an aggregate measurement of 42 × 44 × 28 mm. Light microscopy revealed dense hypocellular sclerotic masses of calcified material (Figures 3–4) with adjacent areas of fibrocellular stroma containing globules of cementum-like material. The specimen also contained areas of normal medullary bone with evidence of acute-on-chronic osteomyelitis. The marrow spaces were involved by fibrosis and a mixed inflammatory cell infiltrate consisting predominantly of plasma cells and neutrophils. Numerous bacterial colonies morphologically in keeping with Actinomyces were identified. After considering the clinical, radiographic, and histopathological findings the lesion in the right maxilla was diagnosed as acute exacerbation of chronic osteomyelitis occurring in a background of familial florid COD. The expansive mass in the right maxilla was therefore thought to be secondary to an inflammatory stimulus. Due to a lack of previous radiographs, this hypothesis cannot be confirmed, as the expansion may have been a result of the benign COD process. The latter theory may be supported by the presence of an expansive lesion in the left maxilla in the absence of clinical or radiographic evidence of osteomyelitis.

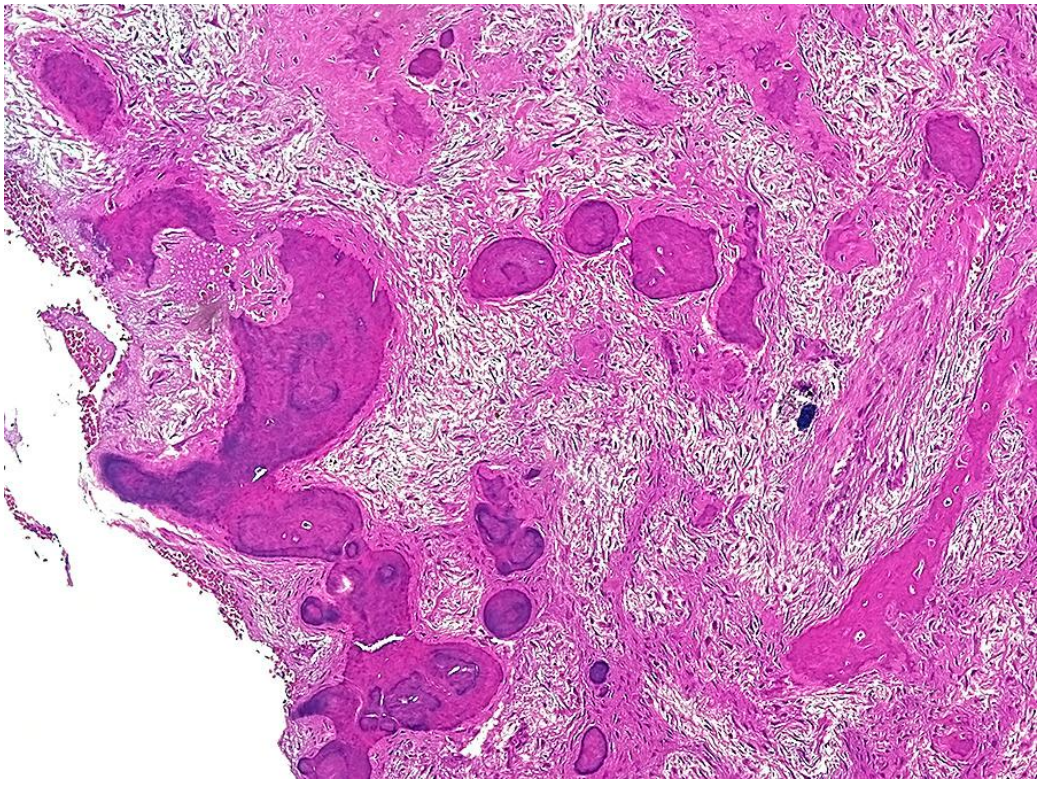

Figure 3. Case1: Light microscopy at 100x magnification showing fibrocellular stroma containing globules of cementum-like calcification and viable osseous tissue.

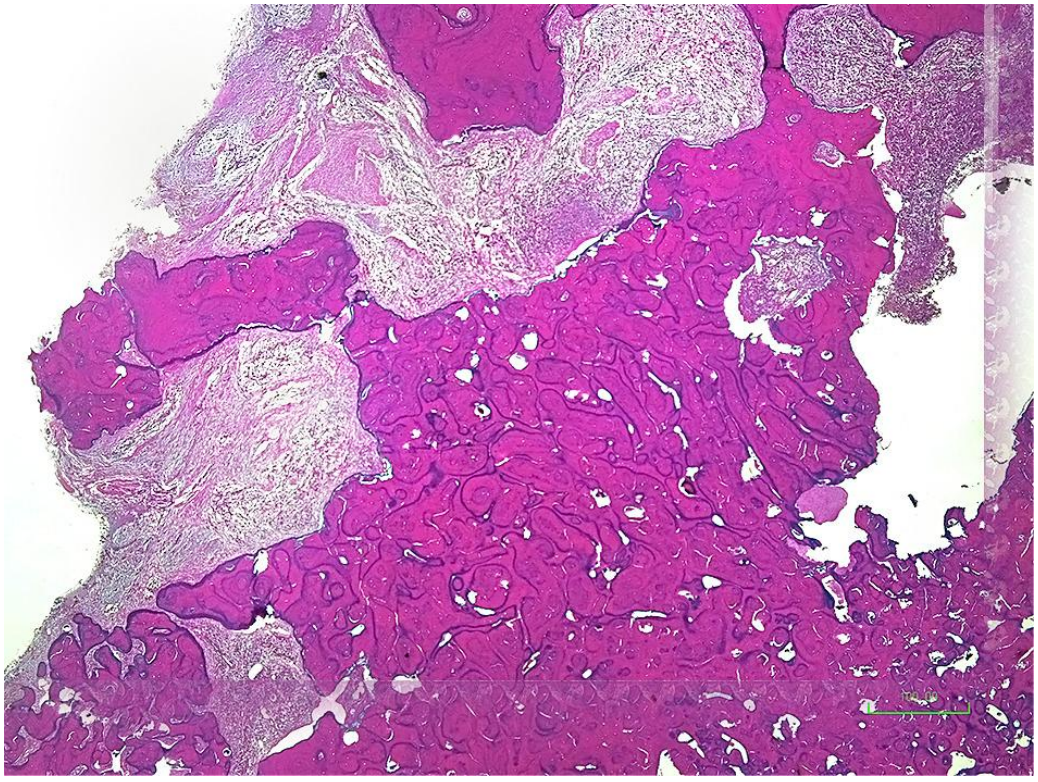

Figure 4. Case1: Light microscopy at 20x magnification showing dense hypocellular sclerotic and necrotic bone, with adjacent fibrosis and mixed inflammation in marrow spaces.

Post-operative healing was uneventful and to date, three follow-up appointments have been kept. The patient will continue to be closely monitored, with subsequent appointments for provision of removable dentures.

Case 2

The 18-year-old daughter of Case 1 presented simultaneously for a general check-up. She did not report any co-morbidities. Extraorally, her mandible appeared expansive and protrusive. On examination, the maxilla showed no evidence of expansion. On questioning, the patient could not recall when the mandibular expansion first began. Intraorally, numerous retained primary teeth were seen. A panoramic radiograph revealed multiple mixed radiolucent-radiopaque areas throughout the maxilla and mandible. Additionally, several teeth were impacted and a supernumerary molar tooth was situated coronal to the right maxillary third molar (Figure 5). The familial presentation in association with the clinical and radiographic findings was regarded as sufficient for a diagnosis of familial florid COD. In this case, the expansive mandibular mass was attributed to the benign COD process, since there were no clinical or radiographic signs of secondary osteomyelitis or an associated simple bone cyst. The patient was referred to the department of orthodontics for management of malposed dentition.

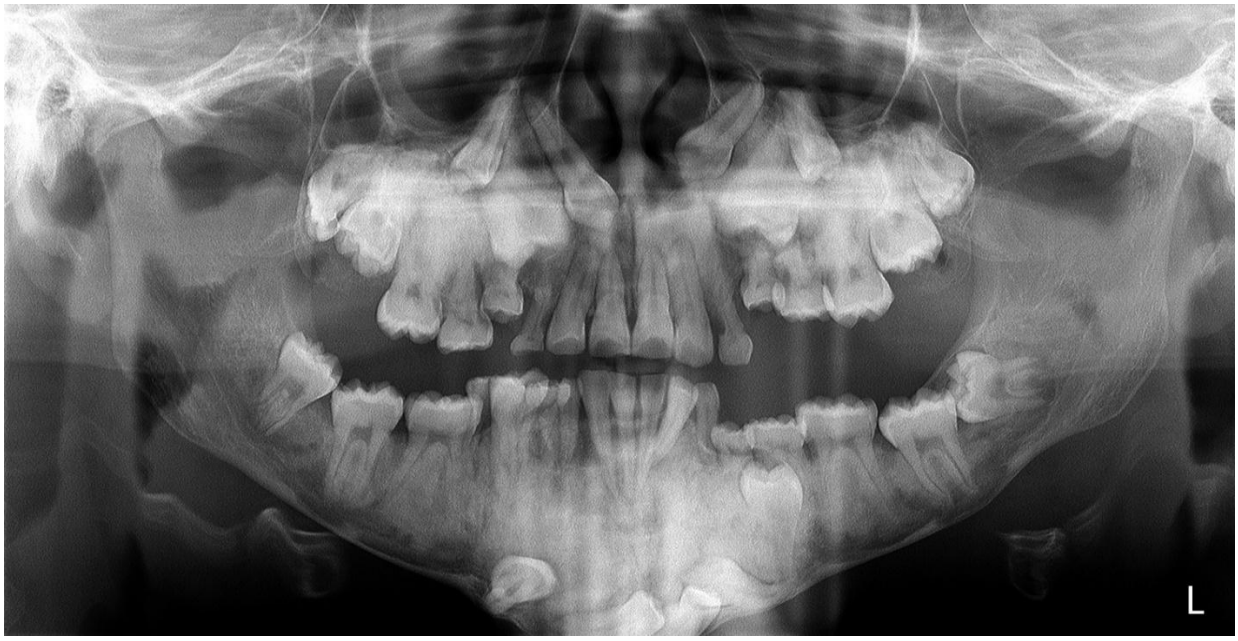

Figure 5. Case 2: Panoramic radiograph showing multifocal mixed radiolucent-radiopaque lesions and numerous impacted teeth.

Case 3

The 21-year-old grandson of Case 1, and nephew of the patient in Case 2 (Figure 6), presented with a chief complaint of pain in the lower-left side of the mandible which had been present for 6 months. The patient complained of difficulty in eating, and during the examination it was apparent that his speech was affected. The patient's medical history included epilepsy and amputation of the right lower leg in 2017 due to "bone cancer" (histology results could not be obtained). The patient did not have other co-morbidities. Extraorally facial asymmetry was evident with an expansive, protrusive mandible and associated malocclusion. In addition to the anterior mandibular jaw expansion, a large expansive swelling was visible intraorally extending from the left mandibular canine to left mandibular first molar-area (Figure 7). The teeth in this region were mobile and the patient reported removing hard tissue material from the affected site, thought to be a tooth. This tumour reportedly started in 2009 and was still enlarging at the time of presentation. The

patient could not recall when the expansion in the anterior mandible started. A large traumatic ulcer was present on the superior surface of this lesion, and the surrounding tissue was firm and fibrotic. Radiographically this left expansive mass was well-demarcated and surrounded by a cortical rim, with loss of cortication at the superior aspect. The panoramic radiograph (Figure 8) further revealed diffuse mixed radiolucent-radiopaque masses throughout all four quadrants with numerous impacted teeth. The clinical differential diagnosis included familial florid COD and FGC with secondary osteomyelitis.

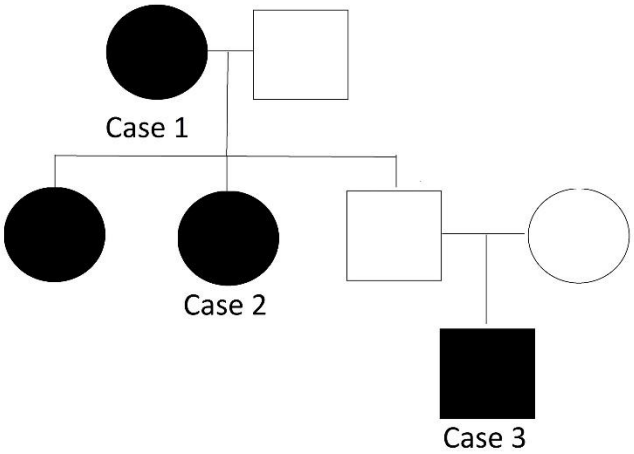

Figure 6. Inheritance pattern of presented cases. ● Affected female, ○ Unaffected female, ■ Affected male, □ Unaffected male.

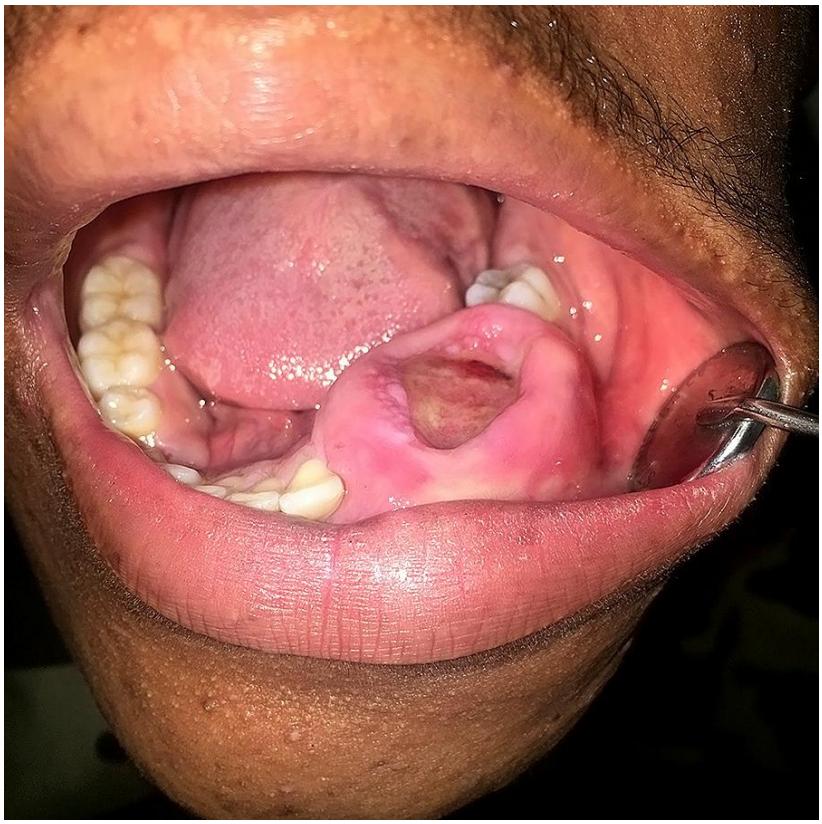

Figure 7. Case 3: Intraoral photograph showing a large expansive swelling with surface ulceration.

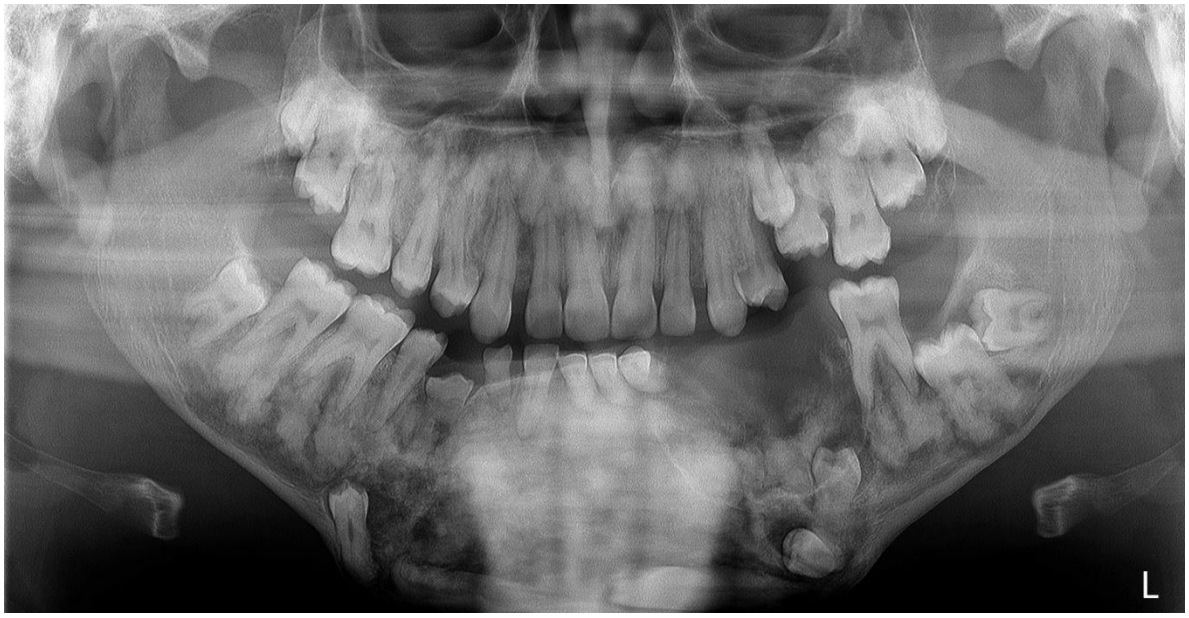

Figure 8. Case 3: Panoramic radiograph showing diffuse mixed radiolucent-radiopaque lesions and expansion in the anterior mandible. An additional expansive mass is visible in the lower left canine to first molar region

An incisional biopsy was taken from the expansive mass in the left mandibular corpus for histological assessment. The specimen consisted of three firm, tan-white soft tissue fragments with the largest fragment measuring 17 × 18 × 5 mm. Light microscopy demonstrated a benign fibro-osseous lesion surfaced by hyperplastic stratified squamous epithelium with ulceration and fibrinopurulent membrane formation. The stroma of the underlying lesion was hypercellular and fibrous, and the stromal fibroblasts showed no evidence of atypia. No mitoses were seen. There were multiple calcified basophilic spherules of cementum-like material within the fibrocellular stroma (Figures 9–10). There were no woven or lamellar bony trabeculae.

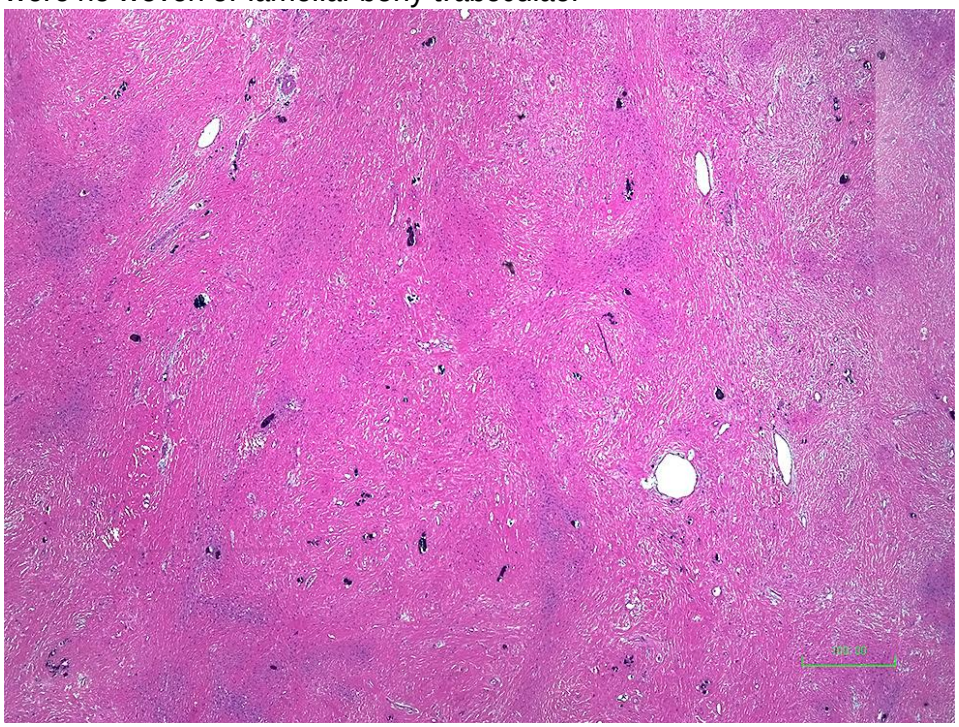
Figure 9. Case 3: Light microscopy at 20x magnification showing dense fibrocellular stroma containing scattered globules of cementum-like calcification.

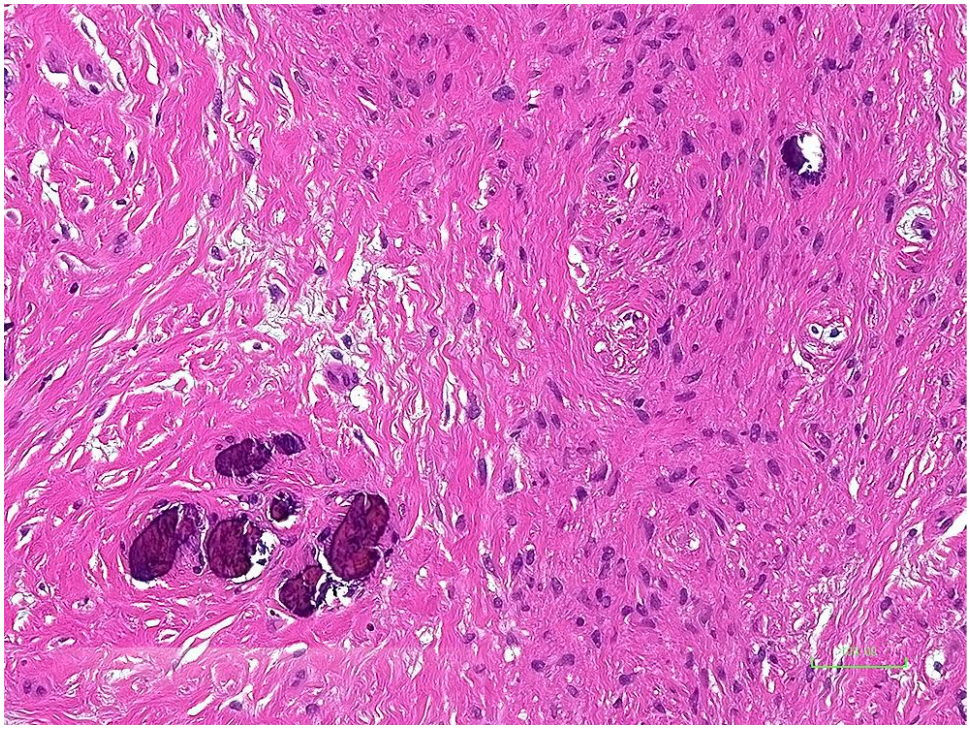

Figure 10. Case 3: Light microscopy at 200x magnification showing cementum-like calcifications surrounded by fibrocellular stroma.

After considering the clinical, radiographic, and histopathological findings, the biopsied expansive mass in the left mandibular corpus was diagnosed as an "ossifying fibromatoid lesion" occurring in a background of familial florid COD. The expansive process in the anterior mandible was attributed to the COD disease process, whereas the expansion in the left mandible was considered a separate slow-growing entity. There was no histologic evidence of osteomyelitis and the patient's pain was attributed to the traumatic ulcer. The patient did not return for follow-up treatment despite numerous telephonic attempts to contact him.

Due to the family history, clinical appearance and radiographic features of all three cases, it was evident that the jaw lesions were of a benign fibro-osseous origin with a hereditary component. Genetic testing was recommended but could not be performed due to financial constraints.

Discussion

Benign fibro-osseous lesions are a diverse group of lesions that share similar histologic features and are diagnosed in a combined assessment of clinical, radiological and microscopic features.8 The differential diagnosis for the above cases included fibro-osseous entities which may exhibit a genetic susceptibility and show extensive involvement of both jaws. Fibrous dysplasia was excluded as a possible diagnosis since there was no radiographic evidence of the classical poorly demarcated ground glass opacification of bone.

To find the best clinicopathological categorisation for the above cases, we investigated familial florid COD, hyperparathyroidism-jaw tumour syndrome (HPT-JT), gnathodiaphysial dysplasia (GDD) and FGC as potential diagnoses. The last three conditions are systemic genetic disorders that are associated with benign fibro-osseous expansive jaw lesions that

histologically resemble COF.[12] Hyperparathyroidism-jaw tumour syndrome is a genetic condition associated with hyperparathyroidism, multiple parathyroid adenomas, renal tumours and multiple ossifying fibromas.[12,13] This condition was excluded as a possible diagnosis, as the patients did not present with the associated co-morbidities and jaw lesions typically seen in hyperparathyroidism-jaw tumour syndrome. Although GDD and FGC have similar clinical features and may be genetically related, patients with GDD typically suffer from the consequences of brittle bone, i.e. numerous long bone fractures.[12,14] The aforementioned was excluded as a possible diagnosis since none of our patients had a history of long bone fractures.

Distinguishing between familial florid COD and FGC is a topic of debate and many conflicting opinions exists in the literature. Both conditions share clinical and radiographic features and have overlapping histologic findings. Some suggest that familial florid COD and FGC represent different spectrums of the same disease process.[15–18] Further research and genetic studies are needed to improve understanding and to assess if the conditions are indeed related.[8] Familial gigantiform cementoma is a rare autosomal dominant hereditary condition with high penetrance and variable expressivity. The condition often presents at a young age with mixed radiolucent-radiopaque lesions affecting multiple (often all four) quadrants of the jaws, showing considerable, diffuse and disfiguring expansion early in the disease process.[8,10] This condition was previously considered to be a variant of COD,[6,19,20] however, the propensity for progressive growth to "gigantic" proportions as the name implies, suggests a neoplastic process.[4,20,21] Some authors propose that FGC should be classified as a variant of ossifying fibroma.21It has been suggested that the term FGC should be discontinued because "cementoma" implies neoplastic transformation of root cementum, and FGC lesions are not fused to the tooth roots.[16,22,23] Several articles report cases of FGC, which are more likely to be familial florid COD since the cases do not show any signs of the uninhibited growth associated with FGC.[24–26] Based on the clinicoradiographic features and aggressive and disfiguring growth pattern associated with FGC, it was excluded as a possible diagnosis.[15,20,27–32]

A PubMed search of the English literature using the terms "familial florid osseous dysplasia" and, "familial florid COD" delivered a total of 11 published articles (Table 1). The lack of clear definitions and the use of interchangeable nomenclature has resulted in inconsistent reporting of lesions, making it difficult to estimate the true prevalence of these conditions.

Table 1. Review of familial florid COD lesions reported in the literature

Author	Reported cases	Sex	Features	Population group	Familial	Expansion	Reported diagnosis
Sedano et al [33] 1982	10	6 ♀ 4 ♂	Radiopacities in tooth-bearing areas (florid COD). Autosomal dominant in 10 family members	White (United States)	√	x	Autosomal dominant cemental dysplasia
Musella et al[34] 1989	2	2♀	Florid COD	White (United States)	√	√ (In one patient)	FFCOD
Thakkar et al[18] 1993	4	3♀ 1♂	Proband has florid COD Proband's children show periapical COD	Afro-Caribbean	√	x	Familial occurrence of periapical cemental dysplasia
Coleman et al[35] 1996	3	2♀ 1♂	Florid COD	African	√	√	FFCOD
Toffanin et al[17] 2000	6	3♀ 3 ♂	Florid COD	White (European)	√	√ (In two patients in mandibular symphysis area)	FFCOD
Hatori et al[36] 2003	2	1♀ 1♂	Florid COD	Japanese	√	N-R	FFCOD
Srivastava et al[37] 2012	2	1♀ 1 ♂	Florid COD	Indian	√	√	FFCOD
Sim et al[5] 2014	3	3♀	Florid COD	Korean	√	N-R	FFCOD
Thorawat et al[38] 2015	2	2♀	Florid COD	N-R	√	√	FFCOD
Kucukkurt et al 2016[39]	3	1♀ 2 ♂	Florid COD	N-R	√	x	FFCOD
Lv et al 2019[40]	4	1♀ 3 ♂	Florid COD	Chinese	√	√	FFCOD

√,Yes;♀,Female;♂,Male;COD,cemento-osseous dysplasia;FFCOD,Familial florid cemento-osseous dysplasia;N-R, Not reported;X,No.

Familial florid COD is inherited in an autosomal dominant fashion with variable expressivity.[5,17,18,33–40] Recently, a mutation in the anoctamin 5 (ANO5) gene was identified as the causative factor in a Chinese family.[40] The ANO5 gene was also implicated in GDD, but the mutation occurs at a different locus.[14] Familial florid COD exhibits dysplastic fibro-osseous lesions similar to the non-familial variant. In distinction, the jaw lesions seen in familial cases present with an earlier age of onset and can commonly exhibit expansion. Additionally, familial cases do not favour a specific gender or ethnic group, whereas non-familial florid COD predominantly affects middle-aged black females and East Asian populations.[8,10] The radiographic features include early radiolucent lesions with a transition to intermediate mixed radiolucent-radiopaque lesions, and eventual sclerotic radiopaque lesions often surrounded by an irregular radiolucent rim. Lesions in close proximity may coalesce to form larger sclerotic zones. There is an inclination towards bilateral and symmetrical distribution in the mandible, and there may be extensive involvement in all four quadrants. The presence of teeth is not essential for the diagnosis of florid COD, as these lesions have been observed in edentulous areas. Impactions and retained primary teeth are also common findings in familial florid COD.[17,22,35,39,41]

There may be associated bony expansion, with some patients exhibiting more than one expansive lesion.[8,10,17,22,35,37,38,40–42] The presence of expansive lesions occurring in the background of florid COD is not a new finding and has a reported prevalence of 0.35% in an African sample.[22] The expansive lesions are found most commonly in the anterior mandible followed by the posterior maxilla. Cases with progressive growth and/or expansion in otherwise typical florid COD have been termed expansive osseous dysplasia by some authors.[11,16,22,41,43] There is considerable controversy as other authors feel that all florid COD lesions do have the potential to cause expansion. It should be kept in mind that the prevalence of expansion in florid COD may be under reported due to the inability of two-dimensional radiographs to assess buccolingual expansion.

In most instances, florid COD has a distinctive clinical and radiographic profile, and histological investigations are not needed to make a diagnosis.8 Florid COD is regarded as non-neoplastic and management is therefore focused toward prevention of exposure of avascular bone to the oral cavity, which causes subsequent development of osteomyelitis. For this reason, surgical procedures (e.g. biopsy, tooth extraction and implant placement) should be avoided where possible.[8,44] There is a consensus that the expansive masses require complete surgical removal, as recontouring can result in significant regrowth.[20,28] However, the need for surgical intervention to attain improved aesthetics and function should be evaluated on a case-by-case basis, and be weighed against the risk of introducing infection in the susceptible avascular bone.

Based on the histology, the final diagnosis of the biopsied tissue in case 3 was that of familial florid COD with a concurrent "ossifying fibromatoid lesion." This association between COF and florid COD has previously been reported,[44] but some authors disagree that COF and florid COD can occur concurrently.[41] Rossbach et al[29] reported similar findings of COF occurring in the background of a benign expansive fibro-osseous process of the jaw. Moreover, the patient's right femur presented with concurrent osteosarcoma. Case 3 in this paper may show similar clinical features, but histology from the professed cancerous growth in the leg is unavailable and therefore our speculation remains unsubstantiated.

It should be noted that COD and COF are separate and independent disease entities in terms of clinical presentation and underlying pathogenesis. While these solitary expansive lesions may clinically and histologically resemble COF, the tendency of these lesions to arise in the background of familial florid COD may suggest that they are not, in fact, true COFs. The term "ossifying fibromatoid lesion" is therefore used to distinguish these lesions from true COFs.

Conclusion

We agree with the statement made by Noffke et al that "the expansion of knowledge regarding pathologic processes is not synchronised with the lethargic processes of adaptation of terminology and classification systems. Terms applied to the diagnosis and descriptions of lesions are therefore often not a reflection of their biologic behaviour."[16]

In conclusion, hereditary cases of florid COD should not be confused with a diagnosis of FGC. It is imperative to use a combination of clinical assessment, special investigations and apply stringent radiological criteria to rule out other possibilities. FGC presents with diffuse expansion in multiple quadrants early in the disease process resulting in marked facial

disfigurement. Familial florid COD, on the other hand, presents with typical florid COD lesions that may exhibit localised areas of expansion.

This study is limited by a lack of genetic testing. The patients all came from a rural community, and the language barrier led to challenges in communicating detailed pertinent clinical histories. The second reportedly affected daughter of Case 1 could not be reached.

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Notes
Patient consent
Written informed consent was obtained from all patients included in the study

Ethics Statement
This study received approval by the University of Pretoria Research Ethics Committee (334/2019) in terms of the National Health Act (Act 61 of 2003), the Code of Ethics for Research of the University of Pretoria and the National Health Research Ethics Council. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. This article does not contain any studies with human or animal subjects performed by any of the authors.

References
1. Koury ME, Regezi JA, Perrott DH, Kaban LB. "Atypical" fibro-osseous lesions: diagnostic challenges and treatment concepts. Int J Oral Maxillofac Surg 1995; 24: 162–169.
2. Speight PM, Carlos R. Maxillofacial fibro-osseous lesions. Curr Diagn Pathol 2006; 12: 1–10.
3. de Noronha Santos Netto J, Cerri JM, Miranda ÁMMA, Pires FR. Benign fibro-osseous lesions: clinicopathologic features from 143 cases diagnosed in an oral diagnosis setting. OOOO 2013; 115: 56–65.
4. MacDonald-Jankowski DS. Florid cemento-osseous dysplasia: a systematic review. Dentomaxillofac Radiol 2003; 32: 141–149.
5. Sim YC, Bakhshalian N, Lee J-H, Ahn K-M. Familial florid cemento-osseous dysplasia in mother and her identical twins: a report with review of the literatures. Oral Surgery 2014; 7: 239–244.
6. Waldron CA. Fibro-Osseous lesions of the jaws. Journal of Oral and Maxillofacial Surgery 1985; 43: 249–262.
7. Gupta A, Nayak S, Das B, Das S. Florid cemento-osseous dysplasia. J Oral Maxillofac Pathol 2013; 17: 150.
8. Neville BW, Damm DD, Allen CM, Chi AC. Oral and maxillofacial pathology. 4th ED. Elsevier Inc. 2016: 99–106p.
9. MacDonald-Jankowski DS. Focal cemento-osseous dysplasia: a systematic review. Dentomaxillofac Radiol 2008; 37: 350–360.

10. El-Naggar A. K, Chan J. K. C, Grandis J. R, Takata T, Slootweg P. J et al. eds. WHO Classification of Head and Neck Tumours. In: 4th. Lyon: International Agency for Research on Cancer; 2017. pp. 253–255.
11. MacDonald DS, lesions Mfibro-osseous. Maxillofacial fibro-osseous lesions. Clin Radiol 2015; 70: 25–36.
12. El-Mofty SK. Fibro-Osseous lesions of the craniofacial skeleton: an update. Head Neck Pathol 2014; 8: 432–444.
13. du Preez H, Adams A, Richards P, Whitley S. Hyperparathyroidism jaw tumour syndrome: a pictoral review. Insights Imaging 2016; 7: 793–800.
14. Duong HA, Le KT, Soulema AL, Yueh RH, Scheuner MT, Holick MF, et al. Gnathodiaphyseal dysplasia: report of a family with a novel mutation of the ANO5 gene. Oral Surg Oral Med Oral Pathol Oral Radiol 2016; 121: e123–128.
15. Cannon JS, Keller EE, Dahlin DC. Gigantiform cementoma: report of two cases (mother and son. J Oral Surg 1980; 38: 65–70.
16. Noffke CE, Raubenheimer EJ, MacDonald D. Fibro-Osseous disease: harmonizing terminology with biology. Oral Surg Oral Med Oral Pathol Oral Radiol 2012; 114: 388–392.
17. Toffanin A, Benetti R, Manconi R. Familial florid cemento-osseous dysplasia: a case report. Journal of Oral and Maxillofacial Surgery 2000; 58: 1440–1446.
18. Thakkar NS, Horner K, Sloan P. Familial occurrence of periapical cemental dysplasia. Virchows Arch A Pathol Anat Histopathol 1993; 423: 233–236.
19. Kramer I, Pindborg J, Shear M. Histologic typing of odontogenic tumors. In: ed.World Health Organization international classification of tumors. 2nd. London: Springer-Verlag; 1992.
20. Abdelsayed RA, Eversole LR, Singh BS, Scarbrough FE. Gigantiform cementoma: clinicopathologic presentation of 3 cases. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology 2001; 91: 438–444.
21. Eversole R, Su L, ElMofty S. Benign fibro-osseous lesions of the craniofacial complex a review. Head Neck Pathol 2008; 2: 177–202.
22. Noffke CE, Raubenheimer EJ. Expansive osseous dysplasia: report of 9 lesions in an African population sample and a review of the literature. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology 2011; 111: e35–41.
23. Noffke CEE, Ngwenya SP, Nzima N, Raubenheimer EJ, Rakgwale NB. Gigantiform cementoma in a child. Dentomaxillofac Radiol 2012; 41: 264–266.
24. Oikarinen K, Altonen M, Happonen R-P. Gigantiform cementoma affecting a Caucasian family. British Journal of Oral and Maxillofacial Surgery 1991; 29: 194–197.
25. Moshref M, Khojasteh A, Kazemi B, Roudsari MV, Varshowsaz M, Eslami B. Autosomal dominant gigantiform cementoma associated with bone fractures. Am J Med Genet A 2008; 146A: 644–648.
26. Şakar O, Aren G, Mumcu Z, Ünalan F, Aksakallı N, Tolgay CG. Familial gigantiform cementoma with Ehlers - Danlos syndrome: A report of 2 cases. J Adv Prosthodont 2015; 7: 178–182.
27. Young SK, Markowitz NR, Sullivan S, Seale TW, Hirschi R. Familial gigantiform cementoma: classification and presentation of a large pedigree. Oral Surgery, Oral Medicine, Oral Pathology 1989; 68: 740–747.
28. Finical SJ, Kane WJ, Clay RP, Bite U. Familial Gigantiform Cementoma. Plast Reconstr Surg 1999; 103: 949–954.

29. Rossbach H-C, Letson D, Lacson A, Ruas E, Salazar P. Familial gigantiform cementoma with brittle bone disease, pathologic fractures, and osteosarcoma: a possible explanation of an ancient mystery. Pediatr Blood Cancer 2005; 44: 390–396.
30. Shah S, Huh K-H, Yi W-J, Heo M-S, Lee S-S, Choi S-C. Follow-Up CT findings of recurrent familial gigantiform cementoma of a female child. Skeletal Radiol 2012; 41: 341–346.
31. Wang H-W, Ma C-Y, Qin X-J, Zhang C-P. Management strategy in patient with familial gigantiform cementoma. Medicine 2017; 96: e9138.
32. Wang HW, Yu M, Qin XJ, Zhang CP. Familial gigantiform cementoma: distinctive clinical features of a large Chinese pedigree. British Journal of Oral and Maxillofacial Surgery 2015; 53: 83–85.
33. Sedano HO, Kuba R, Gorlin RJ. Autosomal dominant cemental dysplasia. Oral Surgery, Oral Medicine, Oral Pathology 1982; 54: 642–646.
34. Musella AE, Slater LJ. Familial florid osseous dysplasia: a case report. Journal of Oral and Maxillofacial Surgery 1989; 47: 636–640.
35. Coleman H, Altini M, Kieser J, Nissenbaum M. Familial florid cemento - osseousdysplasia - a case report and review of the literature. J Dent Ass South Africa 1996; 51: 766–770.
36. Hatori M, Ito I, Tachikawa T, Nagumo M. Familial Florid Cemento-osseous dysplasia. Asian Journal of Oral and Maxillofacial Surgery 2003; 15: 135–137.
37. Srivastava A, Agarwal R, Soni R, Sachan A, Shivakumar GC, Chaturvedi TP. Case Report Cemento-Osseous Dysplasia: A Rare Manifestation in an Indian Family. Case Rep Dent 2012; 2012: 1–5.
38. Thorawat A, Kalkur C, Naikmasur VG, Tarakji B. Familial florid Cemento-osseous dysplasia - case report and review of literature. Clin Case Rep 2015; 3: 1034–1037.
39. Kucukkurt S, Rzayev S, Baris E, Atac MS. Familial florid osseous dysplasia: a report with review of the literature. BMJ Case Rep 2016; 1-4.
40. Lv M, You G, Wang J, Fu Q, Gupta A, Li J, et al. Identification of a novel ANO5 missense mutation in a Chinese family with familial florid osseous dysplasia. J Hum Genet 2019; 64: 599–607.
41. Raubenheimer EJ, Noffke CE, Boy SC. Osseous dysplasia with gross jaw expansion: a review of 18 lesions. Head Neck Pathol 2016; 10: 437–443.
42. Yonetsu K, Nakamura T. Ct of calcifying jaw bone diseases. American Journal of Roentgenology 2001; 177: 937–943.
43. Bulut EU, Acikgoz A, Ozan B, Zengin AZ, Gunhan O. Expansive focal Cemento-Osseous dysplasia. J Contemp Dent Pract 2012; 13: 115–118.
44. Gerlach RC, Dixon DR, Goksel T, Castle JT, Henry WA. Case presentation of florid cemento-osseous dysplasia with concomitant cemento-ossifying fibroma discovered during implant explantation. Oral Surg Oral Med Oral Pathol Oral Radiol 2013; 115: e44–e52.