Frontiers in Dentistry

Central Odontogenic Fibroma Accompanied by a Central Giant Cell Granuloma-Like Lesion: Report of a Case and Review of Literature

Monir Moradzadeh Khiavi[1], Abbas Karimi[2], Hassan Mirmohammad Sadeghi[3], Samira Derakhshan[1], Seyed Mobin Tafreshi[4], Samar Jalali[4*]

1. Department of Oral and Maxillofacial Pathology, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran
2. Department of Oral and Maxillofacial Surgery, School of Dentistry; Craniomaxillofacial Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
3. Department of Oral & Maxillofacial Surgery, School of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran
4. Private Practice, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran

Article Info

Article type:
Case Report

Article History:
Received: 29 Feb 2021
Accepted: 13 Nov 2021
Published: 28 Dec 2021

**** Corresponding author:***
Private Practice, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran

Email: Samarjalali96@gmail.com

A B S T R A C T

Central giant cell granuloma (CGCG) is a benign non-neoplastic intraosseous lesion mainly found in the anterior mandible. It is characterized by multinucleated giant cells, representing osteoclasts or macrophages. Central odontogenic fibroma (COF) is an uncommon benign lesion of the jaws. It originates from the odontogenic ectomesenchyme. In rare cases, COF may accompany a CGCG. To date, 49 cases of COF accompanied by CGCG-like lesions have been reported in the literature. In this paper, we present another case of COF-CGCG in a 46-year-old female. The lesion was located in the posterior mandible. Excisional biopsy was carried out, and histopathological analysis revealed multinucleated giant cells with numerous strands of odontogenic epithelium. A literature review of previously reported cases was also performed.

Keywords: Granuloma, Giant Cell; Fibroma; Odontogenic Tumors

➢ Cite this article as: Moradzadeh Khiavi M, Karimi A, Sadeghi HMM, Derakhshan S, Tafreshi SM, Jalali S. Central Odontogenic Fibroma Accompanied by a Central Giant Cell Granuloma-Like Lesion: Report of a Case and Review of Literature. *Front Dent.* 2021;18:44.

INTRODUCTION

Central giant cell granuloma (CGCG) is a benign non-neoplastic intraosseous lesion found mainly in the anterior mandible, and often crossing the midline [1]. Although there is controversy about the nature of this lesion, some theories describe it as a reactive lesion, a developmental anomaly, or a benign neoplasm. The World Health Organization considers CGCG as a bone-related lesion [2]. Extragnathic CGCG can occur mainly in the craniofacial region and small long bones of the hands and feet [3]. Most of the reported cases have occurred in patients between 10 to 25 years, and it is more common in females than males with a 2:1 ratio [4]. Based on the radiographic features, CGCG can be divided into non-aggressive and aggressive types with non-aggressive lesions making up most of the cases [1]. They usually present as an asymptomatic, painless, slow-growing swelling in the jaw, and can often cause tooth displacement [5]. Histopathologically, CGCG is composed of giant cells that are believed to represent osteoclasts while some others suggest that they might be macrophages. These lesions are similar to brown tumors of hyperthyroidism and giant cell

lesions in cherubism and Noonan syndrome and neurofibromatosis type 1 [4,6].

Radiographically, CGCG is a unilocular or multilocular well-defined radiolucency. Large lesions may cause tooth displacement, root resorption, or cortical perforation [5]. These lesions are often treated by curettage or en bloc resection [7]. Central odontogenic fibroma (COF) is an uncommon benign lesion of the jaws. It originates from the odontogenic ectomesenchyme. The maxilla and mandible are affected almost equally. Most maxillary lesions tend to occur in the anterior region; however, mandibular lesions are mostly located posterior to the first molar [8]. An unerupted tooth is involved in one-third of the lesions [8]. COF lesions that are associated with unerupted teeth are believed to originate from the dental follicle; while, those that are not associated with an unerupted tooth arise from the periodontal ligament [7]. The occurrence of COF with CGCG is quite rare. Such a case was first reported in 1985 by Wangerin and Harms [9]. Over the years, more reports of this lesion were documented. In addition to the published cases, several cases have been presented at professional meetings. In 1993, Fowler et al. [10] reported an associated giant cell reaction in 3 out of 24 cases of COF. Kruse-Lösler et al. [11] presented a case diagnosed with COF accompanied by CGCG in the 2006 Meeting of the Western Society of Teachers of Oral Pathology. In 2008, Hassan et al. [12] presented 7 cases of the hybrid lesion at the 62nd Annual Meeting of the American Academy of Oral and Maxillofacial Pathology. Two cases were presented at the 71st Annual Meeting of the American Academy of Oral and Maxillofacial Pathology in 2017 [13, 14]. To date, 49 cases of COF with CGCG have been reported, considering the national conferences and reports (Table 1). Allen et al. [15] presented three cases, all in women and in the mandibular region, and suggested that “this pathological process does not represent a "collision lesion" but instead, is a unique presentation of a central odontogenic fibroma” [15]. Herein, we report a case of COF with CGCG in a 46-year-old female and also perform a literature review of the previous cases.

Table 1 shows all the reported cases of this hybrid lesion.

CASE REPORT

A 46-year-old female was referred to an oral surgeon for evaluation of a radiolucent lesion in her left lower jaw which was accidentally found on radiographic examination by her dentist. On radiographic examination, the lesion was a well-defined radiolucency located between the premolar and molar area (i.e., teeth #19-20) (Fig.1).

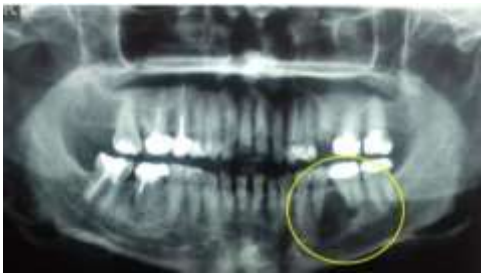

Fig. 1. Panoramic radiograph showing a radiolucent lesion in the left posterior mandible, between second premolar and first molar

The patient did not report any pain or numbness in the area. However, expansion and perforation of the buccal cortical plate were noted on cone-beam computed tomography scan (Fig. 2A and 2B).

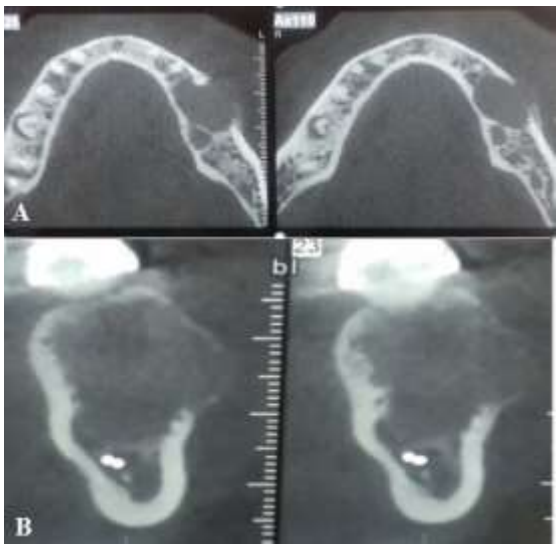

Fig. 2. Cone-beam computed tomography scan demonstrating a unilocular radiolucency with buccal expansion and perforation: (A) axial and (B) sagittal views

Table 1. Reported cases of hybrid central odontogenic fibroma-central giant cell granuloma in the literature

	Author	Age (y)	Sex	Location	Year	Associated features	Radiographic findings	Treatment	Recurrence
1	Wangerin & Harms [9]	7	N/A	L Mandible (M)	1985	Unerupted molars	MRL	N/A	Yes, after one year of FU
2	Allen et al, [15]	66	F	R Mandible (PM-M)	1992	RCT tooth	MRL	Curettage	None after 6 months of FU
3	Allen et al, [15]	14	F	L Mandible (PM-M)	1992	Vital teeth, no expansion	URL, 3.5cm	Curettage	None after 48 months of FU
4	Allen et al, [15]	30	F	L Mandible (PM-M)	1992	Orthodontic treatment, some expansion	MRL 1.5×2cm	Curettage, curettage of recurrent lesion	Yes, after 14months of FU
5-7	Fowler et al, [10] (3 cases)	N/A	N/A	N/A	1993	N/A	N/A	N/A	N/A
8	Odell et al, [16]	5	F	Anterior maxilla	1997	Buccal expansion	N/A	Curettage	None
9	Odell et al, [16]	11	M	Posterior maxilla	1997	Buccal expansion	URL	Curettage, conservative excision of recurrent lesion	Yes, after 36 months
10	Odell et al, [16]	20	F	Mandible (PM-M)	1997	N/A	URL 1.5×1cm	Curettage	None
11	Odell et al, [16]	21	F	Posterior Mandible	1997	Buccal expansion	URL, 3×2 cm	Curettage	None
12	Odell et al, [16]	22	F	Mandible (PM-M)	1997	Buccal expansion, cortical perforation	N/A	Curettage and extraction of involved teeth	None
13	Odell et al, [16]	39	F	Mandible (PM-M)	1997	Expansion, mobile teeth	N/A	Curettage	None
14	Odell et al, [16]	43	F	Mandible	1997	N/A	N/A	Curettage, curettage of recurrent lesion	Yes, after 36 months

15	Odell et al, [16]	50	F	Mandible PM	1997	N/A	URL	Curettage	None
16	Taylor et al, [19]	17	F	R Mandible (C-PM)	1999	Buccal expansion	MRL 2.5 × 2cm	Curettage	None after 72 months of FU
17	Kruse-Losler et al, [11]	22	F	R Mandible (LI-M)	2006	Lingual & inferior expansion	Mostly URL with scalloped edge, with hint of MRL in post. area	Surgical excision	None after 24 months of FU
18-24	Hassan et al, [12]	Average 49	5 M 2 F	Mandible	2008	N/A	N/A	N/A	Yes, 3 cases
25	Younis et al, [25]	57	F	R Mandible (PM-M)	2008	Buccal expansion	URL 2×2.5cm	Curettage	None after 18 months of FU
26	Tosios et al, [23]	18	M	Mandible (PM-M)	2008	N/A	RL	Surgical excision	Lost to FU
27	Tosios et al, [23]	20	F	Mandible (PM-M)	2008	N/A	RL	Surgical excision	None after 117 months of FU
28	Tosios et al, [23]	N/A	N/A	Mandible (PM-M)	2008	N/A	RL	Surgical excision	None after 28 months FU
29	Tosios et al, [23]	N/A	N/A	Mandible (PM-M)	2008	N/A	RL	Surgical excision	None after 43 months of FU
30	Tosios et al, [23]	N/A	N/A	Mandible (PM-M)	2008	N/A	RL	Surgical excision	None after 76 months of FU
31	Tosios et al, [23]	N/A	N/A	Mandible (PM-M)	2008	N/A	RL	Surgical excision	None after 39 months of FU
32	Tosios et al, [23]	N/A	N/A	Mandible (PM-M)	2008	N/A	RL	Surgical excision	Lost to FU
33	Marina de Deus Moura de et al, [17]	24	F	Mandible (R M-L M)	2008	Cortical Expansion	N/A	Curettage	None after 8 months of FU
34	Mosqueda-Taylor et al, [21]	14	M	L Mandible (M)	2011	Buccal & lingual swelling	URL 4×3.2cm	Surgical excision	None after 16 months of FU
35	Mosqueda-Taylor et al, [21]	14	M	L Mandible (PM-M)	2011	Buccal expansion	MRL 4.5×3cm	Surgical excision	None after 24 months of FU
36	Eversole [24]	42	F	Mandible, body	2011	N/A	RL	Enucleation/ Curettage	None

37	Eversole [24]	27	F	Mandible, ramus	2011	Impaction	RL	Enucleation/ Curettage	None
38	Bologna-Molina et al, [27]	14	M	L Mandible (PM-M)	2011	Asymptomatic	Panoramic: URL in the body of the mandible, CT: MRL vestibular cortical expansion	Curettage with milling of the bone walls	None after 2 years of FU
39	Castillo et al, [20]	14	M	Mandible (M)	2011	Expansion and tenderness	URL	Curettage	None
40	Damm [18]	75	F	Ant Mandible	2013	N/A	URL	Curettage	None
41	Eliot & Kessler [28]	22	F	R Mandible (PM-M)	2014	Expansion & swelling	MRL	Surgical excision	None
42	Schultz & Rosebush [14]	12	F	Ant Mandible	2017	Asymptomatic	RL	N/A	N/A
43	Leite et al, [13]	42	F	L Mandible (M)	2017	Edentulous area		Surgical excision	None after12 months of FU
44	Upadhyaya et al, [7]	10	M	Ant Mandible (C-I)	2018	Buccal and lingual expansion, impaction	URL 1.9×1.8cm	Curettage	None after 72 months of FU
45	Upadhyaya et al, [7]	63	F	L Mandible (M)	2018	Buccal expansion	URL 1.7×1cm	N/A	Awaiting treatment
46	Upadhyaya et al, [7]	62	M	R Mandible (PM)	2018	Asymptomatic	URL	Curettage	None after 12 months of FU
47	Vijintanawan et al, [26]	27	M	L Mandible (PM)	2019	Asymptomatic	URL	Curettage	None after 6 months of FU
48	Flores-Hidalgo et al, [22]	65	F	L Mandible (PM)	2019	Paresthesia	MRL	Excisional biopsy	Yes, after 9 months
49	Ramadan & Essawy [29]	33	F	L Mandible (PM-M)	2020	Buccal expansion	URL	Curettage	None after 12 months of FU
50	Our case	46	F	L Mandible (PM-M)	2020	Buccal expansion and perforation	URL	Excisional biopsy	None after 25 months of FU

N/A: not available; Ant: anterior; R: Right, L: Left, RL: Radiolucent, URL: Unilocular radiolucency, MRL: Multilocular radiolucency, PM: Premolar, M: Molar, FU: Follow-up

The greatest diameter of the lesion was 1 cm. The differential diagnosis included CGCG and aneurysmal bone cyst. An excisional biopsy was performed. Microscopic examination revealed hypercellular connective tissue and plump spindle-shaped cells in a hemorrhagic background admixed with numerous multinucleated giant cells. Also, nests and strands of bland odontogenic epithelium were evident (Fig. 3).

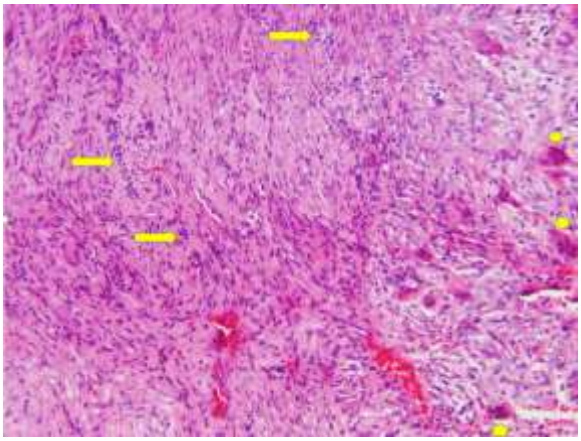

Fig. 3. Nests of odontogenic epithelium (arrows) and multinucleated giant cells (arrowheads) with a low magnification (x20) showing the two lesions relative to each other

The results of immunohistochemical staining with pan-cytokeratin and CD68 confirmed the odontogenic epithelium and multinucleated giant cells (Fig. 4A and 4B). According to the histopathological features and the results of immunohistochemical assessment, the diagnosis of COF with CGCG-like lesion was made.

It should be mentioned that all biochemical and hematological parameters of the patient including serum calcium, phosphorous, and alkaline phosphatase were within the normal range. The patient was periodically followed-up for 2 years, and no recurrence occurred during this time period.

DISCUSSION

Hybrid COF-CGCG is a rare condition, which was first reported by Wangerin and Harms [9] in 1985. Although they introduced the case as a rare combination of two lesions, ameloblastic

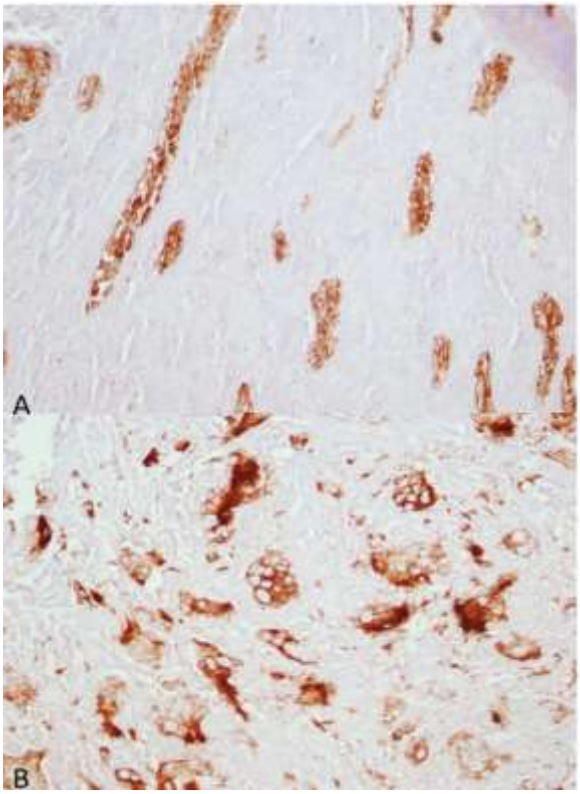

Fig. 4. Immunoreactivity of odontogenic epithelium for pan-cytokeratin (A, x40) and giant cells for CD68 (B, x40)

fibroma and CGCG, they concluded that the primary neoplastic COF induced the secondary reactive CGCG. Most of the previously reported cases were located in the mandible (mostly in the posterior section) except for two lesions which were located in the maxilla (one in the anterior and the other in the posterior maxilla) [16].

The lesions were variable in size and rarely crossed the midline [3,17]. The age of patients has been widely variable ranging from 5 to 75 years, with a mean age of 32.5 years [16,18]. It was more common in women, with a 1.4: female-to-male ratio. Of all cases, only two were associated with pain and tenderness [19-21]. Although the clinical features often include painless swelling and buccal cortical expansion, some documented cases have reported buccal perforation [16,22,23]. According to three reports, this hybrid lesion can cause tooth displacement [17,20,24]. Due to such aggressive behavior, careful follow-up is of utmost importance [22]. Of 48 documented cases, only five showed recurrence [12,15,16].

Sufficient data are not available to determine the frequency of COF-CGCG. Younis et al. [25] stated that this hybrid lesion is associated with some reactive stimuli such as orthodontic treatment, tooth impaction, root canal therapy, and history of extraction [25]. Tosios et al. [23] reported a case that occurred in a patient with cherubism. Radiographically, the hybrid COF with CGCG can be presented as either a unilocular or a multilocular radiolucency with sharp borders. Unilocular radiolucent lesions outnumber multilocular ones with a 2.4:1 ratio. Odell et al. [16] reported a case in the maxilla that extended to the antrum. The previous cases of COF-CGCG were treated by curettage (18 cases) or surgical excision (14 cases). Curettage has shown 33% recurrence rate. Recurrence occurred in seven patients [12,15,16,22]. All the recurrent lesions occurred in patients that were initially treated by curettage except for one case that was treated by surgical excision [22]. The histopathology of six recurrent lesions was similar to that of primary lesions, containing both COF and CGCG components. One recurrent lesion consisted of CGCG components only [12].

The exact pathogenesis of the hybrid CGCG-COF is still unknown. Allen et al. [15] described this hybrid lesion as a unique presentation of COF. Odell et al. [16] postulated that clinical features such as gender, age, and site of occurrence were more suggestive of CGCG. In general, three theories have been proposed regarding the nature of this lesion [25]. The first theory describes this lesion as a "collision tumor", which is characterized by synchronized occurrence of both COF and CGCG. Despite the unlikeliness of this theory due to the rare nature of COF and CGCG, Vijintanwan et al. [26] described their case as a collision tumor.

The second theory is about a primary CGCG which produces some growth factors and chemokines that result in formation of COF [7]. The third theory proposes that the primary lesion is COF, in which trauma or other stimuli induce a giant cell reaction. Our case was reported in a middle-aged woman, which is similar to some previously reported cases [12, 13,16,24]. The clinical and radiographic features showed no significant difference compared with other documented cases.

CONCLUSION

In this report, we added one more case to the documented cases of hybrid COF-CGCG, bringing the total to 50 cases. The recurrence rate is higher in this lesion compared with COF, indicating that the CGCG component is mainly responsible for the recurrence. Hybrid COF with CGCG-like lesion is usually treated by curettage or excision of the lesion. Due to the possibility of recurrence, close follow-up is important. The nature of this lesion is still unknown, and more studies should be carried out in order to find the exact origin and pathogenesis of this lesion.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Hosur MB, Puranik RS, Vanaki SS, Puranik SR, Ingaleshwar PS. Clinicopathological profile of central giant cell granulomas: An institutional experience and study of immunohistochemistry expression of p63 in central giant cell granuloma. J Oral Maxillofacial Pathol. 2018 May;22(2):173-9.
2. Jadu F, Pharoah M, Lee L, Baker G, Allidina A. Central giant cell granuloma of the mandibular condyle: a case report and review of the literature. Dentomaxillofac Rad 2011 Jan;40(1):60-4.
3. Kruse-Losler B, Diallo R, Gaertner C, Mischke KL, Joos U, Kleinheinz J. Central giant cell granuloma of the jaws: a clinical, radiologic, and histopathologic study of 26 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006 Mar;101(3):346-54.
4. de Lange J, van den Akker HP, van den Berg H. Central giant cell granuloma of the jaw: a review of the literature with emphasis on therapy options. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007 Nov;104(5):603-15.
5. Abdelkarim AZ, el Sadat SMA, Chmieliauskaite M, Syed AZ. Radiographic diagnosis of a central giant cell granuloma using advanced imaging: cone beam computed tomography. Cureus 2018 Jun;10(6): e2735.
6. de Lange J, van Maarle MC, van den Akker HP, Redeker EJ. DNA analysis of the SH3BP2 gene in patients with aggressive central giant cell granuloma. Br J Oral Maxillofac Surg. 2007 Sep;45(6):499-500.
7. Upadhyaya JD, Cohen DM, Islam MN, Bhattacharyya I. Hybrid central odontogenic fibroma

with giant cell granuloma like lesion: a report of three additional cases and review of the literature. Head and Neck Pathol. 2018;12(2):166-74.
8. Neville BW, Damm DD, Allen CM, Chi AC. Oral and maxillofacial pathology. 4th ed. St. Louis: Elsevier; 2016:676.
9. Wangerin K, Harms D. Seltene Variationen des ameloblastischen Fibroms. Dtsch Z Mund Kiefer Gesichtschir. May-Jun 1985;9(3):227-31.
10. Fowler C, Tomich C, Brannon R, Houston G. Central odontogenic fibroma: clinicopathologic features of 24 cases and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1993;76:587.
11. Kruse-Lösler B, Diallo R, Gaertner C, Mischke KL, Joos U, Kleinheinz J. Central giant cell granuloma of the jaws: a clinical, radiologic, and histopathologic study of 26 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006 Mar;101(3):346-54.
12. Hassan S, Reich R, Freedman P, editors. Central odontogenic fibroma with associated central giant cell granuloma (Collision tumor?): report of 7 cases. 62nd Annual Meeting, American Academy of Oral and Maxillofacial Pathology San Francisca; 2008.
13. Leite T, Mendes E, Abrahao A, Andrade B, Canedo N, Agostini M, et al. Central odontogenic fibroma: report of three new cases from Brazil. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2017 Sep;124(3):e229-30.
14. Schultz K, Rosebush M, editors. Clinical pathologic conference case 3. Annual Meeting of the American Academy of Oral and Maxillofacial Pathology Newport, Rhode Island; 2017.
15. Allen CM, Hammond HL, Stimson PG. Central odontogenic fibroma, WHO∗ type: a report of three cases with an unusual associated giant cell reaction. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1992 Jan;73(1):62-6.
16. Odell E, Lombardi T, Barrett A, Morgan P, Speight P. Hybrid central giant cell granuloma and central odontogenic fibroma-like lesions of the jaws. Histopathology 1997 Feb;30(2):165-71.
17. Marina de Deus Moura de L, de Aquino Xavier FC, Vanti LA, de Lima PS, de Sousa SC. Hybrid central giant cell granuloma and central odontogenic fibroma-like lesion of the mandible. Otolaryngol Head Neck 2008 Dec;139(6):867-8.
18. Damm D. Interradicular radiolucency. Hybrid giant cell granuloma and odontogenic fibroma. Gen Dent. 2013 May-Jun;61(3):77-8.
19. Taylor AM, Flores VB, Franco MAD. Combined central odontogenic fibroma and giant cell granuloma-like lesion of the mandible: report of a case and review of the literature. J Oral and Maxillofac Surg. 1999 Oct;57(10):1258-62.
20. Castillo GC, Reyes RL, Mosqueda Taylor A. Lesión mandibular inusual de fibroma odontogénico central combinado con granuloma central de células gigantes mandibular. Revista Odontológica Mexicana. 2011;15(2):126-31.
21. Mosqueda-Taylor A, Martínez-Mata G, Carlos-Bregni R, Vargas PA, Toral-Rizo V, Cano-Valdéz AM, et al. Central odontogenic fibroma: new findings and report of a multicentric collaborative study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2011 Sep;112(3):349-58.
22. Flores-Hidalgo A, Biggerstaff T, Murrah V. Hybrid central odontogenic fibroma and central giant cell granuloma lesion–A case report of an aggressive and recurrent lesion. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2019 Nov;31(6):432-4.
23. Tosios KI, Gopalakrishnan R, Koutlas IG. So-called hybrid central odontogenic fibroma/central giant cell lesion of the jaws. A report on seven additional cases, including an example in a patient with cherubism, and hypotheses on the pathogenesis. Head Neck Pathol 2008 Dec;2(4):333-8.
24. Eversole LR. Odontogenic fibroma, including amyloid and ossifying variants. Head Neck Pathol 2011 Dec;5(4):335-43.
25. Younis RH, Scheper MA, Lindquist C, Levy B. Hybrid central odontogenic fibroma with giant cell granuloma-like component: case report and review of literature. Head Neck Pathol 2008 Sep;2(3):222-6.
26. Vijintanawan S, Chettri K, Aittiwarapoj A, Wongsirichat N. Hybrid central odontogenic fibroma with central giant cell granuloma like lesion; A case report and review of the literature. Siriraj Med J 2019 Sep;71(5):426-31.
27. Bologna-Molina R, Pacheco Ruiz L, Mosqueda Taylor A, Huesca Ramirez HG, Ponce Lonato JA, González González R. Central odontogenic fibroma combined with central giant cell lesion of the mandible. Immunohistochemical profile. J Clin Exp Dent 2011; 3(4):e348-51.
28. Eliot C, Kessler HP. Clinical pathologic conference case 1: a multilocular radiolucency in the posterior mandible. Oral Surg Oral Med Oral Pathol Oral Radiol. 2015 Jun;119(6):e289-92.
29. Ramadan OR, Essawy MM. Central odontogenic fibroma with giant cell granuloma-like lesion: A report of an additional case and review of literature. Head Neck Pathol. 2021 Mar;15(1):275.