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Case Report

Hybrid central giant cell granuloma and central ossifying fibroma: Case report and literature review

A. Rai[a,*], S.A. Ahmad[b], M. Saleem[c], M. Faisal[d]

[a] Associate Professor, Oral Medicine and Radiology, Faculty of Dentistry, Jamia Millia Islamia, India
[b] Associate Professor, Oral and Maxillofacial surgery, Faculty of Dentistry, Jamia Millia Islamia, India
[c] Associate Professor, Department of Pathology, Faculty of Dentistry, Jamia Millia Islamia, India
[d] Professor, Oral & Maxillofacial Surgery, Faculty, of dentistry, Jamia Millia Islamia, India

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ABSTRACT

Central giant cell granuloma (CGCG) and central ossifying fibroma (COF) are clinicopathologically distinct entities commonly included in the differential diagnosis of benign focal central tumors. Hybrid CGCG-COF is a combined lesion characterized by the presence of microscopically large areas with features of CGCG, and large areas with features of COF within a single clinical lesion, separated from each other by a transition zone.

We report a hybrid CGCG-COF lesion in a 31 year old female patient which presented as a painless right mandibular swelling of 6 months duration. The existing literature review revealed only 6 similar cases reported so far. The presence of impacted tooth in association with the hybrid CGCG-COF has been reported for the first time. A thorough review of clinical, histopathological and radiological aspects of this interesting entity is presented. The combined CGCG-COF lesions have a female predilection, occur commonly after the 3rd decade, and are predominantly found on the left side of the mandible and present as an expansile mass.

1. Introduction

Hybrid tumors are the extraordinary tumor entities comprising of two distinct tumor types, each of which conforms to a precisely distinct tumor category. Several combinations of the so-called hybrid odontogenic tumors have been reported in the literature such as central giant cell granuloma (CGCG) and aneurysmal bone cyst [1,2], CGCG with ameloblastoma [3], CGCG with odontogenic keraratocyst [4], central odontogenic fibroma with CGCG [5–7] and CGCG in association with fibro-osseous lesions [8–15].

Central giant cell granuloma and central ossifying fibroma (COF) are clinicopathologically distinct entities, though they are commonly included in the differential diagnosis of benign focal central tumors. A thorough review of literature encompassing, Pubmed, Medline, Ovid and world wide web search through Google revealed only 4 reports of the hybrid central giant cell granuloma-central ossifying fibroma (CGCG-COF) describing 6 such cases [8,16–18].

We present a case of hybrid CGCG-COF lesion in a 31-year-old female patient presenting as a right mandibular swelling. The presence of an impacted premolar in our case makes the presentation more challenging and unique. A detailed review of this rare entity encompassing clinical, radiological and histopathological characteristics is presented to understand the biologic behavior of these tumors.

2. Case report

A 31-year-old female patient reported to our OPD complaining of swelling on right side of the face since last 6 months which was insidious in onset and had slowly grown to the present size over last 6 months. There was no history of pain and paraesthesia and no previous history of trauma. Extra-oral examination revealed right facial asymmetry due to a mandibular swelling approximately 4 x 3 cms in size, mainly localized to lower third of the face, hard on palpation and covered by normal skin (Fig. 1). The swelling was non-tender, no signs of parasthesia or lymphadenopathy were observed. Intraoral examination revealed mild expansion of buccal cortical plate on the right side of the mandible posterior to first permanent premolar. The mucosa over the swelling was intact and it was mildly tender on firm palpation. Second premolar (45) was clinically missing and deep proximal caries was evident in relation to 46. Lower border of the mandible was intact.

Intra-oral periapical radiograph (IOPA) revealed impacted 45 with follicular radiolucency around the crown (Fig. 2). There was presence of mixed radiopaque – radiolucent lesion in the periapical region in relation to 46, 47 with non-corticated borders. The inferior extent of the

* Corresponding author at: Oral Medicine and Radiology, Faculty of Dentistry, Jamia Millia Islamia, New Delhi, 110025, India.
E-mail address: arpitadoc@gmail.com (A. Rai).

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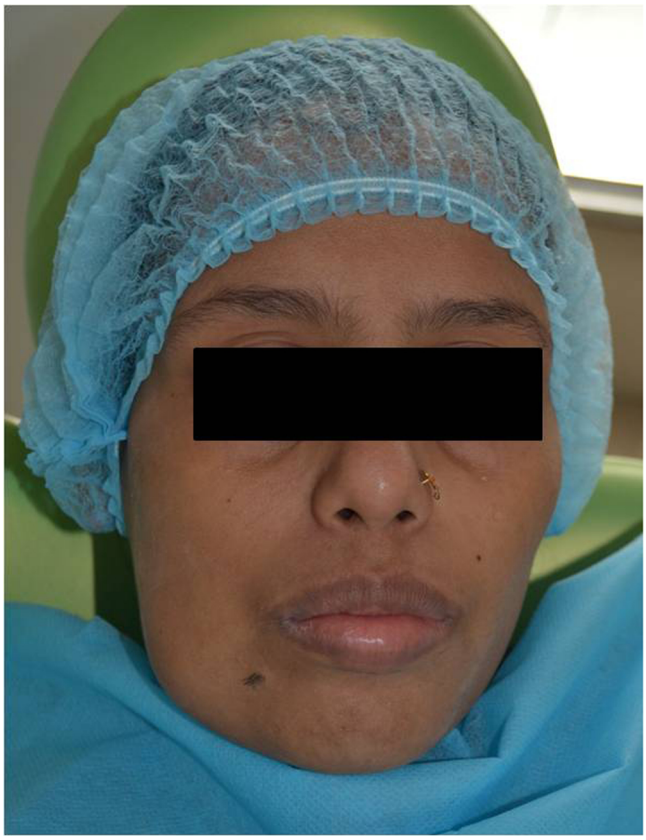

Fig. 1. Clinical photograph of the patient showing extra-oral swelling on right side of the face localized to lower third.

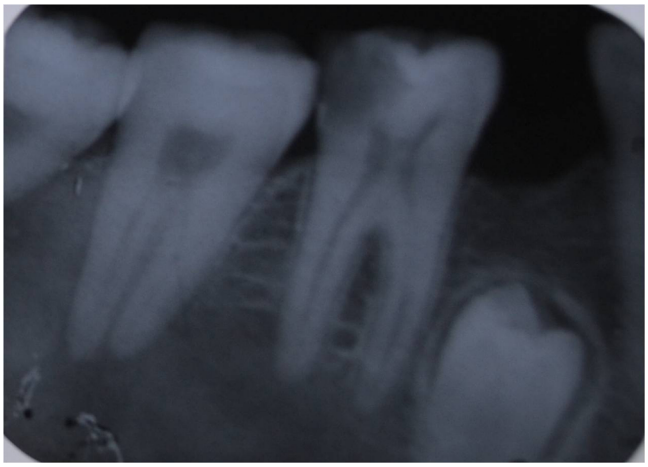

Fig. 2. Intra-oral periapical radiograph of the patient showing presence of mixed radiopaque – radiolucent lesion in the periapical region in relation to 46, 47 with non corticated borders. Also, impacted 45 seen.

lesion could not be completely evaluated in IOPA radiograph. Orthopantamograph revealed a solitary, unilocular, ill-defined predominantly radiolucent lesion in the right mandibular region involving the roots of 45, 46, 47 with areas of radiopacity diffusely spread though out the centre of the lesion (Fig. 3). There was presence of impacted first premolar (45), decayed 46, 36, 17 and 18. The teeth associated with the lesion did not show root resorption or widening of periodontal space. The lower border of the mandible was intact, though thining of cortex in the 46 region was observed. Fine needle aspiration from the lesion was negative. Cone beam computed tomography of the lesion (Fig. 4) showed a solitary, unilocular, expansile hypodense mass on the right side of mandible with central areas of hyperdensity in the inferior aspect and patchy hyperdensity in the superior aspect. The mass measured approximately 29 mm medio-laterally, 27 mm antero-posteriorly and 19 mm superior-inferiorly. The buccal cortical plate was discontinuous at several places. The lingual cortex was thinned but not expanded. Impacted tooth was seen in association with the mixed radiopaque-radiolucent lesion.

Based on the clinical and radiographic findings of the case, a provisional diagnosis of localized fibro-osseous lesion was made. Differential diagnosis included -COF, focal cement-osseous dysplasia, calcifying epithelial odontogenic tumor and CGCG. Incisional biopsy of the lesion was done after making a small window through the thick cortical plate. Histopathology of the tissue was suggestive of central giant cell granuloma with clear cut giant cells.

Surgical management of the lesion through intra oral approach under local anesthesia was planned. Buccal cortex was initially exposed. The pink encapsulated mass protruding from the buccal side of the mandible was removed from the jaw in toto (Fig. 5). After removing the tumor curettage was done and soft bone was removed. Extraction of 46, 47 and impacted 45 was done. Haemostasis was achieved and proper contouring of the bone was done. Interrupted suturing was done by 3-0 silk suture.

Microscopic examination of histopathological sections revealed bone trabeculae with focal osteoblastic rimming in a background of fibrous connective tissue stroma (Fig. 6A & B). Other sections revealed paucicellular cementum like material in a background of fibrous connective tissue stroma (Fig. 6C). Numerous multinucleated giant cells in a background of cellular fibrillar connective tissue stroma are seen in other areas. Bony trabeculae in a background of fibrous connective tissue and multinucleated giant cells in a background of fibrillar connective tissue stroma were seen at the transition zone (Fig. 6D).

The post-operative period remained uneventful. The patient was regularly followed up for 18 months. At 12th month follow-up, OPG revealed increase in radiopacity of the surgical defect signifying osteofibrous scar tissue (Fig. 7).

3. Discussion

Fibro-osseous lesion is an umbrella term given to a heterogenous group of entities in which normal bone is replaced by fibrous connective tissue and consists of cellular to fibrovascular stroma along with the presence of variable amounts of mineralized material (bone or cementum) [19]. It includes disorders like fibrous dysplasia, cemento-osseous dysplasia, and cemento-ossifying fibroma [20]. COF is a well-demarcated fibro-osseous lesion which usually occurs in the third and fourth decade and has mandibular predilection [21]. Focal clusters of giant cells are frequently observed in COF either randomly distributed in small aggregates within the stroma or associated with mineralized material [16].

Central giant cell granuloma (CGCG) was first reported by Jaffe in 1953 as a giant cell “reparative” granuloma of the jaw bones [22]. The World Health Organization has defined CGCG as an intraosseous lesion consisting of cellular fibrous tissue that contains multiple foci of hemorrhage, aggregations of multinucleated giant cells, and occasional trabeculae of woven bone [23]. CGCG occurs more commonly in females under 40 years of age and presents as multilocular radiolucent lesion [17]. There have been reports of presence of focal areas of osteoid or bone formation within CGCG [16].

CGCG – COF represents an association of characteristics from both the pathologies in a single tumor. Kaplan et al. have described the histological diagnostic criteria for this combined lesion as presence of microscopically large areas with features of CGCG, and large areas with features of COF within a single clinical lesion, separated from each other [16]. Central ossifying fibroma with occasional scattered giant cells or CGCG with focal osteoid or mineralized material should be excluded from the diagnosis of hybrid tumor.

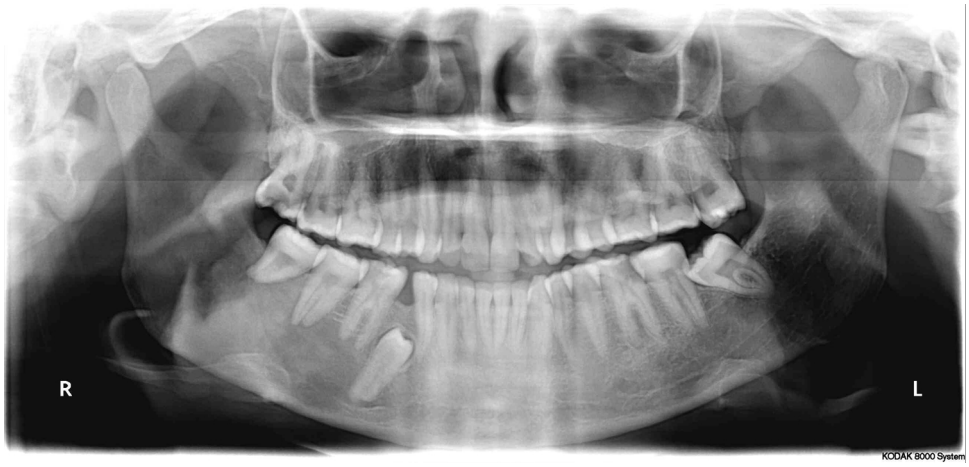

Fig. 3. Orthopantomogram showing solitary, unilocular, ill-defined predominantly radiolucent lesion in the right mandibular region involving the roots of 45, 46, 47 with areas of radiopacity diffusely spread though out the centre of the lesion.

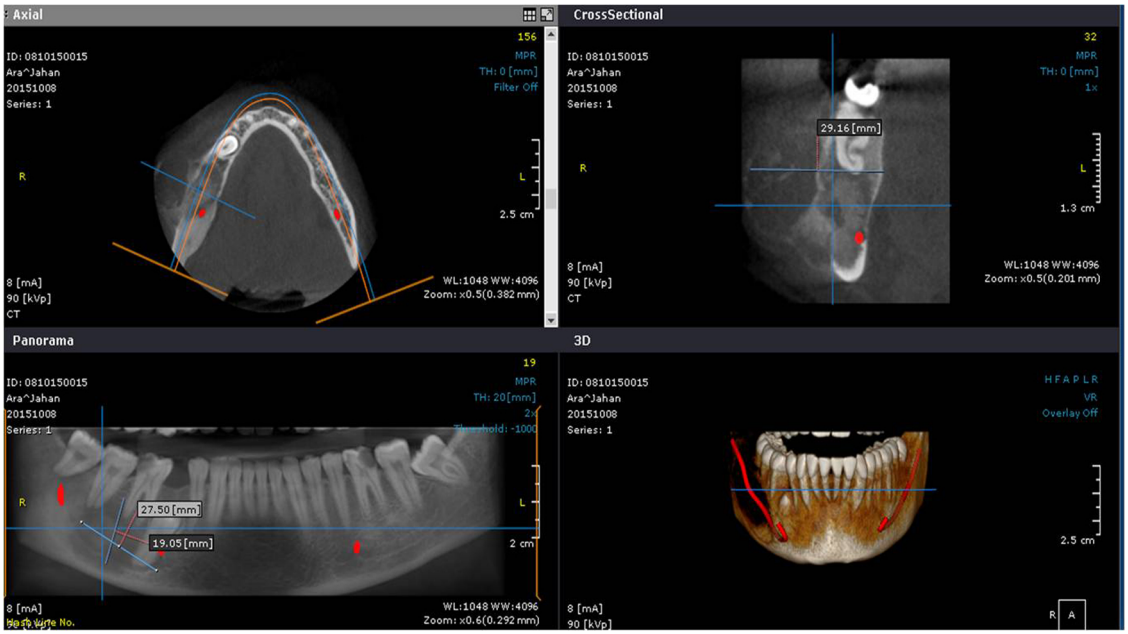

Fig. 4. Cone beam computed tomography showing the mixed radiopaque-radiolucent lesion in the axial, cross-sectional, panoramic and 3D views.

Several theories have been suggested to describe the etiopathogenesis of CGCG-COF. Based on their observation of mandibular premolar-molar occurrence and presence of spindle cells in the transition areas, Kaplan et al. have hypothesized that the primary lesion in CGCG – COF is COF [16]. The mesenchymal spindle cells of the tumor release cytokines in response to unknown trigger that induces differentiation toward osteoclast/giant cells. Farzaneh et al. [14] and Penfold et al. [8] have also proposed similar mechanism wherein osteoblasts may activate osteoclast-type giant cells through paracrine mechanisms. Recently, Liu et al. suggested that the multinucleated giant cells (MGC) in CGCG, ABC, and cherubism show characteristics of the osteoclast phenotype, and suggested that mononuclear stromal cells play an important role in the formation of MGC supporting the theory by others [24].

A search of available literature reveals report of 6 cases describing CGCG in association with COF. The first such case was reported by Penfold et al. [8] in 1993 in a series of 3 cases describing CGCG in association with FOL. Kaplan et al. in their clinicopathological study, examined the prevalence of combined CGCG and COF lesions and compared the clinical, radiographic and histopathologic characteristics of 3 CGCG – COF lesions with the classical CGCG and COF [16]. Crusoe-Rebello et al. in 2009 reported in detail radiographic findings of a similar lesion [17]. Recently, Asthana et al. have reported one more case [18]. The present case is another addition in the series, where CGCG – COF lesion was present in association with an impacted tooth.

Including the case reported here, the mean age of presentation of CGCG – COF is 35.8 years (range 5–68 years) with a male:female of 3:4 (Table 1). There is strong mandibular predilection with the lesion occurring in mandible in 71.4% cases and involving molar premolar region in 57% of cases. Three of the 5 mandibular cases have been reported on the left side. Almost all the cases presented as a firm, painless, slow growing swelling. None of the previously reported cases have been associated with impacted teeth. In our case, presence of impacted 2nd premolar could be an incidental finding of unequivocal importance. Surgical management was performed in all but one case in which growth arrest using calcitonin spray was attempted. Only one case out of the 7 has reported recurrence within one year, whereas in one case data regarding follow-up is not mentioned. In the present case, at the 12th month follow-up of the patient OPG was suggestive of osteofibrous scar tissue.

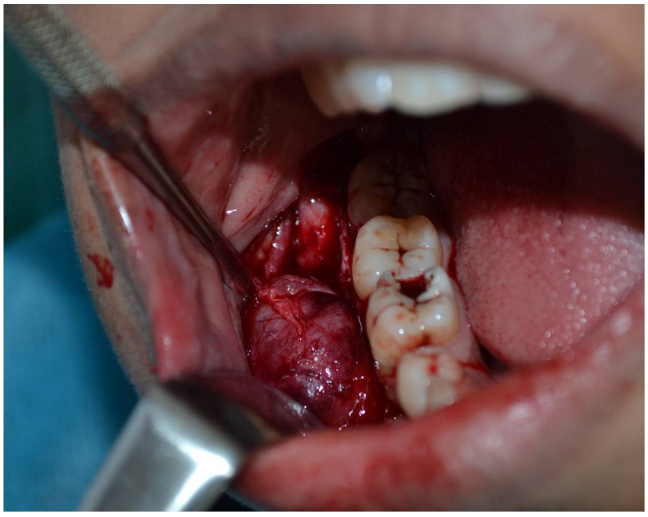

Fig. 5. Clinical photograph showing pink encapsulated mass protruding from the buccal side of the mandible after removal of the buccal cortex.

The CGCG-COF lesion presented as a mixed radiopaque-radiolucent lesion in 5 (71.4%) cases and as radiolucent and radiopaque lesion in one patient each (Table 2). Among the 6 predominantly radiolucent or mixed lesions, 5 (83.6%) presented as unilocular radiolucencies. Expansion of cortical plate was observed in almost all the cases. Resorption of roots was observed in 2 cases, whereas tooth displacement was observed in a single case. In the present case, the lesion was associated with an impacted second premolar.

Histopathologically, most of the lesions showed distinct areas of benign fibrosseous lesions such as bony trabeculae or lamellar bone in fibrocellular connective tissue. Distinct areas with CGCG characteristics of multinuclear giant cells in well vascularized connective tissue were observed. The presence of transition zone composed of densely packed packed spindle cells with varying degrees of collagenization and indistinct vascularity was observed.

4. Conclusion

We have reported a case of combined CGCG-COF lesion in association with an impacted tooth. The existing literature regarding this hybrid tumor was reviewed. The combined CGCG-COF lesions have a

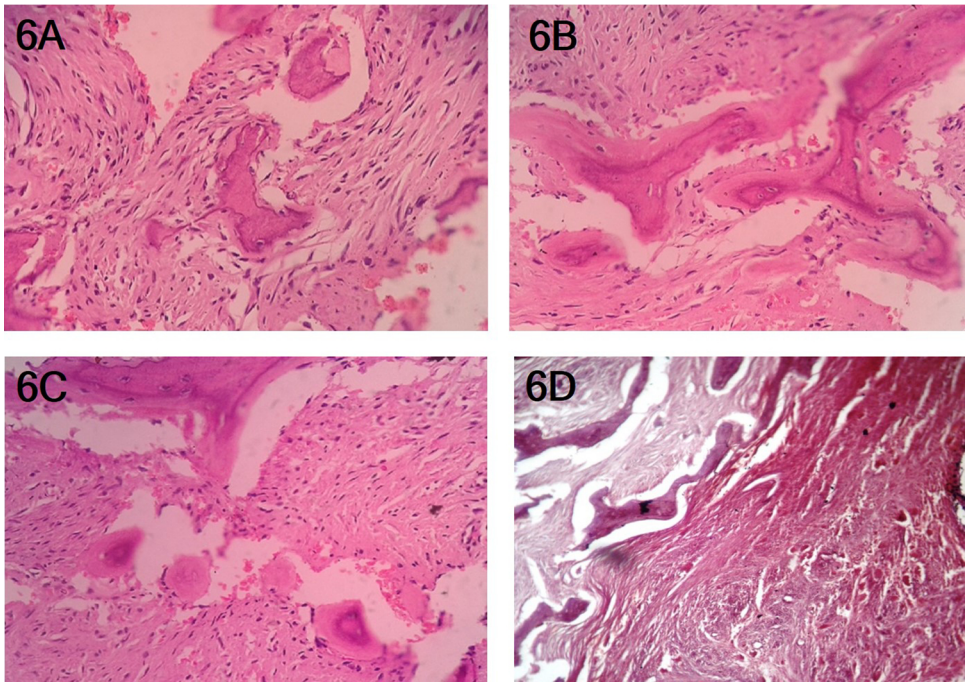

Fig. 6. A & B: Histopathological section showing bone trabeculae with focal osteoblastic rimming in a background of fibrous connective tissue stroma. 6C: Histopathological section showing cementum like material in a background of fibrous connective tissue stroma. 6D: Low power photomicrograph showing transition zone. Bony trabeculae in a background of fibrous connective tissue (left) and multinucleated giant cells in a background of fibrillar connective tissue stroma (right).

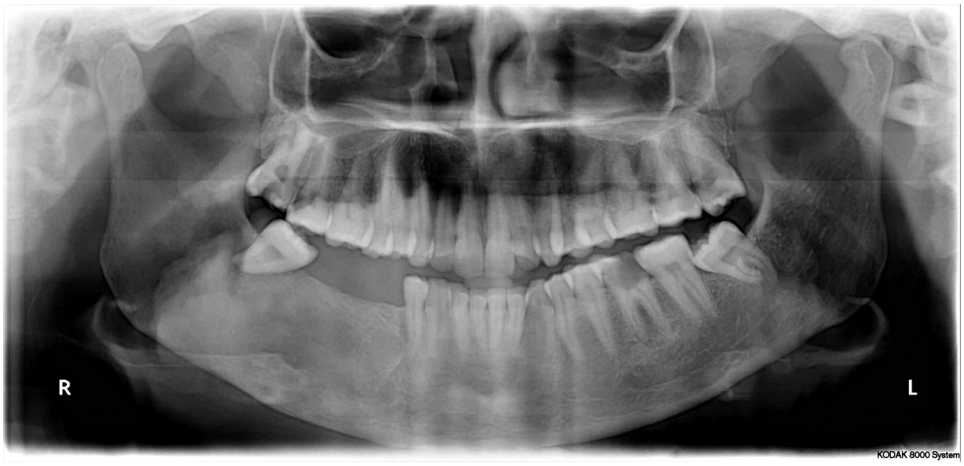

Fig. 7. Orthopantomogram at oneyear follow-up showing increase in radiopacity of the surgical defect signifying osteofibrous scar tissue.

Table 1
showing the clinical features of hybrid CGCG – COF tumors reported so far in the literature.

Author (year of publication)	Gender	Age	Location	Side	Clinical presentation	Treatment	Follow up period	Prognosis
Penfold et al (1993)	M	41	Maxilla	Left	Long standing, hard, bony swelling of the left maxilla	Partial maxillectomy	8 months	No recurrence
Kaplan et al (2007)	M	68	Maxilla	Not known	Painless swelling	Partial maxillectomy	4 years	No Recurrence
Kaplan et al (2007)	F	5	Mandible (molar-premolar area)	Right	Painless swelling	Curettage	3 years	Recurrence after 1 year, repeat curettage, no recurrence for 2 years
Kaplan et al (2007)	F	12	Mandible (molar area)	Right	Painless swelling	Calcitonin nasal spray for 2 yrs. Refused surgery	5 years	Growth arrest achieved in 2 years maintained
Crusoe´-Rebello (2009)	F	38	Mandible (parasymphyseal area)	Left	Firm, painless swelling	Peripheral ostectomy	2 years	No recurrence
Asthana et al (2014)	M	56	Mandible (incisor to molar)	Left	Firm, painless, slow growing swelling	Peripheral ostectomy	Not reported	Not reported
Rai et al (2017)	F	31	Mandible (premolar molar area)	Left	Firm, painless, slow growing swelling	Peripheral ostectomy with curretage	1.5 years	No recurrence

Table 2
showing the radiological features of hybrid CGCG – COF tumors reported so far in the literature.

Author (year of publication)	**Gender**	**Age**	**Location**	**Side**	**RO/RL/ MX**	**Unilocular/ multilocular**	**Size(mm)**	**Expansion/ perforation**	**Root resorption**	**Tooth displacement/ impaction**
Penfold et al (1993)	M	41	Maxilla	Left	RO	NA	Not reported	Mottled radiopacity	Not reported	Not reported
Kaplan et al (2007)	M	68	Maxilla	Not reported	MX	Unilocular	10-30 (mean 20)	Expansion	Present	Absent
Kaplan et al (2007)	F	5	Mandible (molar-premolar area)	Right	MX	Unilocular		Expansion	Absent	Present
Kaplan et al (2007)	F	12	Mandible (molar area)	Right	RL	Unilocular		Expansion	Present	Absent
Crusoe´-Rebello (2009)	F	38	Mandible (parasymphyseal area)	Left	MX	Unilocular	17.9 × 22.6 × 12.3	Expansion	Edentulous patient	Edentulous patient
Asthana et al (2014)	M	56	Mandible (incisor to molar)	Left	MX	multilocular	Not reported	Not reported	Not reported	Not reported
Rai et al (2017)	F	31	Mandible (premolar molar area)	Left	MX	unilocular	29 × 27 × 19	Expansion	Absent	Impacted second pemolar

female predilection, occur commonly after the 3rd decade, are predominantly found on the left side of the mandible and present as an expansile mass. Since only six such cases have been reported in the literature, it is difficult to conclude on the biological behavior of this entity. However, regular follow –up is recommended in these cases, as CGCG is associated with aggressive behavior.

Conflict of interest

None.

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None.

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