

Hybrid Central Odontogenic Fibroma with Central Giant Cell Granuloma Like Lesion ; A Case Report and Review of the Literature

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ABSTRACT

The combination of central odontogenic fibroma and central giant cell granuloma is extremely rare and has been reported in only 46 cases worldwide in previous articles. The lesion is called a hybrid central odontogenic fibroma with central giant cell granuloma like lesion (HCOF-CGCG) due to a histopathological characteristics of multinucleated giant cell and odontogenic epithelium in fibro-cellular background. We report a case of HCOF-CGCG in a 27-year old Thai male patient who was identified as the first case in Thailand. Radiographic examination showed a well-defined radiolucency lesion at posterior mandibular area. Enucleation and curettage were done and microscopic study revealed a fibro-cellular proliferating tissue containing numerous strands, cord of odontogenic epithelium, and numerous multinucleated giant cells. This report also included a literature review of the previous 45 cases.

Keywords: Central odontogenic fibroma; central giant cell granuloma; hybrid (Siriraj Med J 2019; 71: 426-431)

INTRODUCTION

The central odontogenic fibroma (COF) is an uncommon disease found in gnathic area.¹ In 2017, WHO defines it as an ectomesenchymal tumor with a mature fibrous connective tissue lesion, which usually combines with an odontogenic epithelium.² It can occur in wide-ranging age distribution and slight female predilection affecting relatively equal frequency in both jaws.

The lesion in maxilla usually occurs anterior to first molar and about half of all mandibular lesions are found posterior to first molar.³ The small COF is often asymptomatic and presents as well-defined unilocular radiolucency whereas the larger lesion may be associated

with a pain, a bony expansion, a root resorption, a divergence of adjacent tooth roots, a loosening of teeth and presents as multilocular radiolucency.^{3,4}

The histological features of the COF are similar to other tumors including enlarging dental follicle, odontogenic myxoma and desmoplastic fibroma.⁵⁻⁷ Histopathological features of COF compose principally of mature collagen fibers along with numerous interspersed fibroblasts. In addition, presence of small nests or strands of inactive odontogenic epithelium are found to be a variable feature.³ It also can present with histological variations such as granular cell, giant cell and pleomorphic fibroblast combination.^{8,9}

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Central giant cell granuloma (CGCG) is a benign neoplasm of jaw comprising a giant cell reparative granuloma.¹⁰ The CGCG occurs in around 10% of jaw lesions and is reported to occur often in patients aged below 20 years with female predilection.^{2,10} The lesion usually develops in the anterior of the mandible with characteristics of slow growing, asymptomatic, and expansible lesion in nature.¹⁰ The radiographic finding shows the well-defined radiolucency, but it can be multilocular in advanced lesion. About 30% of CGCGs exhibit aggressive behavior associated with pain, root resorption, displacement of adjacent tooth, and cortical perforation.²

Histopathological feature of the CGCG is shown with a non-encapsulated proliferation of mononuclear spindle-shaped and polygonal cells with osteoclast-type multinucleated giant cells in a vascular background with hemorrhage and haemosiderin pigment.^{10,11} Likewise, there is a similar histological feature between CGCG and giant cell lesion of bone comprising cherubism, hyperparathyroidism, aneurysmal bone cyst and Noonan syndrome.¹²⁻¹⁴

In 1992, Allen reported the first case of hybrid central odontogenic fibroma with central giant cell granuloma like lesion (HCOF-CGCG). The histological finding revealed the fibro-cellular tissue, odontogenic epithelium, and distribution of the giant multinucleated cells.¹⁵ HCOF-CGCG has been reported in only 45 cases worldwide in history and considered as a rare lesion. This study aimed to report a rare case and provide a literature review of HCOF-CGCG.

CASE REPORT

A 27-year-old Thai male was referred by general dentist for management of a radiolucent lesion which was accidentally found on a radiographic examination prior to a third molar surgery. According to a history taking, the patient did not notice the presence of lesion in his lower left jaw and did not report numbness or pain in any area. He also underwent a tooth extraction in this area 3 years ago. Clinical examination found a buccal expansion with obliteration of mucobuccal fold and a root fragment of mandibular left first molar. The teeth involved in this area were vital in response to an electric pulp test.

The routine radiograph (Fig 1A) which was obtained 3 years ago did not present any sign of the lesion, but it presented an endodontic lesion of a first mandibular left molar. Preoperative radiograph (Fig 1B) revealed a well-defined unilocular radiolucent lesion, measuring approximately 18x18 mm, extending from a left mandibular



Fig 1A. The routine Panoramic Radiograph 3 years ago.

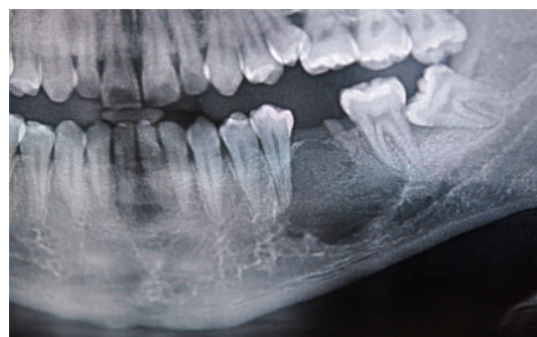


Fig 1B. The preoperative Panoramic Radiograph.



Fig 1C. The 6-month follow-up Panoramic Radiograph.

second premolar to left mandibular second molar. The lesion was superimposed with a mental foramen and inferior alveolar canal. The root fragment was identified as a radiopaque mass at superior border of the lesion.

The differential diagnosis included a radicular cyst, odontogenic keratocyst, and unicystic ameloblastoma. The treatment plan was enucleation by curettage of the total lesion. During the surgical procedure, we found a buccal bone perforation and soft tissue mass within the lesion detached from the surrounding bone. Both inferior alveolar nerve and mental nerve were exposed during the surgery, the inferior alveolar artery was also injured. The bleeding was controlled using bone wax. The lesion was completely removed. The macroscopic appearance (Fig 2) of the lesion was red-pink soft tissue mass with hemorrhage. The primary wound closure with

3-0 silk was done. At one-week follow-up, the patient presented with slight numbness at his lower left lip.

Multiple 4µm-thick formalin-fixed paraffin-embedded sections of the specimen were stained with hematoxylin and eosin. Microscopic examination (Fig 3A, 3B) revealed that it mainly composed of a fibrocellular proliferating tissue containing numerous strands, and cord of odontogenic epithelium. Numerous multinucleated giant cells were seen to be dispersed into the connective tissue with a whorled pattern. Small areas of the connective tissue containing odontogenic epithelium and multinucleated giant cells were separated together. Areas of myxoid stroma and hemorrhage were also observed. Immuno-histochemical stains of cytokeratin 19 was used to confirm the structure that mimicked odontogenic epithelium. The immuno-histochemical was positive on cytoplasm of odontogenic epithelial cells (Fig 3C). Morphology was compatible with HCOF-CGCG. At six-months follow up, no evidence of recurrence occurred, both clinically and radiographically (Fig 1C). The numbness was completely resolved.

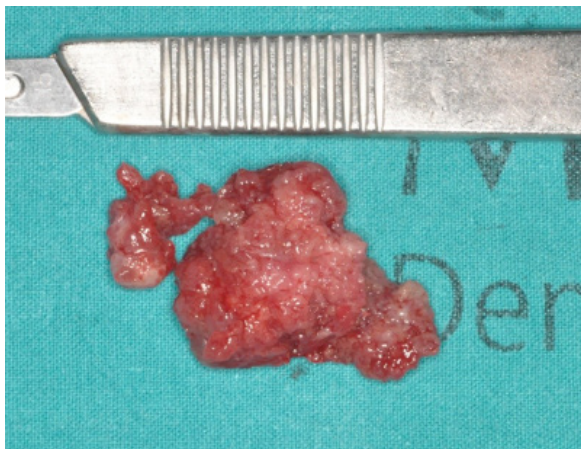


Fig 2. The specimen of the lesion that was completely enucleated.

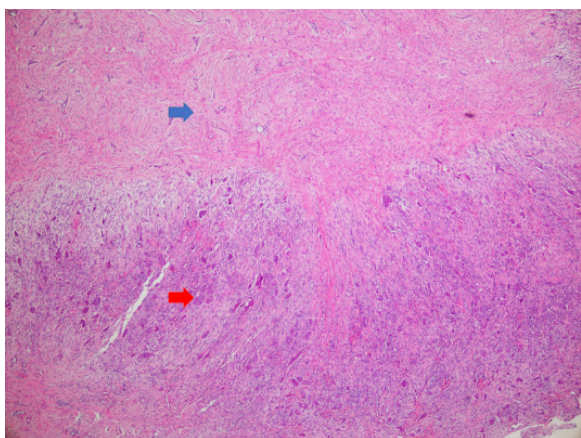


Fig 3A. The histopathology of the combined lesion was composed of areas of giant cell granuloma and odontogenic fibroma. The areas of sole giant cell granuloma (red arrow) and odontogenic fibroma (blue arrow) areas were demonstrate at periphery of the lesion.

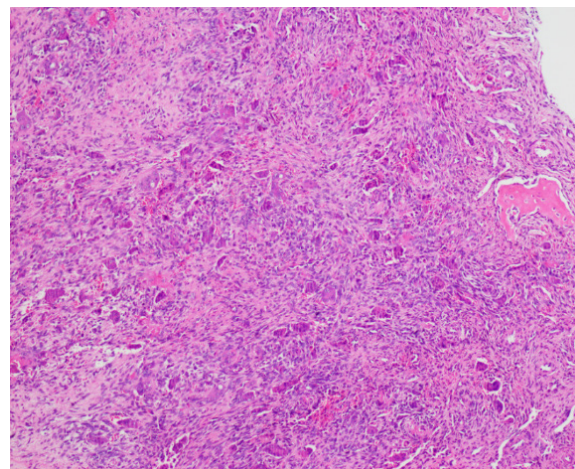


Fig 3B. The histopathology of the areas of giant cell granuloma presented scattering multinucleated giant cells are in the inflamed fibrous tissue.

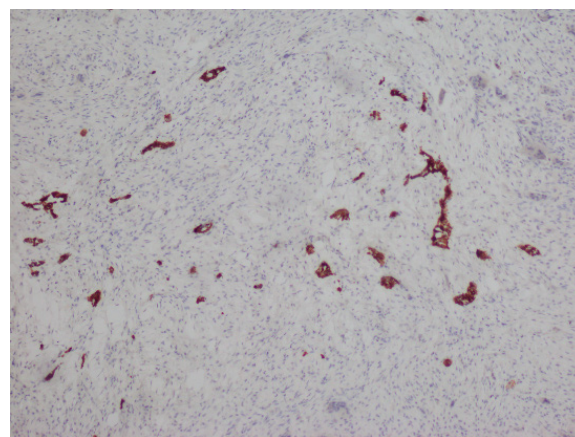


Fig 3C. The histopathology a cytokeratin 19 staining was presented in cytoplasm of odontogenic epithelial rests.

DISCUSSION

The HCOF-CGCG is a rare combination and was first reported by Allen in 1992.¹⁵ The previous reports and the international conferences so far found the number of cases has increased gradually and is reckoned to be 46 cases including this case. The available information of all cases are presented in Table 1. The lesion occurs mostly in second and third decade of life with a female predilection and is more frequent in a tooth bearing posterior mandibular area (86%) alongside the buccal expansion. The tooth displacement is also found in some cases.¹⁶⁻¹⁸ A few cases report the relation of the lesion with an orthodontic, root canal treated tooth, embedded tooth, and cherubism.^{15,19,20} There are only 2 cases reporting pain whilst the remaining have been asymptomatic.^{9,17}

Radiographically, 60% presented as a well-defined unilocular radiolucency and the rest of the lesions presented with multilocular radiolucency. The ill-defined border characteristic can be found in some cases.¹⁵ The extensive

TABLE 1. Information of previously reported cases.

Case No.	Author/Year	Age/Sex	Location	Clinical features	Radiographic findings	Treatment	Recurrence
1-3	Allen, 1992 ¹⁵	3F; 66/14/30	Mandible premolar/molar area	Root canal treated tooth involvement, orthodontic treatment, expansion	Multi/unilocular	Curettage	Recurrence
4-6.	Fowler, 1993 ²⁴			Reported 3 cases but no clinical data available			
7-14	Odell, 1997 ²¹	5F; 5/20/21/22/39/43/50, M; 11	Maxilla, posterior mandible	Buccal expansion, history of extraction, rapid growth, buccal perforation, tooth mobility	Unilocular	Curettage	Recurrence
15.	Taylor, 1999 ⁹	17/F	Mandible/ canine/premolar area	Buccal expansion, tooth displacement, thinning cortex	Unilocular	Curettage	None
16.	Kruse-Losler, 2006 ¹¹	22/F	Mandible/ from right to left molar area	Lingual and inferior expansion	Multilocular, scalloped border	Surgical excision	None
17-23	Pontes, 2008 ¹			Reported 7 cases with 5 males and 2 females at mandible			Recurrence 3 cases
24-30	Tosios, 2008 ¹⁹	6M; 18/50/73/15/59/25, F; 20	Mandible/ premolar/molar area	Cherubism, perforation	Multi/unilocular, premolar apex	Surgical excision	None
31.	Younis, 2008 ²³	57/F	Mandible/ premolar/molar area	Buccal expansion	Unilocular	Curettage	None
32.	Marina, 2008 ¹⁶	24/F	Mandible/ from right to left molar area	Mandibular swelling progressively for 8 years, tooth displacement	N/A	Curettage and reconstruction	None
33.	Bologna-Molina, 2011 ²²	14/M	Mandible/ premolar/molar area	Buccal expansion	Multilocular	Resection and reconstruction	None
34.	Castillo, 2011 ¹⁷	14/M	Mandible/ molar area	Expansion, tenderness, tooth displacement	Unilocular	Curettage	None
35-36	Eversole, 2011 ⁸	42/F, 27/F	Body of mandible, Body of mandible and ramus	N/A	N/A	N/A	N/A
37-38	Mosqueda-Taylor, 2011 ¹⁸	14/M, 14/M	Mandible/ molar area, Mandible/ premolar/molar area	Both buccal and lingual expansion, tooth displacement, tenderness on palpation, 6 months evolution	Unilocular, Multilocular	Surgical excision	None
39.	Damm, 2013 ²⁵	75/F	Mandible/ anterior	N/A	Unilocular	Curettage	None
40.	Eliot, 2015 ²⁶	22/F	Mandible/ canine/ premolar/molar area	Swelling at mandible and submandibular area	Multilocular	Curettage	None
41.	Schultz, 2017 ²⁷	12/F	Mandible/ anterior	Asymptomatic	Multilocular	Enucleation and selective extraction	None
42.	Leite, 2017 ^{28,29}	42/F	Mandible/ molar area	N/A	N/A	Surgical excision	None
43-46	Upadhyaya, 2018 ²⁰	2M; 10/62, F; 63	Mandible anterior, posterior	Buccal and lingual expansion, embedded tooth	Unilocular	Curettage	None
46.	Current case report	27/M	Mandible premolar/ molar area	Asymptomatic, buccal expansion, progression less than 3 years, retained root	Unilocular	Curettage	None

N/A is defined as no available data.

Noted that cases from Fowler and Hassan provided insufficient information but the cases are still accumulated the total number of the cases.

lesions have been reported in a few cases which included a sinus involvement and crossing the midline.²¹ Taylor et al., reported that the lesion was distinctive from surrounding bone and had no encapsulation.⁹ Also, some authors reported that the lesion caused a bony cortex thinning and perforation.^{9,19,21} Most of COF and CGCG, were treated by curettage. One case was treated by resection and reconstruction to prevent a mandibular fracture.²² The recurrent lesions reported 17% which were treated by curettage. Similar to the nature of COF and CGCG, recurrences have been observed with slightly higher rate in the aggressive behavior, ill-defined margin and multilocular lesions.^{1,10,11} Odell et al., stated that the lesion tends to behave like the CGCG much more than the COF due to its prevalence and behavior.²¹

Histo-pathologically, several cases of the HCOF-CGCG were found to be contained as densely collagenous to fibromyxoid stroma with several nests of inactive odontogenic epithelium. The areas have been revealed to merge independently with a variably plump to narrow spindle-shaped fibrocellular connective tissue containing multinucleated giant cells.^{18,21,23} Similarly, in this reported case, features of HCOF-CGCG like components and the odontogenic epithelial nests in the mature fibrous connective tissue were seen histologically.

The pathogenesis of hybrid lesion is still unclear. There are 3 theories mentioning the origin.

1. The first theory was proposed by Allen et al, who first reported the hybrid lesion. The theory suggested “collision tumor” which is defined by synchronous occurrence of COF and CGCG. This theory seems seldom to happen and is opposed by recurrent lesion. Almost all the recurrence presented with combination of COF and CGCG. The combination seems to be a specific characteristic of it.¹⁵

2. The second theory is “primary CGCG induced secondary COF”. This theory stated the cells present within CGCG produce factors like growth factors, chemokines, and cytokines which induce the growth of odontogenic cell line and can result in development of COF.¹⁵

3. The third one is opposite to the second theory. The primary tumor is COF and the trauma or other stimulus induces a giant cell reaction.²¹

Now, it cannot certainly conclude the origin of this hybrid lesion. The evidences of lesion vicinity, histopathology, and recurrence are a conjecture of the pathogenesis.

According to this current case, the lesion occurred in an early adult male which is different from the other studies. The clinical features were similar to the other reports which are buccal expansion and asymptomatic.

The radiographic finding was well-defined with corticated border which corresponded to the characteristics during removal. The lesion showed no infiltration pattern and was detached from the surrounding bone. It caused the buccal bone thinning which is similar other reported cases. In addition, the lesion progressed within 3 years since the past radiograph confirmed the presence of the lesion. In surgical point of view, this intra-bony lesion was easy to remove by enucleation and curettage.

Our opinion suggested a possibility that this lesion could be a “collision tumor”. The growth of collision tumor arose from the synchronous occurrence of COF in the same area as a CGCG.^{9,21} This theory correlated with our case due to the presence of intrabony mixed-up area of these two lesions. This case displayed three different areas including: odontogenic fibroma, giant cell granuloma and two merged lesions. The sole areas of COF and CGCG were present only at the border of the specimen. The central area of the specimen demonstrated mixed histopathologic features of odontogenic fibroma and giant cell granuloma-like lesion. In conclusion, the HCOF-CGCG was considered as a rare oral lesion. The nature of the lesion was mostly non-aggressive behavior. The treatment by enucleation and curettage seemed to be promising. The histopathological feature was characterized by the presence of the fibro-cellular proliferating tissue containing numerous strands, cord of odontogenic epithelium, and numerous multinucleated giant cells. The presence of COF and CGCG could be merged or independent.

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