J Korean Soc Radiol 2010 ; 62 : 11-15

Multiple Synchronous Central Giant Cell Granulomas of the Maxillofacial Region: A Case Report[1]

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Multifocal central giant cell granulomas (CGCG) in the maxillofacial region are suggestive of systemic disease such as hyperparathyroidism or an inherited syndrome such as Noonan-like multiple giant cell lesion syndrome. Only 5 cases of multifocal CGCGs in the maxillofacial region without any concomitant systemic disease have currently been reported. We report here on an unusual case of 17-year-old man who presented with multifocal CGCGs of the bilateral posterior mandible and right maxilla and he was without any concomitant systemic disease.

Index words : Granuloma, Giant Cell
Jaw disease
Neoplasms, Multiple Primary

Central giant cell granulomas (CGCG) of the jaws usually present as a painless lesion and a solitary radiolucent expansion is seen on the simple radiographs. This disease is most commonly diagnosed in the third decade of life, and females are twice as likely to be affected as males (1). The gnathic cases of giant cell granuloma have accounted for 1-7% of all the benign lesions in several previously reported oral surgical series. Jaw lesions affect women more frequently than men (2:1 ratio) (2). The presence of multiple CGCGs in the maxillofacial region is suggestive of hyperparathyroidism or a number of syndromes (3, 4). To the best of our knowledge, only 5 cases of multifocal CGCGs without any concomitant systemic disease have currently been reported (4, 5). We report here on a case of multifocal CGCGs in the maxillofacial region of a 17-year-old male and the patient was without any concomitant systemic disease.

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This work was supported for two years by a research grant from Pusan National University.
Received April 24, 2009 ; Accepted August 4, 2009
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Case Report

A 17-year-old man presented with right nasal obstruction and rhinorrhea that he had suffered with for the previous five months. There was no history of prior trauma or surgery to the mandible. The clinical examination revealed a mass in the right posterior nasal cavity. We then performed computed tomography (CT) and magnetic resonance imaging (MRI) of the paranasal sinuses and nasal cavity.

The CT scan of the right maxilla with the bone window setting showed a relatively well defined, heterogeneous isodense mass with mineralized septa, expansile boney remodeling with cortical thinning of the medial and lateral walls of the antrum and opacification of the antrum and the posterior nasal cavity. The mass had eroded the adjacent bony structures, such as the anterior wall of the sphenoid sinus, and it extended to the surrounding spaces, such as the right maxillary sinus and the posterior nasal cavity. There were also bilateral oste-

olytic lesions with cortical expansion, boney thinning and mineralized septa in both sides of the posterior mandible (Fig. 1).

On MR imaging, multifocal lesions in the right maxilla and bilateral mandible showed low signal intensity on the T1-weighted images and heterogeneous low to intermediate signal intensity on the T2-weighted images. The mass showed intense enhancement after the administration of contrast material (Fig. 2).

Considering these imaging findings, we considered brown tumor of hyperparathyroidism, ameloblastoma, odontogenic myxoma and odontogenic fibroma as possible options for making the differential diagnosis.

The blood serum levels of parathyroid hormone, alkaline phosphatase and calcium were within normal limits (Table 1). There were no other bony lesions in the entire body.

Biopsy was performed on the mass in the right maxillary sinus. Histologically, the mass showed a proliferation of multinucleated giant cells within a background of plump, ovoid and spindle-shaped mesenchymal cells. The giant cells contained only a few nuclei, up to dozen (Fig. 3). Thus, the pathologic diagnosis was central giant cell granuloma.

Discussion

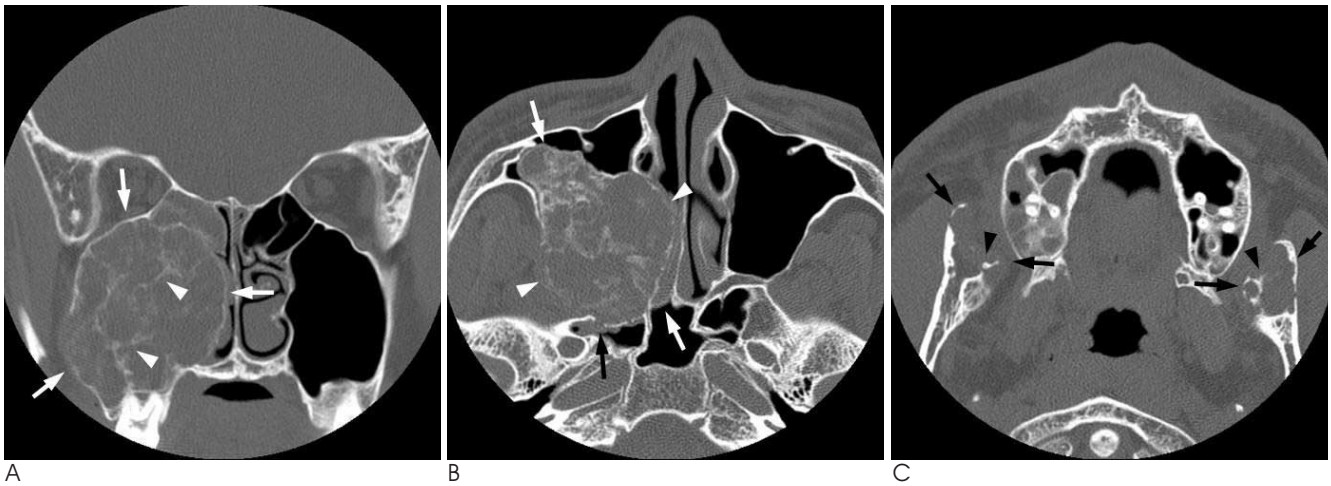
Jaffe in 1953 first described giant cell reparative granuloma (GCRG) as a benign lesion that affects the mandible and maxilla, and Jaffe suggested that this is a reactive response to intraosseous hemorrhage (6). It was initially termed giant cell reparative granuloma, yet these lesions are no longer believed to represent a reparative process (3).

The gnathic cases of GCRG are categorized based on their location as central (i.e., occurring in bone) or peripheral (i.e., occurring in the gingival soft tissues), and these gnathic cases of GCRG account for 1–7% of all the benign lesions in several previously reported oral surgical series. Jaw lesions affect women more frequently than they do men (2:1 ratio) (2). CGCG is more uncommon than peripheral giant cell granuloma, at a ratio 1:3 (4).

CGCG of the jaws usually presents as a solitary radiolucent expansion on simple radiograph and most of the cases are painless; CGCG is usually diagnosed in the third decade of life with females being twice as likely to be affected as males (1). CGCG is a benign lesion of bone with a variably aggressive nature (3). Some of these lesions are more destructive and they show a

Table 1. Results of the Preoperative Workup

Chemistry	Test Result	Normal Range
Parathyroid hormone (PTH)	17.9 pg/mL	10 to 65 pg/mL
Calcium level	9.1 mg/dL	8.5 to 10.3 mg/dL
Phosphorus	4.2 mg/dL	2.0 to 4.6 mg/dL
Alkaline phosphatase	269 IU/L	95 to 280 IU/L
Ionized calcium	1.2 mmol/L	1 to 1.2 mmol/L



A B C

Fig. 1. A. The coronal CT scan with a bone window setting shows a relatively well defined, heterogeneous isodense mass (arrows) with diffuse mineralized septa (arrowheads) in the right maxilla.
B. The axial CT scan with a bone window setting shows expansile remodeling with cortical thinning of the medial and lateral walls of the maxillary antrum (arrowheads). The mass eroded the adjacent bony structures, such as the anterior wall of the sphenoid sinus (black arrow) and the mass extends to the right antrum and the posterior nasal cavity (white arrow).
C. The axial CT scan (below the level of B) shows multiple osteolytic lesions (arrows) with cortical expansion, bone thinning and mineralized septa (arrowheads) in the bilateral posterior mandible.

marked tendency to recur (1).

CGCGs are unifocal lesions that are generally seen in the anterior mandible, and to a lesser extent, in the other facial bones, hands and feet (5). Multicentric CGCGs have only rarely been reported in the medical literature (7). Most of the previously reported cases of multiple concurrent CGCGs were associated with some form of inherited syndrome or systemic disease (3).

Davis and Cassatly (7) reported on the first case of multicentric CGCGs in the absence of hyperthyroidism. To the best of our knowledge, only 5 cases of multifocal CGCGs without concomitant systemic disease have currently been reported in the English-language medical literature and there has been no reported case that occurred in the 2nd decade of life (1 male patient and 4 female patients; mean age 31.4 years; range: 23–41 years)

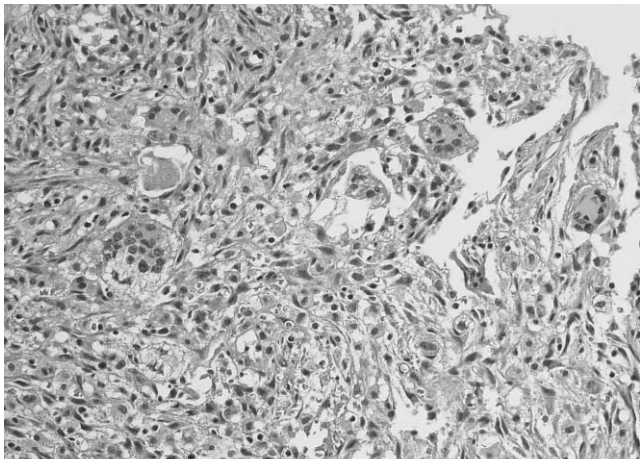


Fig. 3. The biopsy specimen shows several multinucleated giant cells within a background of ovoid and spindle-shaped mesenchymal cells (hematoxylin and eosin staining, magnification × 400).

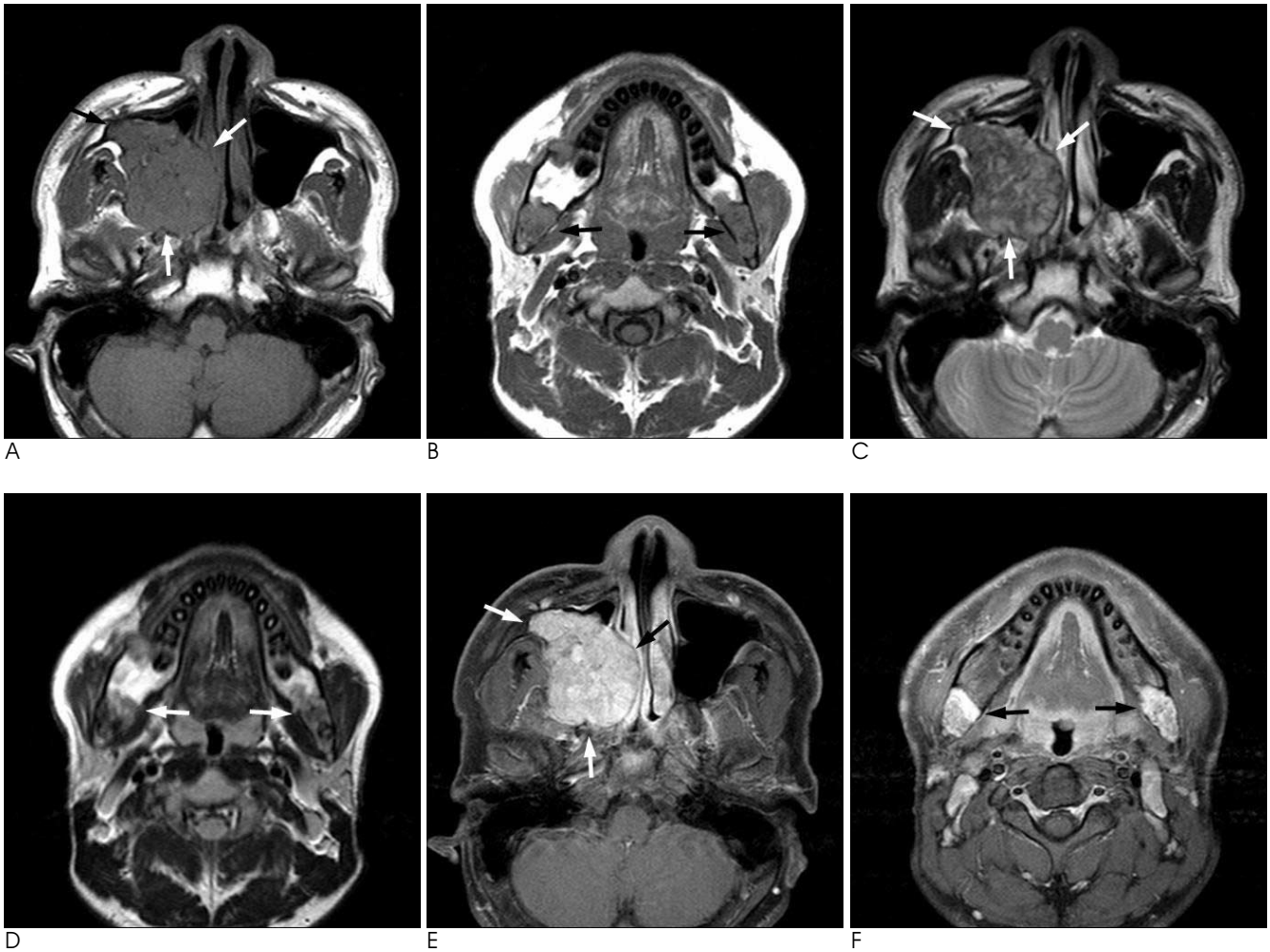


Fig. 2. A-F. The multiple masses (arrows) in the right maxillary sinus and bilateral posterior mandible show low signal intensity on the T1-weighted images (A, B), heterogeneous low to intermediate signal intensity on the T2-weighted images (C, D) and intense enhancement of the masses (E, F) after the administration of contrast agent.

Table 2. The Reported Cases of Multifocal Central Giant Cell Granulomas of the Maxillofacial Region

Study	Age/Gender	Location
Davis and Tideman, 1977	31/F	Right mandibular body, left maxilla
Cassatly et al, 1988	27/F	Parasymphysis and mandibular body
Smith et al, 1990	41/F	Right mandibular ramus, left maxillary sinus, nasal bone, orbit and right maxillary sinus
Wise and Bridbord, 1993	23/M	Left mandibular body; left and right nasomaxillary areas
Wilson et al, 2007	35/F	Left maxilla and right mandible

(Table 2) (4, 5).

The most commonly reported radiological finding of GCRG is lysis with expansile remodeling of the bone. The cortex around the lesion is thin with or without bone destruction (8). However, these radiological appearances are indistinguishable from other radiolucent bony lesions such as odontogenic cyst, aneurysmal bone cyst, ameloblastoma, odontogenic myxoma and odontogenic fibroma (2). The CT appearance of GCRG is not distinctive either. Cortical thinning and destruction, soft tissue extension and a lesion density similar to that of muscle are the usual findings of giant cell granuloma (8). Fibrous septa are a usual finding of giant cell granuloma (8). Mineralization can be seen in CGCG lesions, but this is uncommon and it is usually limited in extent (2). However, diffuse mineralized fibrous septa were noted in our case.

In the present case, the CT scan with a bone window setting showed relatively well defined, heterogeneous isodense multifocal masses with mineralized septa and expansile boney remodeling, and there was cortical thinning of the right maxilla and bilateral mandible. On the MR imaging, the multifocal lesions in the right maxilla and bilateral mandible showed low signal intensity on the T1-weighted images and heterogeneous low to intermediate signal intensity on the T2-weighted images without a cystic component. The mass showed intense enhancement after administration of contrast material. These radiologic findings of our patient are relatively typical findings of a usual CGCG (8). However, diffuse mineralized fibrous septa for this type of lesion have not been reported in the previous literature.

Multifocal CGCGs may be associated with hyperparathyroidism, cherubism or Noonan-like multiple giant cell lesion syndrome (1). The most difficult diagnosis to rule out when presented with multiple giant cell lesions is brown tumor of hyperparathyroidism (7). Our patient had no other biochemical or radiological evidence of hyperparathyroidism (1). Multiple giant cell lesions form part of Noonan-like syndrome, but our patient lacked any of the other features such as a short stature, low intelligence or developmental delay, ocular hyperteleorism, posteriorly angulated ears, pectus excavatum or pulmonary stenosis (1). Cherubism is an autosomal dominantly inherited condition with variable expressivity, and this is characterized by multiquadrant radiolucent lesions of the jaws. Clinically, cherubism most commonly manifests as a progressive and symmetrical enlargement of the mandible and/or the maxilla, and this is first noted between the ages of 1 and 4 years. There is no family history of similarly affected family members for cases of CGCG (3). Yet there are rare reported instances of synchronous multiple CGCGs of the maxillofacial region for which other causes or associated disorders have been excluded (3).

In conclusion, multifocal CGCGs in the maxillofacial region are suggestive of a systemic disease such as hyperparathyroidism or an inherited syndrome such as Noonan-like multiple giant cell lesion syndrome. The present study presents a case of multifocal, synchronous CGCGs in the bilateral mandible and right maxilla without any concomitant systemic disease. Although it is very rare, multiple CGCGs should be considered in the differential diagnosis of benign fibroosseous lesion that typically present as an expansile soft tissue mass of the maxillofacial region.

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대한영상의학회지 2010 ; 62 : 11-15

악안면부에 발생한 동시다발성 중심성 거대세포 육아종: 증례 보고[1]

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강민석 · 김학진

악안면부에 발생한 다발성 중심성 거대세포 육아종은 부갑상샘기능항진증이나 유전성질환 등의 전신병을 시사한다. 수반된 전신병 없이 악안면부에 발생한 다발성 중심성 거대세포 육아종은 매우 드물며 현재까지 5개의 증례만 보고되어 있다. 저자들은 양측 하악과 우측 상악에 발생한 17세 남자환자의 전신병을 동반하지 않은 다발성 중심성 거대세포 육아종 1예를 경험하였기에 문헌고찰과 함께 보고한다.