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## Up-to Date Review And Case Report

# Central giant cell granuloma: a case report

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**Abstract – Introduction:** Central giant cell granuloma (CGCG) is an uncommon benign bony lesion that occurs in the mandible and maxilla. **Observation:** A 30-year-old woman was evaluated for a radiolucent lesion of the mandible, which was discovered by chance. This image was associated with a painless swelling covered by normal mucosa. No symptoms were associated. After surgical excision, histological examination of the surgical specimen concluded a CGCG. Surgical follow-up was simple, and the first radiological test performed 3 months after confirming the onset of bone healing. **Comments:** The clinical behavior of CGCG ranges from a slow-growing asymptomatic swelling to an aggressive lesion with pain, local osteolysis, root resorption and tooth displacement. Therapeutic options have greatly varied in recent years. Nonsurgical treatments with alpha-interferon, calcitonin, and corticosteroids have been described and their benefits may be worthy of consideration. **Conclusion:** A surgical approach is considered as the traditional treatment and is still the most accepted one. However, in some publications, authors disagree on the type of surgery that should be performed.

## Introduction

Giant cell central granuloma (GCCG) is an uncommon pseudotumor of the maxilla. It accounts for 7% benign maxillary tumors, and females are predominantly affected in 2/3 of cases before age 20 years [1]. The origin of this lesion is unclear [2]; some factors such as local trauma, inflammation, intraosseous hemorrhage, and genetic anomalies may be involved [3].

There are two types of clinical progression: nonaggressive and aggressive. Chuong *et al.* described the criteria for aggressive lesions: pain, paresthesia, root resorption, rapid tumor evolution, cortical bone perforation, and a high rate of postoperative relapses [4]. Other authors classify GCCG according to their clinical and radiographic characteristics [5–8]. The aggressive forms are found mainly in younger patients.

Surgery is considered the best course of treatment. However, in the literature, the authors do not agree on the type of surgery that should be performed. Resection by surgical curettage has a low recurrence rate for small lesions. In the event of a relapse or larger lesions, surgical curettage by peripheral ostectomy and/or block resection should be considered by some surgeons [9].

## Observation

A 30-year-old woman was referred by a dentist for the incidental discovery of a radiolucent lesion in the right mandibular body during pulpitis treatment on 46. The medical history revealed stress-related asthma that was being treated with salbutamol and seasonal allergic rhinitis that was being treated symptomatically with levocetrizine 5 mg tablets. There was no surgical history. Dental monitoring was regular till date. The radiological lesion had never been detected before. The patient was checked while his teeth 46/47 have been treated endodontically. There were no neurological signs or functional signs. There was no facial asymmetry, and integuments appeared normal.

However, the intraoral clinical examination showed bone deformity of the right mandibular cortex in its dentate and basilar portion at the premolar–canine area. The mucous membrane was healthy. The overlying teeth were immobile. However, teeth 42/43/44/45 did not respond to vitality tests, which led us to suspect inflammatory lesions of endodontic origin (negative vitality test). Soft tissues were not affected and had a normal appearance.

The orthopantomogram (Fig. 1) showed a radiological lesion in the right mandibular body with a 5 cm axis, with resorption of the dental roots in relation to the lesion: 43, 44, and 45.

Conical-beam computed tomography (CBCT) was performed on the day of the first consultation. It showed the osteolysis of

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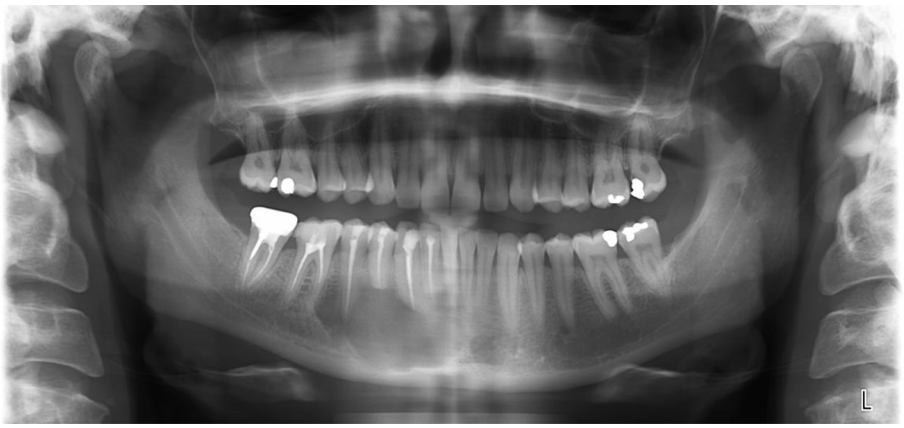


**Fig. 1.** Orthopantomogram. Osteolytic lesion of the horizontal branch of the mandible with root resorption of 43, 44, and 45.

the right mandibular body in both the dental and basilar regions. The lesion had a diameter of 5 cm at its widest point. It extended from the mesial face of 31 to the mesial face of 46. The outer cortex was damaged and fenestrated in some places. The lingual and basilar cortices were unaffected. Its appearance was heterogeneous in places. However, we were unable to determine from these images whether the tumor was pushing or enclosing the mandibular canal and the mental foramen (Figs. 2 and 3).

To rule out any pathology related to bone metabolism, a blood test was prescribed. All parameters were normal, including PTH (associated with brown tumors, indicative of primary hyperparathyroidism) and alkaline phosphatase. The erythrocyte sedimentation rate, C-reactive protein, and calcium–phosphorus levels were within normal ranges. GCCG was diagnosed and a surgical resection was indicated.

The treatment was performed under general anesthesia. After lifting the mucosubperiosteal flap, the tumor was exposed and described as "a fleshy, reddish brown mass, resembling splenic pulp" [10].

Teeth 31, 41, 42, 43, 44, 45 had been previously treated endodontically because they were in direct contact with the bony lesion. In addition, teeth 43, 44, and 45 were presumably nonvital.

Antibiotic prophylaxis (amoxicillin 2 g per day for 7 days) started 24 h before surgery was prescribed before the surgical procedure and was continued 6 days after the surgery.

The resection of the lesion with anatomic and pathological analysis of various fragments was supplemented by the deep curettage of the surrounding bone until seemingly healthy bone tissue was observed. The mental neurovascular bundle was preserved.

Surgical curettage was completed by the apical resection of all the teeth included in the tumor process until gutta percha was impermeable within the periapical complex.

The integrity of the lingual cortical, as well as the basilar region, prevented intermaxillary blocking as well as implantation of plates for osteosynthesis. Bone reconstruction was not required despite the large volume of the lesion on CBCT.

A vestibular flap was repositioned and sutured using Vicryl® 3/0. The resected material, consisting of approximately 20 fragments 5–15 mm in diameter, was subjected to histological examination.

Level-1 painkillers (paracetamol 4 g per day), a corticosteroid (prednisone, 1 mg/kg for 3 days), and 0.12% chlorohexidine mouthwash were prescribed.

The patient started brushing their teeth the day after the surgery using a 7/100th surgical toothbrush for 10 days.

The following dietary advice was given: liquid feeds in the first 2 weeks after surgery, then mixed for 1 month to avoid any risk of mandibular fracture. Similarly, sports practice was prohibited until the bone has healed.

Two weeks after surgery, the mucosal healing was quite satisfactory, and the patient did not complain about any pain.

The anatomical and pathological examination suggested a diagnosis of GCCG, and was confirmed by a secondary analysis carried out at the Anatomy-Pathology Laboratory of CHRU in Tours, which specializes in bone pathologies. The distribution of giant plurinuclear osteoclast cells, clustering in islets around foci of hemorrhagic suffusions, the overall fibrous appearance of the tumor, the cytological aspect of the mononuclear elements, the existence of neo-osteogenesis, and the negative immunostaining with the anti-P63 antibody (thus eliminating a giant cell tumor) were in favor of the diagnosis of a central giant cell granuloma (CGCG).

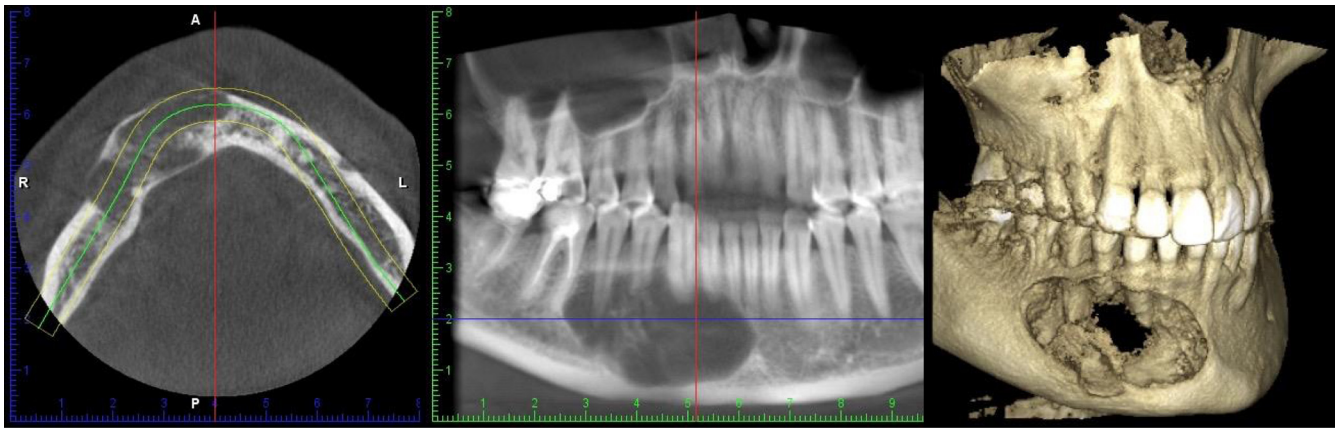
The patient followed up 3 months after the surgery. There was no residual symptomatology. A orthopantomogram showed a heterogeneous bone structure of the mandible (Fig. 4).

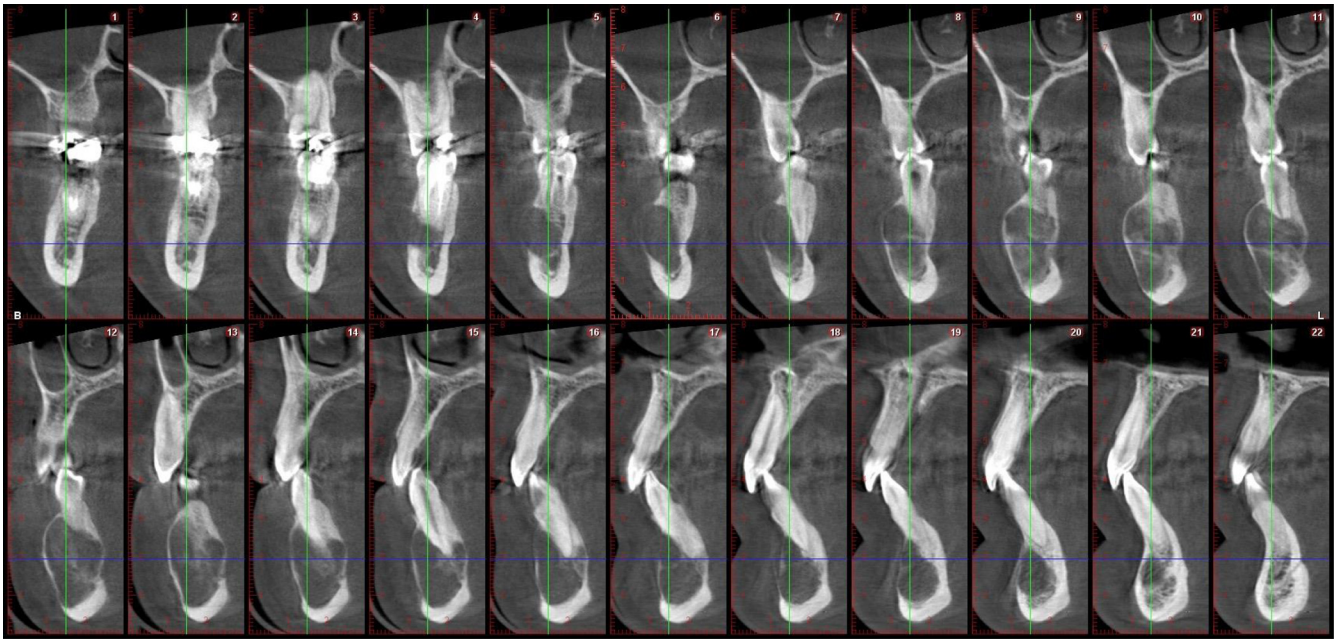
## Discussion

Jaffe initially described the term "reparative GCCG" to describe lesions that he believed were a response to an intraosseous traumatic hemorrhage of the jaw [11].

GCCG occurs mainly in children or young adults, with approximately 75% cases reported before age 30 years, but may appear at any age [12].

Women are affected much more often than men, with a sex ratio of 2:1 [13–15]. Over 70% of CGCG occur in the mandible and $<30\%$ occur in the maxilla, with a predilection for the anterior region [14–16].




**Figs. 2 and 3.** Axial and curvilinear section and 3D representation of right mandibular substance loss.

In the literature, most maxillary lesions are described as being located in the anterior region, whereas in the mandible, these lesions appear to be distributed equally between the anterior and posterior regions.

Jacoway *et al.* were the first in 1988 to report the treatment of a GCCG with corticosteroids. In practice, they proposed weekly intralesional injection of steroids to decrease its size, according to volume tumor. The injection protocol corresponds to 150 mg of prednisolone equivalent per cubic centimeter of tumor spread over 6 weeks. This study showed a complete resolution in three out of the four patients, although one patient needed additional surgery [17]. Some authors have a weak systemic spread of corticosteroids due to intratumoral injection and the use of epinephrine in the solution; but this is difficult to assess because of the hypervascularization of the tumor. One case of Cushing's syndrome after intralesional steroid treatment has been reported [18].

"Giant" cells in GCCG act as calcitonin receptors [19]. Some authors have reported the inhibition of the activity of giant cells after calcitonin injection within the lesion [20]. The adverse effects listed are chronic diarrhea, nausea, flushing, and dizziness, which most often occur immediately after inhalation of calcitonin and epistaxis directly related to the mode of administration (inhalation by intranasal spray of salmon calcitonin to 200 units per day) [21]. However, patients' responses to this treatment vary [19].

Chien *et al.* reported cases of GCCG in children treated with bisphosphonates, with three out of the four cases showing secondary reossification of the treated granuloma [22]. Alendronate is the most commonly used bisphosphonate; it is mixed with intralesional injections of corticosteroids to improve its efficacy [23]. However, alendronate is often found in patients with osteochemical necrosis [24,25].

Denosumab is a human monoclonal antibody (IgG2) that targets RANKL, the ligand of the RANK receptor. Blocking of the

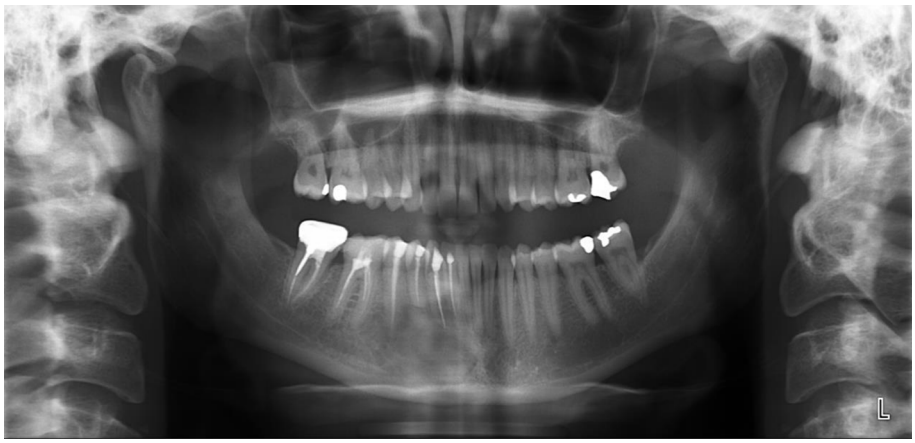


**Fig. 4.** Follow-up orthopantomogram after 3 months.

RANK/RANKL interaction inhibits the formation, function, and survival of osteoclasts, thus decreasing bone resorption in cortical and trabecular bone. Isolated cases are found in the literature with less comparable results but with side effects comparable to bisphosphonates and other calcitonin injections.

Alpha interferon was proposed both because of their antiangiogenic potential and as a mediator in the differentiation of mesenchymal cells into osteoblasts, thus leading to an increase in osteogenesis [26–28]. Alpha IFN administered for aggressive GCCG seems capable of halting the rapid growth of lesions, decreasing their size and even consolidating the bone, but it is still necessary to intervene surgically to eliminate the lesion [29]. In addition, there are severe side effects. This protocol does not result in a complete remission.

Several studies and isolated cases highlighting the interest of antiangiogenic and antiosteoclastic molecules in the treatment of GCCG have been reported in the literature. However these substances have very variable efficacy with severe side effects in the short term and are poorly documented in the medium term [30].

According to Eisenbud and his collaborators, in the event of a recurrence, a surgical vacuum and a peripheral ostectomy with a bone resection must be performed [31].

An *en bloc* resection offers the best chance for a full recovery. In a study of 18 patients with aggressive CGCG, the treatment consisted of an *en bloc* surgical resection with a 5 mm margin of healthy tissue. Only one patient had a relapse [32].

Unal *et al.* propose to obtain safety margins by means of microperforations of the resection field with a diamond cutter. In this study, a curettage, an osteotmy, a tumor resection and microperforations were performed in order to improve a better bone healing [33]. It should be noted that only a few cases described after *en bloc* resection were followed by bone reconstruction with an iliac crest graft [34–36].

The treatment of these lesions involves the suppression of local irritants (tartar, bacterial plaque, defective restorations), complete surgical resection of the lesion, and extraction of mobile adjacent teeth. Relapses are rare (5–11% cases) [37].

## Conclusion

The diagnosis of GCCG is clinical, radiological, and, above all, biological and anatomopathological in nature. Calcium and phosphorus levels must be mandatorily assessed (to differentiate from bone metabolism disorders and brown tumors caused by hyperparathyroidism) and the absence of the p63 protein must be confirmed using immuno-labeling. This indicate a diagnosis of GCCG.

Despite the apparently significant radiological volume of the lesion, surgical exploration allowed us to achieve a conservative and nonmutilating approach. Indeed, the surgical team initially decided to follow the conservative therapeutic approach after the clinical discovery of the lesion. The synthesis of clinical and radiological elements and profound theoretical knowledge make it possible to guide the diagnostic hypothesis and the therapeutic approach; the clinical sense and the experience of the surgeon make sense when treating this type of rare pathology. The skills and the experience of the surgeon are essential when treating this type of rare pathology.

However, Block surgery proceure resection is the best option to cure the condition completely. The risk/benefit ratio of angiogenic and/or antiosteoclast molecule injection, which we found to have negative results, justified our choice of treatment. Regular monitoring is indispensable in all cases because of the significant potential for a relapse.

## Conflict of interest

The authors declare that they have no conflicts of interest in relation to this article.

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