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CASE REPORT

Surgical dilemma in a mandibular central giant cell granuloma – a case report

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Abstract:

Central giant cell granuloma (CGCG) is a benign osteolytic lesion that may display non-aggressive or aggressive behavior. This report describes a 27-year-old male with a mandibular CGCG initially classified as non-aggressive due to its radiographic features and absence of cortical perforation or root resorption. Initial treatment with intralesional corticosteroid injections and enucleation failed to control the lesion, which progressed rapidly, reaching 7 cm and causing buccal cortical perforation. A new biopsy confirmed aggressive features, prompting surgical management via segmental osteotomy with curettage and cryotherapy, preserving the lingual cortex. Immediate reconstruction was performed using an autogenous iliac bone graft and titanium plate fixation. Postoperative healing was uneventful, with good functional and aesthetic outcomes. After 9 years and 7 months of follow-up, no recurrence was observed. This case highlights the potential for behavioral shift in CGCG and emphasizes the need for individualized treatment and timely surgical intervention when conservative therapy fails.

Keywords: Giant cell; Granuloma; Trauma surgery; Drug therapy; Traumas.

INTRODUCTION

The central giant cell granuloma (CGCG) is considered a benign osteolytic lesion of uncertain origin, defined as a lesion comprised of osteoclasts and characterized by the presence of multinucleated giant cells of the osteoclast type, arranged in a fibroblastic stroma with spindle cells, also prominent areas of red blood cell extravasation and may also contain foci of newly formed bone tissue[1]. It is more frequently found in females, at the anterior mandible and until the third decade of life[2]. Radiographically, CGCG presents as a radiolucent lesion, ranging from a small periapical lesion to a large multinucleated lesion[3].

The lesion can be classified as "non-aggressive", when it has a slow and painless growth, is smaller than 5 cm in diameter[4], does not cause tooth displacement and root resorption and preserve the cortical bone[5]. On the other hand, the "aggressive" variant has a rapid and painful growth, is larger than 5cm in diameter with tooth displacement and root resorption, perforation of the alveolar cortical and tends to recur[4,6].

Statement of Clinical Significance
This case highlights the potential for behavioral change in central giant cell granuloma, which may progress from non-aggressive to aggressive despite conservative treatment. Clinicians should ensure timely surgical intervention and long-term follow-up to optimize functional and aesthetic outcomes.

The traditional treatment of CGCG is surgical curettage or enucleation[2]. However, depending on the aggressive behavior of the lesion, size and location, the extent of the surgical procedures can compromise vital structures of the patients, therefore, the combination of pharmacological treatment and surgery, or pharmacological treatment alone, have been used to avoid or reduce these damages[2]. The use of calcitonin, corticosteroids, interferon-alpha, and more recently, denosumab have been reported in the literature[2,7].

According to a recent systematic review, the injection of triamcinolone acetonide, in varying concentrations (10, 20 and 40 mg), is the most used

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pharmacological treatment to CGCG[8]. The mechanism of action of the corticosteroids in the CGCG is not fully understood, but it is suggested that the drug inhibits osteoclast activity, resulting in bone regeneration and the recovery of the bone normal functionality[9].

Therefore, this article aims to report a case of a CGCG in the mandible of a male young adult that was first defined as non-aggressive, did not respond to the conservative treatment of triamcinolone acetonide and enucleation, and was redefined as aggressive, needing a more invasive approach.

CASE REPORT

A 27-year-old male patient was referred to the Diagnostic Center for Oral Diseases (DCOD) of the Faculty of Dentistry of the Federal University of Pelotas (UFPel) for evaluation of an intraosseous lesion in the mandible, comprising the region between teeth 32, 33 and 34, measuring 2 cm in diameter, associated with tenderness on palpation and a 4-month history.

Intraoral clinical evaluation showed a slight swelling at the bottom of the buccal sulcus between the lower incisors and canines on the left side (Figure 1A). On panoramic radiographic examination, a radiolucent, unilocular lesion with well defined borders was observed, without causing root resorption or displacement of adjacent teeth. Tomographic examination reveals destruction of the buccal alveolar cortex between the teeth 33 and 34 (Figure 1B).

An incisional biopsy was performed by Department of Oral and Maxillofacial Surgery and Maxillofacial Prosthodontics, School of Dentistry UFPel, in November 2015, and histopathological analysis revealed a connective tissue containing proliferation of mononuclear spindle-shaped and polygonal cells that permeated multinucleated giant cells and blood vessels (Figure 2A). Serological tests were requested to detect levels of parathyroid hormone (PTH), alkaline phosphatase, calcium and phosphorus, which ruled out hyperparathyroidism (Table 1). Thus, with the diagnosis of non-agressive central giant cell granuloma, the proposed treatment was injections of 10mg of triamcinolone hexacetonide diluted in 5% bupivacaine without vasoconstrictor for each cm^3 of lesion, so 2 ml of this solution were applied[10].

The first application was made in December 2015 and the following ones within an interval of 15 days. However, there was no positive response to the use of corticosteroids after 3 intralesional injections. Due to the lack of response to triamcinolone protocol, a new treatment was proposed. In February 2016 the enucleation was performed and in April 2016 we started again the triamcinolone acetonide injections at 10 mg fortnightly, totaling 4 more applications. The patient had no adverse effects from the corticosteroid injections. However, after this period, in June 2016, the patient returned and the lesion had increased to 7 cm in diameter, causing perforation of the buccal cortical and presenting a multiloculated appearance (Figures 3A and 3B). When performing a new biopsy, in addition to the presence of multinucleated giant cells, the sample revealed the presence of an area of bone neoformation and fibrosis (Figure 2B-D).

Given the aggressive nature of the lesion, resection of the anterior segment of the mandible was indicated. Preoperative cone-beam computed tomography (CBCT) allowed detailed assessment of the lesion, revealing osteolytic extension to the buccal cortical plate, with preservation of the lingual cortical plate.

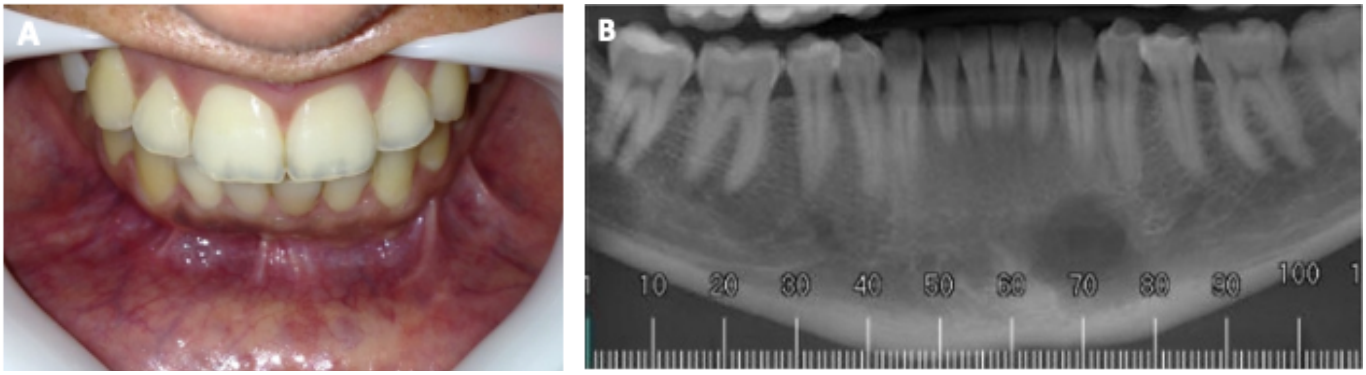

Figure 1. First documentation before treatment. A: Intraoral photo showing a slight increase in volume at the bottom of the buccal sulcus between the lower incisors and canines on the left side. B: Computed tomography revealing a well-delimited hypodense image, measuring approximately 20 mm in diameter.

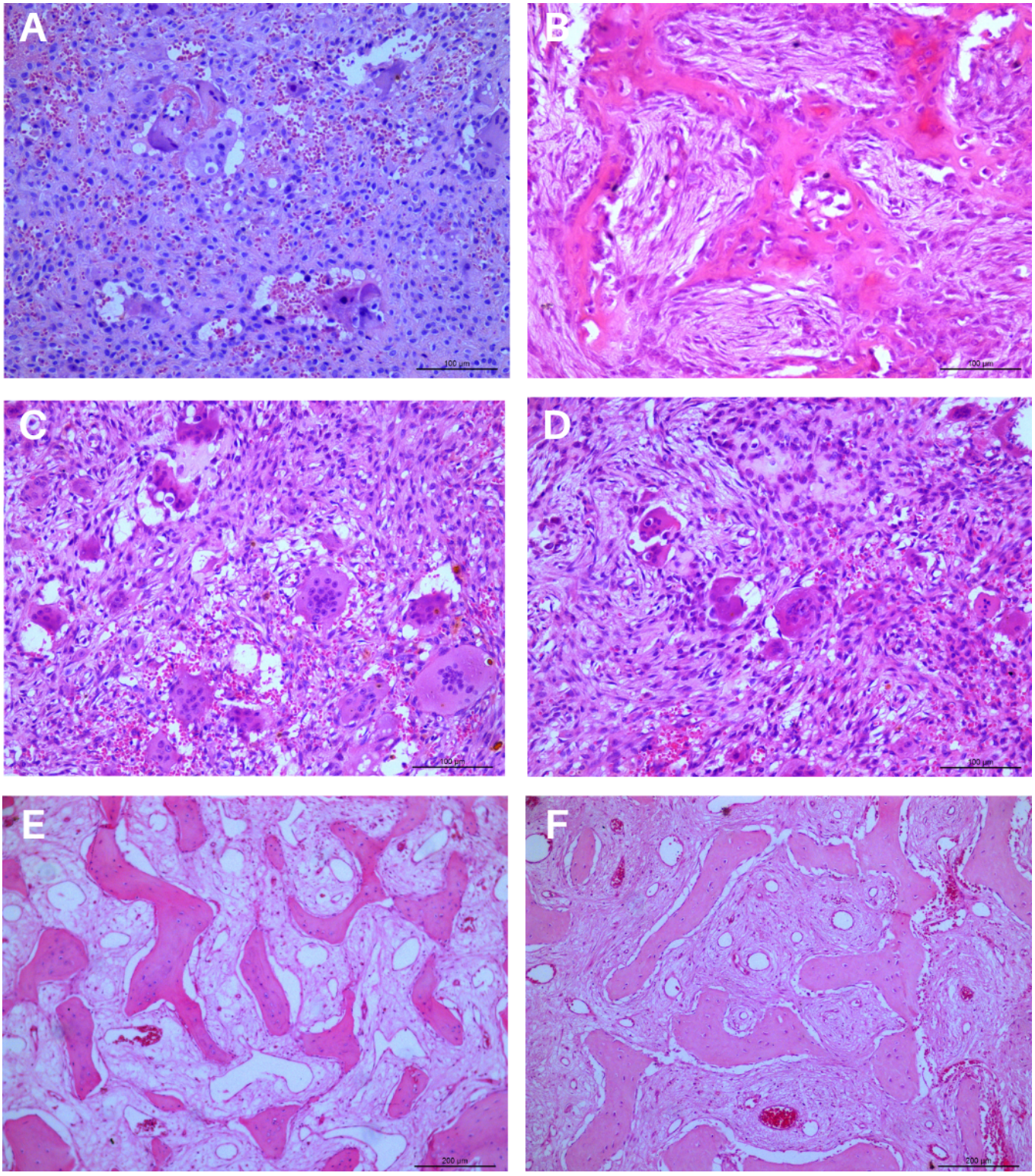

Figure 2. Histopathological images. A) Image of the first biopsy showing numerous multinucleated giant cells within a highly cellular stroma composed of polyhedral and spindle-shaped cells, with prominent vascularization (100x). B) Image of the second biopsy demonstrating fibrous stroma with spindle-shaped cells and areas of immature bone neoformation (100x). C-D) Highly cellular fibrovascular stroma containing numerous multinucleated giant cells, with focal areas of cellular cannibalism (100x). E) Areas of bone neoformation associated with fibrillar stroma and blood vessels (200x). F) Connective tissue with a denser and more vascularized stroma, with areas of bone neoformation (200x).

This anatomical condition enabled the planning of a segmental osteotomy while minimizing the morbidity typically associated with more extensive mandibular resections.

To optimize surgical planning, the DICOM (Digital Imaging and Communications in Medicine) data obtained from CBCT were exported and processed to generate a three-dimensional stereolithographic (.stl) model. This biomodel allowed accurate visualization of the lesion and facilitated preoperative assessment of osteotomy margins, estimation of the iliac crest graft dimensions, and pre-bending of a 2.4-mm standard (non-locking) reconstruction plate. In addition, the biomodel supported estimation of the appropriate length of bicortical screws. No cutting guides were fabricated for either the mandible or the iliac crest (Figure 4).

Thus, segmental osteotomy and curettage were performed under general anesthesia via a lower extraoral submandibular approach. Following lesion removal, cryotherapy was applied to the surgical bed using liquid nitrogen. The protocol consisted of three direct applications of 1 minute each, with 3-minute intervals between applications. During these intervals, copious irrigation with sterile 0.9% saline solution at body temperature (36.5°C) was performed. The surrounding tissues were carefully protected with dry compresses, which were replaced after each application to minimize collateral damage.

Reconstruction of the mandible was achieved with the placement of a reconstruction plate to ensure stabilization and prevent pathological fractures, followed by immediate reconstruction using an autogenous iliac crest bone graft to restore mandibular continuity and contour (Figures 5 and 6).

Immediately after surgery, the patient presented good healing of the surgical area. During the follow-up period, there was a fistula in the region where the surgical intervention was performed and, therefore, root

Table 1. Serological test results.

Serological test	Results
Parathyroid hormone	93,8 pg/ml
Calcium	9,70 mg/dl
Phosphorus	5 mg/dl
Alkaline phosphatase	235 U/l

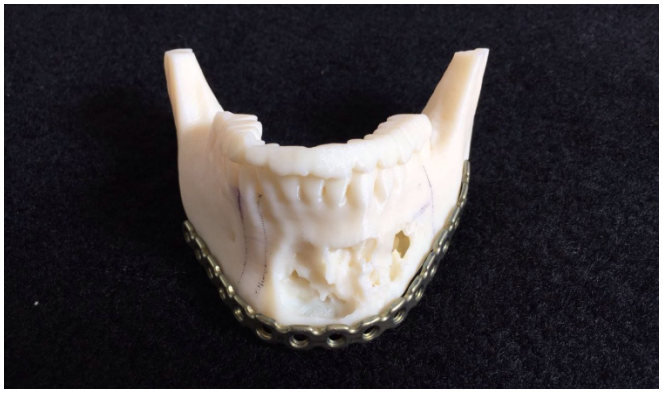

Figure 4. Biomodel used for surgical planning, including visualization of osteotomy safety margins, estimation of iliac crest graft size, and pre-bending of a 2.4-mm standard (non-locking) reconstruction plate.

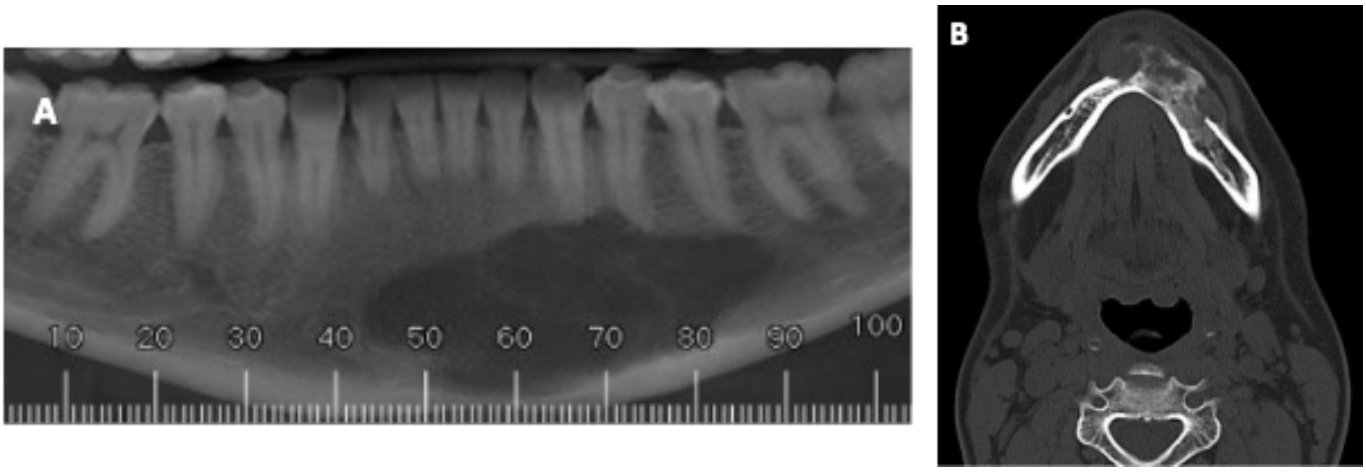

Figure 3. Computed tomography (June 2016) after triamcinolone applications, showing osteolytic expansion of the lesion and perforation of the buccal cortex, measuring 7 cm in diameter.

canal therapy of the lower anterior teeth was performed. After nine years and seven months of follow up, the patient's masticatory and phonetic functions are preserved and aesthetics as well. There was no recurrence of the central giant cell granuloma (Figure 6).

DISCUSSION

In our case, CGCG occurred in a 27-year-old male patient, with involvement of the anterior portion of the mandible. Although CGCG is more frequent in females, the location of the lesion in this case was consistent with the literature[2].

The diagnosis of central giant cell granuloma (CGCG) requires complementary tests to identify possible alterations in the parathyroid glands. In the present case, PTH, calcium, alkaline phosphatase, and phosphorus levels were normal, which helped distinguish between brown tumor and CGCG, since these lesions are histologically identical and altered laboratory values are

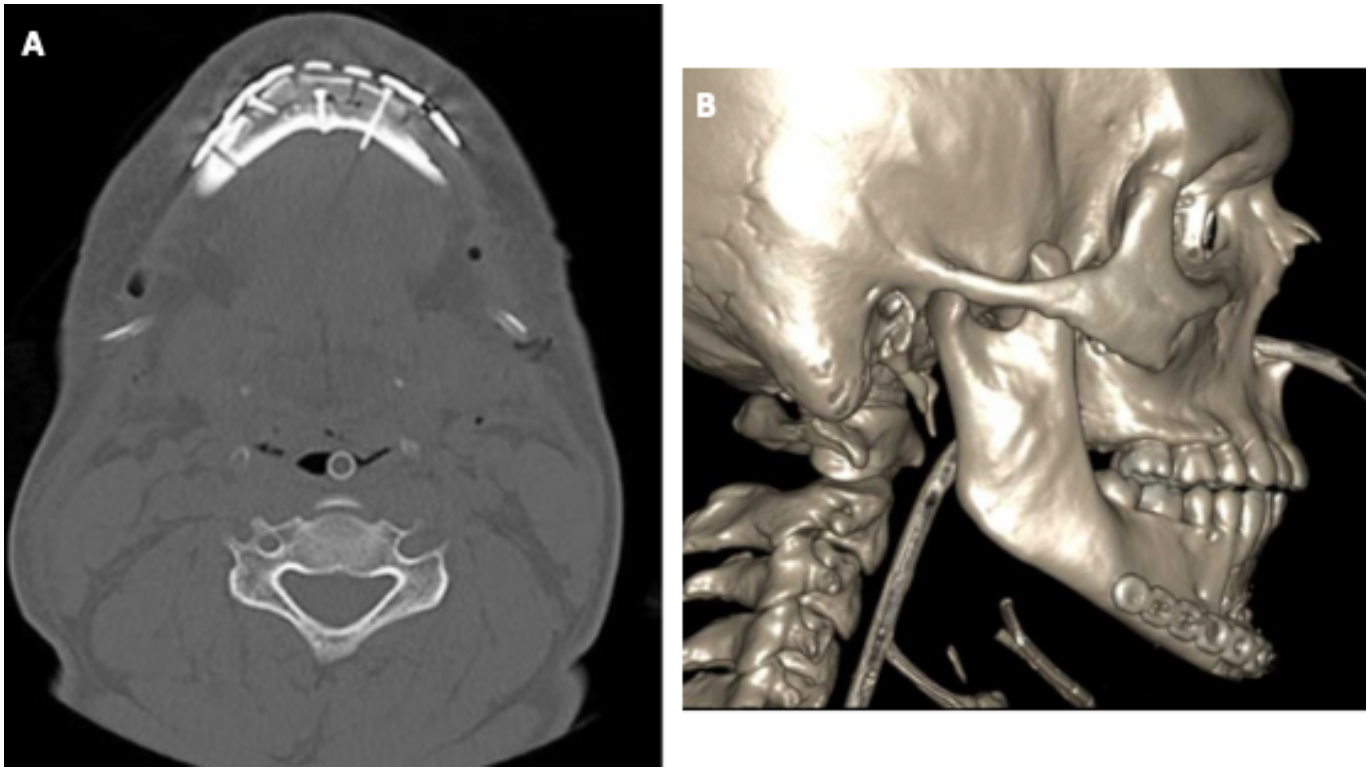

Figure 5. Trans-surgical images. A: Segmental osteotomy. B: Installation of a fixation plate for autogenous iliac grafts.

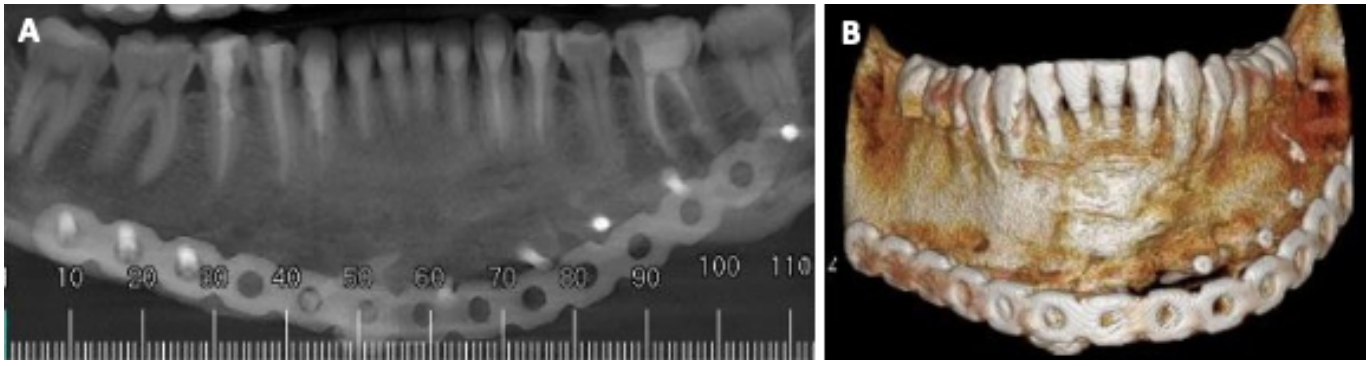

Figure 6. Immediate postoperative. A: Computed tomography showing adaptation of the plate and autogenous graft. B: Maintenance of the mandibular profile.

required to define the lesion as a brown tumor[7,10]. Genetic alterations are associated with the occurrence of multiple CGCGs in rare syndromes, such as mutations in the *SH3BP2* gene in Cherubism, the *PTPN11* gene in Noonan syndrome, and *NF1* in type 1 neurofibromatosis[7]. Other unilocular or multilocular radiolucent lesions in the jaws, such as ameloblastoma, periapical granuloma, and bone cysts, should also be considered in the differential diagnosis of CGCG[7,10]. In the present case, the diagnosis was established based on histopathological analysis from an incisional biopsy, in conjunction with imaging findings and laboratory tests. Genetic testing was not performed, as the lesion was solitary (Table 1).

First described in 1986, Choung et al. differentiated CGCG into aggressive and non-aggressive variants based on clinical signs, symptoms, and histological features[6]. Later, Kaban et al. proposed additional parameters for classifying the aggressiveness of the lesion: lesions larger than 5 cm and those that recurred after curettage were considered aggressive. In the absence of these criteria, a lesion was also classified as aggressive if at least three of the following features were present: cortical bone perforation, root resorption, tooth displacement, rapid growth, and cortical thinning[4]. Initially, we classified the lesion as non-aggressive, as it did not fulfill the criteria for aggressiveness. However, changes observed during the follow-up period indicated a more aggressive behavior, leading to a reclassification of the lesion.

Initially, we opted for treatment with intralesional injections of 10 mg of triamcinolone. The decision to use intralesional corticosteroid therapy was based on the size and location of the lesion, which suggested non-aggressive behavior[4,6], on favorable outcomes reported in the literature[7], and on the fact that this is a conservative and relatively low-cost treatment option[9]. In 1994, Terry and Jacoway established a protocol involving 10 mg of triamcinolone acetonide combined with 0.5% Marcaine containing 1:200,000 epinephrine, at a dosage of 1 mL per cm^3 of lesion, administered weekly for six weeks[10]. Alternatively, triamcinolone acetonide may also be used in different concentration[11,12].

Given the rapid growth and lack of response to pharmacological treatment, the most notable clinical feature in our case was the aggressive behavior of the lesion. The failure of pharmacological therapy, combined with the significant increase in lesion size, indicates an aggressive clinical course[3,4].

Recent advances in molecular pathology have provided new insights into the pathogenesis of central giant cell granuloma (CGCG). Alterations in the MAPK signaling pathway, particularly involving KRAS mutations, have been increasingly reported in giant cell lesions of the jaws[13,14]. These findings suggest that such lesions may represent clonal proliferative processes rather than purely reactive conditions[15]. Moreover, activation of the MAPK pathway has been associated with increased cellular proliferation and may help explain the aggressive clinical behavior observed in some cases[15]. In the present case, the rapid increase in lesion size from 2 cm to 7 cm over seven months may be indicative of an underlying molecular driver, although genetic testing was not performed. These observations reinforce the importance of considering molecular mechanisms in the biological behavior and management of CGCG.

Osterne et al., in a review of 41 cases of CGCG treated with intralesional corticosteroids published between 1998 and 2011, reported that 78% of cases showed a good response to treatment, 14.6% had a moderate response, and 7.3% did not respond[12]. The expected outcome of corticosteroid therapy is bone formation, which was observed in 87.5% of cases following intralesional injections, although 12.5% of patients did not respond[9].

Despite these favorable outcomes, glucocorticoids may exert adverse effects on bone metabolism, including increased bone resorption[11,16]. Their mechanism of action is not fully understood but is thought to involve inhibition of extracellular lysosomal proteases and induction of apoptosis in multinucleated giant cells. Conversely, stimulation of osteoclast differentiation and activity has also been reported, which may contribute to variable treatment responses[16]. Unfortunately, in our case, the lesion increased in size from 2 cm to 7 cm in diameter over seven months, despite seven intralesional applications, confirming its aggressive behavior and ultimately requiring surgical removal.

Another factor that may have significantly contributed to the lesion's progression was the irregular timing of the corticosteroid applications. The protocol adopted for our case[10], advises weekly intralesional injections over a six-week cycle. However, due to difficulties in maintaining consistent follow-up with the patient, we performed seven applications at intervals that did not conform to the established protocol, which may have influenced the shift in clinical behavior of the lesion.

This deviation from the established interval may have triggered a biological 'rebound effect' or exacerbated the paradoxical stimulation of osteoclasts. As described by Komori[16], while corticosteroids are intended

to inhibit lesions, they can paradoxically enhance bone resorption by increasing the RANKL/OPG ratio, elevating reactive oxygen species (ROS), and prolonging osteoclast lifespan[13]. In this case, the irregular application intervals likely permitted these pro-resorptive mechanisms to dominate, leading to aggressive expansion. Although histopathological evidence in Figure 2B-D shows areas of bone neoformation that indicated that the corticosteroid did initiate some osteoblastic repair, this response was insufficient to counteract the steroid-induced osteoclast stimulation[16].

Given the aggressive nature of CGCG, several therapeutic approaches have been proposed. Surgical procedures such as curettage, enucleation, and even segmental resection remain common options. However, in extensive lesions, surgery can result in both aesthetic and functional impairments. In cases of aggressive lesions treated with curettage, recurrence rates can reach up to 37.2%[2]. Conversely, segmental resections, although more invasive, are associated with lower recurrence rates (5.9%), even in aggressive cases[2].

In our case, the preservation of the lingual cortical bone allowed for a segmental osteotomy with reconstruction using an autogenous iliac crest graft and plate fixation, avoiding the need for complete mandibular resection[17,18]. This approach was deliberately chosen to minimize the known morbidities associated with resection of the anterior mandibular region, particularly in the lingual aspect, where the genial tubercles and digastric fossa are located[14]. Beyond aesthetic considerations, this region serves as the origin and insertion site for muscles essential to respiratory and swallowing functions, including the genioglossus, mylohyoid, geniohyoid, and anterior belly of the digastric muscle[17,18].

Furthermore, preservation of the lingual cortex, when feasible, facilitates mandibular reconstruction and contributes to improved functional outcomes[17,18]. The success of this approach in the present case is evidenced by long-term follow-up, which demonstrated no recurrence and no functional or aesthetic deficits.

The long-term (9-y, 7-m) follow-up of anterior mandibular reconstruction after resection of the CGCG provides compelling evidence that the reconstructed segment undergoes not only initial incorporation but also sustained functional remodeling, ultimately resembling native mandibular bone in both structure and biomechanics. The observed progressive corticalization, trabecular reorganization, and loss of graft-host interface definition are consistent with the principles of bone remodeling described by Wolff's law, whereby mechanical loading drives structural adaptation over time[19]. The anterior mandible is subjected to complex biomechanical forces, including incisal loading and muscular attachments such as the genioglossus, geniohyoid, and anterior belly of the digastric, which contribute to continuous stimulus for bone turnover and reinforcement[20]. Furthermore, the absence of radiographic signs of recurrence, coupled with increasing radiopacity and trabecular organization, aligns with previously described patterns of osseous regeneration following CGCG treatment[2]. Therefore, this case supports the concept that, in the absence of residual pathology, reconstructed mandibular bone is a dynamic tissue capable of long-term adaptation, achieving structural stability and biomechanical competence comparable to native bone.

Thus, this case illustrates a central challenge in the management of CGCG: selecting the most appropriate treatment while minimizing functional and aesthetic compromise. Although extensive surgery is often required in aggressive cases, particularly in young patients, detailed preoperative 3D planning can enable immediate reconstruction and optimize outcomes[2]. In our case, this approach resulted in successful functional and aesthetic rehabilitation, with no signs of recurrence after nine years and seven months of follow-up.

CONCLUSION

This case highlights the challenges in treating aggressive CGCG and the limitations of conservative therapy when follow-up is irregular. Despite initial non-surgical management, surgical intervention proved necessary. Careful preoperative planning enabled functional and aesthetic reconstruction, emphasizing the importance of individualized treatment based on lesion behavior and patient context.

AUTHORS' CONTRIBUTIONS

IVBC: Conceptualization, Data curation, Methodology, Writing – original draft, Writing – review & editing. BFO: Conceptualization, Data curation, Methodology, Writing – original draft, Writing – review & editing. FAC: Writing – original draft, Writing – review & editing. MAT: Investigation, Supervision, Validation, Writing – review & editing. OLCJ: Investigation, Supervision, Validation, Writing – review & editing. APNG: Investigation, Supervision, Validation, Writing – review & editing. AE: Investigation, Supervision, Validation, Writing – review & editing.

CONFLICT OF INTEREST STATEMENT

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Competing interests: The authors have no relevant financial or non-financial interests to disclose.

Ethics approval: This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the Hospital (no. 5.099.339).

Declaration of generative AI and AI-assisted technologies in the writing process: During the preparation of this work the authors used ChatGPT in order to improve readability and language. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Data availability statement: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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