

Dilemma in the Treatment of a Central Giant Cell Granuloma

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Management of central giant cell granuloma (CGCG) presents a clinical challenge. While eradicating a lesion known for its high recurrence rate calls for radical surgical approaches, these cause significant esthetic and functional impairment. We present an eight-year-old boy suffering from an extraordinarily large CGCG expanding into the mandible and base of the mouth in the whole anterior region. Combined treatment with surgical intervention and corticosteroid application was successfully applied, and all six attached dental germs could be preserved. Different approaches for clinical management in pediatric cases are discussed.

INTRODUCTION

Central giant cell granuloma (CGCG) is described as a giant cell-rich tumor with histopathologic characteristics resembling a giant cell lesion of the small bones. Until 2017, CGCG of the jaws was classified by the World Health Organization as an entity in its own right.¹

Since the locally aggressive behavior and high recurrence rate of CGCG call for invasive treatment, clinical management has traditionally featured radical surgical interventions up to en bloc resection. This may result in a loss of teeth, dental germs, and related structures, with a high impact on facial growth in young patients.² Recently, pharmacologic agents have been introduced as a more conservative alternative. Calcitonin, corticosteroids, and alpha-interferon were increasingly used and showed promising results³ though some lesions do not respond to pharmacologic therapy. To date, four genetic subgroups of lesions have been identified, and their molecular heterogeneity offers a preliminary explanation for the clinical and radiological variations in granulomas.⁴ CGCG has unpredictable behavior, unknown etiology, and varying responses to therapeutic options. At this point, no evidence-based therapy is available.

This 8-year-old boy presented with an unusually large CGCG, just when permanent dentition was set to come in as the jaw and face matured. Therefore, an appropriate therapeutic strategy was needed to remove the lesion with minimal side effects while guaranteeing a fast and satisfactory outcome to continue with his growth process. Surgical and pharmacologic approaches in pediatrics are discussed.

Case report

An 8-year-old boy was referred to the Department of Oral and Maxillofacial Surgery (Medical University Graz, Austria) for further management. His dentist detected an incidental enlargement located in the anterior mandible during the intraoral examination, with a hard, painless expansion in the whole anterior base of the mouth, covered by healthy-appearing gingiva and mucosa. The lesion was clinically painless.

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A panoramic radiograph showed a well-defined unilocular radiolucent area extending from the lingual aspect of 46 to the other side of the left molar region, involving the whole anterior floor of the mouth (Figures 1-3). The permanent mandibular tooth germs 34, 35, 36, 44, 45, 46 were associated and already displaced on the lower border of the mandible; the incisors were affected but not clinically mobile. Tooth resorption was not visible in the radiograph. Histopathology of a guided biopsy revealed a central giant cell lesion destroying the mandibular bone. (Figure 4). A giant cell lesion surrounded remnants of the missing pre-existing bony tissue.

Blood parameters (serum calcium, phosphate, parathormone, and alkaline phosphatase levels) were within normal limits and excluded hyperparathyroidism and brown tumor. A further MRI revealed a lesion of 8 x 4 x 5 with only a thin layer of mandibular basal bone left. In total, radiography showed no typical signs like lucent regions with soap-bubble appearance compatible with cherubism. In addition, aneurysmal bone cyst, non-ossifying fibroma, and osteosarcoma were excluded by histopathologic re-examination. Based on the above findings, the diagnosis was a central giant cell granuloma; further management was discussed in the conference on bone diseases of the Medical University Graz.

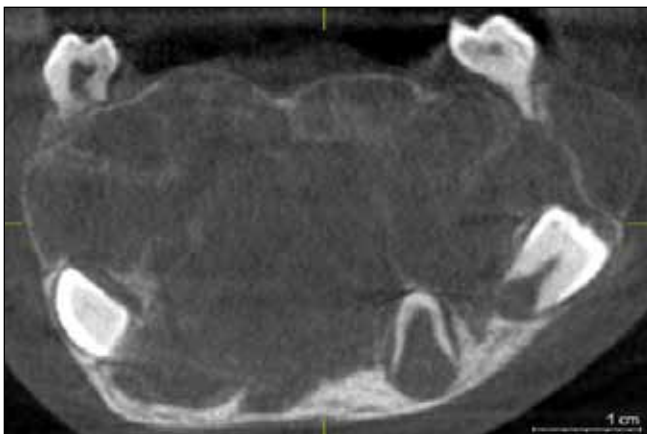
Figure 1: radiographic finding, (March 2017, age 8).

The panoramic radiograph showed a well-defined unilocular radiolucent area extending from the lingual aspect of 46 to the other side of left molar region.



Figure 2: coronal digital volume tomography of the oral cavity (March 2017, age 8)

The permanent mandibular tooth germs 34, 35, 36, 44, 45, 46 were associated and already displaced on the lower border of the mandible. The incisors were affected but not clinically mobile.



We performed a careful curettage of the lesion under general anesthesia instead of a standard resection. The intraoral approach was localized in the chin area so that the teeth germs remained undamaged (Fig. 5). In the same session, an intralesional corticosteroid application consisting of 2 ml per cm³ of a solution containing triamcinolone 10 mg/ml diluted in 0,5% bupivacaine was initiated. Postoperatively, the diagnosis of CGCG was again confirmed by an experienced pathologist. There were no postoperative complications.

Further corticosteroid applications were planned postoperatively. However, after three months, the lesion had regressed in size, and radio-opacity had increased. Due to the positive response, further corticosteroid applications were adjourned at this point. Close follow-up examinations were arranged to detect a recurrence at an early stage and, if necessary, start corticosteroid application immediately. As follow-up examinations revealed a positive outcome, no further corticosteroid applications were scheduled.

Two years later, the dental germs appeared ready to erupt spontaneously, with orthodontic treatment as needed (Fig. 6). In the meantime, a placeholder was used. Follow-up clinical and radiographic examinations show bone remodeling and formation of the mandible without any recurrence to date.

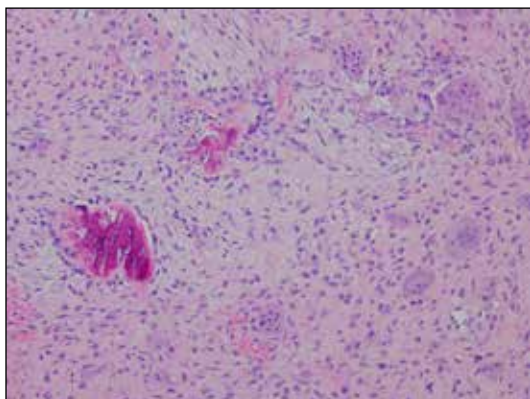
Figure 3: coronal T1 magnetic resonance imaging (MRI) of the face

MRI was carried out under general anesthesia. The MRI shows a cyst-like radiolucent area with a well-defined margin. A typical multilocular honeycomb appearance of the lesion can be seen.



Figure 4: Histopathology, H& E staining

Central giant cell lesion destroying the mandibular bone. The aggressive lesion is composed of osteoclast-like multinucleated giant cells and mononuclear polygonal or spindled cells set in a fibrovascular stroma. At the left side remnants of the destroyed preexistent mandibular bone can be seen. 100 μ m

**Figure 5: Surgical approach**

The intraoral approach was localized in the chin area, so that the teeth germs remained undamaged. Therefore, a careful curettage of the whole lesion could be performed.

**Figure 6: Follow-up radiographic examination, (November 2019, age 11)**

Two years later, the dental germs 34, 35, 36, 44, 45, 46 appeared ready to erupt spontaneously, with orthodontic treatment as needed.



DISCUSSION

Since there are still no universally accepted guidelines, the clinical management of CGCG is still discussed.⁵ The process starts with an appropriate diagnosis covering clinical, radiographic and histopathologic features and excluding very similar differential diagnoses.¹

The most significant clinical aspect of CGCG is its broad spectrum of behavior. It differs in tumor size and aggressiveness, varying from relatively small indolent lesions to rapidly growing aggressive lesions;³ accordingly, it is hard to create reliable therapy guidelines. Considering an extremely low incidence rate of 0.00011%,¹ therapeutic options are mostly discussed in single case reports. There are only a few reviews involving small populations.²

Chrcanovic and colleagues⁵ reported a higher incidence among female patients and very rare occurrence of lesions in the anterior mandible affecting more than one region of the jaw (anterior/premolar, crossing the midline of the mandible). The mean lesion size was 3.9 cm,⁵ while our patient's tumor was massive, with 8 x 5 x 4 cm. Our case in a male child was unique because of the enormous size of the granuloma in an unusual localization with six attached teeth germs that had to be rescued.

Invasive surgery (en bloc surgical resection with 5 mm margins) seems to be the safest option to control recurrence. All soft tissues involved in the lesion had to be peeled off.⁶ In the present case this would have led to a huge defect, followed by bone reconstruction. A complete excision of the lesion and thorough curettage would still have meant a loss of at least six permanent teeth. Aggressive surgical approaches are often accompanied by a high rate of morbidity, treatment complications, and additional procedures. Negative impact on facial growth may influence psychological health. All these factors may lead to a lower quality of life. Accordingly, more conservative approaches are the only acceptable strategy for children in their primary dentition.^{2,7}

Among pharmacologic agents, corticosteroids, calcitonin and interferon present promising results.⁵ We excluded the antiviral cytokine interferon alpha for our young patient due to its many reported serious side effects.⁸

The application of calcitonin, bisphosphonates or corticosteroids seemed to be an appropriate alternative without dangerous side effects, but with the disadvantages of long duration of treatment and the possibility of a minimally or non-responsive lesion.² This entailed the risk that the dental germs might not erupt and that they could not be brought into the proper position. Furthermore, no pediatric reports for the use of bisphosphonates could be found. Therefore, this treatment was not appropriate as a first line therapy. Our case demonstrates that no modality alone could offer a promising solution.

A multidisciplinary approach will achieve the best results when it is well planned and implemented. After due consideration, it was apparent that a more conservative surgical approach would call for additional pharmacologic supportive therapy.⁹

We decided to perform a careful excision with regard to the eruption process of dental germs first. Corticosteroid therapy was essential to avoid the recurrence of the obviously aggressive tumor.

In the literature, calcitonin and corticosteroid showed similar positive results.¹⁰ Due to the heterogeneity of the lesions, they either do or do not respond to a single agent. We chose a

corticosteroid application because steroids are able to increase the cell-surface calcitonin receptor.¹⁰ If there had been no or poor response, we could still have switched to a calcitonin application with perhaps a better result.

CONCLUSION

We conclude that management of CGCG in pediatrics is a clinical challenge with the risk of lifelong cosmetic and functional problems. The treatment choice should be individualized and based on the anatomical location and extent of the lesion, status of the patient and expertise available.^{2,7} In our case, a careful curettage to preserve the dental germs and facial structures combined with intralesional corticosteroid application was successful and can be suggested for similar cases. Demanding cases of CGCG need sophisticated therapeutic strategies to prevent unnecessary structural damage and minimize the risk of recurrence.

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