

## Case Report

# Central Giant Cell Granuloma of the Jaws Complicated with Hemorrhagic Hypovolemic Shock: A Case Report

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## ABSTRACT

Central giant cell granulomas (CGCGs) are localized, benign proliferations of fibrous tissue that, in some cases, exhibit aggressive biological behavior. These last are more common in pediatric patients. CGCGs are unusual, accounting for less than 7% of benign maxillary tumors. The mandible is the most common location. Surgical treatment is the gold standard to manage aggressive CGCGs. Prognosis is favorable if complete removal is achieved. Herein, we present a case of a right mandibular CGCG in a teenage female patient. Among the differential histopathological diagnoses, the brown tumor of hyperparathyroidism was discarded. During hospitalization, she presented with profuse active bleeding from the tumor. Unsuccessful hemostasis was initiated using gauze pads with epinephrine and sutures due to the extremely friable tissue. During the event, approximately 1500 ml of blood loss was reported, with clinical signs of hypovolemic shock. She was admitted urgently for right mandibular embolization. Finally, a hemimandibulectomy, tumoral lesion resection and cervical ganglion biopsy was performed. Within, we document the multidisciplinary approach that led to a successful treatment and recovery as well as the expected course in her future. Nevertheless, there are still opportunities to establish the ideal management in patients with further anatomical, aesthetic, and functional growth ahead of them. In conclusion we strongly recommend establishing a prompt and accurate diagnosis; a complete resection with surgical and non-surgical strategies and an early definitive management to reduce recurrence

## INTRODUCTION

Central giant cell granulomas (CGCGs) are localized proliferations of fibrous tissue that are considered benign, however, in some cases, they exhibit aggressive biological behavior (1). They

can be discerned by three main characteristics: hemorrhagic foci, fibrous connective tissue of multinucleated giant cells, and bone trabeculations (2). CGCGs are unusual, accounting for less than 7% of benign maxillary

tumors (3). According to previous studies, 75% are present before 30 years of age, being most frequent in the second and third decades of life (4); 80% will occur under 20 years of age. There is a prevalence in the female population of about two thirds of cases (3). CGCGs can be classified into two types: the most common being non-aggressive granulomas (80.9%) and characterized by a quiescent, non-tender and asymptomatic lesion (5,6). On the other hand, aggressive granulomas (19.1% of cases) (6) are faster growing, with displacement of the teeth, cortical bone perforation (7) and more common in pediatric patients (5). Regarding its topography, the mandible is its most common location (43.1%), followed by the temporal bone (33.3%) and paranasal sinuses (11.8%) (6). Diagnosis is achieved through the sum of clinical, laboratory, and histological studies. At the radiographic level it is expected to find an image of a honeycomb or soap bubble (8). In terms of histological features, giant cells with a breastplate of mononuclear cells make a diagnosis. Immunohistochemical stains show a positivity for CD68 and CD163, by which diagnosis can be confirmed (4). Interestingly, CGCGs are histologically indistinguishable from Brown hyperparathyroidism tumors (7); therefore, phosphocalcic profiles are used to differentiate between the two. CGCGs having normal calcium, phosphorus, and alkaline phosphatase (9). Treatment wise, a surgical approach, like enucleation, curettage, and resection, is the gold standard to manage aggressive CGCGs (5,7) in lieu of non-surgical strategies such as radiation, intralesional steroids, interferon, and tyrosine kinase inhibitors (imatinib) (5). However, there is still more research needed to evaluate the benefits of mixed treatments. Prognosis is favorable if complete removal is achieved, only 6.8% of cases present recurrence, depending on the surgical technique used (6). Providing a margin of healthy tissue (9) as well as aggressive local

curettage reduces recurrence risk (1). Herein, we present a case of a CGCG in a teenage female patient with hemodynamic complications to document the multidisciplinary approach that led to a successful treatment and recovery as well it's the expected course in her future.

## BRIEF INFORMATION

A 16-year-old Mexican girl presented on March 23rd, 2023, with pain and an increase of volume located in the right retromandibular region, accompanied by bleeding and fever. She was evaluated by a dentist, who encountered a lateralized and semi-erupted third molar removing it on the 27th. However, no improvement of her symptoms was seen; hence, an orthopantomography was performed, which reported a tumor lesion not compromising the dental cortex. A biopsy was performed with an official pathology report of an osteosarcoma rich in giant cells, multifragmented and extensively ulcerated. However, a new biopsy reported aggressive central giant cell granuloma. She arrived at this medical unit to receive an evaluation from the oncology service. She had an unremarkable family history and other medical history was noncontributory.

## CLINICAL FINDINGS

External examination revealed an asymmetrical spherical, smooth, bulbous, tender, and indurated lesion that extended to the right preauricular region as well as both sides of the gingiva with extremely friable tissue that bled readily. Mouth opening, temporomandibular joint and condylar movements were restricted. There was adequate intraoral hygiene, there was no disturbance of the dental arches or of the occlusion, and no displacement of teeth was noted in the region. The patient was in the mixed dentition stage. The oral mucosa was a normal

pink. There was no regional lymphadenopathy, splenomegaly or hepatomegaly.

## TIMELINE

Upon her arrival and after reviewing the histopathology tissue slides a central giant cell granuloma was the favored diagnosis. A referral to the maxillofacial surgery service was made. Scant blood fluid expenditure from the tumoral lesion was present on most days that subsided spontaneously or with the application of gauze with hydrogen peroxide. However, at this point, there was repercussion on the hemoglobin level, requiring blood transfusions during her stay. Enteral diet was restarted with little acceptance due to the interference caused by the tumor to swallow as well as nauseas. On her 13th day of stay, she presented with profuse active bleeding through the oral cavity.

During her assessment no observable bleeding site was identified. Haemostasis was initiated using gauze pads with epinephrine unsuccessfully. Emergency evaluation by the maxillofacial surgery service was done, who placed a suture without success due to the extremely friable tissue. Gelfoam was thus placed at the bleeding site in an intralesional strip, achieving hemostasis. During the event, bleeding of approximately 1500 ml was reported, with clinical signs of hypovolemic shock (blood pressure below the 5th percentile, prolonged capillary refill and tachycardia). At par, fluid resuscitation was started with crystalloid as well as transfusion of 500 ml of concentrated erythrocytes, reports of clotting times were slightly prolonged hence, 250 ml of fresh frozen plasma was indicated to improve transfusion quality.



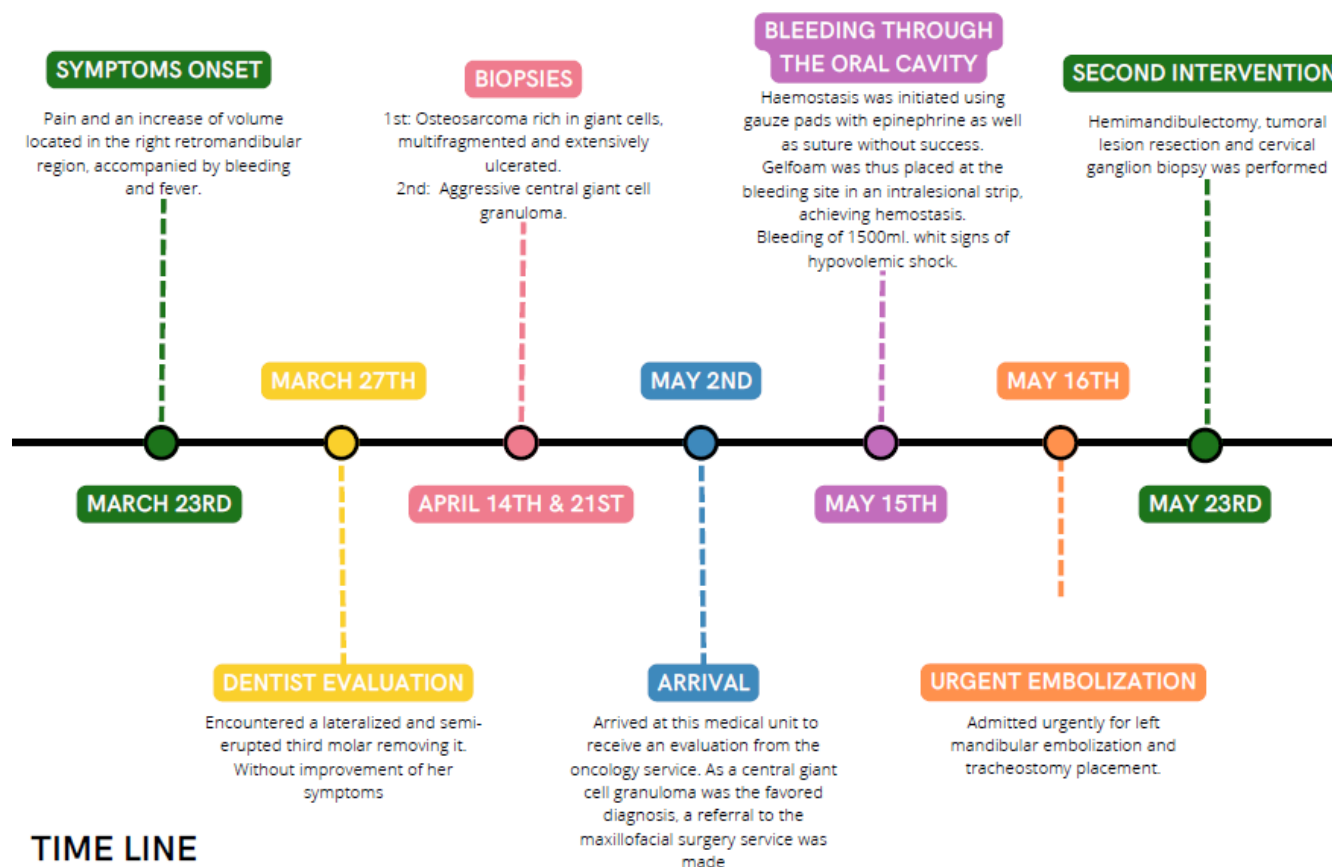
**Photo 1.**

Right frontal view of a 16-year-old female patient at the time of hospital admission. An asymmetric, smooth, bulbous, and indurated lesion is observed with extension to both sides of the dental gum corresponding to a CGCG. The lesion has a brown and pink surface with extremely friable tissue and areas of active bleeding.

She was admitted urgently for left mandibular embolization and tracheostomy placement. During the second surgical event desaturation events of up to 40% were reported, performing emergency cricothyroidotomy with subsequent recovery. She was then moved to the intensive care service for post-surgical management.

## DIAGNOSTIC ASSESSMENT

External panoramic X-ray of the mandible (03.31.2023) showed jaws in the mixed dentition stage typical for the age, as well as a lytic lesion of the right mandibular ramus with destruction, no destruction of the cortex was observed, however invasion of the soft tissue was described.



## TIME LINE

Furthermore, bone scintigram (05.03.2023) showed a lesion in the zygomatic bone, maxilla, and mandible. Negative for the presence of metastatic lesions. A positron emission tomography (PET) scan and a computed tomography (CT) of the head and neck (04.17.2023) revealed a lytic lesion in the right mandibular ramus with soft tissue components, with maximum diameters of 67x53 mm, which extends to the alveolar roots of the ipsilateral upper second and first molars, invades the chewing space, involving the pterygoid and masseter muscle, as well as extension to the masticator space, with involvement of the pterygoid and masseter muscle, as well as extension to the submandibular space, with involvement of the platysma and digastric, ipsilateral submandibular, presents focal

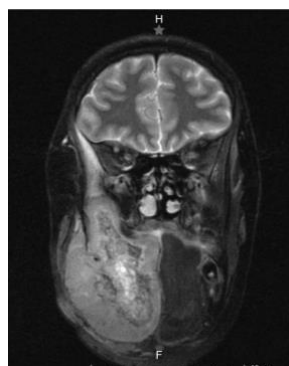
hypometabolism with suv max 7.8 (highly suggestive of cancer).

Hypermetabolic tumor activity in a right mandibular lesion with involvement of adjacent soft tissues and ipsilateral cervical adenopathies. The remaining structures showed no apparent alterations.

The histological features were consistent with an aggressive central giant cell granuloma of the right jaw, extensively ulcerated and multifragmented. The immunohistochemical (IHC) stains showed that the cells were negative for P53, Cytokeratin, P63, Clusterine, MDM2 and SATB2. Diffuse nuclear was positive as well as Ki67 in less than 10%. Lastly, CDK4 showed a positive diffuse cytoplasmic pattern. This conclusion was concordant in two biopsies out of

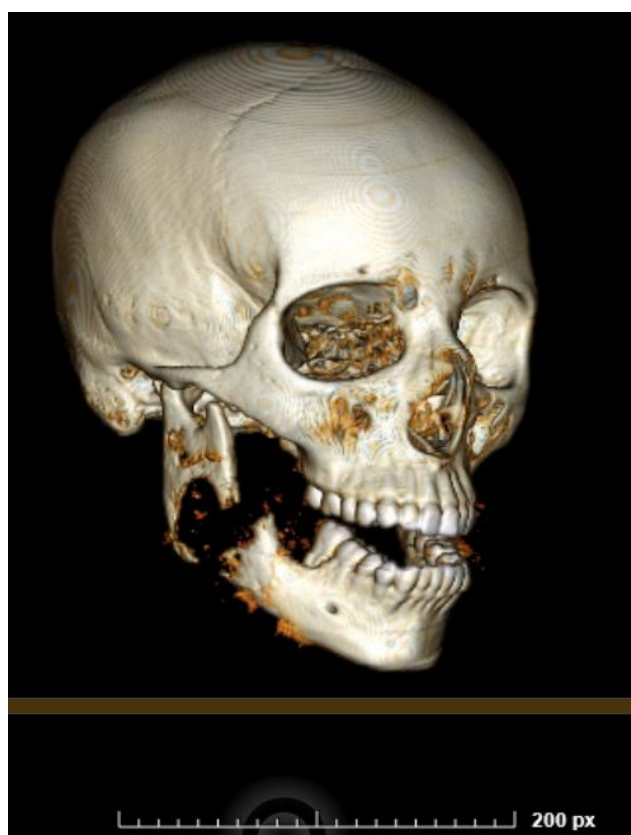


three, with the last one reporting osteosarcoma and not granuloma.



**Image 1.**

Simple, high-resolution contrast CT scan with a 3-dimensional reconstruction. Right frontolateral view. An osteolytic lesion is observed in the body, angle and ramus of the right hemimandible, with irregular edges and peripheral calcified lesions.



**Image 2.**

MRI T2 in simple phase, coronal section, shows the presence of a lesion arising from subcutaneous cellular soft tissue in the right mandibular region. Maximum dimensions are 10 x7 cm with extension to the anterior face, submandibular, zygomatic-temporal region, and oral cavity. There is peripheral enhancement consistent with perilesional edema and osteolytic lesions of the body, angle, and ramus of the right hemimandible. Right dental pieces are missing, and tongue is displaced to the left in its entirety.

Among the differential histopathological diagnoses the brown tumor of hyperparathyroidism, biochemical tests to assess for hyperparathyroidism associated with hypercalcemia and hypophosphatemia, were carried out. Phosphocalcic profiles were within normal ranges thus the differential diagnosis was ruled out.

## THERAPEUTIC INTERVENTION

Correspondingly, on the 23rd of May of 2023 a hemimandibulectomy, tumoral lesion resection and cervical ganglion biopsy was performed. A total bleeding of 500 mL was reported with transfusion of 300 mL of platelets and 500 mL of red blood cells. Botulinum toxin was applied in the region of the submandibular gland on the right side. Only neurological deficit was a right mandibular branch palsy may be secondary to surgical manipulation of the facial nerve.

## FOLLOW-UP AND OUTCOMES

As additional comorbidities we integrated secondary dysphagia with disruption of phase one, surgical site infection by *S. epidermidis* and *S. sanguinis*, probable catheter colonization with secondary bacteremia by *S. hominis*, adaptive reaction with anxious symptoms and unspecified anxiety disorder. Otherwise, her post-surgical recovery was uneventful, and no further events of bleeding were presented. Future follow-up will include periodical reassessments by the maxillofacial surgery service as well as definitive reconstruction.

## DISCUSSION

Central giant cell granulomas (CGCGs) are localized, benign proliferations of fibrous tissue, however, in some cases, they exhibit aggressive biological behavior (1). They can be discerned by three main characteristics: hemorrhagic foci,

fibrous connective tissue of multinucleated giant cells, and bone trabeculations (2). CGCGs are unusual, accounting for less than 7% of benign maxillary tumors (3) and can be classified into: non-aggressive granulomas (80.9%) and aggressive granulomas (19.1%) (6), which are more common in pediatric patients (5). The mandible is the most common location (43.1%) (6). Radiographs show an image of a honeycomb or soap bubble (8). Histological features include giant cells with a breastplate of mononuclear cells, immunohistochemical stains positive for CD68 and CD163, which confirm the diagnosis (4). Surgical treatment is the gold standard to manage aggressive CGCGs (5,7). Prognosis is favorable if complete removal is achieved (6). Herein we report a case of the rare Giant Cell Central Granuloma with aggressive behavior. To our knowledge, there is only one systematic review concerning these types of masses and it is evident that there is still a lack of information in all areas of investigation to propose concrete and general recommendations. Thus, the publication of successful medical approaches to CGCGs is key to contributing to their knowledge, management and control. Furthermore, in pediatric patients, it is crucial for clinical suspicion to be regarded earnestly due to CGCGs aggressiveness and risk of significant bone loss with negative implications on patients' future growth and functionality.

This case specifically presented a very aggressive behavior and a difficult surgical assessment due to its rich vasculature and anatomical site. Its management (clinical, imaging, histopathological and immunohistochemical) entailed a multitude of pediatric subspecialties (general pediatrics, oral and maxillofacial surgery, otorhinolaryngology, endocrinology, oncology, infectiology, psychology, interventional radiology, critical care and

nutriologist among others). This permitted its early identification and key differential diagnosis with malignant neoplasms, arteriovenous malformations, localized infection, and identical histological diagnoses.

Likewise, this case is an example of the more severe complications that CGCG can lead to. Urgent embolization was necessary due to uncoerced bleeding of the mass that led to hypovolemic shock. Ostensibly, this surgery has not been described or reported in literature in the management protocol of this lesion. Consequently, it is highly advisable for other medical teams to establish early on the anatomical vasculature of the mass and consider embolization as a valuable ancillary measure to reduce these types of complications. Appropriate airway management and protection is an integral part of the treatment of these cases, the main strategies include tracheostomy or emergency cricothyroidotomy as was needed in this case.

After stabilization of the patient, she received the gold standard of treatment with complete enucleation. The use of aggressive surgical treatment as established in other literary papers minimizes the likelihood of possible recurrence. (2,5) According to the literature, the risk of relapse in this specific case is expected to be minimal, with a good prognosis. However, it will be necessary to continue a close follow-up during the patient's final stage of growth to ensure functionality, both anatomical and aesthetically, of her jaw.

Nonetheless, there is still room to improve the approach within our medical team. For instance, the implementation of non-surgical adjunctive treatments during the diagnostic approach to decelerate the rapid progression and thus prevent hemorrhagic hypovolemic shock as well

as enhance the results of surgical management. Multiple studies have contributed innovative methods such as autologous platelet-rich fibrin, anti-angiogenic therapy with interferon alpha-2a, radiation, intralesional steroids and tyrosine kinase inhibitors (Imatinib), calcitonin, and denosumab. (1, 2, 5, 6) that, although require more scientific evidence, are within reach of many medical centers.

Until now, there are multiple theories concerning the origin of this lesion; the most accepted concerning its rise from a localized trauma. It is of interest to highlight that our patient had no history of injury or damage to the mandible prior to the CGCG, reinforcing that the nature of these lesions is still unclear. (1) Another limitation was due to the limited resources to carry out a more extensive molecular identification of the oncogenes that, although nonessential for diagnosis or therapeutic decisions, would supply information regarding the etiology of this tumor.

Overall, two main concepts can be retrieved from this case report. Few clinical cases reflect upon the significant bleeding that these tumors may produce, which, along with their destructiveness, is basis enough to justify aggressive and swift treatment. Finally, the ultimate decision of extensive surgical treatment must consider the benefits of reduced recurrence against the risk of sacrificing growing and developing tissue.

## CONCLUSION

Central giant cell granuloma (CGCG) is a rare benign tumor of the jaw with a more aggressive behavior in the pediatric population. We have presented the case of a proven CGCG complicated with hypovolemic shock secondary to tumor hemorrhage. Emergency treatment

with vascular embolization should be considered prompt and accurate. Furthermore, she received a successful primary surgical treatment despite the extremely friable tissue and rich vascularization of the tumor. Nevertheless, there are still opportunities to establish the ideal management, either surgical, nonsurgical strategies or in conjunction, in patients with further anatomical, aesthetic, and functional growth ahead of them. Thus, it is fundamental to contribute to the scarce pool of information regarding these tumors, particularly the aggressive type which is of interest to the pediatric medical community. In conclusion we strongly recommend establishing a prompt, early, and accurate diagnosis; a complete elimination of the neoplasm with surgical and non-surgical treatment strategies and an early definitive management to reduce the rate of recurrence.

## INFORMED CONSENT

Fully informed parental consent as well as patient assent was obtained. Protection of private health care records was kept through the publication process (including but not limited to imaging studies and their reports, pathology reports, pictures, and any type of clinical file). Precautions were taken to keep the patient's indenture confidential.

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