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Diagnosis and management of central giant cell granulomas of the jaws: a European and multicenter study

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ABSTRACT

Introduction: Central giant cell granulomas (CGCGs) are benign but locally aggressive rare neoplasms that affect the bony skeleton, particularly the maxillofacial region. The purpose of this European multicenter study was to describe and assess the characteristics, diagnosis, management, and recurrence of CGCGs at different European oral and maxillofacial surgery centers.

Methods: The data from all the treated CGCGs from the involved oral and maxillofacial surgical units across Europe between January 1st, 2014 and December 31st, 2023 were recorded.

Results: A total of 76 patients, including 37 males and 39 females diagnosed with CGCG met the inclusion criteria and were included. The mean age of the study population at diagnosis was 41.8 years.

Fifty-three lesions were found in the mandible, with the most frequently involved subsite being the mandibular parasymphysis. Overall, 75.0 % of included CGCGs were unilocular. The most frequent treatment option was surgery alone. A total of 12 recurrences (15.8 %) were observed with a mean follow up of 41 months.

Discussion: Further genetic and molecular studies regarding the pathways underlying CGCGs are needed, in order to predict their natural history and to direct non-surgical therapies. In the meantime, surgeons should balance the risks of higher recurrence rates associated with lower surgical morbidity, performing an individualized treatment plan, taking into consideration the clinical and radiological features together with the patients' age and comorbidities. A radiographic follow-up of patients with treated CGCGs could advised for the first 5 years.

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1. Introduction

Central giant cell granulomas (CGCGs) are benign but locally aggressive rare neoplasms that affect the bony skeleton, particularly the maxillofacial region. CGCGs are characterized by destruction of the bone, loss of symmetry of the face and displacement or resorption of teeth (Capucha et al., 2024; Etoz et al., 2020; Rhou et al., 2022; Sun et al., 2009). These osteolytic lesions seem to have osteoclastic origin, with cellular fibrous tissue including haemorrhage foci, multinucleated giant cells, and woven bone trabeculae. In the literature (Capucha et al., 2024; Chrcanovic et al., 2018; Etoz et al., 2020; Pogrel and Hossaini-Zadeh, 2021; Shrestha et al., 2021, Tahmasbi-Arashlow et al., 2022), CGCGs have been reported to occur mainly in patients under the age of 30, predominantly in females, accounting for about 7 % of all benign tumors of the jaws. Both previous trauma and inflammatory responses have been hypothesized to have a role in the etiopathogenesis of such lesions (Capucha et al., 2024; Chrcanovic et al., 2018; Etoz et al., 2020; Pogrel and Hossaini-Zadeh, 2021; Shrestha et al., 2021, Tahmasbi-Arashlow et al., 2022).

Clinically, CGCG may have variable features although it often presents as a slow growing lesion causing expansion, thinning, or perforation of the cortical bone. Instead, their size, the eventual associated resorption or displacement of tooth roots, and the locularity is highly variable.

Diagnosis relies on clinical and radiological findings (Amorós et al., 2024; Ari et al., 2024; Capucha et al., 2024; Corrêa et al., 2024; Etoz et al., 2020; Rhou et al., 2022; Suárez-Roa et al., 2009; Sun et al., 2009).

The management of CGCGs can include conventional surgery with or without medical adjunctive treatment or en bloc resection for the aggressive variant. Although the most common therapy is surgical curettage, the high recurrence rate, especially in aggressive lesions, has raised concern and led to a search for other treatment options (Ari et al., 2024; Capucha et al., 2024; Etoz et al., 2020; Rhou et al., 2022; Suárez-Roa et al., 2009; Sun et al., 2009).

In the last decades, alternative non-surgical treatments have been proposed, including calcitonin, intralesional corticosteroids, interferon α, bisphosphonates, and denosumab. The mechanism of action of non-surgical options would be based on the capacity to reduce the size of the lesions and, eventually, to eradicate them by anti-angiogenic properties of the used drugs, thus avoiding large resections that result in major functional and aesthetic deformities (Capucha et al., 2024; Chrcanovic et al., 2018; Etoz et al., 2020; Pogrel and Hossaini-Zadeh, 2021; Shrestha et al., 2021, Tahmasbi-Arashlow et al., 2022).

Nevertheless, there is still no consensus regarding the management of CGCG.

The purpose of this European multicenter study was to describe and assess the characteristics, diagnosis, management, and recurrence of CGCGs at different European oral and maxillofacial surgery centers, in order to decrease the bias of patient selection, increase the size of the study population, and provide information about the current trends in CGCG management across Europe.

2. Materials and methods

This study was based on a systematic computer-assisted database (by the use of a standardized case report form with a uniform checklist, and a standardized shared registry) that allowed the recording of data from all the treated CGCGs from the involved oral and maxillofacial surgical units across Europe between January 1st, 2014 and December 31st, 2023. The outcome of interest was the collection of uniform data regarding the epidemiology and management of CGCGs. As for inclusion criteria, biopsy or removed specimen's histology proven CGCG lesions were collected only.

The following data were recorded for each patient: gender, age, voluptuary habits, comorbidities, site and size of CGCG, imaging features (locularity, displacement/resorption of adjacent teeth, cortical bone expansion/thinning/perforation, radiolucency), treatment, length of hospital stay, complications, recurrence, follow up.

The following treatment options were considered and noted for each patient either alone or in association: curettage, enucleation, peripheral ostectomy, marginal resection, segmental resection, calcitonin, corticosteroids, denosumab, bisphosphonates, interferon, monoclonal antibody, radiotherapy.

Statistical significance was determined using the χ^2 test or, if the sample sizes were too small, the Fisher exact test. Statistical significance was set at 0.05. Helsinki Declaration guidelines were followed, according to local laws. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) criteria for observational studies were followed. Ethical approval was obtained by the individual centers, if needed, according to local laws.

3. Results

A total of 76 patients, including 37 males (48.7 %) and 39 females (51.3 %) diagnosed with CGCG met the inclusion criteria and were included in the study (Figs. 1–3).

The mean age of the study population at diagnosis was 41.8 years (median, 44 years; standard deviation, 23.1 years; range, 6–86 years). According to decades, patients were most frequently distributed in the decades of age between 10 and 19 years (12 patients), 30 and 39 years (10 patients), 40 and 49 years (11 patients), 50 and 59 years (11 patients), and 60 and 69 years (11 patients), as showed in Fig. 4.

A total of 19 patients (25.0 %) reported voluptuary habits: 15 patients reported smoking or former smoking, 4 smoking (or former smoking) and alcohol drinking.

On the whole, 32 patients (42.1 %) reported no comorbidities, whereas the most frequent comorbidity was hypertension (19 patients), followed by diabetes (11 patients), asthma (5 patients), and neurofibromatosis type 1 (3 patients).

Six patients reported history of previous trauma to the facial region (7.9 %).

Of the 76 CGCGs, 53 lesions were found in the mandible (69.7 %), whereas 22 were found in the maxilla (28.9 %) and a lesion in the zygomatic bone.

The most frequently involved subsite was the mandibular parasymphysis (24.3 %), followed by the mandibular body (20.9 %), and the symphysis (16.5 %), as depicted in Fig. 5.

Mean size of included CGCGs was 3.3 cm (standard deviation, 1.8; range, 0.6–7 cm).

Overall, 75.0 % of included CGCGs were unilocular (57 lesions), whereas the remaining 19 lesions were multilocular. Additionally, 51 lesions were radiolucent (67.1 %), 19 showed a mixed radiolucent and radiopaque pattern (25.0 %), and 6 were entirely radiopaque (7.9 %). As for the observed radiographic features of the effects of CGCGs on adjacent teeth, neither teeth displacement nor resorption were noticed in 33 CGCGs (43.4 %). Root displacement or divergence was observed in 15 of the lesions, root resorption in 16 CGCGs, and both teeth displacement and resorption in the remaining 12 patients (Fig. 6).

As for their effects on cortical bone, CGCGs were almost equally distributed in CGCGs determining cortical bone expansion (35.5 %), cortical bone thinning (33.3 %), and cortical bone perforation (31.2 %).

The treatment options and their corresponding recurrences are presented in Table 1. A total of 12 recurrences (15.8 %) were observed with a mean follow up of 41 months. The most frequently performed treatment options were bony (marginal or segmental) resection in 18 cases, peripheral ostectomy in 15 lesions, and enucleation plus curettage in 14 CGCGs. Excluding the treatment options that were performed in only a single case, curettage (recurrence rate, 37 %), enucleation (recurrence rate, 23 %), enucleation with curettage (recurrence rate, 14 %), and peripheral ostectomy (recurrence rate, 13 %) were the treatment options with the highest recurrence rate.

The four patients that only underwent medical treatment without

any surgical option associated had all severe comorbidities.

As for the relationships between CGCGs and teeth, in patients that would have undergone conservative surgery (for example, enucleation), the vitality as well as the involvement of teeth in the neoplasms were assessed: in positive cases, endodontic treatment followed by apicoectomy during surgery was performed.

Overall, 22 patients (28.9 %) had postoperative complications. An inferior alveolar nerve (IAN) deficit was reported in 17 patients (in 10 cases temporarily, in 7 cases permanently); in 5 cases a postoperative infection occurred; and one patient had a notable postoperative wound dehiscence. Additionally, a patient, following treatment by denosumab, presented hypophosphatemia and hypercalcemia which required medical interventions. All the 7 cases of permanent IAN deficit occurred following a mandibular resection in cases in which IAN could not be spared by the neoplasm.

No statistically significant association ($p > .05$) was found among recurrence among age, gender, site, size, or radiographic features. No statistically significant association ($p > .05$) was also found among locularity and site, size, or root resorption.

4. Discussion

The aim of this European multicenter study was to characterize and evaluate the clinical features, diagnostic approaches, management strategies, and recurrence patterns of CGCGs, while also providing insights into the current trends in CGCG management across Europe. Despite the comprehensive multicenter study, the assessment of treatment modalities proved challenging due to the diversity of available options and the relative rarity of the tumor. Notably, it is promising for the development of future treatments that 5.2 % of patients were managed successfully with pharmacological therapies alone. We also noted differences in patient demographics and tumor etiological factors compared to previous studies.

Multiple concurrent CGCGs are associated with inherited syndrome or systemic disease, as in almost all patients multiple CGCGs are mainly observed in patients with germline mutations involving the RAS/MAPK pathway (Capucha et al., 2024; Chrcanovic et al., 2018; Etoz et al., 2020; Pogrel and Hossaini-Zadeh, 2021; Shrestha et al., 2021, Tahmasbi-Arashlow et al., 2022). Therefore, patients with multiple CGCGs should be checked for underlying concomitant diseases, such as heart disease, cardiomyopathy, mental retardation, and skeletal anomalies. Multifocal and solitary CGCGs should be considered separate entities with different pathogenic pathways. In the present study, only four patients (5.3 %) had known inherited syndrome. As aforementioned, the four patients that only underwent medical treatment without any surgical option associated had all severe comorbidities.

The consistency of the study population of the current multicenter study confirmed no gender predilection by CGCGs, with a mean age of 41.8 years, but showing, in contrast with the previous literature (Capucha et al., 2024; Chrcanovic et al., 2018; Etoz et al., 2020; Pogrel and Hossaini-Zadeh, 2021; Shrestha et al., 2021, Tahmasbi-Arashlow et al., 2022), a wide diffusion in several decades of age from 10 to 69 years. Earlier studies have emphasized the occurrence of granulomas, particularly in children and young adults. The largest age group in the

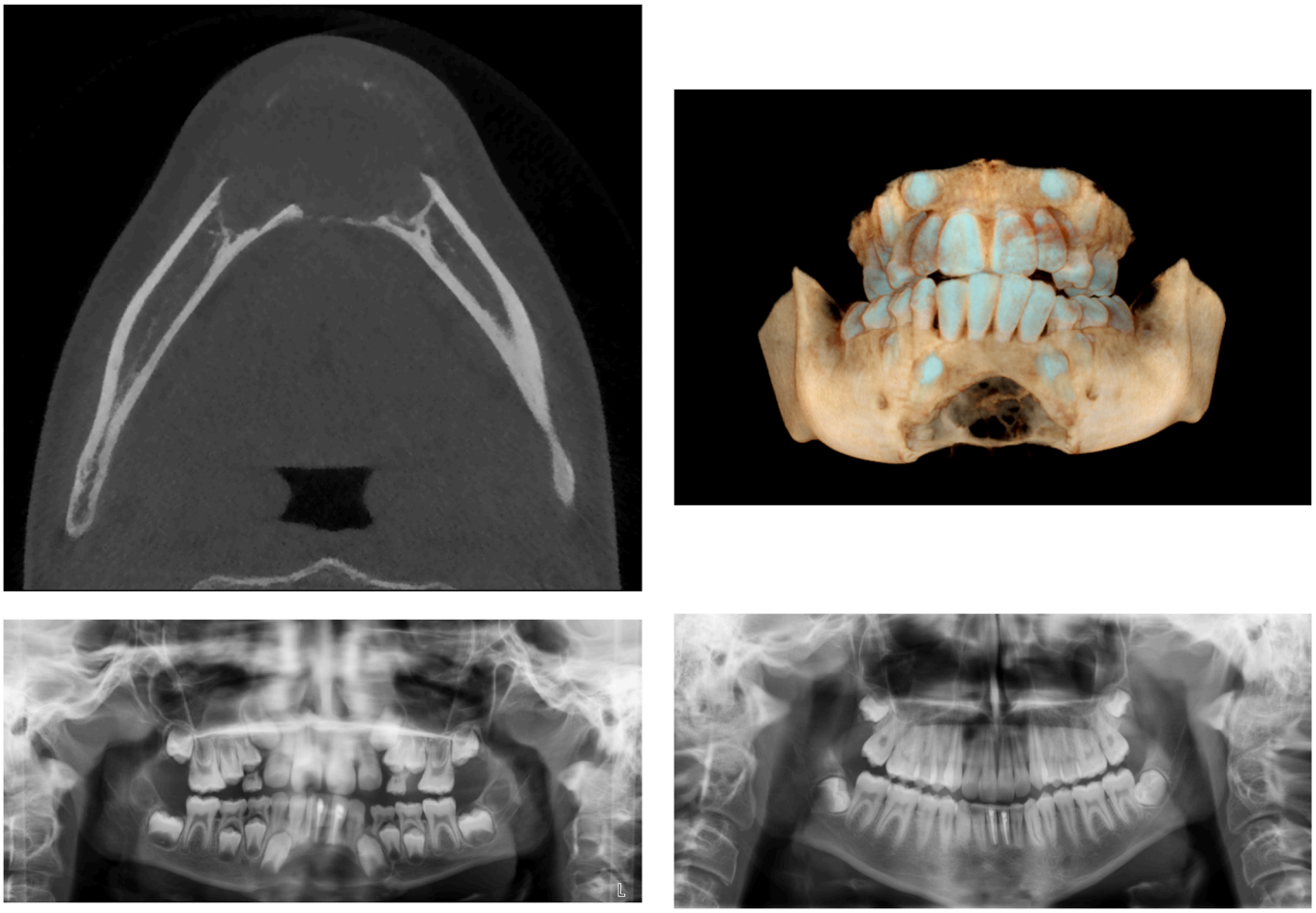

Fig. 1. Imaging examinations of a 12-year-old female patient from the Besancon center. Preoperative axial (A) and tridimensional (B) CT scan show a CGCG of the mandibular symphysis, that underwent enucleation and curettage (together with the endodontic treatment of the inferior central incisors). Postoperative panoramic radiographs performed one year (C) and 6 years (D) after surgery can be observed.

dataset consisted of children and young adults, which supports previous findings suggesting that jaw growth may also contribute to GCGC growth. However, CGCGs should be recognized as a lesion that can affect individuals of all ages. A more detailed evaluation of treatment modalities across age groups could provide valuable insights for selecting the most effective CGCG treatment.

Early hypotheses regarding granuloma development suggested that traumatic events and infectious processes could serve as potential triggers for the onset of the condition (Capucha et al., 2024; Chrcanovic et al., 2018; Etoz et al., 2020; Pogrel and Hossaini-Zadeh, 2021; Shrestha et al., 2021, Tahmasbi-Arashlow et al., 2022). Only 7.9 % of patients reported a history of previous trauma to the facial region, thus not confirming the etiopathogenesis theory of a role by trauma in the development of CGCGs.

Consistent with the literature (Capucha et al., 2024; Chrcanovic et al., 2018; Etoz et al., 2020; Pogrel and Hossaini-Zadeh, 2021; Shrestha et al., 2021, Tahmasbi-Arashlow et al., 2022), the present study population confirmed a wide predominance of the mandibular location with the 70 % of mandibular CGCGs. Accordingly, the most frequently observed subsites were the mandibular parasymphysis (24.3 %), followed by the mandibular body (20.9 %), and the symphysis (16.5 %).

Histopathologically, CGCGs are characterized by unencapsulated proliferation of mononuclear spindle-shaped and polygonal cells with osteoclast-type multinucleated giant cells in a vascular background, with haemorrhage foci and haemosiderin pigments (Fig. 7).

Conventional radiography is traditionally the first imaging modality used in patients with CGCGs and may reveal valuable information about the dimensions and the internal structure of the CGCGs. However, the use of Cone Beam Computed Tomography (CBCT) and Computed tomography (CT) modalities, in particular when facing multilocular lesions, could be considered as an aid for the identification of the presence of cortical perforation/thinning, and root resorption (Capucha et al., 2024; Chrcanovic et al., 2018; Etoz et al., 2020; Pogrel and Hossaini-Zadeh, 2021; Shrestha et al., 2021).

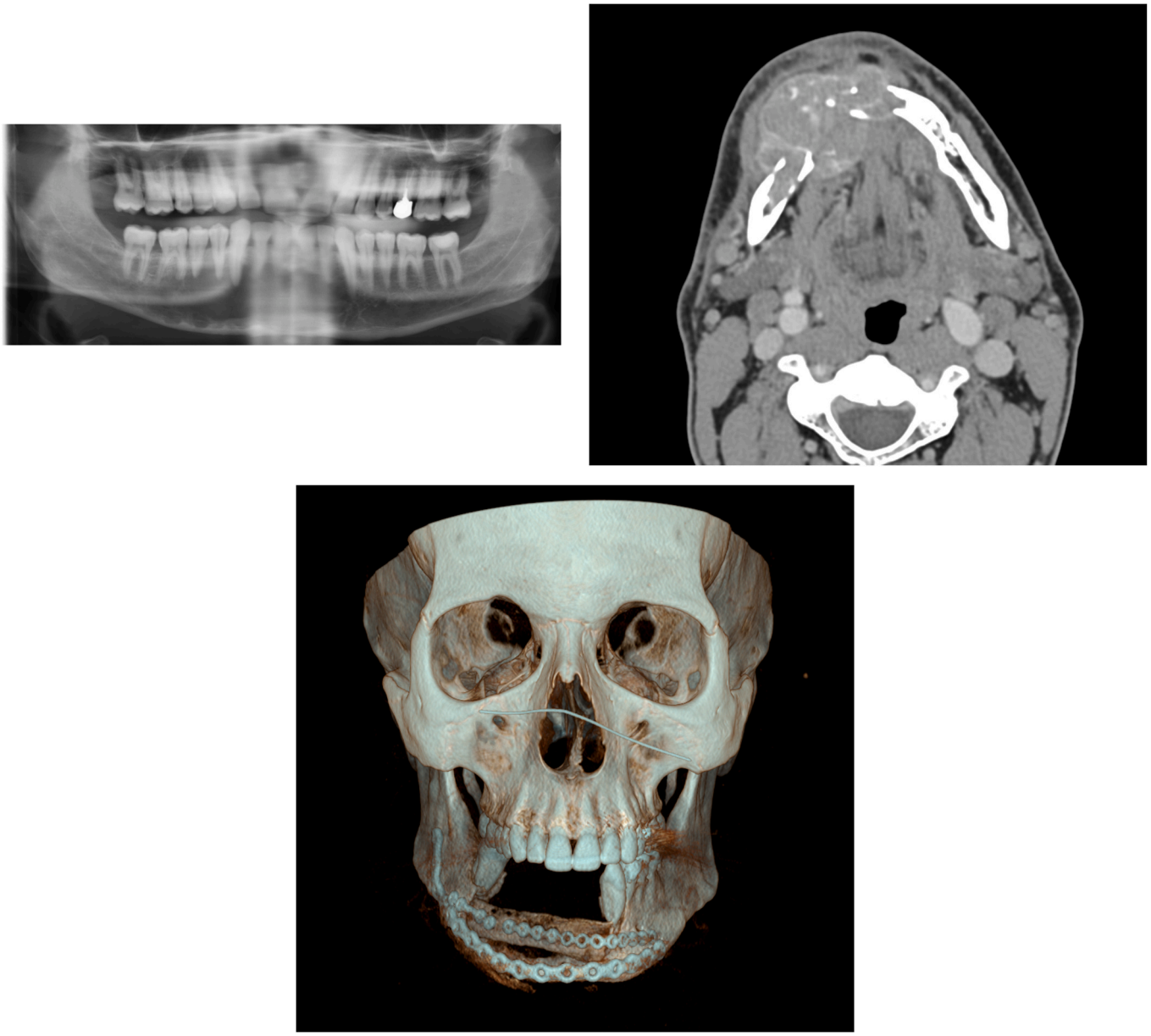

Fig. 2. Imaging examinations of a 33-year-old male patient from the Besancon center. Preoperative panoramic radiograph (A) and axial CT scan (B) show a CGCG involving the symphysis and right parasymphisis-body regions of the mandible that underwent a segmental resection and reconstruction, as shown by the postoperative tridimensional CT scan (C).

These lesions are frequently diagnosed by routine radiographs and thus tend to be large at diagnosis with a consequent need of extensive surgical management. In the present study population, a mean size of 3.3 cm of diameter was found. Nevertheless, when such lesions are diagnosed in pediatric patients or in patients with severe comorbidities, the successful rates of an aggressive/radical surgical treatment or even a

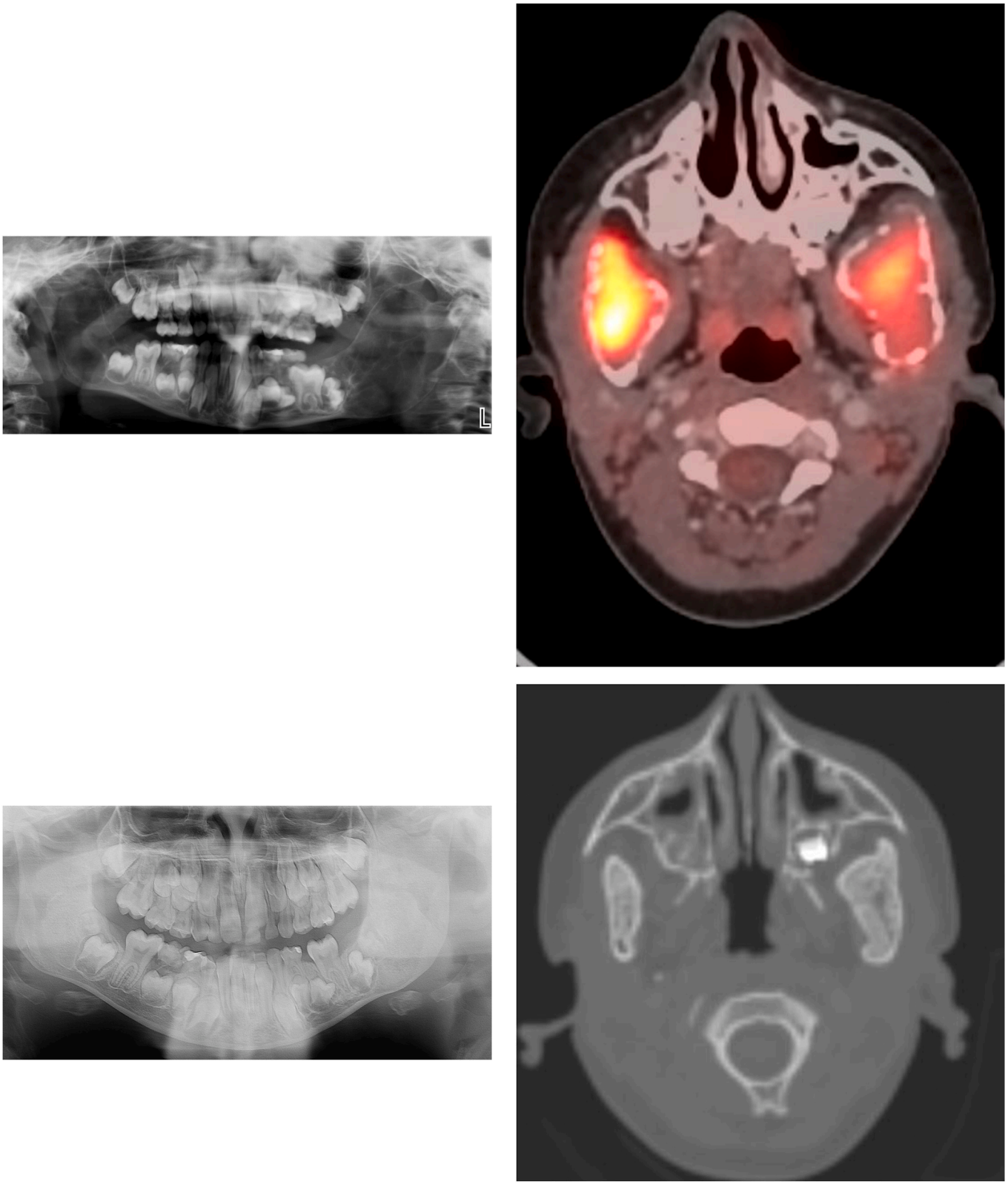

Fig. 3. Imaging examinations of a 7-year-old male patient affected by Noonan syndrome, from the Oviedo center. Preoperative panoramic radiograph (A) and PET/CT scan (B) show a CGCG involving the mandibular ramus, coronoid, and angle, bilaterally. The patient underwent administration of denosumab (30 mg/month) for a year. Because of the occurrence of 3 episodes of hypercalcemia, corticosteroids were administered in such occasions. Postoperative panoramic radiograph (C) and axial CT scan (D) performed at the end of the treatment can be observed, as well as a panoramic radiograph (E) that was taken one year after the treatment.

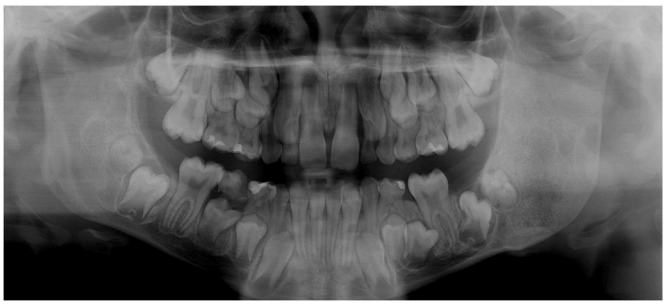

Fig. 3. (*continued*).

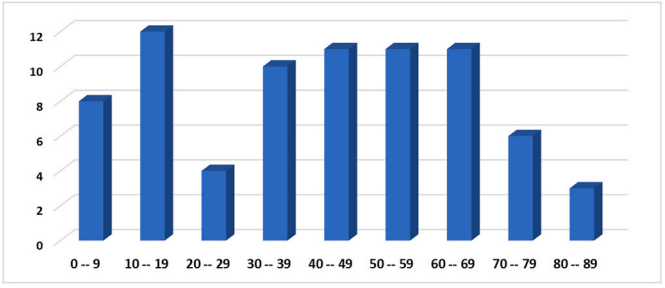

Fig. 4. Distribution of the study population according to decades of age.

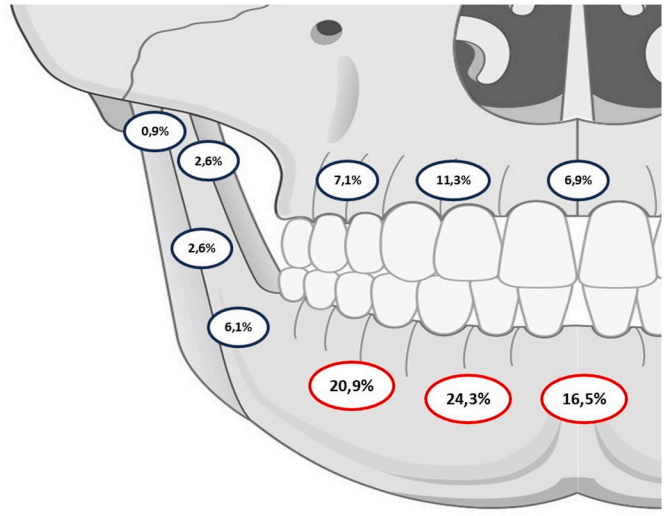

Fig. 5. Distribution of the CGCGs according to subsites.

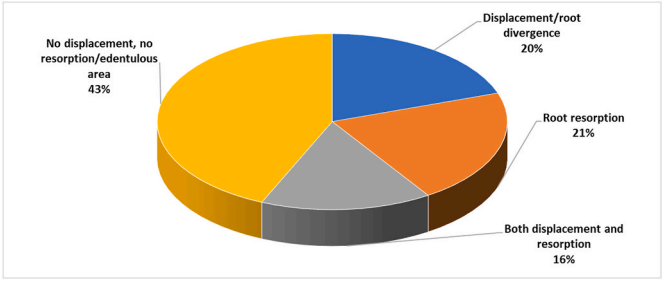

Fig. 6. Radiographic features of the effects of CGCGs on adjacent teeth in the study population.

Table 1
Treatment of CGCGs.

	Number of patients	Mean length of hospital stay	Number of recurrences	Mean follow up (months)
Curettage	8	2. 9	3	36
Enucleation	13	3	3	30
Enucleation + Curettage	14	1.6	2	44
Peripheral ostectomy alone or combined with enucleation or curettage	15	4.9	2	46
Bony Resection (marginal or segmental)	18	5.7	0	42
Total only surgical options	*68*			
Curettage + Denosumab	2	0,5	0	67
Enucleation + Curettage + Corticosteroids	1	1	1	48
Marginal resection + Corticosteroids	1	5	0	47
Total mixed surgical-medical options	*4*			
Calcitonin + Denosumab + Bisphosphonates	1	0	0	66
Denosumab	1	1	1	64
Denosumab + Corticosteroids	1	0	0	NA
Denosumab + Bisphosphonates	1	2	0	NA
Total only medical options	*4*			

NA: Not Available.

conservative surgical treatment should be balanced with the possibility of a high morbidity. These features led to the development of different pharmacological treatment options for CGCGs such as corticosteroids, calcitonin, Interferon α-2a, bisphosphonates, and denosumab.

Most of included CGCGs were unilocular (75 % of lesions), whereas 19 CGCGs were multilocular. Instead, 51 lesions were radiolucent, 19 had a mixed radiolucent – radiopaque appearance, and 6 were radiopaque. As for the observed radiographic features of aggressiveness of CGCGs, neither teeth displacement or resorption was noticed in 33 patients. Displacement/root divergence was observed in 15 patients, root resorption in 16 CGCGs, and both teeth displacement and resorption in the remaining 12 patients. As for their effects on cortical bone, CGCGs were almost equally distributed in CGCGs determining cortical bone expansion (35.5 %), cortical bone thinning (33.3 %), and cortical bone perforation (31.2 %).

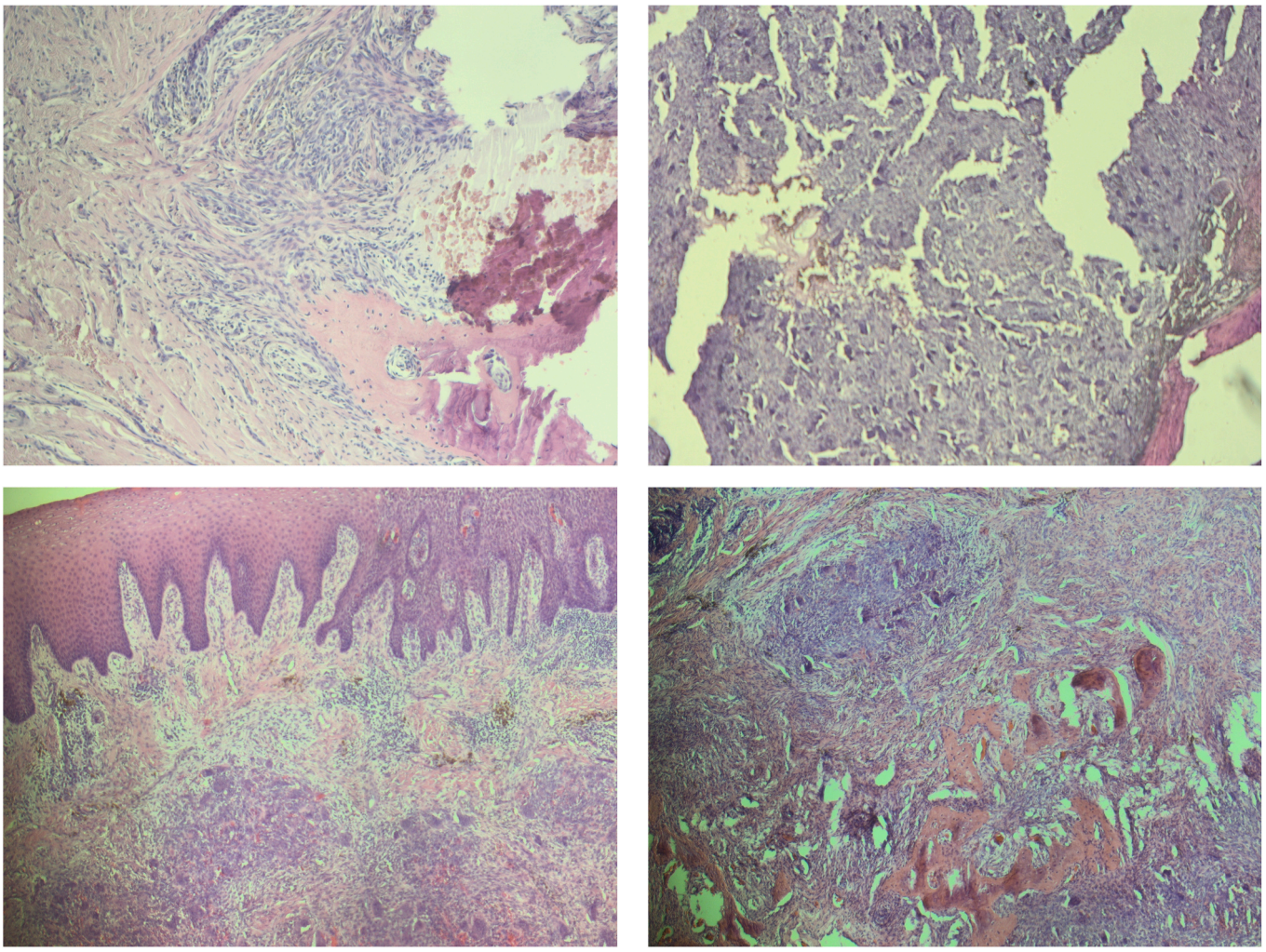

Fig. 7. Histopathological images (Hematoxylin Eosin staining) from Novi Sad center, showing unencapsulated proliferation of spindle shaped cells with multinuclear giant osteoclast type cells in vascular stroma (A, 50x; B, 100x). Gingiva or alveolar mucosa with proliferation of mononuclear and osteoclast type giant cells in deep lamina propria compartment can be seen, as well as foci of haemorrhage (C, 50x). Aggressive osteolytic spindle cells and multinuclear giant cells in the vicinity of the osteoid and woven bone can be observed too (D, 50x).

Non-aggressive CGCGs are usually slowly growing, with rarely observed cortical bone perforation/thinning and root resorption. In contrast, aggressive CGCGs usually present with rapid growth, thinning and perforation of the cortical bone, root resorption, and a higher possibility of recurrence after surgical treatment (Chrcanovic et al., 2018; Rhou et al., 2022; Shrestha et al., 2021, Tahmasbi-Arashlow et al., 2022). Therefore, aggressive subtypes of CGCGs seem to represent about the half of the present study population. This feature, in slight contrast with some recent articles, could be explained by the reduced bias of the current study due to the multicenter nature of the project.

Central giant cell granulomas seem to have an unpredictable course, with some lesions showing a very good response to drugs or conservative surgical therapy, while others recurring even after more radical surgical treatment. Such diverse biological behavior may be explained with a molecular heterogeneity of the lesions.

In spite of the not so high numerosity of the study population, the results of the present study seem to confirm that radical surgical approaches (such as marginal or segmental resections) decrease the recurrence rate of CGCGs.

Unfortunately, aggressive surgical options are associated with morbidities and, sometimes, a poorer quality of life.

In the present multicenter study, pharmacological only treatment options seemed to have been reserved to pediatric and high-risk patients, where an aggressive surgery could be too destructive or dangerous.

In spite of the low numbers and with no statistical confirmation, we could speculate that in case of conservative surgical options the associations of two surgical methods (e.g. enucleation and curettage, curettage and peripheral ostectomy) might reduce the recurrence rate from the higher recurrence rates of single surgical options of curettage (37 %) and enucleation (23 %) to low values included between a range of 10–15 %. Although this suggestion regarding the CGCG management cannot represent a reliable conclusion, despite the limitations of the present study this information might be taken into consideration by surgeons in the treatment plan of selected patients with CGCGs.

Several pharmacological treatment options have been proposed for the management of CGCGs, as aforementioned.

Calcitonin therapy for CGCG was introduced following the demonstration that giant cells of CGCGs are osteoclasts and that such cells would be responsive to calcitonin, resulting in cytoplasmic quiescence and bone resorption inhibition (Capucha et al., 2024; Etoz et al., 2020; Rhou et al., 2022, Suárez-Roa et al., 2009). The use of corticosteroids for CGCG management was proposed following the finding that in vitro dexamethasone would have a direct effect on osteoclast formation and activity, stimulating the proliferation and differentiation of human osteoclast precursors while inhibiting the bone resorbing activity by

mature osteoclasts (Capucha et al., 2024; Etoz et al., 2020, Suárez-Roa et al., 2009).

The proposal of interferon for CGCGs would follow the hypothesis that they are proliferative lesions that would, therefore, respond to angiogenic therapy (Capucha et al., 2024; Etoz et al., 2020; Rhou et al., 2022, Suárez-Roa et al., 2009).

Denosumab, a monoclonal antibody targeting nuclear factor kB-ligand (RANKL), is an effective treatment for giant cell tumor of bone, for which a treatment regimen of denosumab 120 mg monthly with loading doses on days 8 and 15 ha been standard Food and Drug Administration (FDA)-approved treatment for giant cell tumor of bone (Chrcanovic et al., 2018; Rhou et al., 2022; Shrestha et al., 2021, Tahmasbi-Arashlow et al., 2022). CGCG presents similar features to the giant cell tumors of bone, as they are both characterized by spindle-shaped neoplastic cells that over-express receptor activator of RANKL and recruit multinucleated, osteoclast-like giant cells leading to bony destruction. In the recent literature (Chrcanovic et al., 2018, Rhou et al., 2022, Suárez-Roa et al., 2009, Shrestha et al., 2021, Tahmasbi-Arashlow et al., 2022), the use of denosumab has been proposed in CGCG, although the optimal dose and treatment strategy in this condition has not been clearly stated.

However, a Cochrane collaboration review in 2009 (Suárez-Roa et al., 2009) concluded that, although a number of therapies have been proposed for treating central giant cell granuloma of the jaws, no evidence for a treatment option predilection could be found.

The limitations of the study included the retrospective nature of the study, the possible differences in surgical interventions among the various centers, and the different follow-ups, as well as despite being a multicenter study, the sample size is small, at least in some therapeutic groups.

The choice of the most appropriate treatment for each patient (depending on the health status of the patient, the site and size of the lesion, and the possible surgical morbidity) make it extremely difficult to identify a gold standard treatment for any CGCG, that is made even more difficult by the rarity of the lesion.

5. Conclusions

In conclusion, further genetic and molecular studies regarding the pathways underlying CGCGs are needed, in order to predict their natural history and to direct non-surgical therapies. In the meantime, surgeons should balance the risks of higher recurrence rates associated with lower surgical morbidity, performing an individualized treatment plan, taking into consideration the clinical and radiological features together with the patients' age and comorbidities. A radiographic follow-up of patients with treated CGCGs could advised for the first 5 years.

References

Amorós, C.M., Bascones, A.E., Leone, R.C., De la Sen Corcuera, Ó., Barone, S., De Pedro Marina, M., 2024. Central giant cell granuloma: off-label treatment with Denosumab in a patient with Noonan syndrome. J. Stomatol. Oral Maxillofac. Surg. 125 (1), 101640.

Ari, I., Adiloglu, S., Aktas, A., Yasan, G.T., Usman, E., Aksoy, S., 2024. Incidence, treatment method and recurrence rate in giant cell granulomas: retrospective study. J. Craniomaxillofac. Surg. 52 (6), 697–703.

Capucha, T., Krasovsky, A., Abdalla-Aslan, R., Ginini, J.G., Noy, D., Emodi, O., Rachmiel, A., Shilo, D., 2024. Central giant cell granuloma of the jaws-long-term clinical and radiological outcomes of surgical and pharmacological management. Clin. Oral Invest. 28 (3), 200.

Chrcanovic, B.R., Gomes, C.C., Gomez, R.S., 2018. Central giant cell lesion of the jaws: an updated analysis of 2270 cases reported in the literature. J. Oral Pathol. Med. 47 (8), 731–739.

Corrêa, F.A., de Arruda, J.A., Drumond, V.Z., Cepeda, I.V., Tarquinio, S.B., Silva, T.A., Abreu, L.G., Rivero, E.R., Mesquita, R.A., Etges, A., 2024. Pharmacological therapy for central giant cell granuloma of the jaws: a systematic review. J Clin Exp Dent 16 (7), e885–e897.

Etoz, M., Asantogrol, F., Akyol, R., 2020. Central giant cell granulomas of the jaws: retrospective radiographic analysis of 13 patients. Oral Radiol. 36 (1), 60–68.

Pogrel, M.A., Hossaini-Zadeh, M., 2021. Denosumab for the management of central giant cell granuloma of the jaws-a case series. Int. J. Oral Maxillofac. Surg. 50 (8), 1019–1022.

Rhou, Y.J., Wang, C.J., Nguyen, M., Vanderniet, J.A., Munns, C.F., Coleman, H., Kim, J., Holmes-Walker, D.J., Lim, L., Girgis, C.M., 2022. Clinical and radiologic response of central giant cell granuloma to denosumab: a 6-year prospective observational study. Calcif. Tissue Int. 110 (4), 464–474.

Shrestha, S., Zhang, J., Yan, J., Zeng, X., Peng, X., He, B., 2021. Radiological features of central giant cell granuloma: comparative study of 7 cases and literature review. Dentomaxillofac Radiol 50 (5), 20200429.

Suárez-Roa, L., Reveiz, L., Ruíz-Godoy Rivera, L.M., Asbun-Bojalil, J., Dávila-Serapio, J. E., Menjívar-Rubio, A.H., Meneses-García, A., 2009. Interventions for central giant cell granuloma (CGCG) of the jaws. Cochrane Database Syst. Rev. (4), CD007404.

Sun, Z.J., Cai, Y., Zwahlen, R.A., Zheng, Y.F., Wang, S.P., Zhao, Y.F., 2009. Central giant cell granuloma of the jaws: clinical and radiological evaluation of 22 cases. Skelet. Radiol. 38 (9), 903–909.

Tahmasbi-Arashlow, M., Patel, P.B., Nair, M.K., Liang, H., Cheng, Y.L., 2022. Cone-beam computed tomographic imaging of central giant cell granuloma: a comprehensive review. Imaging Sci Dent 52 (2), 123–131.