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CASE REPORT

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Surgical management of mandibular and maxillary central giant cell granuloma

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Abstract

Background Central giant cell granuloma is a benign intraosseous lesion of bone. It frequently affects the head and neck region, particularly the maxillary and mandibular bones. Despite the availability of various nonsurgical treatment options, surgery is still the most effective treatment option for granulomas that do not respond to medical treatment, cause significant bone deformities, or result in extensive bleeding. In this article, we aimed to show the importance of surgery in certain patients by sharing our experience with five patients who were operated on in our clinic.

Case presentation In this case series, five patients who attended our clinic with central giant cell granuloma disease and underwent surgical treatments were retrospectively evaluated utilizing the hospital database records. Demographic and medical information, symptoms at admission, the results of CT and MRI imaging, pathologic results, previous treatments, and the surgical therapy performed at our clinic were all considered. Surgical procedures were performed in five patients; marginal mandibulectomy in two, segmental mandibulectomy in one, and partial maxillectomy in the other two. The granulation tissues in the cavity were removed using curettage and a diamond burr. Primary suture, secondary healing, palatal obturator repair, and free fibula flap reconstruction techniques were performed.

Conclusions The objective of surgical therapy for central giant cell granuloma is to remove the mass with appropriate surgery and repair it properly with the least amount of morbidity and risk of recurrence possible.

Keywords Central giant cell granuloma, Maxillectomy, Mandibulectomy, Craniofacial granuloma

Background

Central giant cell granuloma (CGCG) is a benign intraosseous lesion first described by Jaffe [1]. CGCG is also described as an intraosseous lesion consisting of cellular fibrous tissue that contains multiple foci of hemorrhage, aggregations of multinucleated giant cells, and some trabeculae of woven bone [2]. It is a nonneoplastic lesion that is found particularly in the maxilla and mandible. Although the etiology is uncertain, it is assumed to be caused by trauma, inflammatory processes, or genetic factors [3].

CGCG is mainly appeared in children or young adults, with a predilection for females [4, 5]. Though it is more common at young ages, it can be diagnosed at advanced ages as it has a slow progressing course. CGCG is more common in the mandible than in the maxilla [4]. CGCGs account for approximately 7% of all benign tumors of the jaws, with an incidence rate of 1.1/million population annually [6]. Radiologically, the CGCGs frequently presented as unilocular lesions with well-defined and ill-defined margins. CT demonstrates lesion margins and trabeculation [7]. CGCG is divided into two subclasses aggressive and non-aggressive [6, 8]. The non-aggressive is the most common subtype, presenting as a slow-growing, painless lesion with the expansion of the cortical

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bone. In contrast, aggressive giant cell granulomas tend to appear in younger patients with the following possible features: greater than 5 cm in size, rapid growth, root resorption, tooth displacement leading to malocclusion, cortical bone thinning or perforation, and recurrence after curettage [6, 8–10]

We can classify treatment options as surgical and non-surgical. Non-surgical treatment options include radiation therapy [3], systemic injections of calcitonin [11], intralesional steroid injection [12], and denosumab treatment [13, 14]. Furthermore, surgical options vary from simple curettage to major excisional and reconstructive surgeries such as maxillectomy or mandibulectomy with proper reconstruction, depending on the size, location, and radiological features of the lesion.

We would like to present a case series of five patients diagnosed with CGCG who underwent surgery in the Hacettepe University Department of Otorhinolaryngology and Head and Neck Surgery (Table 1).

Case presentation

Case 1

A 13-year-old female patient applied to the clinic with the complaint of swelling in the mouth. It had been enlarging in the last 6 months. She has no known medical disease. On physical examination, a mass was noticed extending from the lower lip to about 2 cm below the anterior lower border of the mandible and between the first canine teeth. CT scan showed an expansive mass lesion extending from the roots of the left canine tooth to the right first molar tooth, causing extensive damage to the outer and inner cortex of the mandible (Fig. 1). The lesion size is 3.7 cm transversely and 2.1 cm vertically. Besides this, her blood test results were at normal levels.

The patient underwent surgery under general anesthesia. Surgical removal of the mass in the mandibular mentum was performed. A 4 cm incision was made from the right canine tooth to the left canine tooth with the help of electrocautery in the gingivobuccal sulcus. The mass was removed along with the central incisor teeth. The granulation tissues in the cavity were also removed with a curette. The focus of bleeding in the cavity floor was stopped with the use of a diamond burr. After the mass excision, a bone graft was taken from the left iliac region to reconstruct the defective area. The pathology confirmed the diagnosis of central giant cell granuloma. After ten months, there was no sign of repetition.

Table 1 A case series of five patients diagnosed with CGCG who underwent surgery in the Hacettepe University Department of Otorhinolaryngology and Head and Neck Surgery

	Case 1	Case 2	Case 3	Case 4	Case 5
Age-gender	13-female	7-female	9-male	35-female	9-male
Medical history	None	Neurofibromatosis type-1	Oculo-ectodermal syndrome	FMF[a]	None
Lesion location	Mandible	Maxilla/mandible	Mandible/maxilla	Mandible	Maxilla
Size of lesion	3.7 cm	2 cm/2 cm	5 cm	5 cm	3.5 cm × 3.5 cm
Previous treatment	None	None	Denosumab + intralesional steroid	Intralesional steroid	None
Surgical modality	Marginal mandibulectomy	Marginal mandibulectomy	Curettage/maxillectomy	Segmental mandibulectomy	Partial maxillectomy

[a] Familial Mediterranean fever

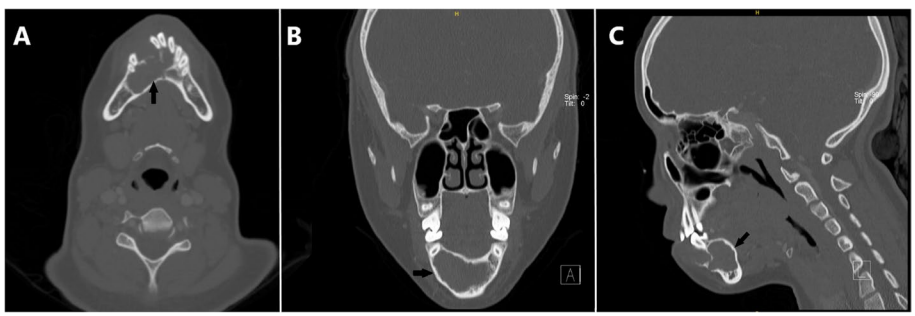

Fig. 1 CT scan of case 1. **a** Axial view. **b** Coronal view. **c** Sagittal view. Black arrows show the lesion

Case 2

A 7-year-old female with neurofibromatosis type 1 attended the clinic with a complaint of swelling in the oral cavity. According to her past medical history, she had undergone two orthopedic operations because of tibial bowing. On physical examination, there was granulomatous mass sealing the gingivobuccal fossa. The lesion extended from the maxillary incisive teeth to about 2 cm above the anterior lower border of the maxilla. About 2 cm mass and the central incisive teeth were removed with partial maxillectomy. No recurrence was found in the surgical area in the first-year controls. Eighteen months postoperatively, the patient presented with a 2 cm mass in the right mandible. CT scan revealed a lytic mass in the right half of the mandible body, at the level of the right mandibular canine and the first premolar. She had undergone an operation with mass removal from the mandibular ramus body by excision and curettage. After making an incision on the area between the gingivobuccal junction and the oral floor with monopolar electrocautery, then the mucosa over the mass was elevated in both directions. The mass was dissected from the mandible, followed by the removal of granulomatous tissue in the cavity with curettage. The incision in the gingivobuccal mucosa was closed. Pathology confirmed the diagnosis of central giant cell granuloma. There were no recurrences in the upper and lower jaw during the last three years of follow-up.

Case 3

This 9-year-old male patient has oculoectodermal syndrome, which is a condition that causes ocular and cutaneous defects. He applied to the clinic with complaints of swelling in the hard palate and bleeding from that lesion. According to his medical history, when he was 2 years old, he developed swelling in the jaw after having his teeth removed, and the biopsy showed that he had a central giant cell granuloma. The patient had undergone eight excision surgeries on the same site over a 5-year period at another clinic. During this period, he also received eight cycles of denosumab treatment for 5 months. At the end of the treatments, the mass in the jaw disappeared. No recurrence was demonstrated in the mandible in the follow-ups of the patient; however, eight months later, a separate hemorrhagic swelling appeared on the hard palate. A biopsy of this new lesion revealed a central giant cell granuloma. The patient received six intralesional triamcinolone injections at the faculty of dentistry. With this treatment, the bleeding decreased somewhat, but the mass remained the same size. The patient applied to us after experiencing these treatments, and he had a hemorrhagic and fragile lesion found in the posterior side of the left hard palate, thinning the bone, and extending to the nasal floor (Fig. 2).

CT and MRI scans showed an expansive mass in the maxillary bone on the left at the level of the 2nd premolar and molar teeth, causing thinning and loss of the inner and outer cortex (Fig. 3).

We performed surgery to remove the granuloma. The upper part of the lesion was removed through the maxillary sinus by entering with a Caldwell-Luc antrostomy. The other part of the lesion in the hard palate was diminished intraorally with the help of curette and diamond burr followed by the repairing of mucosa on the Caldwell Luc window. The mucosa of the hard palate was left for secondary healing. The pathology confirmed the diagnosis of central giant cell granuloma. There were no recurrences in the first-year follow-ups.

Case 4

A 35-year-old pregnant woman with familial Mediterranean fever (FMF) presented with bleeding, facial pain, and a mandibular mass. About 2 years ago, the patient applied to the dentist with symptoms of toothache and swelling. The patient had a tooth extracted then the biopsy revealed a central giant cell granuloma. Based on biopsy results, seven cycles of intralesional steroid therapy were administered, though a sufficient response to treatment could not be achieved. After the non-surgical treatment, she underwent surgery at the faculty of dentistry which was interrupted because the patient had massive intraoperative bleeding.

When the patient applied to our clinic, she was 7 months pregnant with a mass of 5 cm diameter, and the patient received several blood transfusions due to bleeding from the mass. The mass had grown significantly during pregnancy, and her bleeding from the lesion had also increased. A CT scan revealed a lesion causing extensive

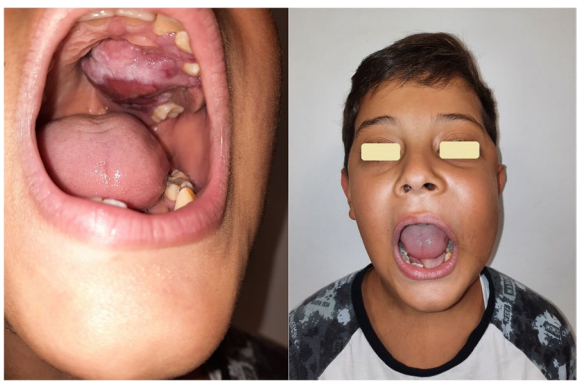

Fig. 2 Case 3. Intraoral view of expansive CGCG, causing destruction on the hard palate (*right*), the outer appearance of left premaxillary swelling (*left*)

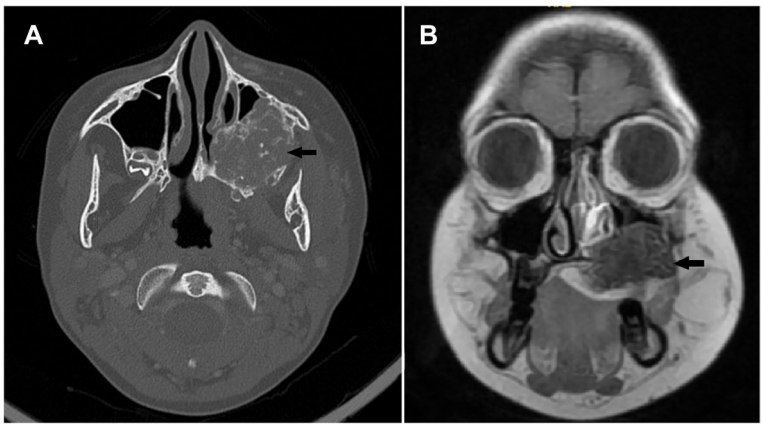

Fig. 3 Case 3. **a** Axial view of CT, thinning and losing of inner and outer cortex. **b** Coronal view of T1 enhanced MRI. Black arrows showing the lateral border of the granuloma

teeth loss in the paramedian part of the right mandible, mentum, and body of the left mandible and also an intensely enhancing lesion in the mandible (Fig. 4). Physical examination revealed a mass attached to the body of the left mandible extending from the midline through the right incisor and to the floor of the mouth, pushing the tongue posteriorly. The operation was delayed until after the baby was born to protect the mother and baby during pregnancy. After the birth, we performed a segmental mandibulectomy, floor-of-mouth reconstruction, and furthermore, tracheostomy operation to achieve a safe airway after a major intraoral surgical procedure. The procedure began with a lip-splitting incision that extended from 2 cm below the mandible's free edge to the mastoid ridge on the left side. After making an incision from the gingivobuccal sulcus on the left and right sides after the lip split incision. The mandible was later dissected from its surrounding tissues and cut with a piezoelectric device on the left and right sides of the lesion. A fibula-free flap surgery was performed to reconstruct the mandibular defect from the right lateral incisive to the left second molar. The pathology confirmed the diagnosis of central giant cell granuloma. The patient had no recurrence throughout post-operative follow-ups. Decannulation, as well as tracheostomy closing, were also accomplished.

Case 5

A 9-year-old boy attended the clinic complaining of swelling in his right cheek and nasal bleeding. According to his medical history, he had no known medical disease. Intralesional triamcinolone therapy was administered at the faculty of dentistry but did not relieve his symptoms. Physical examination revealed an ulcerative lesion extending from the right central incisive through all the molar teeth on the right side. CT and MRI scans showed an expanding mass lesion in the right maxillary sinus encompassing the alveolar process of the maxillary bone, the medial–lateral walls of the maxillary sinus, and the right side of the hard palate. Its dimensions at the widest point are $35 \times 31 \times 35$ mm. Furthermore, the inferior concha was deviated medially by the mass (Fig. 5).

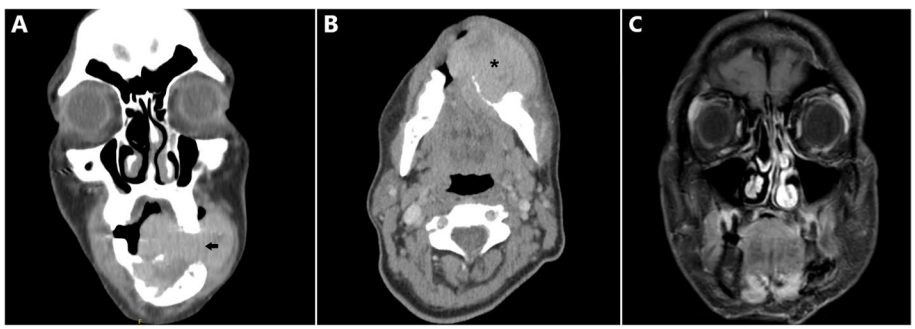

Fig. 4 **a** Coronal view of CT, black arrow showing the destruction of the left mandibular body. **b** Axial view of CT, * showing destructive mass. **c** A postoperative coronal T1 MRI image shows that there is no residual contrast-enhanced lesion after surgery

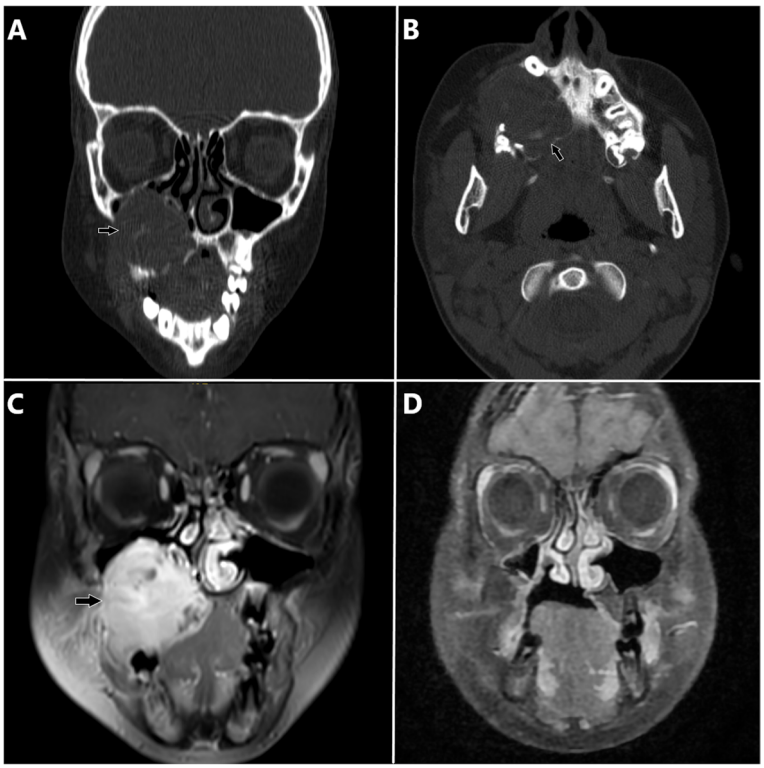

Fig. 5 Case 5. **a** Coronal view of CT, destruction of lateral maxillary sinus wall. **b** Axial view of CT, destruction of the hard palate. **c** Preoperative coronal view of T1 enhanced MRI. **d** Postoperative coronal view of T1 enhanced MRI

The patient had a partial maxillectomy and excision during the procedure. First, an incision was made in the right gingivobuccal sulcus. It was noticed that the mass had abraded the anterior wall of the maxilla. The mass further proceeded to be dissected from surrounding tissues. The lesion also was observed to be extensively hemorrhaging. Following that, a partial maxillectomy was performed. Intraorally, the maxillary bone's boundaries were drilled using a diamond burr. Eventually, the defective area was sutured with the palatal obturator. The pathology confirmed the diagnosis of central giant cell granuloma. On post-surgical follow-ups, there were no recurrences (Fig. 5).

Discussion

Central giant cell granuloma disease is a benign intraosseous lesion. Although this disease mostly appears in children and young people, it can also appear in adults. Head and neck CGCGs frequently involve the maxillary and mandibular bones. Locally invasive, expansile, and bleeding lesions are the most common symptoms.

Peripheral and central giant cell granuloma (GCG) are the two types of GCG that have been identified. Although both types have comparable clinical and histological characteristics, the main difference is that PGCG originates from extraosseous tissues, while CGCG originates from intraosseous tissue. Both are non-neoplastic lesions with similar pathophysiology of local trauma and inflammation. CGCG is more aggressive clinically, manifesting as lytic, expansile masses in the mandible and maxilla, and is less common than PGCG [15–17].

Along with histology, one of the most crucial diagnostic techniques in the diagnosis of the disease is imaging. CT is specifically helpful in imaging its relationship with bone tissue. On the other hand, MRI is quite successful in showing the relationship between the nature of the mass and the soft tissue.

A CT scan can reveal well-circumscribed lytic lesions and expansile mass with the existence of a subtle granular bone pattern at the periphery of the expanded bone with some internal septa [18]. MRI reveals a soft tissue area of low signal intensities on both T1 and T2 weighted images along with variable intensities within the lesion if there is the presence of fibrosis, osteoid, hemorrhage, or hemosiderin deposits. The lesion mass can show enhancement, but the degree of enhancement can vary [19].

Various syndromes and systemic disorders may contribute to the genesis of CGCG development in certain patients [20, 21]. Cases 2 and 3 demonstrated that CGCG in the maxilla or mandible might recur in another bone

over time. The lesion was identified in the maxillary or mandibular bone in all five of our patients, and no other bones were affected. There is no clear information about when or in which patients the secondary lesion will occur later. The fact is that the third case has Oculo-ectodermal syndrome, a rare disease with characteristic clinical findings of ocular and cutaneous defects including epibulbar dermoids, aplasia cutis congenita, macrocephaly, and areas of skin hyperpigmentation [22]. Patients with Oculo-ectodermal syndrome who develop giant cell granulomas of the jaw have been documented by Toriello et al. (1999) [23] and Lacombe et al. (2004) [22]. In the second case, the presence of NF-1 disease might be the reason for recurrent CGCG. Reports of CGCG in patients with Neurofibromatosis type-1 have been described in the literature by Chrcanovic et al. (2011) [24], Edwards et al. (2006) [25], and Krammer et al. (2003) [26]. In the fourth case, the patient had FMF (Familial Mediterranean Fever) disease, a rare autosomal recessive autoinflammatory disease characterized by paroxysmal fever, peritonitis, arthritis, and myalgia [27]. In the literature, there is no unknown association between FMF and CGCG. There were various medical treatment options, these mainly consist of radiation treatment [3], systemic injections of calcitonin [11], intralesional steroid injection [12], and denosumab treatment [13, 14].

Despite the availability of several medical treatments, surgery remains the most crucial step in the treatment of disease today. The type of surgery is determined by considering factors such as the lesion's location, shape, size, and invasion of the surrounding tissues. Although non-surgical treatments are crucial for a patient's quality of life, surgery may be recommended in situations when non-surgical treatments have failed or are ineffective. As shown in cases 3 and 4, patients who did not respond to nonsurgical treatment required surgery.

Making a treatment decision and selecting the best surgery for these patients requires a multidisciplinary approach. Both pre-operative and post-operative care should be provided by dentists, speech and swallowing therapists, and plastic surgeons. A multidisciplinary team meeting was used to decide on the care plans for each of our patients. The patient's post-surgical dental care and speech and swallowing therapies were all followed by the appropriate departments.

In most cases, excision or curettage of the mass is adequate, but in large lesions, further major procedures may be indicated such as segmental or marginal mandibulectomy or partial maxillectomy. Each of these surgical decisions should be considered after a thorough examination of the patient.

The age and morbidity of the patient, the size and location of the lesion, the severity of symptoms such as frequency of bleeding, facial deformity, chewing difficulties, pain, visual disturbances, numbness, and response to previous treatments are the main concerns we have, especially when making a surgical decision.

The primary surgical strategy is to excise the lesion and repair the defect. There are several surgical treatment options for eradicating the lesion. Segmental or marginal mandibulectomy, partial maxillectomy, curettage, and functional endoscopic sinus surgery are the main components of the surgical treatments in our cases. After the surgical excision, either a diamond burr or curettage is required to remove the granulation tissues in the cavity to diminish the risk of recurrence.

In patients with a large mass, reconstruction of the defect is also required after surgical excision. Primary closure, secondary healing, or free flap surgery are the most common procedures utilized in reconstruction. For example, in case 1, the defective area was reconstructed with a bone graft which was taken from the left iliac region; in case 2, the defective area was primarily sutured; in case 3, the defective mucosa of the hard pale was left to secondary healing; in case 4, fibula free flap surgery was performed; and in case 5, palatal obturator was used.

Conclusion

Although many non-surgical therapies are now incorporated into the treatment of CGCG with the various treatment methods developed today, surgery remains to play an essential role in the treatment of refractory cases. Choosing the best excision procedure may not be enough; suitable reconstruction therapy is also required.

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Authors' contributions
All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by ED. All authors (ED, ROG) commented on previous versions of the manuscript. All authors (ED, ROG) read and approved the final manuscript.

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Availability of data and materials
The data of the patients were obtained from the Hospital database system (nucleus software).

Declarations

Ethics approval and consent to participate
This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Hacettepe University non- interventional clinical investigations committee with the number GO 21/1356. Informed written consent to participate in the study was provided by all adult participants and parents of the participants under 16.

Consent for publication
Both written and verbal informed consent was obtained from the patient and their parents.

Competing interests
The authors declare that they have no competing interests.

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References

1. Jaffe HL (1953) Giant-cell reparative granuloma, traumatic bone cyst, and fibrous (fibro-osseous) dysplasia of the jawbones. Oral Surg Oral Med Oral Pathol 6(1):159–175
2. Kramer IR, Pindborg JJ, Shear M (1992) The WHO Histological Typing of Odontogenic Tumours. A commentary on the Second Edition. Cancer 70(12):2988–2994. https://doi.org/10.1002/1097-0142(19921215)70:12<2988::aid-cncr2820701242>3.0.co;2-v
3. Eisenbud, Leon, et al. (1988) Central giant cell granuloma of the jaws: experiences in the management of thirty-seven cases. J Oral Maxillofacial Surg 46(5):376–384
4. Auclair, Paul L, et al. (1988) A clinical and histomorphologic comparison of the central giant cell granuloma and the giant cell tumor. Oral Surg Oral Med Oral Pathol 66(2):197–208
5. Abu-El-Naaj, Imad, et al. (2002) Central giant cell granuloma of the mandibular condyle: a rare presentation. J Oral Maxillofacial Surg 60(8):939–941
6. de Lange J, van den Akker HP, Klip H (2004) Incidence and disease-free survival after surgical therapy of central giant cell granulomas of the jaw in The Netherlands: 1990–1995. Head Neck 26(9):792–795. https://doi.org/10.1002/hed.20069
7. Sun, Zhi-Jun, et al. (2009) Central giant cell granuloma of the jaws: clinical and radiological evaluation of 22 cases. Skeletal Radiol 38(9):903–909
8. Wang Y, Le A, El Demellawy D et al (2019) An aggressive central giant cell granuloma in a pediatric patient: case report and review of literature. J Otolaryngol Head Neck Surg 48:32. https://doi.org/10.1186/s40463-019-0356-5
9. Kruse-Losler B, Diallo R, Gaertner C, Mischke KL, Joos U, Kleinheinz J (2006) Central giant cell granuloma of the jaws: a clinical, radiologic, and histopathologic study of 26 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 101(3):346–354
10. Chuong R, Kaban LB, Kozakewich H, Perez-Atayde A (1986) Central giant cell lesions of the jaws: a clinicopathologic study. J Oral Maxillofac Surg 44(9):708–713
11. Harris M (1993) Central giant cell granulomas of the jaws regress with calcitonin therapy. Br J Oral Maxillofac Surg 31(2):89–94
12. Carlos R, Sedano HO (2002) Intralesional corticosteroids as an alternative treatment for central giant cell granuloma. Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol 93(2):161–166
13. Schreuder, Willem H., et al. (2014) Alternative pharmacologic therapy for aggressive central giant cell granuloma: denosumab. J Oral Maxillofac Surg 72(7):1301–1309
14. Bredell, Marius, et al. (2018) Denosumab as a treatment alternative for central giant cell granuloma: a long-term retrospective cohort study. J Oral Maxillofacial Surg 76(4):775–784
15. Bhalodiya N, Singh N (2005) Giant cell reparative granuloma of posterior ethmoid: a case report. Indian J Otolaryngol Head Neck Surg 57:325–327. https://doi.org/10.1007/BF02907701
16. Flórez-Moreno GA, Henao-Ruiz M, Santa-Sáenz DM, Castañeda-Peláez DA, Tobón-Arroyave SI (2008) Cytomorphometric and immunohistochemical comparison between central and peripheral giant cell lesions of the jaws. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 105(5):625–632. https://doi.org/10.1016/j.tripleo.2007.08.032
17. Ishinaga H, Otsu K, Mouri G, Takeuchi K (2013) Aggressive Giant Cell Reparative Granuloma of the Nasal Cavity. Case Rep Otolaryngol 2013:690194. https://doi.org/10.1155/2013/690194
18. Jadu FM, Pharoah MJ, Lee L, Baker GI, Allidina A (2011) Central giant cell granuloma of the mandibular condyle: a case report and review of the literature. Dentomaxillofac Radiol 40(1):60–64. https://doi.org/10.1259/dmfr/85668294
19. 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. https://doi.org/10.1259/dmfr.20200429. Epub 2021 Apr 21. PMID: 33881907; PMCID: PMC8231678
20. de Lange, Jan, Hans P. van den Akker, and Henk van den Berg (2007) Central giant cell granuloma of the jaw: a review of the literature with emphasis on therapy options." Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol 104(5):603–615
21. Uçar Birsen et al. (1998) Noonan syndrome associated with central giant cell granuloma. Clin Genet 53(5):411–414
22. Toriello HV, Lacassie Y, Droste P, Higgins JV (1993) Provisionary unique syndrome of ocular and ectodermal defects in two unrelated boys. Am J Med Genet 45:764–766
23. Federici S, Griffiths D, Siberchicot F, Chateil JF, Gilbert B, Lacombe D (2004) Oculo-ectodermal syndrome: a new tumour predisposition syndrome. Clin Dysmorphol 13(2):81–83
24. Chrcanovic BR, Gomez RS, Freire-Maia B (2011) Neurofibromatosis type 1 associated with bilateral central giant cell granuloma of the mandible. J Craniomaxillofac Surg 39(7):538–543. https://doi.org/10.1016/j.jcms.2010.10.014
25. Edwards, Paul C, et al. (2006) Clinically aggressive central giant cell granulomas in two patients with neurofibromatosis 1. Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol 102(6):765–772
26. Krammer Uta, et al. (2003) Neurofibromatosis 1: a novel NF1 mutation in an 11-year-old girl with a giant cell granuloma. J Child Neurol 18(5):371–373
27. Komatsu Shigetsuna, et al. (2014) Cutaneous necrotizing vasculitis as a manifestation of familial Mediterranean fever. J Dermatol 41(9):827–829

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