

A CASE OF CENTRAL GIANT CELL GRANULOMA (CGCG) AND ITS LONG-TERM FOLLOW-UP

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يعتبر الورم الحبيبي المركزي ذو الخلايا العريضة الأكثر مشاهدة في الأطفال والبالغين الشباب، من الآفات السليمة النادرة الحدوث في الفكين. تضمنت هذه الدراسة متابعة لمدة ٦ سنوات بعد التجريف الجراحي لإحدى الإصابات لدى طفل بعمر ٦ سنوات. دلت النتائج على تعظم كامل تمت أيضا مناقشة النتائج الشعاعية والنسجية.

A case of central giant cell reparative granuloma (CGCRG), which is one of the benign and rarely encountered jaw lesions and which has been postulated to have been more frequently encountered in children and young adults, is being reported together with a review of pertinent literature. A lesion localized in the ramus was curetted surgically in a 6-year-old boy and was followed-up for six years. It was found that the lesion in the ramus was completely ossified and there was no sign of recurrence at the end of the long-term follow-up. Radiologic and histopathologic findings are presented.

CGCG of the jaw is one of the relatively rare pathologic processes and encountered, less than 7% of all of the jaw lesions.¹ It is considered by Jaffe² as a local reparative reaction of bone to the intra-osseous hemorrhage and trauma.

CGCG is seen clinically in patients younger than 30 years old, in women more than in men, and in mandible more than in maxilla.³⁶ Signs and symptoms vary considerably. Pain is very rare. Luxation and migration of teeth with root resorption may be seen.⁶

In this report, we aimed to emphasize that curettage and enucleation are curative for CGCG jaw bone lesions. Remodelling of the bone was followed-up radiographically.

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Literature Review

Giant cell lesions of the maxillofacial area can vary from asymptomatic radiolucency of slowly growing lesion to aggressive tumors showing high recurrence rate as well as rapid expansive progression characterized by root resorption and pain.³

Jaw lesions of CGCG are frequently compared with giant cell tumors (GCT) of other tissues due to the similarity in histologic appearances of these lesions.⁷ Rate of recurrence and metastasis are high in long bone lesions. Malignant giant cell lesions are very rare in jaws.⁷

GCT, GCG, and brown tumor of hyperparathyroidism have different histological features and clinical entities. The histologic criteria is that the number of stromal nuclei distribution of giant cells are somewhat helpful in differentiating between the GCT and GCG.⁸ Pathologists tried recently to determine the histopathologic parameters for predicting the prognosis and clinical distribution of GCG. Studies have been focused on the stromal cells, vascularity, hemorrhage and presence or

absence of mitosis, but definitive results remain to be elucidated.⁸

Unlike osteoblastoma and giant cell lesions of hyperparathyroidism, a great majority of cases with CGCG are found under 20 years of age and this may be helpful in the differential diagnosis.⁶ In their study, Auclair et al⁹ determined that the mean age for 42 cases with GCT of long bones and 49 cases with CGCG of jaws were 25 and 21 years, respectively where its clinical and histomorphologic findings were compared. Eisenbud et al¹⁰ also determined the incidence by age, sex, and localization of lesions. They stated that 89% of CGCG cases was found under the age of 50 years, of which 62% were females with the mandible being affected more than the maxilla.

Brown tumor of primary or secondary hyperparathyroidism, cherubism, fibrous dysplasia, xantofibroma, osteogenic sarcoma and GCT have identical histologic appearances. Definitive diagnosis was established by detailed anamnesis and full clinical examination.⁴

Adekeye et al¹¹ considered the CGCG and Burkitt's lymphoma in differential diagnosis of histoplasmosis granuloma, a fungal infection that caused progressive destruction in mandible of a 14-year-old boy. The foam-like fungal body appearance of histoplasmosis granuloma is similar to giant vacuole of mononuclear histiocytes and multinucleated giant cells of CGCG.

Diffuse lesions should be treated by resection while simple curettage is an effective method in the great majority of cases with CGCG.³ Simple curettage of aggressive lesions is frequently not curative, however, resection is the contemporary mode of therapy for this type of tumor.⁹

Case Report

A 6-year-old boy was admitted to our clinic on October 7, 1987 with a complaint of painless swelling in his right lower jaw extending from right angle to the front of the ear, with an open wound from an old surgery in his mouth. It was understood that he was operated on by an otorhinolaryngologist one year ago.

A panoramic radiograph revealed multilocular radiolucency extending from the distal of the second deciduous molar to the coronoid process and condylar neck along the angle and the ramus [Fig.

1]. Brown-colored tumor tissue was completely removed under local anesthesia with the presumptive differential diagnosis of ameloblastoma and central giant cell reparative granuloma. The surgical site was filled by gauze tamponade and furacin [Fig. 2].

Histological findings showed fibrocytes, arranged like bundles in various areas and copious capillaries with fibrous tissue, as well as lymphocytic infiltration. Multinucleated giant cells were observed [Fig. 3].

During postoperative follow-ups, gauze tamponade with furacin was changed once a week. Further follow-ups was made at three-month intervals. Healing was observed at the end of the sixth month [Fig. 4]. Six-years later, clinical and radiologic examinations were performed and the patient had no complaint. No sign of recurrence was noticed yet the development of third molar tooth germ was observed [Fig. 5].



Figure 1. Appearance of an extensive and multilocular lesion on panoramic radiograph.



Figure 2. Postoperative radiograph showing the appearance and disappearance of multilocular lesion after surgical enucleation. The cavity was packed with furacin gauze.

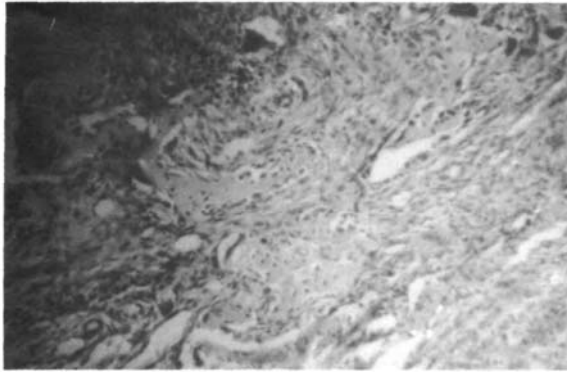


Figure 3. Histopathologic slide showing multinucleated giant cells (hematoxylin and eosin X 200).



Figure 4. Panoramic radiograph taken six-month after operation showing regeneration of bone.



Figure 5. Six-years follow-up radiograph showing complete healing and third molar germ.

Discussion

The term "GCRG (CGCG)" was first established by Jaffe² in 1953 and it was the first approach for indicating the clinical and histologic differences between GCT and CGCGs of bone. The word "reparative" is not used currently as a convenient marker because GCT was actually destructive in structure. Austin et al agreed that these pathologic conditions (GCT and CGCG) were different in clinical entities and emphasized their histologic differences. They thought that GCT was rarely seen in jaws. Shklar and Meyer¹² stated that GCT of the jaw was more common than previously considered.

Waldron and Shafer¹³ reviewed 38 cases and concluded that these two clinical entities were mainly different processes of the same disease. Many authors thought that most CGCGs of the jaw, which are relatively more common lesions, were reactive in nature rather than neoplastic.^{1,2,13}

Various concepts were proposed regarding the pathogenesis of GCGs. Waldron and Shafer¹³ proposed that these lesions were similar and perhaps the same. It was reported that the development of aneurysmal bone cyst might be helpful in determining the pathogenesis of giant cell granulomas.¹⁰ The most important criteria to distinguish the CGCG from aneurysmal bone cyst is that the latter has large blood spaces.

Numerous lesions as cherubism, fibrous dysplasia, primary and secondary hyperparathyroidism, xantofibroma, aneurysmal bony cyst, osteogenic sarcoma and GCT are considered in differential diagnosis.^{5,8}

Cherubism is a benign fibro-osseous lesion where bilateral and symmetric enlargement is seen at early childhood.⁴ It is a hereditary disorder inherited by 100% autosomal dominant genes in men. Its histopathologic appearance looks like GCG (it shows marked vascularity, and fibrous stroma containing multinucleated giant cells).

It was concluded that the aggressive type of CGCGs was more common in the younger age-group, larger when diagnosed and had more frequent tendency of recurrence than the nonaggressive type. Cytometric imaging study proved that clinical criteria used by Chuong et al⁸ in diagnosing the aggressive type were reliable, not only in determining the extent of tumor but also in showing its rapid growth and destructive behavior.

In a clinicopathologic and cytometric study of the CGCG of maxilla and mandible of 22 patients, Ficarra et al¹⁴ used a computer-guided image analysis in defining the four histopathologic parameters (numbers of giant cell, mean nucleus number of giant cells, functional surface area and relative size index). The parameters were used for investigating the presumptive initial histologic signs of clinical behavior of CGCG.

The CGCG of jaw and GCT of long bones were discussed with respect to their biological behavior, histopathologic features and clinical responses to conservative therapy.¹⁴ The latter is locally aggressive and has a high rate of recurrence. Malignant transformation occurs in 15-20% of cases.¹⁴ The majority of CGCG of the jaw are generally benign in character. However, some showed tendency of recurrence and an aggressive biologic behavior.^{3,8-14}

A study¹⁵ showed that increased levels of estrogen were responsible for the progression of CGCG in jaw. Waldron and Shafer¹³ stated that 68% of the CGCG cases were seen in women. Flaggort et al¹⁶ also reported a case of recurrent mandibular CGCG in a patient with Sotos'syndrome (cerebral gigantism) during high-dose estrogen therapy. They proposed that while the hormonal therapy of the cases has no positive correlation with CGCG, excessively increased levels of estrogen lead to the development of CGCG in the jaws.

While the therapy of choice is conservative surgical curettage, enucleation plus resection may be necessary in aggressive lesions of extensively destructive type.³ Eisenbud et al¹⁰ noted that curettage with peripheral osteotomy was a convenient method for the treatment of giant cell granuloma of the mandible (recurrence in three cases only).

In this case curettage and enucleation has been applied and the extensive bone defect was completely ossified. There was no sign of recurrence at the end of the six years follow-up.

References

1. Austin LT, Dahlin DC, Royer RQ. Giant cell reparative granuloma and related conditions affecting the jawbones. *Oral Surg Oral Med Oral Pathol* 1959; 12:1285-95.
2. Jaffe HL. Giant cell reparative granuloma, traumatic bone cyst, and fibrous (fibro-osseous) dysplasia of the jawbones. *Oral Surg Oral Med Oral Pathol* 1953;6:159-75.
3. Cohen MA, Hertzanu Y. Radiologic features, including those seen with computed tomography, of central giant cell granuloma of the jaws. *Oral Surg Oral Med Oral Pathol* 1988;65:255-61.
4. Kerley TR, Schow CE Jr. Central giant cell granuloma or cherubism. Report of a case. *Oral Surg Oral Med Oral Pathol* 1981;51:128-30.
5. Urade M, Furusawa K, Watatani K, Matsuya T. Mandibular giant cell granuloma. *Oral Surg Oral Med Oral Pathol* 1988;66:121-22.
6. Spouge JD. *Oral Pathology: Central giant cell reparative granuloma*. St. Louis: CV Mosby Co, 1973:352.
7. Cohen MA. Management of a huge central giant cell granuloma of the maxilla. *J Oral Maxillofac Surg* 1988;46:509-13.
8. Chuong R, Kaban LB, Kozakewich H, Atayde AP. Central giant cell lesions of the jaws: A clinicopathologic study. *J Oral Maxillofac Surg* 1986;44:708-13.
9. Auclair PL, Cuenin P, Kratochvil FJ, Slater LJ, Ellis GL. A clinical and histomorphologic comparison of the central giant cell granuloma and the giant cell tumor. *Oral Surg Oral Med Oral Pathol* 1988;66:197-208.
10. Eisenbud L, Stem M, Rothberg M, Sachs SA. Central giant cell granuloma of the jaws: Experiences in the management of thirty-seven cases. *J Oral Maxillofac Surg* 1988;46:376-84.
11. Adekeye EO, Edwards MB, Williams HK. Mandibular African histoplasmosis: Imitation of neoplasia or giant-cell granuloma? *Oral Surg Oral Med Oral Pathol* 1988;65:81-4.
12. Shklar G, Meyer I. Giant cell tumors of the mandible and maxilla. *Oral Surg Oral Med Oral Pathol* 1961;14:809-27.
13. Waldron CA, Shafer WG. The central giant cell reparative granuloma of the jaws. An analysis of 38 cases. *Am J Clin Pathol* 1966;45:437-47.
14. Ficarra G, Kaban LB, Hansen LS. Central giant cell lesions of the mandible and maxilla: A clinicopathologic and cytometric study. *Oral Surg Oral Med Oral Pathol* 1987;64:44-9.
15. Littler BO. Central giant cell granuloma of the jaw - a hormonal influence. *Br J Oral Surg* 1980; 17:43.
16. Flaggert JS, Heldt LV, Gareis FJ. Recurrent giant cell granuloma occurring in the mandible of a patient on high dose estrogen therapy for the treatment of Sotos' syndrome. *J Oral Maxillofac Surg* 1987;45:1074-76.