# Central giant cell granuloma of the mandible in a 7-year-old boy: A case report

Yu-Ju Lin, DDS[1]/Hong-San Chen, DDS, PhD[2]/
Hong-Rong Chen, DDS, PhD[3]/Wen-Chen Wang, DDS, MS[4]/
Yuk-Kwan Chen, DDS, MS[5]/Li-Min Lin, DDS, MS, PhD[6]

Central giant cell granuloma is a relatively uncommon benign bony lesion of a variably aggressive nature. This paper presents the case of a 7-year-old boy with central giant cell granuloma in the anterior mandible. In children with mixed dentition, a pathologic lesion could be the underlying cause of regular tooth mobility and exfoliation of primary teeth and can easily be overlooked, especially in cases that are not accompanied by an obvious bony expansion. The clinician needs to be aware of possible oral pathology when tooth mobility and displacement are present, and central giant cell granuloma should be considered in the differential diagnosis for children with maligned and mobile teeth.
*(Quintessence Int 2007;38:253–259)*

**Key words:** central giant cell granuloma, child, differential diagnosis, tooth exfoliation

Central giant cell granuloma (CGCG) is a relatively uncommon benign bony lesion of a variably aggressive nature, accounting for less than 7% of all benign jaw lesions.[1] The condition was first identified in 1953 by Jaffe,[2] who initially termed this lesion a *central giant cell reparative granuloma*. Nowadays, as a reparative response is quite rare and most lesions of CGCG are destructive, the word *reparative* has been deleted from that term.[3,4] In contrast to the giant cell tumors of the long bone, CGCG of the jaw tends to involve a younger age group, and, though categorized as "aggressive," CGCG is much less destructive than giant cell tumors, which are usually painful and fast growing, with a pathologic fracture being the first sign in about 10% of cases.[5]

Auclair et al[6] performed a histomorphologic comparison of 49 CGCGs of the jaw and 42 giant cell tumors of long bones; the only statistically significant histologic difference between these 2 lesions was the higher number of nuclei in the giant cell tumors. Al Sheddi et al[7] performed a similar comparison between 18 CGCGs of the jaw and 22 giant cell tumors of bone. A result similar to Auclair et al's report[6] was obtained, but, in addition, necrosis was a significant finding in lesions of CGCG. Wold et al[8] also compared the CGCGs of the small bones of the hands and feet with giant cell tumors of the same bones. They reported 100% osteoid formation, 93% stromal hemorrhage, 73% clustering of giant cells, and a 20% stromal storiform pattern in their 30 cases of CGCG lesions, whereas all these were lacking in giant cell tumors of the same bones, except for hemorrhage in 44%.

[1]Chief Resident, Department of Oral Pathology, Kaohsiung Medical University, Kaohsiung, Taiwan.

[2]Associate Professor and Head, Department of Pediatric Dentistry, Kaohsiung Medical University, Kaohsiung, Taiwan.

[3]Professor, Department of Oral and Maxillofacial Surgery, Kaohsiung Medical University, Kaohsiung, Taiwan.

[4]Attending staff, Department of Oral Pathology, Kaohsiung Medical University, Kaohsiung, Taiwan.

[5]Assistant Professor and Head, Department of Oral Pathology, Kaohsiung Medical University, Kaohsiung, Taiwan.

[6]Professor, Department of Oral Pathology, Kaohsiung Medical University, Kaohsiung, Taiwan.

**Reprint requests:** Dr Yuk-Kwan Chen/Dr Li-Min Lin, Department of Oral Pathology, School of Dentistry, Kaohsiung Medical University, 100 Shih-Chuan 1st Road, Kaohsiung, Taiwan. E-mail: k0285@ms22.hinet.net

**Table 1** **Differential diagnosis of lesions with histology indistinguishable from central giant cell granuloma in the jaw[15–18]**

| Lesions* | Traditional diagnostic tools | Molecular approach |
|---|---|---|
| Brown tumor of hyperparathyroidism† | Radiographic finding: Loss of lamina dura of teeth, multiple lytic radiolucencies<br>Blood chemistry: Elevated parathyroid hormone secretion, hypercalcemia, hypophosphatemia | NA |
| Cherubism | Radiographic finding: Multiple lytic radiolucencies | Mutation in SH3BP2 on p-arm of chromosome 4 |
| Neurofibromatosis type 1 (NF1) | Radiographic finding: Multiple lytic radiolucencies | Mutation in a NF-1 gene on q-arm of chromosome 17 |
| Noonan syndrome | Radiographic finding: Multiple lytic radiolucencies | Mutation in PTPN11 on q-arm of chromosome 12 |

(NA) Not yet clinically available.
*Histologically and radiographically, all of these lesions are essentially indistinguishable. A clinical-radiological-molecular approach is required to obtain a final diagnosis.
†Primary occurrence is due to hyperplasia or neoplasia of the parathyroid gland; secondary occurrence is associated with renal osteodystrophy.

Furthermore, in contrast to the giant cell tumors of the long bone, in which en bloc excision is the treatment of choice, curettage is usually the first line of treatment and is frequently adequate for CGCG of the jaw. Small fragments that may be left behind do not necessarily require further treatment, and sometimes appear to resolve spontaneously. A minority of these tumors is more aggressive, and recurrence follows incomplete removal; frequently, however, a second curettage appears to be adequate. Wide excision is only occasionally required for otherwise uncontrollable lesions.[9] Therefore, the failure to distinguish between CGCG of the jaw and giant cell tumors prior to 1953, resulted, according to Jaffe, in overtreatment of many young patients.[2]

The origin of CGCG is unknown, but some indications implicate genetic abnormality. Two small genetic studies on lesions of CGCG have been reported.[10,11] Cytogenetic abnormalities involving translocations between sex chromosomes and autosomes were identified in a case of CGCG of the phalanx.[10] Also, by using DNA microarray, several genes covering a wide range of functional activities, including cell cycle regulation, signal transduction, and vesicular transport, have been discovered to be up- or downregulated in 2 surgically resected CGCGs of the mandible; some genetic markers have been identified that can potentially assist in identifying the biologic behavior (such as quiescent versus aggressive) or that are potential disease-specific targets for therapy.[11] Additional cases of CGCG must therefore be studied to determine the specificity and significance of these findings.[10,11]

On the other hand, cyclin D1 protein overexpression has been found to be involved in the formation of the giant cells of CGCG of the jaw; hence, deregulation of the cell cycle may contribute to the pathogenesis of CGCG.[12] The light microscopic, enzymatic, histochemical, immunochemical, and ultrastructural features of these giant cells are similar to those of normal osteoclasts.[12] Furthermore, there has been experimental evidence to indicate that the multinucleated giant cells of CGCG are formed by the fusion of the mononuclear stromal cells, endothelial cells of capillaries, fibroblasts, myofibroblasts, or osteoclast progenitor cells.[13] However, a more recent study has claimed that although the multinucleated giant cells of CGCG share some similarities with the osteoclasts, they demonstrate phenotypic differences from each other, suggesting a distinct precursor.[14]

Importantly, a number of lesions are histologically indistinguishable from CGCG of the jaw, including brown tumor of primary or secondary hyperparathyroidism,[15] cherubism,[16] and a number of other inherited syndromes, such as neurofibromatosis type 1[17] and Noonan syndrome.[18] The differential diagnosis using traditional diagnostic tools together with a molecular approach is summarized in Table 1.[15–18]

In a review of English-language medical literature, most cases of CGCG were reported to appear between the ages of 10 and 30 years.[1,3,4,19–22] Well-documented cases of CGCG in children under 10 years old without association with an inherited syndrome have seldom been reported.[23–26] Furthermore, while CGCG is generally an asymptomatic lesion, enlarged cases have been known to cause tooth mobility or tooth displacement.[1,3,4,19–22] Such symptoms and signs may easily be overlooked as regular tooth exfoliation of primary teeth in children with mixed dentition.

This report presents an interesting case of a 7-year-old boy who initially presented with the symptoms and signs of tooth mobility and was ultimately diagnosed with CGCG.

## CASE REPORT

A 7-year-old Chinese boy presented with a 4-month history of a painless swelling over the anterior mandibular area. According to his mother, the mandibular right primary central incisor had exfoliated itself, and no swelling of the mandibular right anterior area was noted. Subsequently, the mandibular left primary lateral incisor had severe mobility and was pulled out by the patient. Mobility of the mandibular left primary central incisor was then evident. The patient was taken to a nearby local dental clinic for examination. It was assumed that the tooth mobility was caused by the underlying undererupted permanent counterparts, and consequently the clinician extracted the mandibular left primary central incisor without conducting a radiographic examination. The swelling continued to enlarge, however, and permanent teeth had not yet erupted.

The patient's family history was unremarkable. His medical history revealed a trauma about 1 year previously consisting of a knock against the anterior mandibular area, accompanied by a laceration to the chin requiring stitches. Extraoral examination revealed a healthy boy with a mild facial asymmetry in the chin area. The swollen area was hard in consistency, without overlying hyperemia. The patient did not have any symptoms or signs of infection. Intraoral examination revealed a 3 × 2-cm firm swelling in the mandibular anterior region, with a smooth, bluish surface (Fig 1). There was no associated tenderness, and the patient did not have any motor or sensory disturbance. Routine laboratory tests revealed that blood chemistry data were within normal limits.

Panoramic radiography revealed a well-defined monolocular radiolucency over the anterior mandibular area, with a maximum diameter of about 3 cm, extending between the mesial aspects of the mandibular right permanent central incisor and the mandibular left primary canine, as well as from the alveolar crest down to about 2 cm above the inferior cortex of the mandible. Displacement of the mandibular left permanent central and lateral incisors was noted, but no root resorption was observed in the affected teeth. Furthermore, the mandibular left primary canine had been pushed downward to the inferior border of the mandible (Fig 2). Mandibular occlusal radiography revealed lingual expansion of the cortical bone (Fig 3).

The patient was subsequently referred to the Department of Oral and Maxillofacial Surgery for an incisional biopsy under local anesthesia, and the specimen was submitted to the Department of Oral Pathology for histopathologic examination. Microscopic examination revealed cellular vascular connective tissue with a proliferation of osteoclast-type giant cells with multiple nuclei. Granulation tissue rich in mononuclear inflammatory cells and hemosiderin pigments was also observed, consistent with CGCG (Fig 4).

The patient subsequently underwent curettage of the mass under general anesthesia. The wound was closed with interrupted sutures to prevent hematoma formation. The patient tolerated the procedure

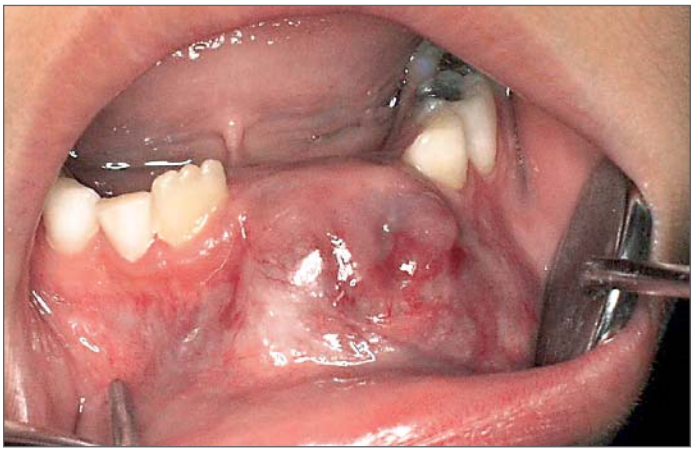

**Fig 1** A swelling with a smooth, bluish surface in the mandibular anterior region.

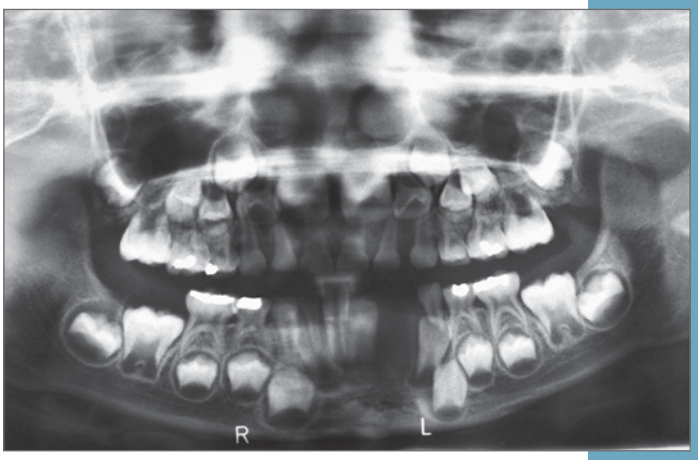


**Fig 2** Panoramic radiography reveals a well-defined monolocular radiolucency over the anterior mandibular area, extending between the mesial aspects of the right permanent central incisor and the left primary canine and from the alveolar crest down to about 2 cm above the inferior cortex of the mandible. Displacement of mandibular left permanent central and lateral incisors is noted.

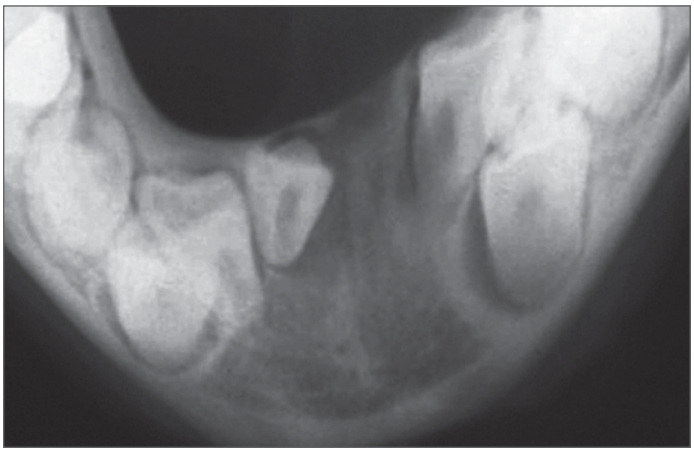

**Fig 3** Mandibular occlusal radiography reveals lingual expansion of the cortical bone.

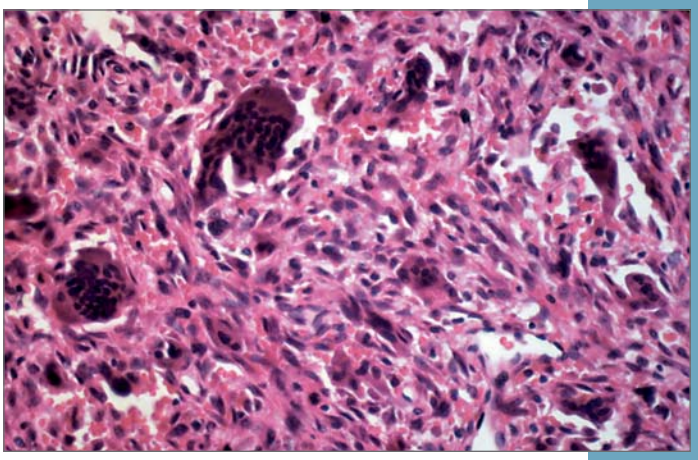

**Fig 4** Histologic examination reveals a cellular vascular connective tissue with a proliferation of osteoclast-type multinucleated giant cells and granulation tissue rich in mononuclear inflammatory cells and hemosiderin pigments (hematoxylin-eosin stain; original magnification × 40).

well. The postoperative course was uncomplicated, and the patient was discharged on postoperative day 3.

The histologic findings of the surgical specimen were similar to the previous incisional biopsy, and a diagnosis of CGCG was again rendered. No recurrence was noted 6 months postoperatively. Unfortunately, we are unable to report beyond 6 months because contact with the patient has been lost.

## DISCUSSION

CGCG primarily occurs in the jaw and facial bones, but it is also found in other areas of the body.[1] It is usually an asymptomatic lesion discovered during routine radiographic examinations, or when the painless expansion of the affected bone is noted by the patient or the parents, as in the present case.[1,3,4] CGCG lesions usually grow slowly; however, as in the present case, they occasionally present with a relatively high growth rate.[20]

Usually, as in this case, lesions of CGCG are painless and do not induce paresthesia.[1,20,27] However, it has been reported that 5% to 11% of these lesions are painful.[4,19,20] Although CGCG can be seen in every age group, it occurs more frequently in patients under the age of 30.[1,3,4,19–22] To the best of our knowledge, there have been only 4 well-documented cases of CGCG in patients under 10 years old without association with an inherited syndrome.[23–26] In children with mixed dentition, a pathologic lesion may be the underlying cause of regular tooth mobility and exfoliation of primary teeth and can easily be overlooked, especially in cases that are not accompanied by an obvious bony expansion. The clinician needs to be aware of any possible oral pathology when tooth mobility and displacement are present. In these circumstances, radiographic examination is of the utmost importance. As evidenced by this case, the possibility of CGCG should be considered in the differential diagnosis for children with maligned and mobile teeth.

While previous studies reported CGCG to predominantly affect females, with occurrence between 56% and 64%,[21,28–31] the present case describes CGCG in a young boy. However, our case is consistent with previous reports of CGCG presenting in the mandible more often than the maxilla and tending to occur in the anterior region of the molars and across the midline (although a recent review of 80 CGCG cases reported an equal predilection for the posterior mandible[29]).

Local trauma and intraosseous bleeding have been regarded as possible causes of CGCG lesions; however, a history of trauma before the development of the lesion was determined in only 1 of 32 CGCG cases in the report of Andersen et al.[21] In the current case, a traumatic event prior to the occurrence of the lesion could be identified. Other hypotheses of the development of CGCG include its association with other preexisting bony lesions, such as fibrous dysplasia, it being of neoplastic nature or representing an idiopathic reactive process.[32] The etiology of CGCG is therefore not well understood but, as mentioned above, genetic mutation is claimed to be involved.[10,11]

The radiographic appearance of CGCG is not pathognomonic.[3,20] Both unilocular and multilocular lesions are possible, but multilocular lesions show a slight predominance over the unilocular lesions.[4,20] Interestingly, a statistically significant correlation between the locularity of lesions and their size has been suggested, with small lesions usually appearing as unilocular radiolucent and large lesions usually appearing as multilocular.[1,20] The present case is consistent with this assumption.

Some reports have divided the lesions of CGCG into 2 categories[4,28,33,34]: *(1)* Nonaggressive lesions exhibit a slow growth rate, do not exhibit root perforation in teeth affected by the lesion or cortical perforation, and often show new bone formation; *(2)* aggressive lesions grow quickly and are associated with pain, cortical perforation, and root resorption. The present case, as demonstrated clinically and radiographically, suggested a nonaggressive lesion. The development of any additional swelling within 4 months of curettage should be a clinical alert for the risk of recurrence. The incidence of recurrence of a nonaggressive lesion is between 4% and 20%, whereas a local aggressive lesion has a higher recurrence rate.[1,28]

As stated in Table 1, histologically, a number of systemic or genetic conditions can present with lesions that are indistinguishable from CGCG lesions of the jaw. Therefore, differential diagnosis based on a clinical-radiological-biochemical-molecular approach is required to obtain a final diagnosis. This case, however, revealed no association with systemic and genetic diseases.

Simultaneous occurrence of CGCG with other lesions, such as odontogenic keratocyst[35] and central odontogenic fibroma,[36] has also been reported. Hybrid CGCG and central odontogenic fibroma of the jaw have been associated with an increased risk of recurrence following curettage.[36] It is recommended that a careful search for a possible lesion coexisting with CGCG always be performed.

Surgical curettage is usually employed for smaller lesions of CGCG of the jaws, as performed in our case. For aggressive lesions, en bloc surgical resection is occasionally used.[9] Recently, weekly intralesional corticosteroid injections,[37,38] daily subcutaneous administration of calcitonin,[39] and the use of interferon alpha[40] have also been suggested as possible treatments for large or multiple lesions to avoid the need for mutilating surgery in growing children. The main drawback to these nonsurgical approaches is the need for continual treatment over a prolonged time period. Radiation treatment is contraindicated because of the potential for malignant transformation.[37–39]

## REFERENCES

1. Potter BJ, Tiner BD. Central giant cell granuloma. Report of a case. Oral Surg Oral Med Oral Pathol 1993;75:286–289.
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;6:159–175.
3. Shafer WG, Hine MK, Levy BM. A Textbook of Oral Pathology, ed 4. Philadelphia: Saunders, 1983: 146–149.
4. Neville BW, Damm DD, Allen CM, Bouquot JE. Oral and Maxillofacial Pathology, ed 4. Philadelphia: Saunders, 2002:705–740.
5. Cawson BRA, Binnie WH, Speight PM, Barrett AW, Wright JM. Lucas's Pathology of Tumors of the Oral Tissues, ed 5. London: Churchill Livingstone, 1998:107–110.
6. 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.
7. Al Sheddi M, Mosadomi H, Al Dayel F. Central giant cell granuloma of the jaws and giant cell tumor of long bones. A clinicopathologic, cytometric, and immunohistochemical comparative study. Oral Surg Oral Med Oral Pathol 2004;98:195–196.
8. Wold LE, Dobyns JH, Swee RG, Dahlin DC. Giant cell reaction (giant cell reparative granuloma) of the small bones of the hands and feet. Am J Surg Pathol 1986;10:491-496.
9. Chuong R, Kaban LB. Diagnosis and treatment of jaw tumors in children. J Oral Maxillofac Surg 1985; 43:323–332.
10. Buresh CJ, Seemayer TA, Nelson M, Neff JR, Dorfman HD, Bridge J. t(X;4)(q22;q31.3) in giant cell reparative granuloma. Cancer Genet Cytogenet 1999; 115:80-81.
11. Carinci F, Piattelli A, Martinelli M, et al. Genetic profiling of central giant cell granuloma of the jaws. J Craniofac Surg 2005;16:399–407.
12. Kauzman A, Li SQ, Bradley G, Bell RS, Wunder JS, Kandel R. Central giant cell granuloma of the jaws: Assessment of cell cycle proteins. J Oral Pathol Med 2004;33:170–176.
13. Liu B, Yu SF, Li TJ. Multinucleated giant cells in various forms of giant cell containing lesions of the jaws express features of osteoclasts. J Oral Pathol Med 2003;32:367–375.
14. Tobon-Arroyave SI, Franco-Gonzalez LM, Isaza-Guzman DM, et al. Immunohistochemical expression of RANK, $GR_a$ and CTR in central giant cell granuloma of the jaws. Oral Oncol 2005;41:480–488.
15. Suarez-Cunqueiro MM, Schoen R, Kersten A, Klisch J, Schmelzeisen R. Brown tumor of the mandible as first manifestation of atypical parathyroid adenoma. J Oral Maxillofac Surg 2004;62:1024–1028.
16. Ueki Y, Tiziani V, Santanna C, et al. Mutations in the gene encoding c-Abl-binding protein SH3BP2 cause cherubism. Nat Genet 2001;28:125–126.
17. Gutmann DHJ. Neurofibromin in the brain. J Child Neurol 2002;17:592–601.
18. Tartaglia M, Kalidas K, Shaw A, et al. PTPN11 mutations in Noonan syndrome: Molecular spectrum, genotype-phenotype correlation, and phenotypic heterogeneity. Am J Hum Genet 2002;70:1555–1563.
19. Spraggs PD, Roth J, Young-Ramsaran J, Goodwin WJ. Giant cell reparative granuloma of the maxilla. Ear Nose Throat J 1997;76:445–446, 449.
20. Goaz PW, White SC. Oral Radiology, ed 2. St Louis: Mosby, 1987:608–611.
21. Andersen L, Fejerskov O, Philipsen HP. Oral giant cell granulomas. A clinical and histological study of 129 new cases. Acta Pathol Microbiol Scand [A] 1973; 81:606–616.
22. Regezi JA, Sciubba JJ. Oral Pathology: Clinical pathologic correlations, ed 3. Philadelphia: Saunders, 1993:368–370.

23. Cannistra C, Fadda T, Guerrieri L, Vero S, Della Rocca C, Iannetti G. Central giant cell granuloma of the palate: Unusual localisation in a five-year-old child. Bull Group Int Rech Sci Stomatol Odontol 1999;41: 112–114.
24. Allen DT, Sheats RD. A central giant cell granuloma in a patient seeking orthodontic treatment. J Am Dent Assoc 2001;132:1255–1260.
25. Ustundag E, Iseri M, Keskin G, Muezzinoglu B. Central giant cell granuloma. Int J Pediatr Otorhinolaryngol 2002;65:143–146.
26. Loyola AM, Fernandes AV, Magalhaes AO, Moreira MR. The central giant cell granuloma in childhood: Clinical case report. J Clin Pediatr Dent 2005;29: 259–262.
27. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 20-1993. A 23-year-old woman with a rapidly enlarging intraoral mass after a tooth extraction. N Engl J Med 1993;328:1478–1483.
28. Whitaker SB, Waldron CA. Central giant cell lesions of the jaws. A clinical, radiologic, and histopathologic study. Oral Surg Oral Med Oral Pathol 1993;75: 199–208.
29. Kaffe I, Ardekian L, Taicher S, Littner MM, Buchner A. Radiologic features of central giant cell granuloma of the jaws. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996;81:720–726.
30. Eisenbud L, Stern 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;46:376–384.
31. 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;65:255–261.
32. Farzaneh AH, Pardis PM. Central giant cell granuloma and fibrous dysplasia occurring in the same jaw. Med Oral Patol Oral Cir Bucal 2005;10(suppl 2): E130–132.
33. Chuong R, Kaban LB, Kozakewich H, Perez-Atayde A. Central giant cell lesions of the jaws: A clinicopathologic study. J Oral Maxillofac Surg 1986;44: 708–713.
34. 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;64:44–49.
35. Yoon JH, Kim SG, Lee SH, Kim J. Simultaneous occurrence of an odontogenic keratocyst and giant cell granuloma–like lesion in the mandible. Int J Oral Maxillofac Surg 2004;33:615–617.
36. Mosqueda Taylor A, Bermudez Flores V, Diaz Franco MA. Combined central odontogenic fibroma and giant cell granuloma–like lesion of the mandible: Report of a case and review of the literature. J Oral Maxillofac Surg 1999;57:1258–1262.
37. Terry BC, Jacoway JR. Central giant cell granulomas: An alternative to surgery. Oral Maxillofac Surg Clin N Am 1994;6:579–600.
38. Kurtz M, Mesa M, Alberto P. Treatment of a central giant cell lesion of the mandible with intralesional glucocorticosteroids. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001;91:636–637.
39. Harris M. Central giant cell granulomas of the jaws regress with calcitonin therapy. Br J Oral Maxillofac Surg 1993;31:89–94.
40. Kaban LB, Mulliken JB, Ezekowitz RA, Ebb D, Smith PS, Folkman J. Antiangiogenic therapy of a recurrent giant cell tumor of the mandible with interferon alfa-2a. Pediatr 1999;103:1145–1149.