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A 10-year review of the occurrence and treatment of central giant cell granulomas, in a District General Hospital

S. L. Farrier[1], J. N. Farrier[2], M. K. Smart[3], E. S. Nash[3]

[1]*Adult Dental Health, University of Wales Dental Hospital, Cardiff;* [2]*Oral and Maxillofacial Surgery, Morriston Hospital, Swansea;* [3]*Oral Surgery, Prince Charles Hospital, Merthyr Tydfil, UK*

BACKGROUND: There is considerable variation in the clinical presentation, behaviour and radiological appearance of central giant cell granulomas (CGCGs), for which multiple treatment modalities have been suggested.
METHOD: A 10-year retrospective review of the clinical presentation, radiological features and treatment received was undertaken.
RESULTS: The cohort of patients included six males and three females, with an age range of 7–61 years. Six lesions were in the mandible and three in the maxilla. Eight lesions presented with swelling, three in relation to teeth. One case was an incidental finding. Six cases were confined within the cortical plates, one involved soft tissue. Radiological presentation was diverse, but within the existing confines of CGCGs. With one exception, primary treatment was surgical resection with excisional curettage of the remaining bone; to date, none have recurred.
CONCLUSION: Diagnosis relies on correct interpretation of clinical, radiographical and histopathological data. Alternative treatments are worthy of consideration, although surgical excision remains the treatment of choice.
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Keywords: calcitonin; corticosteroid; diagnosis; giant cell; granuloma; oral; outcome; treatment

Introduction

Giant cell lesions affecting the jaws are usually granulomatous in nature and their aetiology remains unknown (1). Giant cell lesions account for approximately 7% of all benign tumours of the jaws (2).

The histological features of a central giant cell granuloma (CGCG) are defined by the WHO (3), as intraosseous lesions consisting of cellular fibrous tissue that contains multiple foci of haemorrhage, aggregations of multinucleated giant cells and, occasionally trabeculae of woven bone (Fig. 1).

There is considerable variation in the clinical behaviour of CGCG. They may present with a rapid onset of symptoms including pain, parasthesia, root resorption and tooth displacement, with expansion and or local destruction of surrounding bone, causing facial asymmetry; or simply discovered incidentally on routine examination as an asymptomatic lesion. Complete loss of sensation of the affected region is not usually a presenting symptom and the overlying mucosa normally has a healthy appearance (4, 5). CGCG usually occur in patients <30 years and are more common in females (2:1). They are more prevalent in the mandible, particularly the anterior portion crossing the midline, than the maxilla (3:1; 2, 4, 6–10). The most common sites, other than the facial bones, for CGCG, are the small bones of the hands and feet (11).

Radiologically, the lesion appears as a radiolucent area and may contain faint trabeculation; it can be unilocular or multilocular with either well-defined or ill-defined margins (Fig. 1). Varying degrees of expansion are seen, allowing for thinning of cortical plates, with possible perforation to involve the surrounding soft tissue (Figs. 2 and 3). Root resorption and tooth displacement may also be evident (Fig. 4; 8, 9, 12). The radiological and histological appearances of CGCG are not pathognomonic, and therefore further relevant clinical investigations must be performed and interpreted to confirm the diagnosis; for example, blood tests, such as calcium, phosphate, parathyroid hormone and alkaline phosphate levels (13, 14).

Some CGCG of the jaws, despite a typical histological, radiological and clinical appearance, show an aggressive behaviour and a tendency to recur (2, 5, 9, 10, 15). Ficarra et al. (15) considered that these lesions should be defined as aggressive CGCG of the jaws and their recurrence following curettage has been reported (16, 17).

The accepted form of treatment of CGCG is surgical excision, varying from curettage to *en bloc*

Correspondence: S. L. Farrier, Lecturer, Adult Dental Health, University of Wales Dental Hospital, Heath Park, Cardiff CF14 4XN, UK. E-mail: farriersl@cardiff.ac.uk
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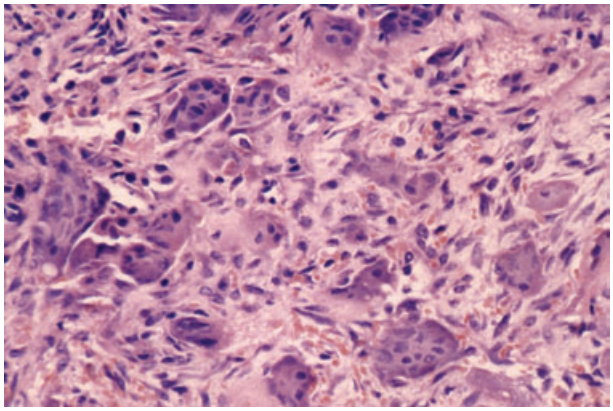

Figure 1 Histological appearance of a central giant cell granuloma (CGCG).

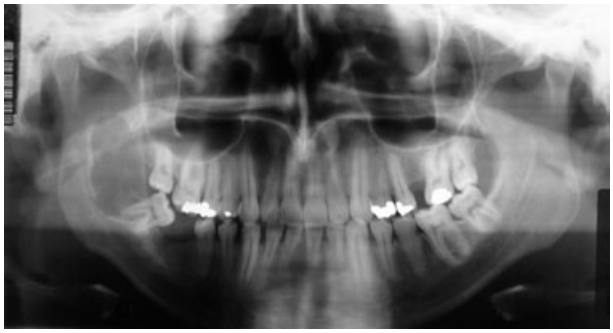

Figure 2 Radiological appearance of a central giant cell granuloma (CGCG).

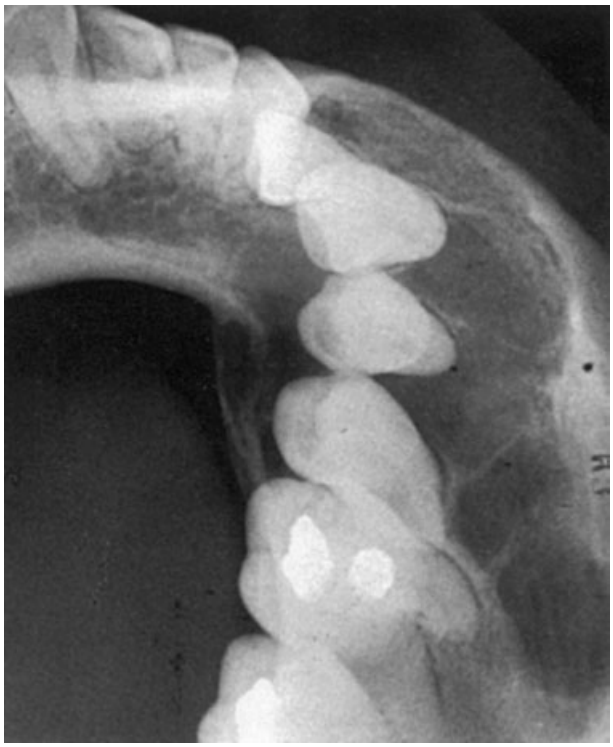

Figure 3 Resulting expansion of cortical plates due to a central giant cell granuloma (CGCG).

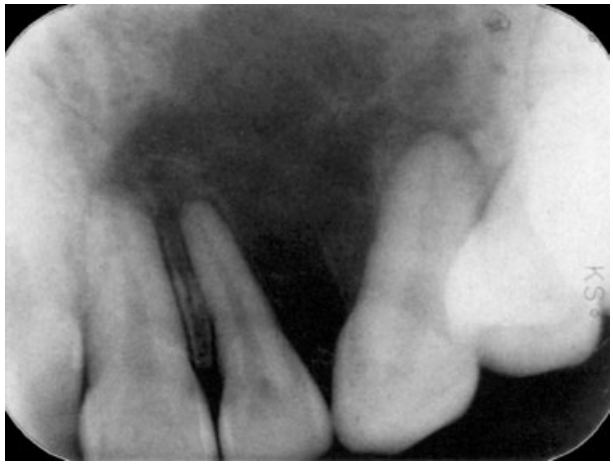

Figure 4 Central giant cell granuloma (CGCG) causing tooth displacement.

resection (18, 19); when curettage is the treatment of choice, cryotherapy may be used as an adjunct to cauterise the remaining bone (20). More extensive surgery may involve peripheral ostectomy and bone replacement with grafts (21–23). Non-surgical methods of treatment that have been advocated are systemic or involve using intralesional calcitonin, intralesional steroids, antiangiogenic therapy and radiotherapy (18, 24–31). Advantages of non-surgical treatments include a reduction in the need for extensive surgery and thus possible consequential deformity. Localized intralesional treatments may be advantageous compared with potentially painful radiotherapy (26, 28). Calcitonin therapy and intralesional corticosteroid injections have been advocated for these reasons (26, 31, 32).

The purpose of this study was to report and evaluate our experiences of presentation, treatment and outcome of CGCG with reference to information currently available.

Method

A retrospective analysis was conducted of patients diagnosed with CGCG who were treated between 1992 and 2003 in the Oral and Maxillofacial Surgery Departments within the North Glamorgan NHS Trust.

Data were analysed with reference to age, gender, anatomical location, presentation, radiological features, method of treatment, complications of treatment, length of review following treatment and incidence of recurrence. All cases were investigated radiographically using orthopantonograms as a minimum standard.

The serum calcium, phosphorus and alkaline phosphatase were measured in all cases to exclude hyperparathyroidism. The aim of treatment was to eradicate the lesion, with minimal facial deformity, with no loss of function or sensation, thus eliminating the need for reconstructive surgery.

Results

During the period of this study nine patients with CGCG were treated with an age range of 7–61 years. Table 1 shows the gender, age and anatomical distribution for the CGCGs. Of the mandibular lesions, four were on the left and two on the right. In the maxilla one was found on the left and two on the right. None of the lesions was found to cross the midline.

Eight cases of CGCG were confined to one bone; however, one maxillary lesion extended into the floor of orbit and medial wall of maxillary sinus. Table 2 represents the various clinical presentations. All but one patient presented with asymmetrical swelling of the affected area; three of these had evident swelling extraorally. Six of the nine CGCGs were confined within the cortical plates. Two had arisen within the sockets of an extracted tooth and one case presented as a non-healing periapical infection. Only one lesion, involving the maxillary alveolar ridge, also involved surrounding soft tissue.

Displacement of teeth was only observed in one patient, and no cases of root resorption were seen. One mandibular case presented with pain, and a further case, reported altered sensation of the lip.

The radiographic presentation of CGCG is inconsistent, as shown in Table 3. All the identified lesions had a radiolucent cystic appearance, with varying degrees of margin definition. Six of the nine CGCG had well-defined margins and four had evidence of both a unilocular and multilocular areas.

The definitive treatment for all patients was surgical resection with excisional curettage of the remaining bone, preserving as much compact bone and periosteum as possible. However, in view of Harris (26), one patient was initially treated with a non-surgical approach using intralesional calcitonin, to reduce the size of the lesion, involving the maxilla, the orbit and the maxillary sinus. About 0.5 mg (100 IU) human calcitonin was administered subcutaneously into the predominantly maxillary lesion daily. The lesion showed no signs of regression following 3 months of treatment and thus a complete surgical excision was performed including extraction of teeth 1–6 in this upper right maxillary quadrant.

Following the surgical excision of all nine CGCG, only one patient has any adverse effects: residual parasthesia of the once affected area. Eight patients presented when requested for review appointments and discharged when appropriate. One patient failed to attend further follow-up appointments and thus was only monitored post-operatively for 4 months (Table 4). No patients have shown any signs of recurrence since treatment or during their review period.

Table 1 The gender, age and anatomical distribution of central giant cell granuloma (CGCG)

	Number of cases						
			Mandible		*Maxilla*		
Age (years)	*Male*	*Female*	*Left*	*Right*	*Left*	*Right*	*Total (%)*
0–9	2		1		1		22.2
10–19	2		1			1	22.2
20–29	1	2	1	1		1	33.3
30–39							0
40–49		1		1			11.1
50–59							0
60–69	1		1				11.1

Mean age: 27 years.

Table 2 Clinical presentation of central giant cell granuloma (CGCG)

Clinical presentation	*Cases (%)*
Asymmetry	33.3
Intra-oral swelling	88.9
Pain or parasthesia	22.2
Displaced tooth	11.1
Associated dental pathology	33.3
Incidental find	11.1

Table 3 Radiological presentation of central giant cell granuloma (CGCG)

Radiological presentation	*Cases (%)*
Expansion of cortex	88.9
Radiolucency	100
Unilocular	55.6
Multilocular	77.8
Well-defined margins	66.7
Ill-defined margins	33.3
Trabeculation	22.2

Table 4 Post-operative follow up

Length of review before discharge (months)	*Patients (%)*	*Patients who failed to return (%)*
< 6	11.1	11.1
6–12	11.1	
13–18	22.2	
19–24	44.4	

Discussion

The CGCGs may occur at any age, but are more common in those under 30 years of age. Females are affected more frequently than males, with the mandible a more common site than the maxilla (2, 4, 6). In this study, 77.8% of patients were younger than 30 years of age, which is in accordance with previous published reports (2, 7, 8); however, we found a male to female ratio of 2:1. This may be due to the small case numbers involved, although some authors have reported an equal M:F ratio (18).

Three cases were found in relation to the apical area of teeth. Two of these presented with swelling of an extraction socket and it was not clear from the notes whether these lesions were present prior to these dental extractions. The third case initially presented as a non-healing periapical infection. These periapically located

CGCGs support studies that discuss the possible misdiagnosis of such lesions when related to teeth with necrotic pulps (33, 34). Another lesion presented with displacement of the upper left maxillary incisors. Following a referral to an orthodontist and subsequent radiographic examination a CGCG was diagnosed; it had been assumed initially this patient had a simple malocclusion or periodontal condition. Incidental findings of CGCG and those presenting in areas more commonly associated with other dental pathology, support the debate for thorough investigation; this includes radiographic investigation, especially with changing symptoms, to form part of continuous and thorough patient care (35).

In the present study, the radiographic features were all typical of the various reported appearances of CGCG. However, due to the diversity of the radiographic presentation, it is well recognized that accurate diagnosis lies on correct interpretation of clinical, radiographical and histopathological data available for each patient. Amalgamating this information enables correct diagnosis from other lesions such as hyperparathyroidism, ameloblastoma and a giant cell tumour of long bones (36–38).

The CGCG are expansive in their growth, but do not invade or grow around nerve trunks (20). One patient with a mandibular CGCG, presented with altered sensation of the lower lip; this is best explained by compression of the inferior alveolar nerve by the growing lesion. One patient had residual parathesia, following surgery, in the right infraorbital region, which is explained by the nature of the radical excision necessary to excise the lesion which involved removing this nerve.

Treatment and complete resolution of CGCG by surgical excision is strongly supported by other authors (7, 18–20). The extent of surgery is related to the size and position of the lesion, ranging from simple excision and curettage to *en bloc* resection and reconstruction. All patients were treated by surgical excision and curettage of remaining bone.

Alternative treatments are now advocated and available for CGCGs and their benefits are worthy of consideration. Harris supports the use of calcitonin therapy (26). Calcitonin is antagonistic to the effects of parathyroid hormone, and its action is mainly within bone by inhibiting osteoclastic bone resorption thus slowing down the release of calcium and phosphate ions from skeletal tissues. Calcitonin has some renal effects, enhancing the excretion of phosphate, calcium and sodium, but these are poorly understood. It also has inherent analgesic properties, although these are of little significance when dealing with CGCG (24, 26, 32, 39). Side-effects to calcitonin therapy include, flushing and nausea, both of which are dose-dependant. Osteoclasts escape the inhibitory effects of calcitonin following continued exposure, and intralesional administration, can be associated with discomfort, which may be intolerable to some patients, especially children (27, 40). Pogrel (41) published the results of 10 patients with CGCG treated with calcitonin therapy. Nine patients showed resolution of the CGCG following 19–21 months of subcutaneous calcitonin injections, one patient ultimately underwent surgery following poor compliance with intranasal calcitonin therapy. The long treatment time is discussed as a disadvantage to this method compared with surgery, and it is advised clacitonin treatment is reserved for recurrent, multiple or aggressive lesions (41).

Successful non-surgical treatment with intralesional corticosteroid injections has been advocated in a variety of cases (18, 24, 30, 31, 42, 43). Steroids, such as triamcinolone acetonide, inhibit osteoclasts in marrow cultures and in conditions of resorption of bone by increased apoptosis (31). Carlos and Sedano (24) used 10 mg/ml of triamcinolone aqueous suspension, SQIBB with either lidocaine 2% or bupivicaine on three males aged 31, 34 and 6 years and on a 21-year-old female. The average dose was 6 ml (30 mg of triamcinolone) for adults and 5 ml (25 mg of triamcinolone) for children; improvement and eventual resolution was seen in all cases (24). Although reducing the inflammatory response they are contraindicated in some medical conditions (18, 39). Kurtz et al. (25) also described a case successfully treated with intralesional glucocorticoids. Advantages of any non-surgical treatment such as intralesional corticosteroid injections are again evident, preventing disfiguring surgery and the potential loss of teeth or tooth germs in children (18, 42, 43). Disadvantages with intralesional steroid treatment are associated with the long treatment time, patient compliance and any systemic effects associated with the steroids used (18, 43). The vast majority of cases subjected to initial intralesional corticosteroid treatment for CGCG involve children, where surgery is potentially a more disfiguring and complicated option (30, 42).

The reasoning behind treatment with antiangiogenic agents is due to CGCG being a rapidly increasing vascular lesion, and thus can be treated as a haemangioma. Antiangiogenic treatment is based on its interaction with the fibrinolytic cascade (29), but little research into this treatment has been documented.

Calcitonin therapy was used as first-line treatment in one patient due to the extent of the lesion. The aim was to reduce the size of the lesion, if not completely resolve it, thus eliminating or restricting extensive disfiguring surgery. However, the lesion failed to reduce in size after 3 months of continual calcitonin treatment and thus this method of initial or absolute treatment was not applied to any future cases.

In the light of our limited experience in using calcitonin to treat CGCGs, we would propose that this, and other such non-surgical treatments, may be more successful and appropriate if restricted to smaller, less extensive lesions.

Although there is a tendency for some CGCGs to recur, successful surgical excision reduces this to an insignificant number (9). Once healing of the bone was evident, following ideal treatment, the post-operative review period was terminated, which is the rationale in the varying follow-up periods. It has also been reported that recurrence is most frequent when the primary lesion

perforates the cortical plate to involve the surrounding soft tissue (30, 44). The cases in our study showed no sign of recurrence, despite three cases not being totally confined within the cortical plates.

In view of the current literature, the CGCGs diagnosed were within given parameters of typical presentation, although more commonly occurring pathologies may confused the diagnosis initially. There is a current trend to move away from surgical treatment, maybe due to its morbidity, but as highlighted previously such cases treated successfully are still relatively few in number. Our experience indicates that a correct diagnosis and complete surgical excision with curettage of any remaining bone, proves to be effective in complete elimination of the lesion.

References

1. Cawson RA, Odell EW. *Essentials of oral pathology and oral medicine*, 6th edn. Edinburgh: Churchill Livingstone, 1998.
2. Austin LT, Dahlin DC, Royer RQ. Giant cell reparative granuloma and related conditions affecting the jaw bones. *Oral Surg Oral Med Oral Pathol* 1959; **12**: 1285–95.
3. Kramer IRH, Pindborg JJ, Shear M. *Histological typing of odontogenic tumours*, 2nd edn. Berlin, Germany: Springer-Verlag, 1991; 31.
4. Mohammed TL, Brummett DP, Hahn FJ, Sharma P. Intracranial giant cell reparative granuloma arising from the temporal lobe area. *AJNR Am J Neuroradiol* 2001; **22**: 873–5.
5. Chuong R, Kaban LB, Kozakewich H, et al. Central giant cell lesions of the jaws: a clinicopathologic study. *J Oral Maxillofac Surg* 1986; **44**: 708.
6. Cohen MA, Hertzanu Y. Radiological features, including those seen with computed tomography of central giant cell granuloma of the jaws. *Oral Surg Oral Med Oral Pathol* 1998; **65**: 255–61.
7. Sidhu MS, Parkash H, Sidhu SS. Central giant cell granulomas of jaws: review of 19 cases. *Br J Oral Maxillofac Surg* 1995; **33**: 43.
8. Kaffe I, Ardekian L, Taicher S, et al. Radiological features of central giant cell granuloma of the jaws. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996; **81**: 720.
9. Heithersay GS, Cohn SA, Parkins DJ. Central giant cell granulomas. *Aust Endod J* 2002; **28**: 18–23.
10. Whitaker SB, Waldron CA. Central giant cell lesions of the jaws. *Oral Surg Oral Med Oral Pathol* 1993; **75**: 199.
11. Yamaguchi T, Dorfman HD. Giant cell reparative granuloma: a comparative clinopathologic study of lesions in gnathic and extragnathic sites. *Int J Surg Pathol* 2001; **9**: 189–200.
12. Murphey MD, Nomikos GC, Flemming DJ, Gannon FH, Temple HT, Kransdorf MJ. From the archives of AFIP. Imaging of giant cell tumour and giant cell reparative granuloma of bone: radiologic-pathologic correlation. *Radiographics* 2001; **21**: 1283–309.
13. Stafne EC, Gibilisco JA. *Oral roentgenographic diagnosis*, 4th edn. Philadelphia, PA, USA: W. B. Saunders, 1975; 200.
14. Shafer WG, Hine MK, Levy BM. *A textbook of oral pathology*, 4th edn. Philadelphia, PA, USA: W. B. Saunders, 1983; 146.
15. 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.
16. Andersen L, Fejerskov O, Phillipsen HP. Oral giant cell granuomas: a clinical and histological study of 129 new cases. *Acta Pathol Microbiol Scand* 1973; **81**: 606.
17. Auclair PL, Cuenin P, Kratochvil FJ, et al. A clinical and histomorphologic comparison of the central giant cell granuloma and the giant cell tumor. *Oral Surg* 1988; **66**: 197.
18. Kermer C, Millesi W, Watzke IM. Local injection of corticosteroids for central giant cell granuloma: a case report. *Int J Oral Maxillofac Surg* 1994; **23**: 366.
19. Bateineh AB, Al-Khateeb T, Rawashdeh MA. The surgical treatment of central giant cell granulomas of the mandible. *J Oral Maxillofac Surg* 2002; **60**: 756–61.
20. Webb DJ, Brockbank J. Combined curettage and cryosurgical treatment for aggressive 'giant cell lesion' of the mandible. *Int J Oral Maxillofac Surg* 1986; **5**: 780.
21. Eisenbud L, Stern M, Rothberg M, et al. Central giant cell granuloma of the jaws: experiences in the management of thirty-seven cases. *J Oral Maxillofac Surg* 1988; **46**: 376–84.
22. Wise AJ, Bridbord JW. Giant cell granuloma of the facial bones. *Ann Plast Surg* 1993; **30**: 564–8.
23. Becelli R, Cerulli G, Gasparini G. Surgical and implantation reconstruction in a patient with giant-cell central reparative granuloma. *J Craniofac Surg* 1998; **9**: 45.
24. Carlos R, Sedano HO. Intralesional corticosteroids as an alternative treatment for central giant cell granulomas. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002; **93**: 161–6.
25. Kurtz M, Mesa M, Alberto P. Treatment of a central giant cell lesion of the mandible with intralesional gluccocorticoids. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001; **91**: 636–7.
26. Harris M. Central giant cell granulomas of the jaws regress with calcitonin therapy. *Br J Oral Maxillofac Surg* 1993; **31**: 89–94.
27. de Long J, Rosenberg AJ, van den Akker HP, Koole R, Wirds JJ, van den Berg H. Treatment of central giant cell granuloma of the jaw with calcitonin. *Int J Oral Maxillofac Surg* 1999; **28**: 372–6.
28. O'Regan EM, Gibb DH, Odell EW. Rapid growth of giant cell granuloma in pregnancy treated with calcitonin. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001; **92**: 532–8.
29. Collins A. Experience with anti-angiogenic therapy of giant cell granuloma of the facial bones. *Ann R Australas Coll Dent Surg* 2000; **15**: 170–5.
30. Adornato MC, Paticoff KA. Intralesional corticosteroid injection for treatment of central giant cell granuloma. *J Am Dent Assoc* 2001; **142**: 186–90.
31. Abdo EN, Alves LC, Rodrigues AS, et al. Treatment of a central giant cell granuloma with intralesional corticosteroid. *J Oral Maxillofac Surg* 2005; **43**: 74–6.
32. Kodaei I, Rowley H, Farrell M, Collins CM, Vianni L, Rawluk D. An unusual cause of tinnitus. *Ir Med J* 2001; **94**: 312–3.
33. Seldon HS. Central giant cell granuloma a troublesome lesion. *J Endod* 2000; **26**: 371–3.
34. Dahlkemper P, Wolocott JF, Pringle GA, Hicks ML. Periapical central giant cell granuloma: a potential endodontic misdiagnosis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000; **90**: 739–45.

35. Allen DT, Sheats RD. A central giant cell granuloma in a patient seeking orthodontic treatment. *J Am Dent Assoc* 2001; **132**: 1255–60.
36. Thoma KH. Cherubism and other intraosseous giant cell lesions. *Oral Surg* 1962; **15**: 1–4.
37. Smith GA, Ward PH. Giant cell lesions of the facial skeleton. *Arch Otolaryngol* 1978; **104**: 186–90.
38. Hamli WB, Lund PC. 'Giant cell tumours' of the mandible and facial bones. *Arch Otolaryngol* 1967; **86**: 658–865.
39. Rajeevan NS, Soumithran CS. Intralesional corticosteroid injection for central giant cell granuloma, a case report. *Int J Oral Maxillofac Surg* 1998; **27**: 303.
40. Berne RM, Levy MN. *Principles of physiology*, 1st edn. St. Louis, MO, USA: Mosby Year Book Inc., 1990; 573.
41. Pogrel MA. Calcitonin therapy for central giant cell granuloma, including commentary by Kaban LB and Dodson TB. *Int J Oral Maxillofac Surg* 2003; **61**: 649–54.
42. Sezer B, Koyuncu B, Gomel M, Gunbay T. Intralesional corticosteroid injection for central giant cell granuloma: a case report and review of the literature. *Turk J Pediatr* 2005; **47**: 75–81.
43. Khafif A, Krempl G, Medina JE. Treatment of giant cell granuloma of the maxilla with intralesional injection of steroids. *Head Neck* 2000; **22**: 822–5.
44. Minic A, Stajcic Z. Prognostic significance of cortical perforation in the recurrence of central giant cell granulomas of the jaws. *J Craniomaxillofac Surg* 1996; **24**: 104.