CASE REPORT

Central giant cell granuloma: a case report

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SUMMARY

Central giant cell granuloma (CGCG) is a relatively uncommon benign bony lesion of a variably aggressive nature. Thought to represent a reparative response to intrabony haemorrhage and inflammation, CGCG was once regarded as a reactive lesion. It is actually an asymptomatic lesion which becomes evident during routine radiographic examination or as a result of painless but visible expansion of the affected jaw. This paper presents the case of a 4-year-old boy with CGCG in the right mandibular region.

BACKGROUND

Diagnosis of many lesions of the oral cavity is challenging to most clinicians because of their uncommon prevalence. A number of cystic, metabolic, osteodystrophic, microbial, tumour and tumour like lesions of the oral cavity present with characteristic giant cell lesions, which makes their diagnosis and study simpler. 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. The condition was first identified in 1953 by Jaffe, who initially termed this lesion as a central giant cell reparative granuloma, but nowadays the reparative word has been deleted from that term. The WHO has defined it as 'an intraosseous lesion consisting of cellular fibrous tissue that contains multiple foci of haemorrhage, aggregations of multinucleated giant cells and occasionally trabeculae of woven bone'. In contrast to the giant cell tumour of long bone, CGCG of the jaw tends to involve a younger age group, with a distinct predilection for the female gender, responsible for 65% of the cases. Giant cell granuloma is often confused with giant cell tumour. However, a giant cell tumour can be distinguished based on the fact that it occurs commonly between the ages of 25 and 40 years, usually involving the long bones and is more aggressive in nature, with frequent recurrence after curettage. Herein, we report a case of a CGCG in a child who was managed by a conservative surgical approach.

CASE PRESENTATION

A 4-year-old boy reported to our outpatient department with swelling over the right lower jaw region since 6 months. The swelling had remained asymptomatic while gradually enlarging to cause the facial disfigurement evident at the time of presentation. No history of trauma was elicited nor any systemic or local infections. The prenatal history was unremarkable and delivery was at full term and normal. There was no history of similar disease in any of the siblings or the parents of the affected

Figure 1 The patient showing facial asymmetry due to a poorly defined swelling over the right angle of the mandible.

child. A physical examination revealed a moderately built and nourished boy with no known systemic disorder. A facial asymmetry due to a poorly defined swelling in the right angle of the mandible measuring 2×3 cm was noted (figure 1). The overlying skin appeared normal, while the swelling itself was bony hard and non-tender to palpation. Intraoral examination showed a diffuse swelling in the alveolar portion of 85 region with slight obliteration of buccal vestibule in the same region (figure 2). Tooth displacement and mobility were

Figure 2 Intraoral examination showed a diffuse swelling in the alveolar portion of 85 region with slight obliteration of buccal vestibule in the same region.

To cite: Mohan RPS, Verma S, Agarwal N, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-009903

not evident in the same quadrant. The overlying mucosa appeared normal. The swelling was non-tender and bony hard on palpation with some areas of fluctuance in the buccal aspect. The adjacent dentition and the oral mucosa did not reveal any abnormality. A tooth vitality test revealed normal pulpal response of the teeth in the same quadrant. A provisional diagnosis of dentigerous cyst was made with the differential diagnosis of ameloblastoma, CGCG, odontogenic myxoma and fibrous dysplasia. Later on the patient was subjected to radiographic examination in the form of orthopantomogram which revealed a solitary well-defined multilocular radiolucent lesion in the region of right mandibular angle and ramus (figure 3). The lesion measured 2×4 cm extending to involve the right coronoid with distinct and sclerotic borders except in the region of the superior aspect. The histopathological examination showed a highly vascularised fibrous stroma with several multinucleated giant cells with 20–30 nuclei, the nuclei mainly confined to the centre of the cells leaving a clear zone of cytoplasm at the periphery (figure 4). Randomly dispersed spindle-shaped fibroblasts were also noted and a conclusive diagnosis of a CGCG was made.

Overall, clinical, radiographic and histological features were suggestive of CGCG.

INVESTIGATIONS

Radiographs and histopathological examination.

DIFFERENTIAL DIAGNOSIS

- ▶ Ameloblastoma and CGCG may appear unilocular or multilocular with a honeycomb or soap bubble appearance.
- ▶ Odontogenic myxoma may appear as a poorly defined or well-circumscribed radiolucent defect, which may be unilocular or multilocular with a tennis racquet appearance.
- ▶ Serum calcium, phosphorous and alkaline phosphatase levels were found to be normal thereby excluding brown tumour of hyperparathyroidism.
- ▶ Aneurysmal bone cyst.
- ▶ Simple bone cyst.
- ▶ Cherubism.

TREATMENT

In view of the young age of the boy, a conservative surgery was performed under general anaesthesia to spare the mandible with an aggressive curettage and marginal resection/peripheral osteotomy of the lesion. The unerupted permanent right mandibular first molar was extracted during the procedure.

Figure 3 Panoramic radiograph showing multilocular radiolucent lesion with faint curved septa in the right ramus-body of mandible.

Figure 4 Histopathological examination revealed numerous multinucleated giant cells which were distributed in a stroma that was highly cellular comprising both spindle-shaped and round cells and were found mostly in the area of haemorrhages.

OUTCOME AND FOLLOW-UP

The prognosis of present case was fair.

DISCUSSION

CGCG occurs predominantly in the jaw and facial bones, but it also appears in other parts of the body. 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 parents as in this case CGCG lesions usually grow slowly, but they occasionally grow fast also.^{1–3} However, it is reported that 5–11% of the lesions are painful. Although it is noted in every age group it is more common in patients below 30 years of age.^{4–7} It occurs more commonly in the mandible than in the maxilla. Women are affected more frequently than men (ratio 2:1). Most mandibular lesion occurs anterior to first molars and often cross the midline. CGCG also occurs in other bones of the facial skeleton and cranial vault.⁵ Thought to represent a reparative response to intrabony haemorrhage and inflammation, CGCG was once regarded as a reactive lesion. However, because of its unpredictable and occasionally aggressive behaviour, and because of its possible relationship to the giant cell tumour of long bones, CGCG is best classified as a benign neoplasm. The histogenesis of CGCG of the jawbones remains controversial, as speculations are still debated regarding the possibility that it represents a reactive, an inflammatory, an infective or a neoplastic process. Another theory is the vascular hypothesis that suggests that CGCG belongs to the spectrum of mesenchymal proliferative vascular primary jaw lesions. Angiogenesis is a phenomenon modulated by several cytokines and growth factors. Vascular endothelial growth factor and basic fibroblast growth factor are the most potent inducers of angiogenesis and have a synergistic effect. It is produced and released from activated monocytes and macrophages.^{6,7} Perhaps the most widely held view is that the initial CGCG is an endosteal haemorrhage. In 1962, Kramer stated that if the process is concerned with the repair following haemorrhage, then the repair follows

a peculiar pattern complicated by repeated new haemorrhages. Trauma has been considered as an important aetiological factor in the initiation of this lesion. The lesions increase by accumulation of tissue which is produced by slow, minute, condition haemorrhages of multicentric nature due to trauma and some defect in capillaries. Giant cell granulomas of the jaw bones may be central or peripheral. Peripheral lesion present as pedunculated or sessile lesion on the gingival while central lesions are endosteal.⁵⁻⁸ To the best of our knowledge, there have been only four well-documented cases of CGCG in patients under 10 years old without association with an inherited syndrome. In children with mixed dentition, a pathological 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 accompanied by an obvious bony expansion. These causes frequently complicate the radiographic analysis, and it can delay diagnosis and aggravate the case.²⁻³ It has been reported that the origin of this lesion could be triggered by trauma or inflammation. The common effects of CGCG are painless swelling that remains undetected until facial asymmetry, impaired nasal breathing and loosening or displacement of teeth. Localised swelling is an important clinical feature. The swelling is smooth, and palpation can reveal a rubbery, elastic sensation where the bone has thinned.⁸ Although the lesion is expansile and invasive, it does not usually involve the perineural sheaths.^{2-4 6-8} For this reason, paraesthesia is not usually observed in these patients. The clinical behaviour of CGCG ranges from a slowly growing asymptomatic swelling to an aggressive lesion. Similar findings were evident in our case. When CGCG is a slow-growing lesion, it can be asymptomatic and discovered on a routine X-ray, while the rapidly expanding, aggressive variety is characterised by pain and facial swelling. These fast growing lesions also have a high rate of recurrence. It has been reported that recurrence is usually found when the lesion perforates the cortical plates to involve the surrounding soft tissue.⁸ The radiological appearance of CGCG is variable. Usually the lesion appears as a unilocular or multilocular radiolucency. It may be well-defined or ill-defined and shows variable expansion and destruction of the cortical plate. The radiological appearance of the lesion is not pathognomonic and may be confused with that of many other lesions of jaws.⁵⁻⁹ The final diagnosis eventually rests on histopathology because the clinical and radiological features are not specific.⁵ Found in their study on 80 cases that 51% of the lesions were multilocular, 44% were unilocular, 5% were not loculated and 68% of the multilocular lesions were in the mandible. They also determined unilocular lesions had a mean size of 4.05 cm, while multilocular lesions' mean size was 7.38 cm. They established a statistically significant correlation between the localisation of lesions and their size. They also described a correlation between root resorption and gender. Root resorption was observed in 24% male patients and only 6% of female patients.⁷ Histologically, CGCG contain focal arrangements of giant cells within a vascular stroma with thin-walled capillaries adjacent to the giant cells. There is a spindle cell stroma which may well be the cell of origin. Similar findings were evident in our case also. Presence of foreign body type giant cell (as seen in our case and absence of stromal tumour cells differentiate CGCG from a giant cell tumour. 'Solid' aneurysmal bone cysts (ABC) are true benign neoplasms containing giant cells while trauma causing intramedullary haemorrhage has been implicated in the past as the aetiology. Normal serum calcium, parathyroid hormone, alkaline phosphatase and phosphorous levels distinguish CGCG from other conditions like Brown tumour of

hyperparathyroidism.⁶⁻⁸ Surgery is the traditional and most accepted form of treatment for CGCG.⁴ However, the extent of tissue removal ranges from simple curettage to en bloc resection. The conservative surgical treatment of CGCG usually involves curettage alone or along with peripheral osteotomy with no evidence of disease in a 2 year follow-up period. The margins of the CGCG may also be thermally sterilised with laser or cryoprobes. Radical surgical techniques of resection without continuity defect and peripheral osteotomy and en bloc resection have sometimes been justified for aggressive CGCG.⁶ However, recurrence with serious facial mutilation, loss of teeth and tooth germs seem unavoidable. Paediatric patients necessitate conservative management to prevent long-term developmental defects. Steroids and calcitonin have been advocated in the recent past and they act by inhibition of osteoclastic activity. Equal parts of triamcinolone acetonide (10 mg/mL) and 0.5% bupivacaine injected into the lesion for a period of 11 weeks have been shown to be effective in a child. Relative contraindications do exist in certain medical conditions, such as diabetes mellitus, peptic ulcer and generalised immunocompromised states.^{4 6-8} Calcitonin nasal spray 200 U/spray once or twice daily was reported to be safe and effective for the treatment of CGCG. But, therapy may be complicated owing to the great amount of discomfort and the relatively long duration of treatment, with poor compliance by children. Where surgery has been conservative daily subcutaneous interferon α (3 million units/m² of body surface area) has been tried as an adjuvant due to its antiangiogenic properties; but significant side effects may limit its utility. A combination of interferon α and imatinib given for 9 months has been shown to initiate regression of the lesion that continued after treatment had ceased. Bisphosphonates have also been attempted intravenously with promising results. Nevertheless, recurrences of CGCG are not uncommon and can be seen in up to 46% of cases.⁶⁻⁸ Radiation treatment is contraindicated because of the potential for malignant transformation.^{3 4}

Learning points

There are two types of central giant cell granulomas, non-aggressive and aggressive.

- ▶ The former has a slow rate of growth and thus less likely to absorb roots and perforate the cortical plate.
- ▶ The aggressive form has rapid growth and thus is much more likely to absorb roots and perforate the cortical plate. It also has a high rate for recurrence and can be painful and cause paraesthesia.
- ▶ Central giant cell granuloma is expansive in its growth; it does not grow around or invade nerve trunks. It also does not invade perineural sheaths or spread via perineural spaces.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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