

Short Case Report

Diagnostic difficulty of an aggressive and recurrent giant cell granuloma: a short case report

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Abstract – Introduction: The central giant cell granuloma (CGCG) is a rare benign lesion of the jaws, rarely aggressive, mostly affecting the mandible in children and young adults. The diagnosis may be difficult, complementary histological analyses being necessary to differentiate it from other giant cell tumours. **Observation:** A 28-year-old woman consulted for a painful gingival swelling surrounding the inferior right second molar. Cone Beam (CBCT) showed a unilocular radiolucent mandibular lesion. Histological examination performed after the curettage of the lesion could not differentiate between a peripheral GCG with bone extension, a giant cell tumour (GCT) or a CGCG. The patient was lost of view for 4 months until an aggressive recurrence. A segmental mandibulectomy in disease-free margin was performed. Immunohistochemical and genetic tests complementary to histology finally permitted to conclude to a CGCG. The patient presented no recurrence in 4 years of follow-up. **Discussion:** Surgical removal in disease-free margin is the gold standard treatment in aggressive CGCG. Nonetheless, literature reports alternative pharmacological treatments alone or in addition to surgery. In this case, the aggressiveness of the tumour and the absence of patient compliance for follow-up have led to the decision of a radical treatment of the recurrence. **Conclusion:** Aggressive CGCG requires a rapid diagnosis and a primary disease-free margin surgical resection to avoid mutilating treatment of the recurrence.

Observation

A 28-year-old woman consulted for a painful oral swelling. There was nothing relevant in her medical history. She underwent the removal of 3rd molars under general anaesthesia a year earlier.

She reported the occurrence in the posterior mandibular region of a rapidly growing tumour without remembering starting period of the swelling. It became painful a week earlier (visual analogue scale for pain, VAS = 10/10 the day of visit).

The extra-oral examination found a firm swelling in the posterior mandibular region with a moderate trismus and without lymphadenopathies.

The intra-oral examination found a 3.5 cm tumour behind the mandibular right 2nd molar which was partially covered with the tumour (Fig. 1). A gingival suppuration was present. The tumour was covered with a whitish mucosa and had a firm consistency.

The panoramic X-Ray showed a circular, well limited unilocular radiolucent lesion behind the mandibular right 2nd molar with on its lower border a 2 mm radio-opaque image compatible with a residual dental apex (Fig. 2).

Diagnostic hypothesis was dental cellulitis caused by a residual cyst after 3rd molar removal. The initial treatment consisted of antibiotics, analgesics and antiseptic mouth washes for 6 days.

The blood test found microcytic anaemia, hyperleukocytosis and high level of C-reactive protein. Parathyroid hormone, calcium and phosphate levels as well as creatinine clearance were normal, so primary or secondary hyperparathyroidism was excluded.

CBCT showed a 22 × 14 × 16 mm unilocular lesion in contact with the inferior alveolar nerve. The lingual cortical plate was perforated and the vestibular one was thinned.

After 1 week, no significant improvement was observed. Other diagnoses were then evoked among which a keratocyst, an ameloblastoma, a myxoma, an aneurismal bone cyst (ABC), a giant cell tumour (GCT) or a central giant cell granuloma (CGCG).

The exeresis of the tumour along with the removal of the residual apex were performed under local anaesthesia.

Histological examination found a great number of multinucleated giant-cells (Fig. 3) but was unable to distinguish between peripheral GCG, CGCG or GCT.

The patient was lost of view for 4 months until the recurrence of the lesion. She presented a 2.5 cm, bleeding on

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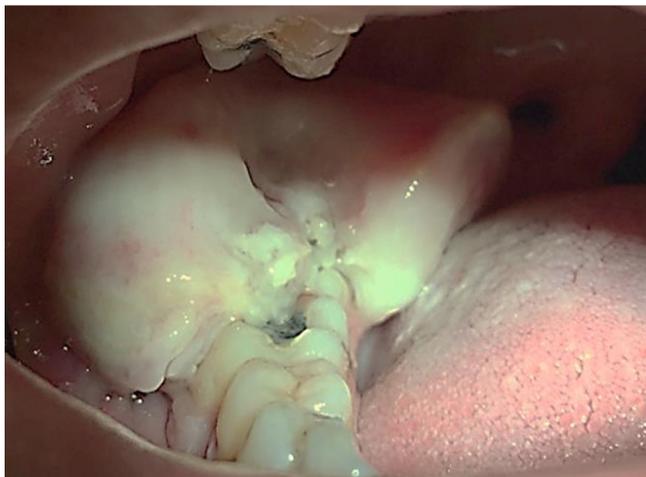


Fig. 1. Gingival large tumour partially covering the mandibular right 2nd molar.



Fig. 2. Orthopantomography performed at the first visit showing an unilocular, well-delimited, radiolucent lesion behind the mandibular right 2nd molar and a residual apex of the 3rd molar.

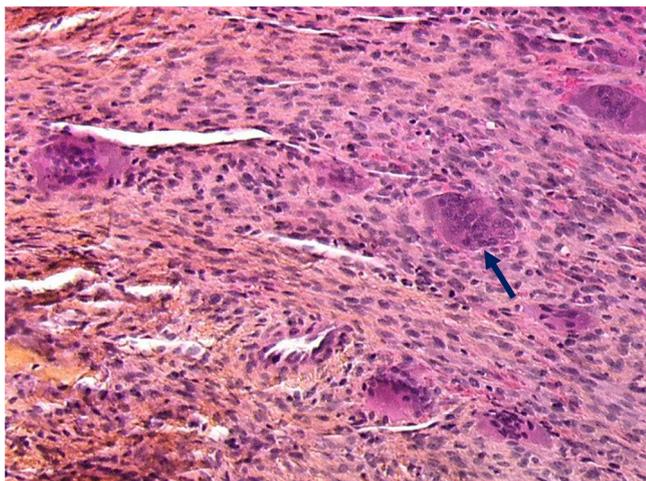


Fig. 3. Histological slide coloured with hematein eosin safran (HES) (magnification $\times 40$) showing numerous multinucleated giant cells (black arrow).

touch, painful gingival tumour behind the mandibular right 2nd molar. Submandibular lymphadenopathies were found.

A new CBCT showed an extensive unilocular radiolucent lesion of 40 mm located in the mandibular angle and ramus, perforating the buccal and lingual cortices and the lower rim of the mandible, and invading the soft tissues (Fig. 4).

Because of the rapid and aggressive recurrence, decision has been made to realise a mandibular resection with 5 mm margin; the mandible was reconstructed with a titanium plate.

Histological examination showed numerous osteoclastic-like multinucleated giant cells, uniformly distributed within a stroma of mononucleated and spindle-shaped cells grouped in islets around haemorrhagic suffusion sites. The diagnosis of giant cell tumour was made, without being able to differentiate between a CGCG or a true GCT. Complementary immunochemical and genetic analyses (searching for G34W mutation of histone H3.3 and USP6 gene rearrangement) have been performed. Both results were negative. The diagnosis retained was that of a CGCG.

No recurrence appeared in the 4-year follow-up.

A secondary reconstruction of the mandible by free fibula flap was refused by the patient because of pregnancies during the follow-up.

Comments

The CGCG is a rare benign tumour of the bone (incidence 1.1 per 10^6) [1]. The CGCG develops more frequently in women and 60% of patients are aged under 30; 65% of the cases occur in the mandible [1].

One possible aetiology of CGCG could be an excessive healing process after an endo-osseous trauma. In the reported case, the removal of the 3rd molar one year earlier may support this hypothesis.

The growth of the tumour is often slow and asymptomatic, but teeth displacements, root resorptions and cortical perforations are sometimes observed [1].

Histological examinations alone are sometimes not able to differentiate between CGCG and GCT. Few studies reported diagnostic difficulties and the use of complementary diagnostic techniques such as immunofluorescence or immunohistochemistry to distinguish CGCG from osteosarcoma or other giant cell tumours such as GCT or ABC [2]. In our case, such tests were necessary – in addition to two anatomopathological examinations – to reach the final diagnosis.

CGCG are classified in aggressive and non-aggressive types [3]. Aggressive lesions are characterised by at least three of the following clinical features: size superior to 5 cm, root resorption, tooth displacement, rapid growth, cortical perforation and high recurrence rate after curettage [3]. The global recurrence rate varies between 11 and 49% after surgical treatment [1], but could rise to 70% after curettage or

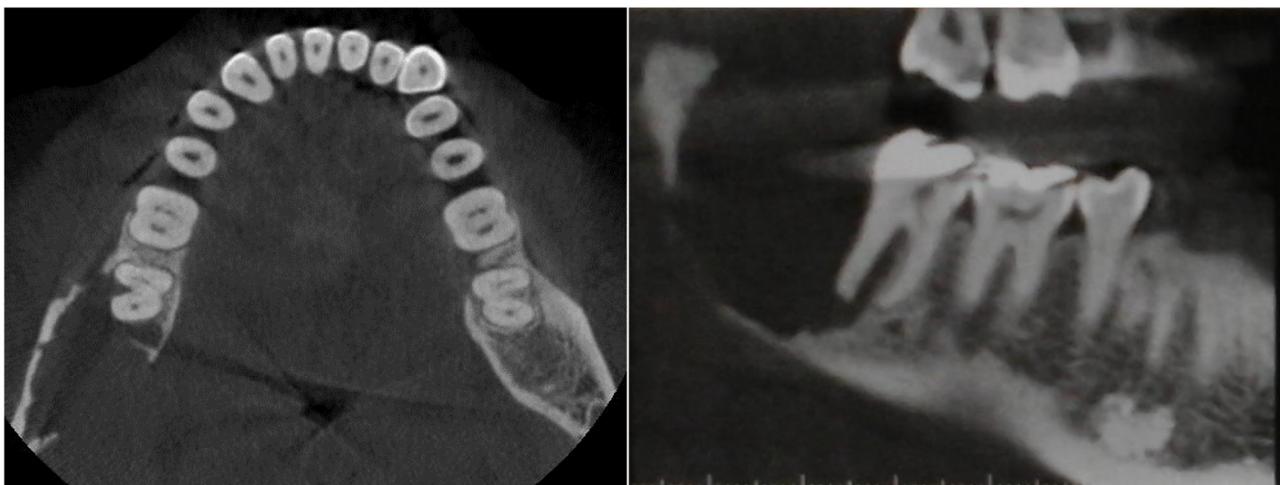


Fig. 4. Axial and coronal CBCT slides showing the tumour extension with cortices perforation.

enucleation of an aggressive type [4]. Some histological aspects such as the number of multinucleated cells, their volume and the number of nuclei seem to be correlated to the aggressiveness of the CGCG [3].

The treatment modalities described in the literature vary widely depending on the size and aggressiveness of the tumour.

For non-aggressive types, simple curettage seems sufficient, but in aggressive types the high recurrence rate does not allow this treatment [1]. Resection with >5 mm margin limits the recurrence rate to 6%, comparing with the 72% rate observed after curettage [3].

Alternative pharmacological treatments acting on the tumour proliferation (*i.e.*, intralesional injection of corticosteroid, calcitonin, interferon alpha, denosumab, imatinib...) are proposed alone or combined with a surgical treatment, in order to limit the functional impact of extensive surgeries in the often-young patients with CGCG [1]. These treatments seem effective on non-aggressive types but are rarely enough to obtain complete healing on aggressive tumours that often require complementary surgery [1].

In the literature, tumour resection is the first-line treatment for aggressive CGCG [2,4,5]. Tosco *et al.* reported the management of 18 cases of CGCG of which 11 were aggressive types. Their treatment consisted in a 5 mm margin en-bloc resection. No recurrence was observed after a 18-month follow-up [4].

Similar to our case report, two publications reported two cases of CGCG treated with segmental mandibulectomy and immediate reconstruction with a titanium plate [2,5]. Yadav *et al.* performed a segmental resection after 2 recurrences of an aggressive CGCG located in the ramus that invaded the nearby soft tissues [5]. Wang *et al.* performed the same surgery

in a child with an aggressive CGCG located in the mandibular ramus and condyle that recurred rapidly after enucleation [2].

In the present case, the very aggressive type of tumour in this young patient and the lack of compliance for follow-up oriented us towards a radical treatment of the recurrence. The decision of immediate reconstruction with a titanium plate rather than a free fibula flap was justified by the risk of recurrence and the opposition of the patient.

Conflict of interest

The authors declare no conflict of interest.

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