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Case Report

Hybrid central odontogenic fibroma and central giant cell granuloma lesion – A case report of an aggressive and recurrent lesion

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ABSTRACT

Central odontogenic fibroma (COF) with central giant cell granuloma (CGCG) features is an uncommon lesion, the origin and true definition of which remains somewhat controversial. To date, it is unclear whether this lesion represents a true collision between the two entities or if the COF or CGCG induces the proliferation of the other. Only a small amount of cases have been published in the literature to this date. We present a case of a hybrid lesion of COF and CGCG. The lesion presented as a radiolucent lesion of the left mandible that caused bony expansion and paresthesia. Microscopic examination revealed a florid population of fibrohistiocytic cells and multinucleated giant cells in a densely collagenized fibrous connective matrix. Interspersed among this proliferation, lobular collections of intensely basophilic cells with benign cytologic appearance were observed. Immunohistochemistry staining with MCK, Calretinin, CK5/6, and CD68 separated these islands of odontogenic cells from the surrounding multinucleated giant cells and histiocytes. Careful review of previously reported cases appears to yield a relationship with previous long-term history of dental extraction in the area. Management reports in the literature suggest the possibility of a slightly more aggressive lesion than pure central giant cell granuloma, with the possibility of recurrence. Therefore, close clinical follow-up is advised. The possibility of hyperparathyroidism should also be ruled out.

1. Introduction

The central odontogenic fibroma (COF) is a somewhat uncommon benign neoplasm of odontogenic mesenchyme and epithelial islands, that has been reported mostly in middle-aged females and in the predominantly in the posterior mandible. It exhibits a proliferation of mature collagenous connective tissue in association with islands or strands of inactive appearing odontogenic epithelium, and sometimes various amounts of calcified material resembling dysplastic dentin or cementum [1,2]. This tumor alone displays a slow-growing, non-aggressive clinical behavior, unless it is associated with central giant cell granuloma (CGCG) features. The presence of multinucleated giant cells within the COF is associated with increased recurrence after surgical removal. This tumor is now known as a hybrid lesion between a COF and CGCG, and it was first described by Odell et al. [3]. Central odontogenic fibroma with central giant cell granuloma (COF/CGCG) features is characterized by the presence of all the components of a COF, with fibrohistiocytic cells and interspersed multinucleated giant cells. Hemorrhage and hemosiderin can be present [1–4].

The origin of COF/CGCG and definition remains somewhat controversial. To date, it is unclear whether this lesion represents a true collision between the two entities or if the COF induces the proliferation of the CGCG or vice versa [4]. Three theories has been postulated to explain the formation of this hybrid lesion. One hypothesis suggests that these lesions are a true collision between COF and CGCG, while some postulate that COF is the initial entity with a multinucleated giant cell reactive component, or that both entities arise synchronously. Other authors have proposed that CGCG produces growth factors and induces proliferation of the odontogenic component and formation of COF [2,4]. Careful review of previously reported cases indicates a relationship with previous long term history of dental extraction, endodontic, or orthodontic treatment, but there is not enough data reported to make solid assessments on epidemiology of the affected patients, the clinical course of the tumor, and recurrence rate, making this entity often overlooked by the practicing oral pathologist and diagnosed as simple CGCG. We present on aggressive case of COF/GCG received by the Division of Oral and Maxillofacial Pathology at the University of North Carolina at Chapel Hill.

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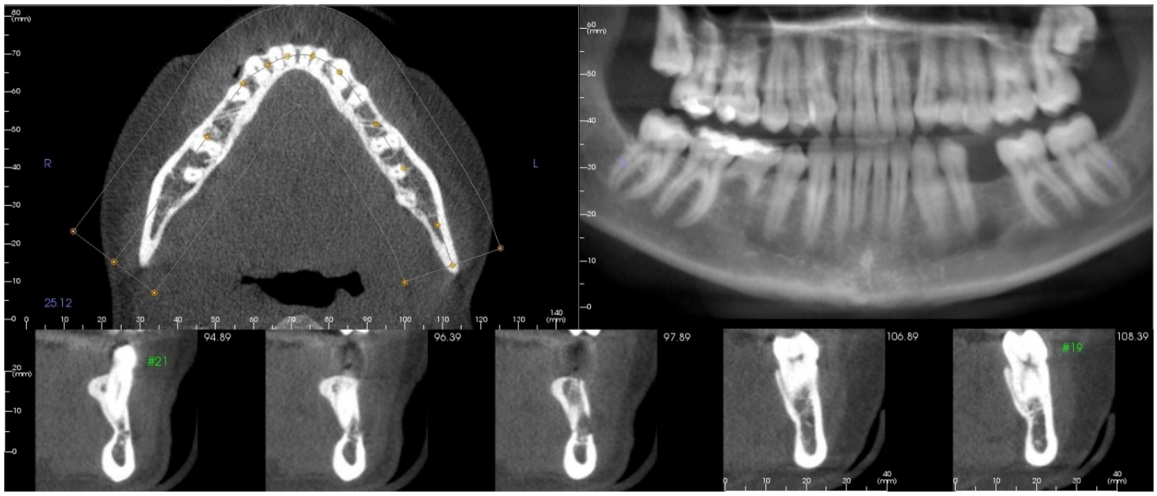

Fig. 1. Cone Beam Computerized Tomography (CBCT) and panoramic radiograph of initial presentation. Note multilocular radiolucency above mental foramen.

2. Case presentation

The patient was a 65-year-old female that presented at oral surgery consultation with left body of the mandible expansion and paresthesia. Tooth #20 was not present at the time of consultation. It was described as congenitally missing and a deciduous tooth has been removed from the area 33 years ago. Radiographic examination revealed a 9 mm × 8 mm multilocular radiolucency superior to the mental foramen (Fig. 1). The clinical differential diagnosis rendered was central giant cell lesion vs botryoid odontogenic cyst. The lesion underwent excisional biopsy and was submitted to our facility for examination.

The specimen consisted of three fragments of tan, brown and black soft tissue and it measured 0.9 × 0.7 × 0.4 cm. Microscopic examination revealed a densely collagenized fibrous connective tissue matrix among a dense population of fibrohistiocytic cells and multinucleated giant cells, as well as hemorrhage and hemosiderin accumulation (Fig. 2). Interspersed among this proliferation, were islands of odontogenic-like epithelium forming lobular collections of darkly basophilic cells with a benign cytologic appearance. The odontogenic epithelium showed strong immunoreactivity for Multiple Cytokeratin (MCK), Calretinin and CK 5/6. The presence of fibrohistiocytic cells and multinucleated giant cells was demonstrated with strong positivity for CD68 staining (Figs. 3–5).

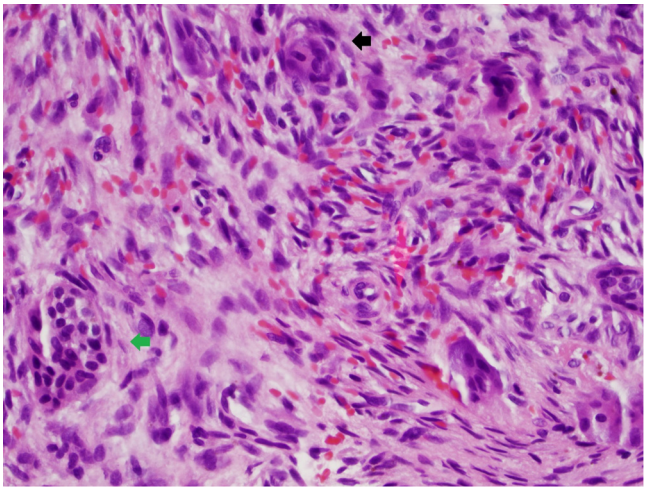

Fig. 2. Fibrohistiocytic proliferation of spindle cells with intermixed multinucleated giant cells and odontogenic epithelial rests. [Black *arrow: multinucleated giant cell. Green arrow: epithelial odontogenic rest*] Stain: Hematoxylin and Eosin. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

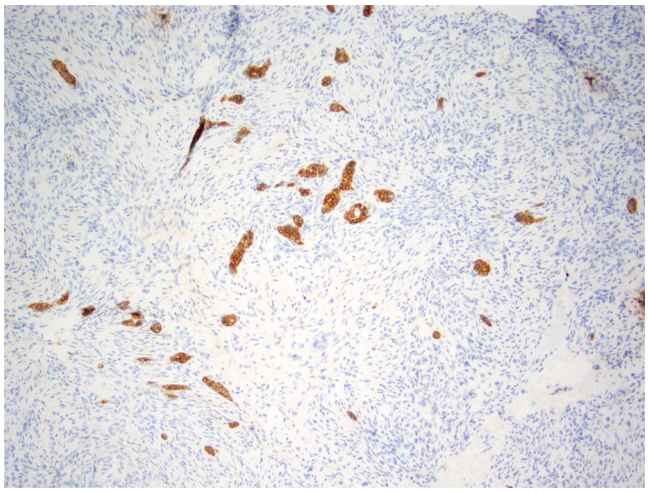

Fig. 3. MCK immunohistochemical stain highlights the cytoplasm of odontogenic epithelial rests through the lesion.

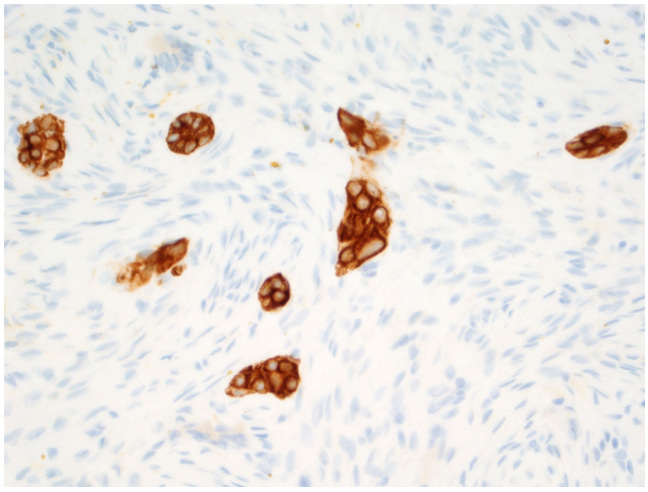

Fig. 4. Odontogenic epithelial rests immunoreactive to CK5/6 antibody.

Nine months after the initial procedure, the patient reported no pain in the area, and slight improvement in the paresthesia of the lower lip.

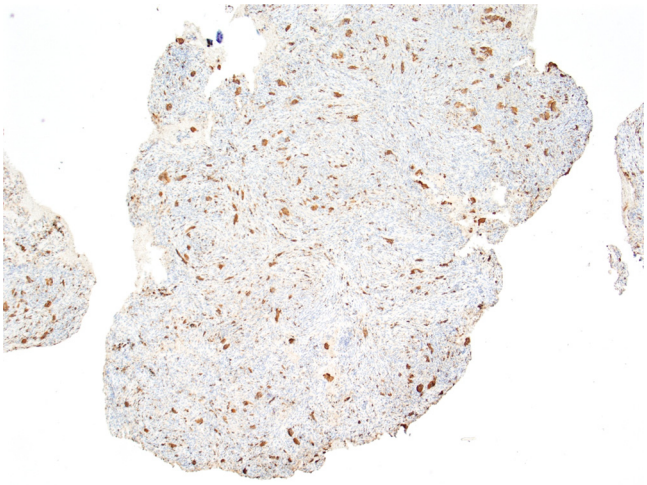

Fig. 5. CD68 antibody highlight fibrohistiocytic cells and multinucleated giant cells throughout the mass.

However, around the periapical area of tooth number 21, a small unilocular radiolucent lesion was observed in the previous surgical site. A second surgical appointment was planned, and the new lesion was removed and submitted for histopathologic examination. The new lesion consisted of two separated lobules attached by a small "bridge" of soft tissue. Both fragments together measured 0.4 × 0.3 × 0.2 cm. The microscopic appearance was consistent with the initial lesion. No cytologic atypia or signs of malignancy could be associated with the recurrence of the lesion. The margins of the specimen did not appear free of pathology; hence a third surgical procedure was conducted in an outside institution, without recurrence to date.

3. Discussion

Three theories have been postulated to explain the formation of this hybrid lesion. The hypothesis suggests that this lesion is a true collision between COF and CGCG, or that COF is the initial entity with a multinucleated giant cell reactive component. Other authors have proposed that CGCG produces growth factors and induces proliferation of the odontogenic component and formation of COF [1–3]. However, Younis et al. stablishes that a high percentage of the cases reported to the date, have a history of reactive stimuli, such as history of dental extraction, root canal therapy and orthodontic treatment, and that may play a role in the etiology of the lesion, suggesting that this event would trigger a primary CGCG reparative response [3]. In our case, the patient presented a long-term history of dental extraction of a deciduous tooth and congenital agenesis of tooth number 22 as well as the contralateral permanent canine. Although the pathogenesis of this hybrid lesion is unknown, the presence of multinucleated giant cells seems to be associated with a high rate of recurrence and aggressiveness [2,4,5]. Cortical expansion of the bone, and paresthesia was encountered in our case, which concords with previously reported cases, although to the best of our knowledge, no cases with paresthesia have been previously reported. No cytologic or architectural features of malignancy were identified. Due to the cortical expansion and paresthesia, careful management and long-term follow-up is recommended [6,7]. To date, no correlation of the architectural changes or atypical features have been related to recurrence of the lesion [8], which supports the behavior of the tumor in our patient. In both specimens, the margins were not free of tumor, which can explain the local recurrence.

4. Conclusion

The COF with CGCG-features is considered an aggressive variant of a conventional COF. This entity can be associated with extensive bone destruction, pain, expansion, increased local recurrence, and in our case paresthesia. We considered that a traumatic event, such as dental extraction in the area, could induce proliferation of odontogenic rests in the area, and differentiation of multinucleated giant cells; however, further research, including a multicenter study and the examination of multiple cases with molecular research, is necessary for this final assessment. In the meantime, clinicians should be encouraged to surgically remove these lesions with clean margins, and closely monitor the patients. In addition, the possibility of hyperparathyroidism should be ruled out.

Ethical approval

The presented case was submitted to the Institutional Review Board for consideration and was deemed extent.

Declaration of Competing Interest

We have no conflicts of interest to report.

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