Case Report
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A Hybrid Lesion of the Mandible with Three Co-existent Pathologies: Report of a Rare Case with Literature Review

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Abstract

Hybrid lesions are rare and microscopically composed of areas of distinct pathologic entities. The occurrence of dual lesions containing Central Giant Cell Lesion (CGCL) and fibro-osseous lesions has been recorded in the literature. Although many similar cases have been reported the pathophysiology of such lesions is yet not well understood. Furthermore, their clinical behaviour and treatment guidelines are also not clearly outlined. Presented here is a unique case of a 17-year-old male with a hybrid lesion with a triad of pathological entities, Ossifying fibroma, CGCL and aneurysmal bone cyst. The clinical presentation, pathogenesis and behaviour of the reported lesion are comprehensively explained. The authors believe that greater knowledge of the hybrid variety of jaw lesions may aid in better understanding and management of these lesions by clinicians.

Keywords: Aneurysmal, Bone Cysts, Fibroma, Giant Cell Granuloma, Mandible, Ossifying Fibroma

1. Introduction

Hybrid lesions consisting of Central Giant Cell Lesion (CGCL) along with either Aneurysmal Bone Cyst (ABC) or other Fibro-osseous Lesions (FOL) are well documented in the literature[1]. However, all the reported hybrid/mixed cases until now were dual lesions with simultaneous occurrence of CGCL with any other FOL. The authors encountered a unique hybrid/combined lesion showing features of three different pathological entities occurring simultaneously, namely Ossifying fibroma, CGCL and Aneurysmal Bone Cyst, in the same lesion.

This case report presents a young patient with painless extra-oral mandibular swelling. The article presents the clinical behaviour and the possible explanation of occurrence along with the treatment rendered for this bony lesion.

2. Case Presentation

A 17-year-old male patient reported to our institution with the chief complaint of pain and swelling of the left side of the lower jaw evident extra-orally from 18 months. The patient was previously treated elsewhere with calcitonin nasal spray for 3 months which proved futile. According to the patient, the lesion kept on increasing and he reported to our institute after 6 months of the initial treatment. On clinical examination, a bony hard swelling was noted on the left side body of the mandible with the expansion of buccal and lingual cortices and gross facial disfigurement (Figure 1-A).

Orthopantomogram (OPG) showed a well-defined multilocular radiolucency on the left side of the mandible extending from the distal aspect of the lateral incisor to the angle region and involving the inferior alveolar nerve

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canal. Blunt root resorption was evident w.r.t # tooth 34, 35, 36, and 37 and distal displacement of roots w.r.t tooth #36#37 was visible. Expansion of the inferior border was well appreciated with a prominent gonial angle. (Figure 1-B). Looking at combined features, the findings pointed more toward a benign tumour rather than a cyst.

An incisional biopsy was then performed which confirmed the diagnosis of CGCL. After ruling out hyperparathyroidism, intralesional corticosteroid injections (Triamcinolone acetonide 10 mg/ml) mixed with Lidocaine and Adrenaline (1:80,000) in 1:1 ratio were given for 6 weeks at weekly intervals.

To assess the response to the treatment, panoramic radiographs were performed after 6 months of completion of steroid therapy at 3-month intervals. In the first two radiographs, new endosteal bone formation was evident, especially in the periphery (Figure 2-A). However, the last X-ray revealed an increase in the size of the osteolytic component of the lesion in the anterior region of the mandible, extending to the right side and causing an expansion of cortical bone (Figure 2-B). Thus, surgical curettage of the lesion was planned under general anaesthesia via an intra-oral approach.

The histopathologic report again established the findings of CGCL. But after 6 months of the procedure, recurrence was noticed in the form of a progressive increase in cortical expansion as well as an increase in radiolucency in the operated site. The lesion was again curetted out via an extra-oral submandibular approach and the excess bone causing buccal expansion and part of the inferior border was removed along with the lesion while maintaining the continuity of the mandible on the

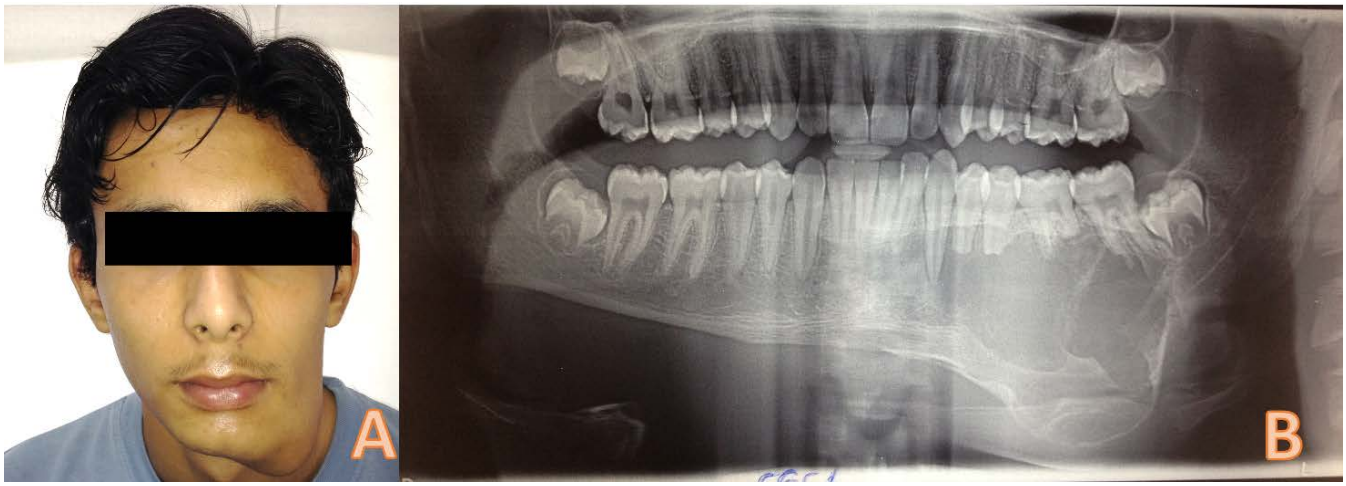


Figure 1. **(A)** Clinical photograph of the patient showing extraoral expansile swelling of the left side of face. **(B)** OPG revealing well defined multilocular radiolucency on left side of mandible extending from the lateral incisor to the angle region.

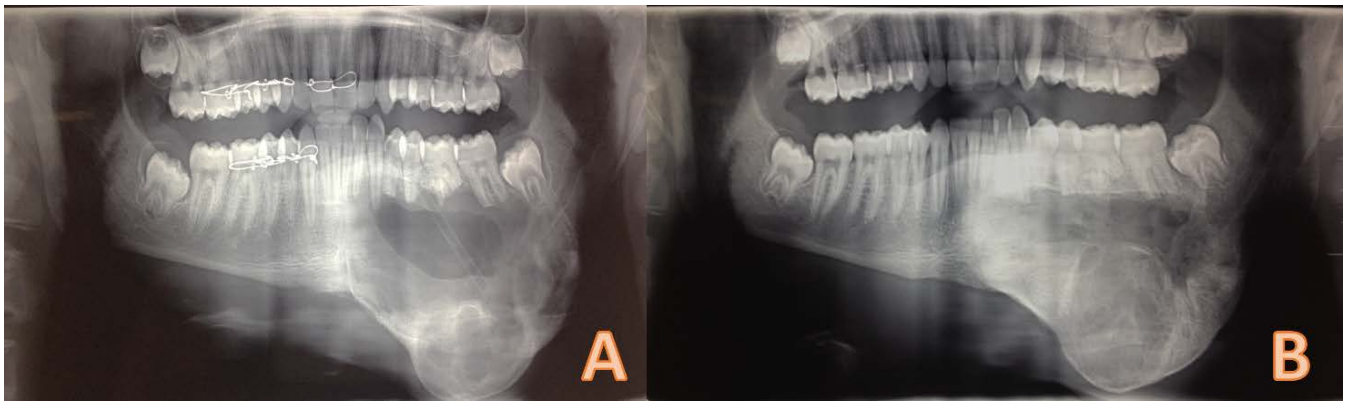


Figure 2. **(A)** OPG depicts new endosteal bone formation after initial phase of steroid therapy. **(B)** OPG demonstrating increased osteolytic lesion at the completion of steroid therapy.

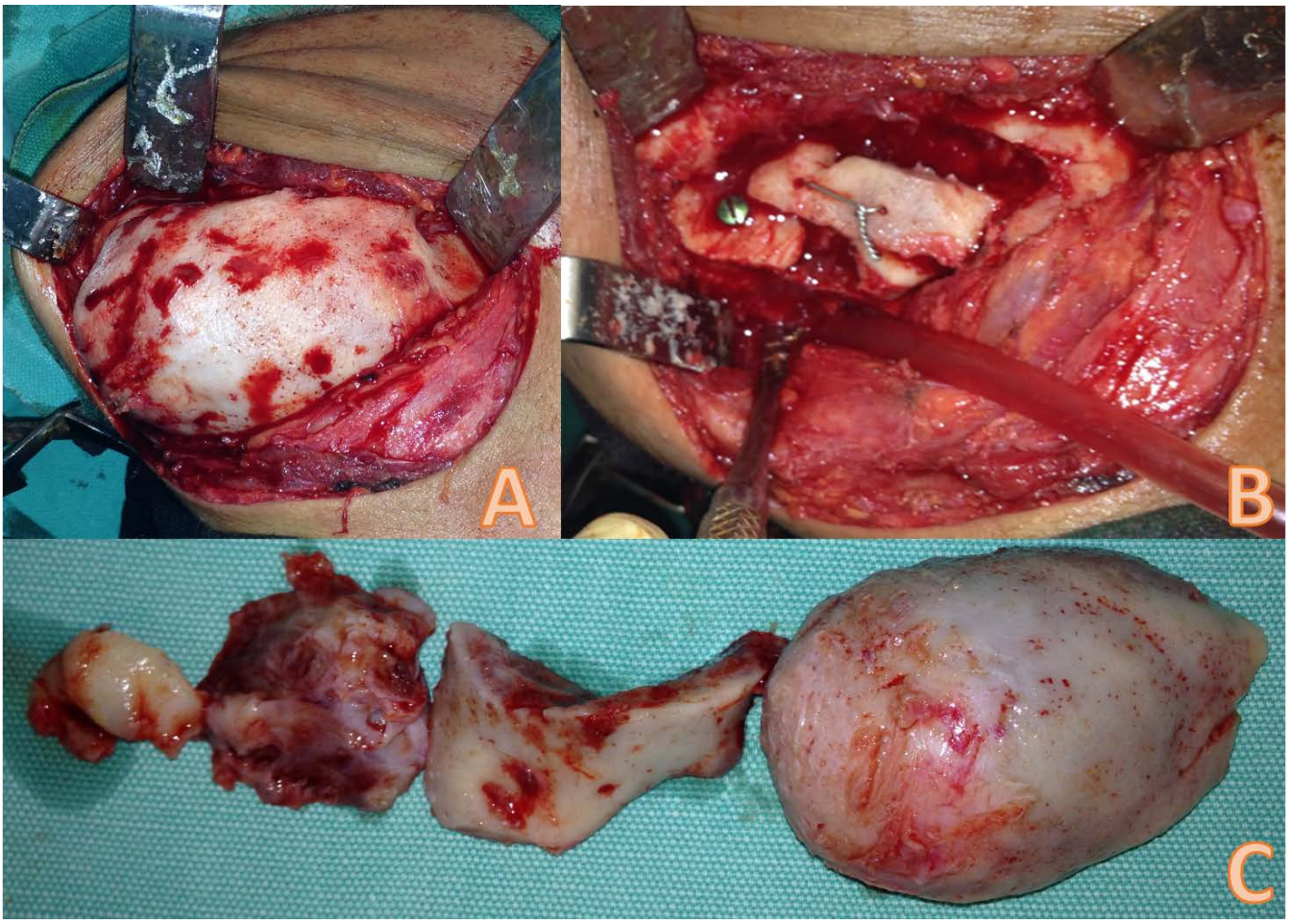


Figure 3. **(A)** Exposure of the pathology using extraoral approach. **(B)** Fixation of the healthy buccal bone using transosseous wire and positional screw to the pathologic defect. **(C)** Pathologic specimen resected.



Figure 4. **(A)** Clinical photograph showing resolution of swelling at the last follow up. **(B)** OPG showing resolution of the lesion at the last follow up.

lingual aspect. The lesion was completely separated from the resected buccal bone. The resected buccal bone was found to be healthy and was replaced into the 3-walled bony cavity created by curettage of the lesion and fixed to its walls with the help of transosseous wires and positional screw to maintain the facial contour (Figure 3).

Following this procedure, complete resolution of the lesion was noticed at 6 months post-operative OPG and clinically the patient was free of the disease at 2.5 years of follow-up (Figure 4-A) which was evident from subsequent OPG (Figure 4-B).

The histopathology report of the patient after the final curettage revealed a highly cellular stroma with strands of trabeculae of varying shapes. The morphology of stromal cells ranged from plump hyperchromatic cells to round cells with vesiculated nuclei. The trabeculae showed immature woven bone with trapped osteocytes exhibiting cellular pleomorphism. In close association with these trabeculae, myxoid areas with stellate cells were seen. Large vascular spaces filled with RBCs and giant cells were seen adjacent to the cavity. Focal areas of giant cells associated with increased vascularity and extravasated RBCs were seen distributed at intervals. These features were suggestive of a lesion predominantly consisting of Ossifying fibroma with areas of CGC and Aneurysmal Bone Cyst (Figure 5).

3. Discussion

The term "hybrid lesions" was first introduced by Waldron and El-Monty in the course of their work on cases of ameloblastoma[2]. Later, it became generally

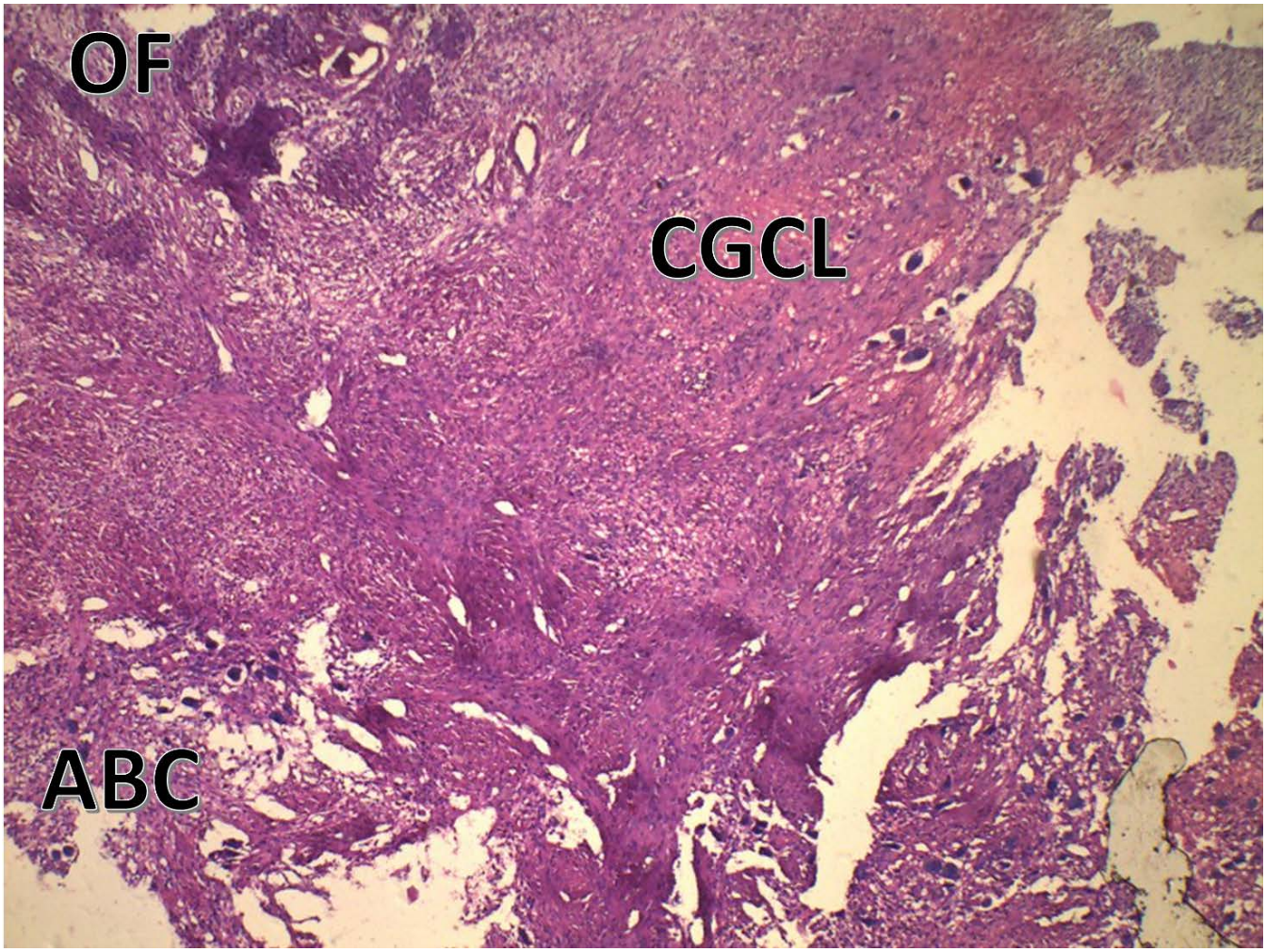


Figure 5. Histopathologic section showing a hybrid lesion with areas of typical Central giant cell lesion (CGCL) adjacent to areas of Ossifying Fibroma (OF) and Aneurysmal Bone Cyst (ABC) (hematoxylin-eosin stain).

accepted that "hybrid" lesions encompass those that include significantly large and discrete portions of histopathological features of multiple, completely distinct entities[3–5]. The exact etiology of these lesions nevertheless remains controversial, therefore making their diagnosis challenging to clinicians.

The incidence of CGCL with various lesions has been reported in the literature. A number of studies wherein simultaneous regions of CGCL were observed along with features of different lesions such as Central Odontogenic Fibroma[3], Aneurysmal bone cyst[4], ossifying fibroma and different fibro-osseous lesions[5] have been mentioned. A scientific review by Alsufyani *et al*.,[1] found out the main hybrid-CGCL lesions, in descending order, have been Central Odontogenic Fibroma (CODF) (n = 14/39;35.8%), Central Ossifying Fibroma (COF) (n = 11/39;28.2%), Fibrous Dysplasia (FD) (n = 7/39;17.9%) and with other bone conditions (n = 7/39;17.9%). All of these reported hybrid lesions were composed of only two different pathologic elements, thus making our current case with a triad of distinct pathologies unique in its presentation. In our case, another interesting finding was that the histopathology of the final specimen after curettage was quite different from the initial biopsy findings. Biopsy of the lesion was suggestive of only CGCL in the first two instances, whereas, the histopathology after curettage/ resection of the entire lesion was suggestive of ossifying fibroma with areas of CGCL and Aneurysmal bone cyst. This occurrence was quite striking and it is difficult to find an exact explanation for the occurrence of 3 types of findings in a single lesion.

This raises another pivotal query of whether these hybrid lesions ought to be considered as simply separate lesions which have joined to form one entity or if this is just a progression of the primary tumour. The second scenario also raises the suspicion of a partially shared pathogenic mechanism of solitary lesions with combined/ hybrid lesions of the jaws. It also cast a doubt on whether the primary lesion in our case converted into the ossifying fibroma or CGCL. Most of the studies to date have considered Ossifying Fibroma to be the primary lesion. For instance, Kaplan *et al*.,[6] believe that these lesions are Ossifying fibromas primarily in which some unknown stimulus causes the osteoblasts to get differentiated into osteoclasts (Giant cells) and give rise to CGCL-like areas. Additionally, Penfold *et al*.,[5] Farzaneh *et al*.,[7] also concur that theoretically, osteoblasts may activate osteoclast-type giant cells through paracrine mechanisms already described in the literature[8]. The present case may also be related to such a phenomenon wherein Ossifying Fibroma stimulated the formation of CGCL. However, the authors believe that there is a chance that the lesion was primarily a CGCL. This assumption is based on two major reasons: First, the initial biopsy revealed only CGCL, leading to the conclusion that CGCL was the predominant lesion in the beginning. The other theory supporting this includes findings of Scaglietti *et al*.,[9] who have shown fibrotic and ossification changes occurring after administration of intralesional corticosteroids in bone cysts. The exact mechanism of action of Triamcinolone is not known but it is believed that it inhibits the production of bone resorption mediating lysosomal proteases by the giant cells and induces apoptosis of osteoclasts[10,11].

Edgerton *et al*.,[12] studied the role of intralesional steroids in the management of hemangiomas and found that intralesional steroids sensitize the vascular beds to vasoconstrictive agents and thus cause the involution of the lesion. Since in our study, we used a combination of Triamcinolone with lidocaine+1:80,000 Adrenaline in a 1:1 ratio, the sensitization of vascular beds to vasoconstrictive action of adrenaline might have resulted in a decrease in areas of the lesion showing extravasation of RBC's and thereby decreasing the overall area having CGCL like features and inducting fibrotic and osseous changes in the lesion resulting in Ossifying fibroma development.

Secondarily, the occurrence of areas of ABC within CGCL is not rare and many of the authors consider it as a cystic variant of CGCL[4]. Liu *et al*.,[13] suggested that the Multinucleated Giant Cells (MGC) in CGCL, ABC and cherubism display characteristics of the osteoclast phenotype and are derived from identical monocyte/ macrophage precursors. Thus, it could be extrapolated that ABC component in the present case probably represented a similar cystic degeneration occurring inside the CGCL. All these changes might have resulted in the occurrence of these three simultaneous pathological entities. Although the transduction mechanism at the cellular level cannot be stated with certainty, it is nevertheless safe to assume that a common pathophysiological mechanism does play a role in the formation of various hybrid jaw lesions.

Owing to the small number of reported hybrid lesions, their biological behaviour cannot be accurately predicted and hence their management is uncertain. As for the chosen treatment in our case, the surgeon initially tried to be as conservative as possible considering the young

age of the patient. Some authors[14] had previously reported successful management of Non-aggressive CGCL mandible with complete resolution using intralesional steroid injections. However, when the lesion failed to show resolution on intra-lesional steroid use, curettage was accepted to be the most reliable surgical option. The patient had an uneventful healing following the curettage and showed no signs of recurrence. Given the relative paucity of studies reported to date, it would be difficult to determine if the hybrid component in the previously reported cases and the present case is related in any way to the aggressiveness or high recurrence of these lesions. Without further similar research/molecular studies, it is also not possible to determine whether hybrid lesions share a similar potential as the aggressive behaviour of CGCL, but until verified, regular monitoring with long term-follow up is required.

4. Conclusion

The reported case was one of its kind in literature where features of three interrelated entities lesions were present in the same lesion. Histopathological diagnosis of such lesions is frequently driven by the predominant component and their hybrid/mixed nature is often missed. Therefore, a thorough microscopic examination of the histologic specimen is warranted to be able to rule out the possibility of any hybrid lesion. Due to its rarity, the clinical behaviour and treatment strategies of these lesions are yet to be understood. The authors, however, found that the hybrid nature had increased aggressiveness to the lesion and the conservative modalities did not prove beneficial in its management.

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The authors declare that they have no conflict of interest.

All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration.

Informed consent was obtained from patients included in this study.

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