Fibro-osseous lesions vs. central giant cell granuloma: A hybrid lesion

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ABSTRACT

Fibro-osseous lesions of the jaws can have certain histologic features in common with central giant cell granuloma (CGCG) including the presence of multinucleated giant cells. The clinical, radiologic and histologic features of these lesions should be carefully evaluated to distinguish between these conditions. Fibro-osseous lesions of the jaws are a heterogenous group of lesions characterized by the replacement of normal bone by fibrovascular tissue containing newly formed mineralized material. Central giant cell lesions are defined as an intraosseous lesion consisting of cellular fibrous tissue containing multiple foci of hemorrhage and aggregation of multinucleated giant cells. These lesions may sometimes lead to a confusion in their diagnosis as many pathologists report them taking into consideration one of the prominent histopathologic feature. These confusions may be because of the small number of cases reported in the literature with uncertain clinical, radiographic and histopathologic features of these lesions. So even surgeons may end up treating these lesions inadequately or patients may need to undergo multiple surgeries. We report such a case of Juvenile ossifying fibroma associated with CGCG and discuss the clinical, imaging, histologic, and treatment aspects of this hybrid lesion.

Keywords: Central giant cell granuloma, fibro-osseous lesions, hybrid lesion

INTRODUCTION

Fibro-osseous lesions mimicking giant cell lesions are not new. Lesions with features from various pathologies have been reported in the literature. These are called “hybrid lesions”. They are lesions comprising of elements of different pathologies in one lesion. Hybrid lesions comprising of central giant cell granuloma (CGCG) with fibroosseous components are very rare with only seven maxillomandibular cases reported in the literature.10

Fibro-osseous lesions of the jaws are a heterogenous group of lesions characterized by the replacement of normal bone by fibrovascular tissue containing newly formed mineralized material.10 Juvenile ossifying fibroma (JOF) is one among these fibro-osseous lesions. JOF is a fibro-osseous neoplasm that arises within the craniofacial bones in individuals under 15 years of age, and the maxilla is more commonly involved than the mandible. JOF may exhibit erosion and invasion of the surrounding bone accompanied by rapid enlargement. It consists of a cell-rich fibrous stroma, containing bands of cellular osteoid without osteoblastic rimming, together with trabeculae of more typical woven bone. Small foci of giant cells may be present. This lesion is nonencapsulated, but well demarcated from the surrounding bone.15-4

Central giant cell lesions are defined by the World Health Organization as an intraosseous lesion consisting of cellular fibrous tissue containing multiple foci of hemorrhage, aggregation of multinucleated giant cells, and occasionally, trabeculae of woven bone. It mainly occurs in children or young adults with a predilection for females. It is more common in the mandible than in maxilla. The radiologic features range from unilocular to a multilocular radiolucency with varying degrees of expansion of the cortical plates.15-4
These lesions may sometimes lead to a confusion in their diagnosis as many pathologists report them taking into consideration one of the prominent histopathologic feature. So even surgeons may end up treating these lesions inadequately or patients may need to undergo multiple surgeries. These confusion may be because of the small number of cases reported in the literature with uncertain clinical, radiographic, and histopathologic features of these lesions. We report a case of JOF associated with CGCG and discuss the clinical, imaging, histologic, and treatment aspects of this hybrid lesion.

**CASE REPORT**

A 9-year-old boy was referred to our unit. He was complaining of swelling in the left mandibular angle region since 4 months. It was insidious in onset, slow growing, hard and not associated with pain. On extraoral examination the lesion was 4 × 3 cm² and hard on palpation covered with normal skin. There was no history of pain or paresthesia and no previous history of trauma. Intraoral examination revealed a mild expansion of buccal cortical plate posterior to left permanent mandibular first molar with tenderness over lingual cortex distal to first permanent molar and mucosa covering the swelling was intact. The lower border continuity of mandible was maintained with a mild bulge in the lower border in the angle region. Mouth opening was 35 mm [Figure 1].

The orthopantomograph revealed a well-defined unilocular radiolucency with scattered radiopacities with a bony sclerotic margin. The lesion extended anteroposteriorly from the distal root of mandibular deciduous second molar to 1.5 cm anterior to posterior border of mandible, superoinferiorly from superior border of mandible to 1 cm below the lower border of mandible with displacement of second permanent molar tooth bud toward the sigmoid notch [Figure 2].

On aspiration of the lesion about 2 ml of blood mixed serous fluid was collected and sent for biochemical analysis. The biochemical analysis showed the protein content of fluid as 7.8 g/dl. An open biopsy was carried out under local anesthesia. After creating a small window through the thick covering bone on the buccal side of the lesion, a soft tissue specimen was taken out and sent for histopathologic examination.

Histopathologic examination showed the presence of dense cellular fibrous connective tissue with numerous spindle-shaped fibroblasts. Focally numerous multinucleated giant cells and irregular trabeculae of osseous tissue rimmed by plump osteoblasts were evident. A Fine Needle Aspiration Cytology report of the fluid showed a protein content of 7.8 g/dl, and cytosmears revealed the presence of debris. Correlating cytologic and histopathologic features, it was reported as CGCG undergoing tumor degeneration leading to solitary bone cyst [Figure 3].

The decision was made to go for the conservative surgical approach that is curettage of the lesion with the removal of displaced second permanent molar tooth bud. Since the lesion was extending along the ramus, it was found to be difficult to completely enucleate the lesion by the intraoral approach, hence, the decision was taken to go extraorally.

The lesion was approached through submandibular incision and the lesion was curetted [Figure 4]. The displaced tooth was removed. The inferior alveolar neurovascular bundle was not encountered during surgery since it was pushed downward. Perforation of the lingual cortex was observed at a higher level.
than the inferior alveolar canal, and lower border continuity was maintained. Postsurgical recovery of the patient was uneventful. The orthopantomograph taken on the first postoperative day shows the extent of surgical exploration [Figure 5].

The excised specimen was sent for histopathologic examination which revealed the presence of connective tissue exhibiting highly cellular fibrous tissue with monotonous uniform plump fusiform fibroblasts interspersed with variable amounts of osteoid and woven bone predominantly arranged in irregular trabeculae. These bony trabeculae show plump osteocytes, rimmed by hyperchromatic basophilic osteoblasts. Some areas showed the presence of dark basophilic round to irregular calcified bodies. Separate foci of multinucleated giant cells were also found within the stroma. It was reported as JOF of the trabeculated type [Figure 6].

The patient is on regular follow-up. The orthopantomographs at 3 months [Figure 7], 6 months [Figure 8], and 1 year [Figure 9] interval show increased radio-opacity of the defect, and the expanded lower border is regaining its normal contour.

DISCUSSION

Fibro-osseous lesions of the jaws can have certain histologic features in common with giant cell granuloma including the

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Figure 4: Curetted lesion

Figure 5: Orthopantomogram taken on first postoperative day showing extent of surgical exploration

Figure 6: Photomicrograph of curetted lesion (H and E, 40x)

Figure 7: Postoperative orthopantomogram taken at 3 months

Figure 8: Postoperative orthopantomogram taken at 6 months

Figure 9: Postoperative orthopantomogram taken at 1 year
presence of multinucleated giant cells. The clinical, radiologic, and histologic features of these lesions should be carefully evaluated to distinguish between these conditions.\(^{[5]}\) The association of CGCG with the fibroosseous lesions in the maxilla and mandible is a very rare condition with only few cases reported in the literature. CGCG associated with cherubism and Paget’s disease has also been reported.\(^{[1]}\)

In our case the incisional biopsy specimen revealed numerous multinucleated giant cells and plump spindle-shaped fibroblasts in a fibrous connective tissue stroma along with irregular trabeculae of osseous tissue rimmed by plump osteoblasts. This was suggestive of central giant cell granuloma.\(^{[5,7,8]}\) Whereas the final histopathology of the excised tumor showed highly cellular fibrous tissue with mononuclear uniform fibroblasts interspersed with variable amounts of osteoid and woven bone arranged in irregular trabeculae. These trabeculae show plump osteocytes, rimmed by hyperchromatic basophilic osteoblasts. Separate foci of multinucleated giant cells were also found. These features are suggestive of JOF of trabeculated variant.\(^{[2,4,9]}\) In classical CGCG though the multinucleated cells are the most prominent feature, the mononuclear spindle cells are the active cycling compartment. It is believed that spindle cells recruit monocytes and induce differentiation into osteoclastic giant cells through cytokine releases. As it is discussed by Kaplan et al. in their cases, the primary lesion was central ossifying fibroma, on the basis of sex, location, and age they speculated that the primary lesion could be an ossifying fibroma and that through some yet unknown trigger, the mesenchymal spindle cells of the tumor release cytokines that induce differentiation toward osteoclast/giant cells. This results in the formation of the CGCG compartment. Therefore, in our case the primary lesion is a JOF-based on age, sex, and clinical, radiographic and histopathologic features.\(^{[2,8,9]}\) The above-mentioned reaction in the stroma could be the reason for the presence of giant cells in JOF. Giant cells in association with fibroosseous conditions may represent a reaction that stimulates modifications in the stroma of the original tumor. Theoretically, osteoblasts may activate osteoclast type giant cells through paracrine mechanisms.\(^{[1,7]}\)

It is possible that these combined lesions are overlooked by the pathologists and diagnosed according to one of the prominent microscopic features. Because of the small number of these cases, their biologic behavior is uncertain, and so is their treatment.

In our case as the initial biopsy report was CGCG going for cystic degeneration, considering the age of the patient and slow growth of the lesion, we restricted ourselves to a conservative treatment approach. Therefore, we went for thorough curettage of the lesion.

The JOF though non-encapsulated, is well demarcated from the surrounding bone. These lesions have got varied biologic behavior with the recurrence rate ranging from 30% to 50% including some with multiple recurrences.\(^{[2,4]}\) In spite of the high recurrence rate local excision is still recommended. The extent of surgical resection should be dictated by the age of the patient, anatomic location of the tumor, and the effect of tumor on surrounding vital structures.\(^{[9,10]}\) Because in our case the patient was a 9-year-old boy, and also the lesion initially was diagnosed as CGCG going for cystic degeneration, we went for a conservative approach by curettage. As the final diagnosis was JOF, strict follow-up of the patient will be considered.

Because of less number of cases reported in the literature and no specific clinical and radiological features, histopathologic examination remains the main stay for the diagnosis of these lesions.

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