Case Report

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Dentistry Section

Fibrous Dysplasia and Central Giant Cell Granuloma: A Report of Hybrid Lesion with its Review and Hypotheticated Pathogenesis

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ABSTRACT

Benign fibro–osseous lesions (BFOLS) of the jaws are a wide array of lesions that actually represent distinct phases of a single benign morphological process. These lesions share certain histopathological features which are in common with giant cell containing lesions, which include central giant cell granulomas (CGCGs). The association of BFOLS and CGCG has to be critically evaluated, pertaining to their clinical, radiologic and histologic features. Many pathologists diagnose these types of lesions, considering only one of the prominent features. Eventually, surgeons end up treating these lesions inadequately. This ambiguity may be because of very small number of cases have been reported in the literature, with uncertain clinical, radiologic and histologic features. We are reporting a case of fibrous dysplasia (FD) which was associated with a central giant cell granuloma (CGCG) and discussing the hypothetical pathogenesis of giant cells.

Key Words: Fibrous dysplasia, Granuloma giant cell, Hybrid, Dimorphic, Stromal cells, Osteoclasts

INTRODUCTION

Benign fibro–osseous lesions (BFOLS) and giant cell lesions are dimorphic conditions that consist of a fibro-osseous component in common. BFOLS such as Fibrous dysplasia (FD) are developmental tumour like conditions that occur Unilaterally, diagnosed in the second decade of life and are relatively common in the maxillae. Females are less affected than males, with variable radiographic appearances and never crossing the midline. The patients may exhibit a subsequent regrowth of the lesion and this is estimated to be around 25-50%.

CGCG mostly occurs in the younger age group, with a predilection for females, being more common in the mandible and prevalent in the anterior than in the posterior jaws, often crossing the midline and producing an asymptomatic expansion of the cortical plates, with variable radiographic appearances which range from a unilocular to a multilocular radiolucency. It has been suggested to be a reparative than a neoplastic lesion. Its clinical behaviour ranges from an indolent, slow growing, asymptomatic mass to an aggressive lesion that causes pain, root resorption and a tendency to recur after its excision.

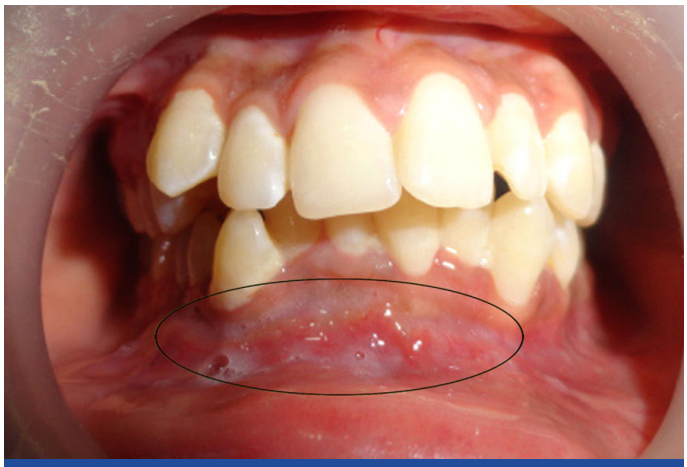
With indifferent clinical and radiologic features, the association of BFOLS and CGCG is always a chance of occurrence. The lesions that present as the elements of different pathologies in one lesion are referred to as “hybrid” lesions. Hybrid lesions which consist of CGCG with fibro-osseous lesions are very rare, with only seven maxilla-mandibular cases being reported in the literature, out of which only one case of CGCG in association with FD has been reported till now.

This may also be because of the negligence of the pathologists in diagnosing the cases by considering only one prominent histopathology feature. With uncertain clinical and radiological features, the histopathological examination remains the main stay of the focus in the diagnosis of these types of lesions. We are reporting a hybrid lesion that consisted of a FD with a CGCG. The uncertainty of these types of lesions, their association, and the presence of giant cells raise a lot of doubts about their origin.

CASE REPORT

An 18 year old female patient reported to the Dental Out Patients Department (OPD) at Sri Sai College of Dental Surgery, Vikarabad, with a swelling that was insidious in onset, slow growing and non-painful, which involved the right angle of the mandible, with a duration of six months. The intra oral examination revealed a lesion which extended from the distal aspect of the lower left canine to the right first molar, causing obliteration of the vestibule, with a swelling which measured approximately 3*1 cm [Table/Fig-1].

The occlusal radiograph revealed a multilocular radiolucency which extended from the mesial side of left mandibular lateral incisor to the right first molar area, crossing the midline, which was in conti-



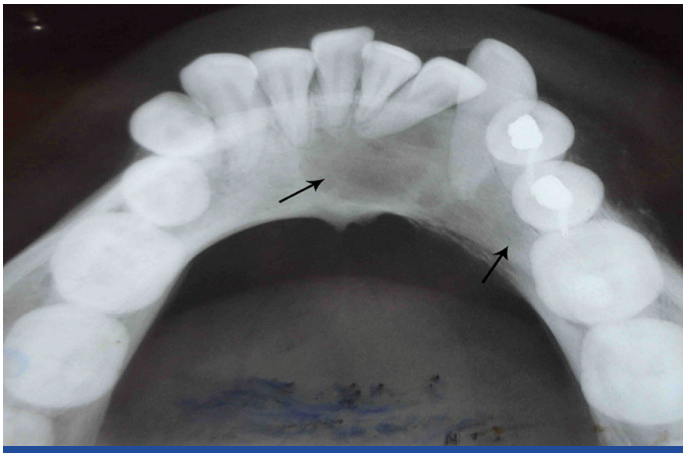
[Table/Fig-1]: Intra-oral view: The lesion is extending from the lower left mandibular canine to the right mandibular first molar area, crossing the mid-line

nuity with the adjacent normal bone [Table/Fig-2]. The orthopantomograph (OPG) revealed a diffuse, multilocular radiolucency which extended anterioposteriorly from the left manibular canine to the right first mandibular molar area, superioinferiorly from the superior border of the mandible to 1 cm below the lower border of the mandible, with root resorption w.r.t to 33-42 and flaring of the roots w.r.t 43-45 [Table/Fig-3].

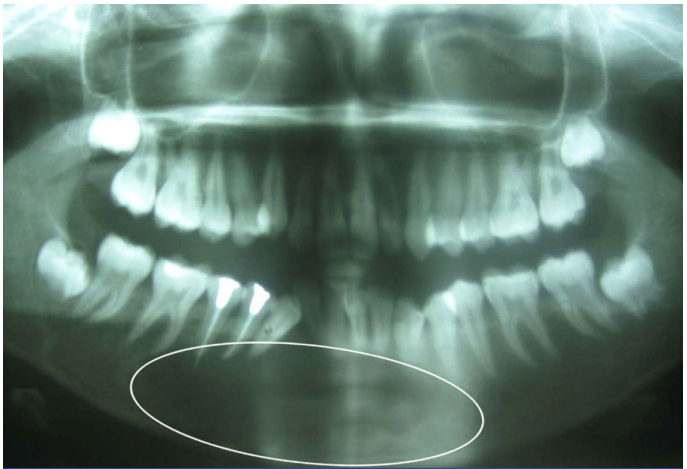
A computed tomography (C.T) scan was carried out and the three-dimensional images showed a well-defined, expansile, destructive, hypodense mass, with thin residual septae like areas [Table/Fig-4]. The routine haemogram and the urine examination were normal.

On aspiration of the lesion, about 1.5 ml of blood mixed serous fluid was collected and sent for a biochemical analysis, that revealed that the serum calcium phosphatase, alkaline phosphatase (ALP) and the parathormone levels were within the normal range, thereby excluding the possibility of hyperparathyroidism. The protein content of the fluid was 7.9g/dl.

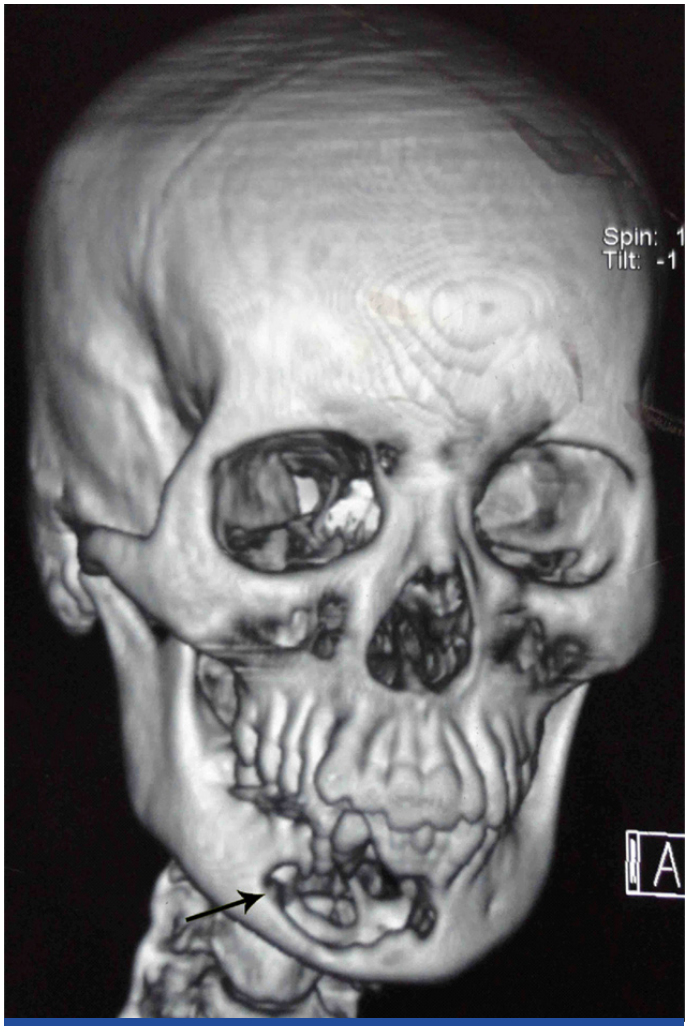
An incisional biopsy was carried out under local anaesthesia, on the buccal side of the lesion, through the thick covering of the bone and a soft tissue specimen was sent for histopathologic analysis. In the gross examination, a tan brown, elliptical tissue which measured 0.5*0.5*1.0 cm, which was hard in consistency, was observed. The microscopic examination revealed irregularly shaped bony trabeculae that were not connected to each other and they had assumed curvilinear shapes (a Chinese letter pattern appearance). These bony trabeculae lacked the osteoblastic border and



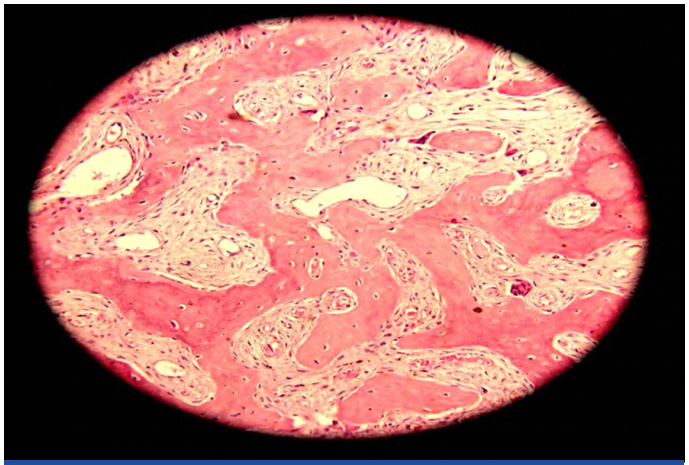
[Table/Fig-2]: Occlusal view: Diffuse multilocular radiolucency with periapical resorption areas i.r.t 32, 31 crossing the midline and extending from 41-46



[Table/Fig-3]: OPG reveals a diffuse, multilocular, radiolucent lesion extending from 34-46, with root resorption and flaring of roots i.r.t 43, 44, and 45



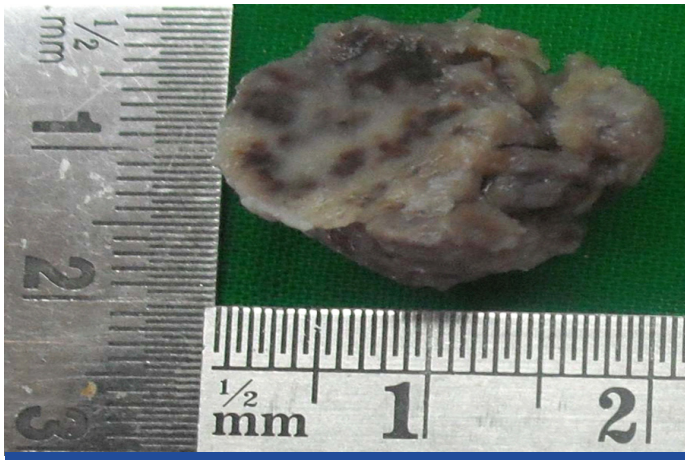
[Table/Fig-4]: C.T scan: Three - dimensional CT volume rendering showing the extension of the tumor



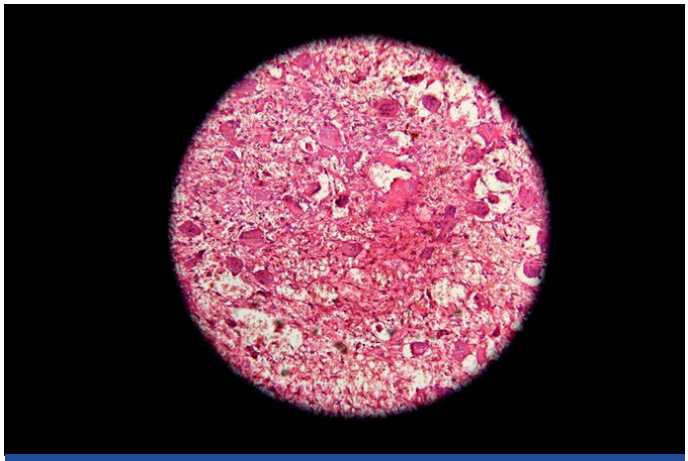
[Table/Fig-5]: Microscopic view of the incisional biopsy specimen showing, interconnecting bony trabeculae that are irregular in shape, lined by osteoblastic rimming at few places and resembling chinese letter pattern. (H&E, 40x)

were arranged in the fibrous stroma with extravasated erythrocytes [Table/Fig-5]. It was reported as Fibrous dysplasia.

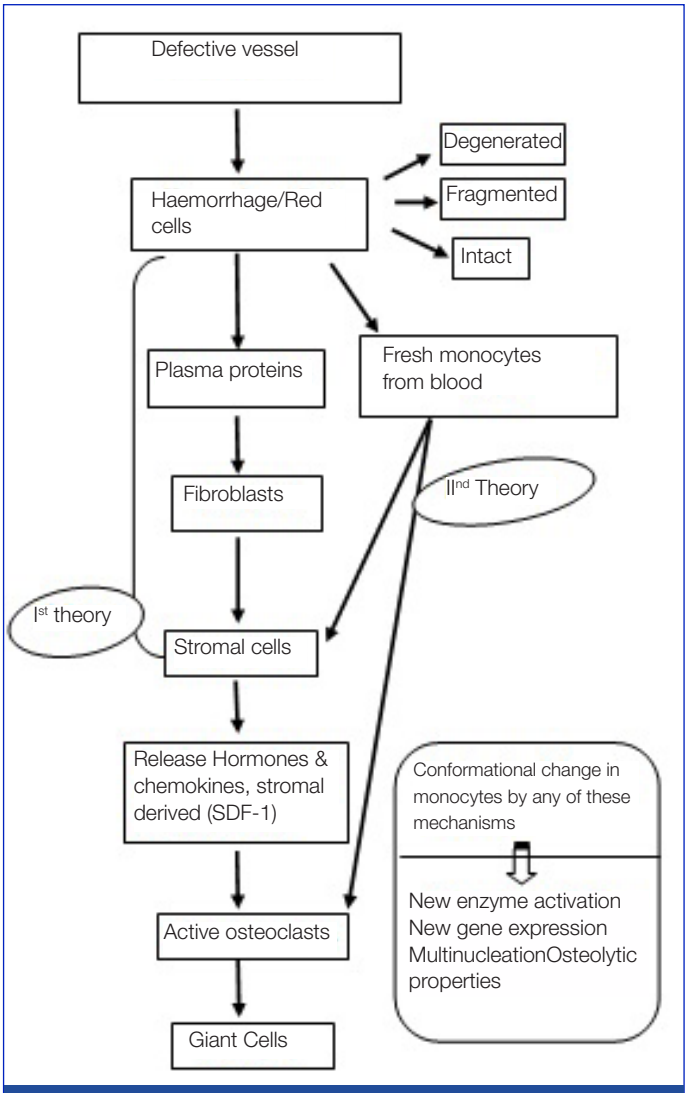
Based on the histopathological diagnosis, a decision was made to excise the whole lesion and it was sent for a histopathologic examination. The gross specimen consisted of a soft tissue mass which was approx 2*2*1.5 cm in dimension and brown in colour at one end and blackish white at the other end, with irregular borders and it was soft to firm in consistency [Table/Fig-6]. The specimen was sectioned into two and sent for a histopathological analysis. The histopathological examination of the excised specimen revealed



[Table/Fig-6]: Macroscopic specimen: A soft tissue mass brown to blackish white in color with regular borders, smooth in surface and firm in consistency



[Table/Fig-7]: Microscopic view of the excisional biopsy specimen showing abundant giant cells in a fibrous stroma along with fibro-histiocytic proliferation (H&E, 40x)



[Table/Fig-8]: Hypothecated mechanism of pathogenesis of giant cell formation

abundant giant cells in a fibrous stroma along with vesiculated fibrohistiocytic proliferation. Evenly dispersed giant cells, each having 2 to 8 nuclei in them, which were in close approximation with the proliferating blood vessels, which were admixed with areas of haemorrhage, were observed [Table/Fig-7]. On the high power field (HPF), 2-3 giant cells were seen.

Few newly forming bony trabeculae with a prominent osteoblastic rimming and osteoid formation were also observed. The tumour mass had infiltrating margins and residual bony spicules towards the periphery. The bony trabeculae displayed a curvy pattern without any osteoblastic rimming in few areas of the peripheral lesion. It was reported as a central giant cell granuloma. The histological aspects pointed to a diagnosis of a central giant cell granuloma which was associated with a benign fibro-osseous lesion, a Fibrous dysplasia.

DISCUSSION

Making a differential diagnosis among these BFOLS is very difficult, as these lesions do not present a well defined behaviour. A substantial correlation between the patient history, the clinical features, the imaging findings and the histopathology is necessary. The case which is being reported here, consisted of two different lesions, one, a fibrous dysplasia and the other, a central giant cell granuloma. The concomitant presence of one entity with other lesions, compelled the authors to think about the de-facto existence. Fibrous dysplasia is a rare lesion which occurs in the mandible and it is more common in men [1,2]. The case which is being described here was unique with respect to its location and gender prelidiction. The lesion in our case was observed in the mandible and in a female patient.

Histologically, Fibrous dysplasia shows irregularly shaped bony trabeculae that are not connected to each other. These trabeculae show a Chinese letter pattern appearance . These bony trabeculae lack osteoblastic borders and are arranged in the fibrous stroma along with extravasated erythrocytes and few giant cells. The lesional tissue which fuses with the adjacent uninvolved bone is typical of a fibrous dysplasia.

CGCG is composed of two distinct populations of cells viz. multi nucleated giant cells (MGCs) and spindle shaped stromal cells [2-9]. The latter are thought to be proliferating tumour cells and they form the active cycling compartment. Histologically, in a giant cell containing lesion, haemorrhage occurs with intact areas of frank or partially degenerated RBCs and numerous MGCs and spindle cells are also observed in the stroma, along with mononuclear fibrohistiocytic cells [9,10].

The presence of multi nucleated giant cells (MGCs) that are common to both a FD and a CGCG can help us in understanding the nature of the giant cells. Although the aetiopathogenesis of CGCG of the jaw bones has not yet been established, it was suggested that it could be the result of an exacerbated reparative process which was related to some previous trauma and an intraosseous haemorrhage

that had triggered the reactive granulomatous process [11,12]. The association of t(X; 4) (q22; q31.3), was also suggested as an aetiology of CGCG [13].

Although, the nature and the origin of giant cells have been discussed by many authors, the concept of a giant cell origin is still not obscure. One of the proposed hypotheses (I st theory) for the giant cells was a haemorrhage [14]. If the bony matrix of the vessel was weak or defective, it could result in a haemorrhage that could be in the form of intact, fragmented or degenerated red blood cells. This could provide plasma proteins, that could further stimulate the fibroblasts and eventually activate the stromal cells, which in turn could facilitate their conversion into osteoclasts that could give rise to giant cells.

The other hypothesis (II nd theory) was also a hemorrhage, but it could directly provide fresh monocytes from the blood, that could get activated in turn and proliferate into stromal cells. These stromal cells release chemokines such as interleukin-1 (IL-1) and proteases that further cause recruitment of the monocytes and get transformed into osteoclasts, and eventually into giant cells [Table/Fig-8] [14].

The stromal derived factor (SDF-1) is a significant chemoattractant which is involved in the recruitment of the haematopoietic osteoclast precursor cells (monocytes) during osteoclastogenesis. They also recruit monocytes and induce their differentiation into osteoclastic giant cells through the release of cytokines [15,16]. There may be some conformational changes in the monocytes that can occur because of the activation of new enzymes, the expression of new genes or due to multinucleation or osteolytic properties.

The mononuclear stromal cells may be the precursors of MGCs that may show characteristics of the osteoclast phenotype and a similar kind of pathogenesis may be involved in the formation of MGCs in the other giant cell containing lesions of the jaws.16, 17 They induce osteoclast formation from the mononuclear blood cells via the RANKL-RANKL interaction. The RANKL which is present on the stromal cells influences the differentiation of the giant cells from RANK, that expresses mononuclear cells [17].

It can also be proposed that giant cells can also arise from the stromal elements and react with the epithelial elements, which may behave as foreign bodies [18].

When the giant cell lesions are associated with fibrous dysplasia or other fibro-osseous conditions of the jaws, the association of these giant cells may represent a reaction that may eventually stimulate the necessary stromal changes within the original lesion. This stromal change could involve the osteoblasts, who have the capacity to activate the osteoclasts into giant cells through a paracrine mechanism [10,18,19].

CONCLUSION

Since very few cases have been reported in the literature, the information on the enigmatic association of a FD with a CGCG is obscure. The clinical, radiographic and the histologic features which have been described here, may contribute to the further diagnosis of new cases. The clarity to their adjunctive association, that is very lucid, will now become very obvious, when more cases are reported in future .They may also lead us to understand the interrelationship between them in a better way. By examining and investigating them properly, a definitive diagnosis can be established.

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