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Fibrous Dysplasia and Ossifying Fibroma - an advent in their diagnosis

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Abstract

Objectives: Fibro-osseous lesions of the craniofacial complex comprise of a diverse, interesting and challenging group of conditions that pose difficulties in classification and treatment. The two most confused benign fibro-osseous lesions are fibrous dysplasia and ossifying fibroma. Sometimes, the classic clinical, radiologic or pathologic features of fibrous dysplasia or ossifying fibroma may not be evident, but overlapping features of both may be seen. The dilemma in diagnosis of these lesions rests in the bony trabeculae as well as in the fibrous stroma. Cases of fibrous dysplasia showing lamellated bony trabeculae and osteoblastic rimming have been reported which may confound diagnosis because of resemblance with ossifying fibroma. In the present study, an attempt has been made to demonstrate the fibrous element of these two lesions using histochemical stains.

Study design: The sections of fibrous dysplasia & ossifying fibroma were stained with Haematoxylin and Eosin, Trichrome stain and Peracetic acid-aldehyde fuschin-modified Halmi stain.

Result: The study revealed that the oxytalan fibers were more numerous in ossifying fibroma (seen with both Trichrome and modified Halmi stains).

Conclusion: Although the ultimate diagnosis of fibrous dysplasia and ossifying fibroma is arrived at by correlating clinical, radiographic and routine histopathologic examination, the differences in the configuration of the stroma using histochemical stains may help in the diagnosis of these two lesions.

Key Words: *Fibro-osseous lesions, fibrous dysplasia, histochemical diagnosis, ossifying fibroma.*

Introduction

Fibro-osseous lesions comprise of a diverse, interesting and challenging group of conditions that pose difficulties in classification and treatment (1, 2). Some benign fibro-osseous lesions of the craniofacial complex are unique to that location, whereas, others are encountered in bones from other regions (3, 4). All these lesions share common histologic features in that the bone is replaced by fibrous cellular tissue composed of collagen fibers and fibroblasts containing variable amounts of substance which may be bone or cementum-like in appearance (1, 5). Whereas, some of these lesions are diagnosable histologically, most require a combined assessment of clinical, microscopic and radiographic features (6).

The two most confused benign fibro-osseous lesions are fibrous dysplasia and ossifying fibroma. Sometimes, the classic clinical, radiologic or pathologic features of fibrous dysplasia or ossifying fibroma may not be evident, but overlapping features of both may be seen.

Fibrous dysplasia is first diagnosed in infancy and childhood (7), mainly in the first and second decades (8). It affects females predominantly and commonly affects the maxilla, presenting itself as a slow growing painless swelling which produces progressive destruction (9). The radiographic picture varies with the maturity of the lesion. Early lesions are largely radiolucent. Lesions showing uniform calcification may show the classic ground-glass appearance but mature lesions show discrete areas of radiopacity. In Haematoxylin and Eosin (H&E) sections, the metaplastic bone is in the form of irregular, feathery, Chinese letter pattern, woven trabeculae with expansile diffuse blending of the margins and occasional osteoblastic rimming (8). The delicate fibrous connective tissue stroma is arranged in a whorled pattern (1).

Ossifying fibroma which is commonly seen in the third and fourth decades (2,8,10,11) and affects females predominantly (8) represents a neoplastic process that presents with expansion of the buccal and lingual cortices & in larger lesions may expand the inferior surface of the mandible (2,12,13). It is seen mainly in the premolar and molar regions of the mandible (2, 8-11) and follows a painless course (9). Radiographically, it appears initially as relatively well-demarcated radiolucency and later more radio-opaque and relatively less well localized (12). In H&E sections, the metaplastic bone is in the form of numerous small trabeculae of lamellar bone which sometimes join to form a large solid mass with a smooth periphery and an osteoblastic rimming. The fibrous stroma reveals haphazard orientation of collagen fibers (10).

Ossifying fibroma and fibrous dysplasia are the most common fibro-osseous lesions, which may be associated with significant cosmetic and functional disturbances. They show distinct patterns of disease progression (13) and as the treatment and prognosis differs for both (14-16), it is important to distinguish between the two (13). The dilemma in diagnosis of these two fibro-osseous lesions rests in the bony trabeculae as well as in the fibrous stroma. Harrison (5), Berger & Jaffe (7), Waldron (8), Harris et al (17) and Cooke (18) reported cases of fibrous dysplasia showing lamellated trabeculae and osteoblastic rimming. These may resemble those of ossifying fibroma and may pose a difficulty in diagnosis.

Objectives

The aim of this study is to differentiate the fibrous dysplasia and ossifying fibroma using histochemical stains.

Materials and Methods

Five cases each of fibrous dysplasia and ossifying fibroma were obtained from the archives of the Department of Oral Pathology and Microbiology. The clinical and radiographic findings of these ten cases are presented in

Case No.	Age	Gender	Site	Radiographic appearance	Clinical diagnosis
1	17	Female	Maxilla	Mixed lesion, predominantly radiolucent	Fibrous dysplasia
2	40	Male	Maxilla (Fig. 1)	Mixed lesion, predominantly radiopaque (Fig. 2)	Fibrous dysplasia
3	24	Female	Mandible	Radiolucent lesion	Fibrous dysplasia
4	35	Male	Maxilla (Fig. 3)	Mixed lesion, predominantly radiopaque (Fig. 4)	Fibrous dysplasia
5	27	Female	Maxilla	Mixed lesion, predominantly radiolucent	Fibrous dysplasia
6	40	Male	Mandible	Predominantly radiopaque	Ossifying fibroma
7	26	Female	Maxilla	Radiolucent lesion	Ossifying fibroma
8	40	Female	Mandible	Mixed lesion predominantly radiopaque (Fig. 5)	Ossifying fibroma
9	35	Male	Maxilla	Mixed lesion	Ossifying fibroma
10	24	Female	Mandible	Mixed lesion, predominantly radiolucent	Ossifying fibroma

Table 1. *Clinicoradiographic presentation*

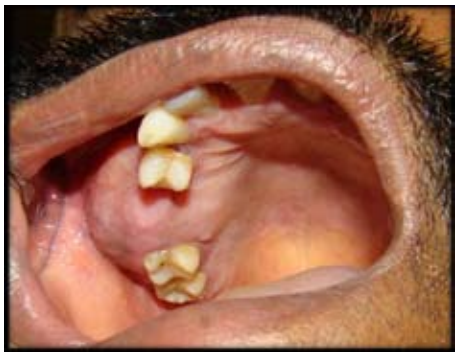

Fig. 1. *Clinical photograph of Case 2 – smooth expansile mass seen on right side of the maxilla measuring 3cm X 4cm extending from distal of first premolar to mesial of third molar*

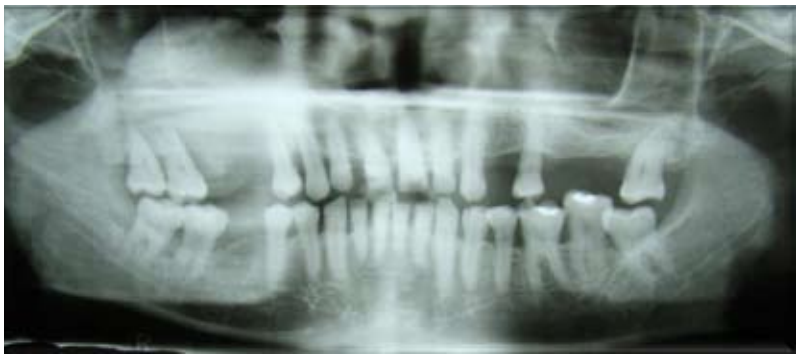

Fig. 2. *Panoramic view of Case 2 – well-defined dome-shaped, homogenous radiopacity seen in the right maxillary posterior region. Floor of the maxillary sinus on this side is not evident.*

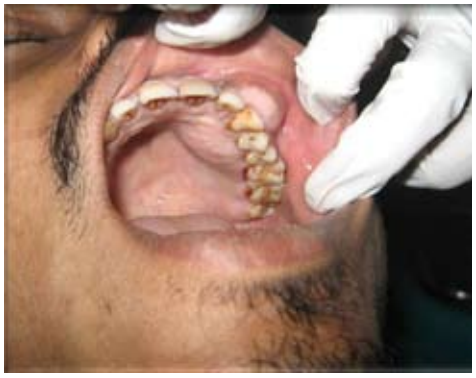

Fig. 3. *Clinical photograph of Case 4 – swelling seen on the left side of the maxilla extending from canine to second premolar causing expansion of the buccal and lingual cortical plates.*

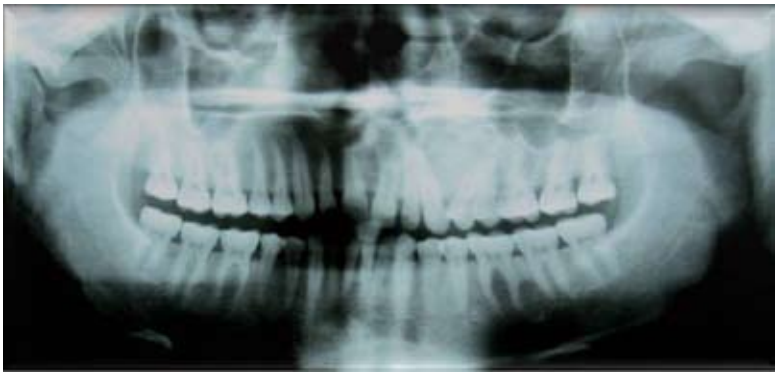

Fig. 4. *Panoramic view of Case 4 – diffuse mixed lesion which is predominantly radiopaque causing divergence of the roots of left maxillary canine and left maxillary first premolar.*

Table 1. The sections were stained with Haematoxylin and Eosin, Trichrome stain and Peracetic acid-aldehyde fuschin-modified Halmi stain.

Results

Trichrome stain – Collagen appeared bluish green; bone appears greenish red in fibrous dysplasia (Fig. 6) and red in ossifying fibroma (Fig. 7) while oxytalan fibers appear reddish brown.

Peracetic acid-aldehyde fuschin-modified Hami stain – collagen appears green; bone appears green in fibrous dysplasia (Fig. 8) and purple in ossifying fibroma (Fig. 9) while oxytalan fibers appear purple.

On comparing the two lesions, if was found that the oxytalan fibers were more numerous in ossifying fibroma (seen with both Trichrome and modified Halmi stains).

Discussion

Fibro-osseous lesions usually present a diagnostic dilemma for the clinicians as well as the pathologists. A variety of investigations have been made in an effort to clarify the problem.

Fibrous dysplasia is a genetic non-inherited condition caused by missense mutation in the gene GNAS1 on chromosome 20, that encodes the alpha subunit of the stimulatory G protein-coupled receptor, Gsα. Fibrous dysplastic lesions have characteristic changes in bone matrix organization, in expression of certain non-collagenous proteins of the extracellular matrix, and in mineralization; and the mutated cells within the lesion are morphologically altered (19, 20). Critical to the diagnosis is the fact that fibrous dysplasia fails to manifest any discrete margins; rather the lesional bone subtly blends into the surrounding normal appearing bone (3, 6, 11). Ultrastructural and biochemical studies have suggested that the fibroblastic component of fibrous dysplasia is related to the osteogenic lineage (21, 22). However, the precise molecular biologic evidence for this has not yet been presented (13).

Ossifying Fibroma is a relatively slow-growing lesion in which the overlying cortical bone and mucosa remain intact and thus the tumour may be present for a number of years before a diagnosis is made. No histopathologic features are available to determine the potential aggressivity of the lesion or its tendency to recur (23). Very few molecular studies have been reported for the ossifying fibroma group of lesions. There have been reports that identify mutations in HRPT2, a gene that encodes parafibromin protein (6).

Until 1948 it was believed that fibrous dysplasia and

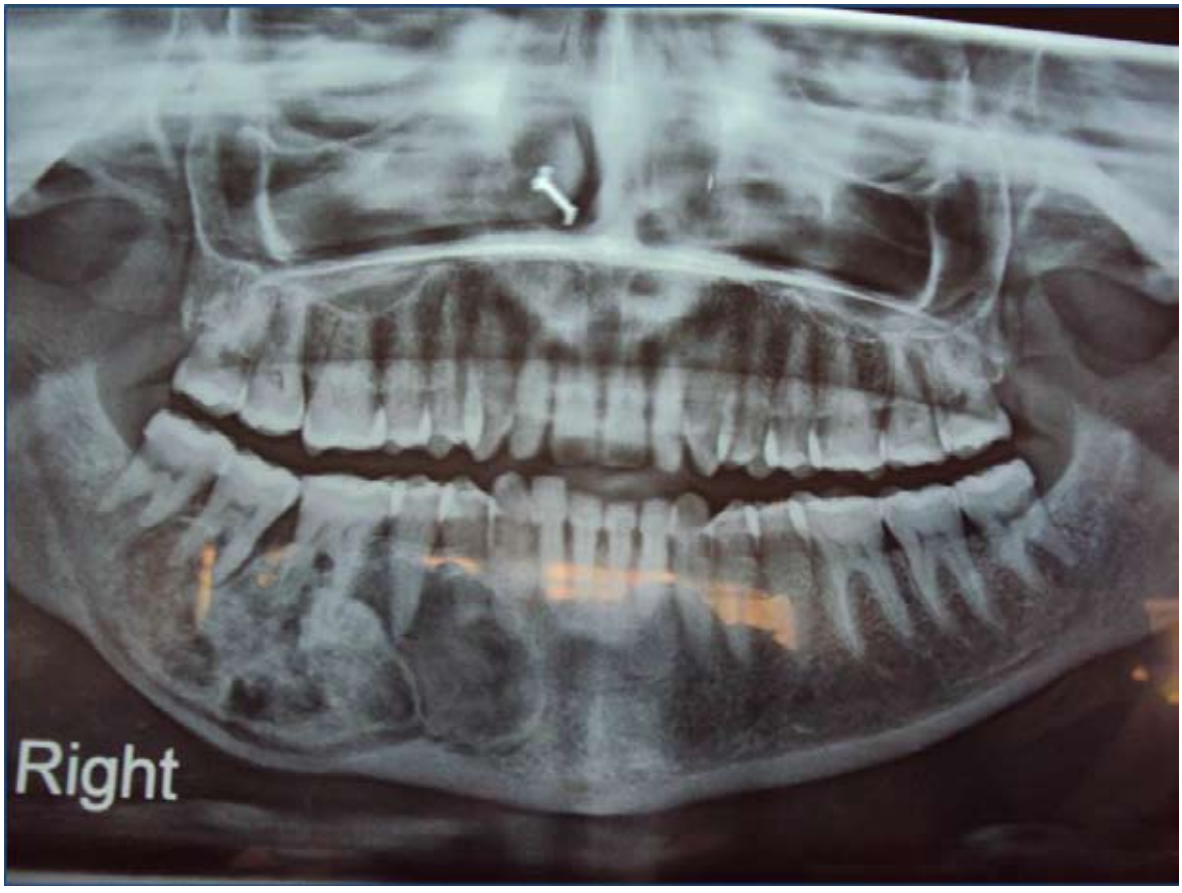

Fig. 5. *Panoramic view of Case 8 – well-defined mixed lesion with predominant radioopaque areas extending from right mandibular canine to mesial of right mandibular third molar.*

ossifying fibroma were either the same entity or variants of the same lesion (24). Studies by Toyosawa et al demonstrated that immunohistochemical analysis of osteocalcin and PCR analysis of GNAS mutations are useful methods in differentiating between the two, and furthermore suggest that they are probably distinct disease entities (13).

It is generally assumed that in the jaws certain fibro-osseous "tumours" and "dysplasia" may arise from either the periodontal membrane or the endosteum because all of these contain fibrous tissue capable of proliferation (25). The fibrous connective tissue of the periodontal membrane is composed chiefly of collagen fibers, oxytalan fibers, mucopolysaccharides and cells which have the capacity of synthesising bone, cementum and fibrous tissue. Under pathologic conditions, such blastic cells are capable of producing tumours composed of cementum, lamellar bone and fibrous tissue (9, 10, 26).

Lille and Fulmer (1958) reported a previously undescribed connective tissue fibre in the periodontal membrane and gingiva and named it oxytalan fibre. It is derived from a Greek word meaning "acid enduring" or "acid resisting" as these fibers are resistant to acid hydrolysis. These fibers were disclosed accidentally after sections of human periodontal membrane were stained with aldehyde fuschin following peracetic acid oxidation (27, 28).

Oxytalan fibers have been reported in various pathologic conditions such as fibrous dysplasia, ossifying fibroma (25) and rarely in dental granulomas, radicular cysts (29) and ameloblastomas (30). Few workers have analysed cases of fibro-osseous lesions and found that oxytalan fibers were present in most of these lesions regardless of their origin, along with mature collagen fibers. They observed more oxytalan fibers in ossifying fibroma than in fibrous dysplasia. Studies by Hamner, Scofield and Cornyn on fibro-osseous lesions showed greater amount of oxytalan fibers in the lesions of periodontal membrane origin compared to fibers seen in fibro-osseous lesions of endosteal origin (25).

In the present study, the basic hard tissue configuration is that of woven bony trabeculae, lamellated bony trabeculae or anastomosing curvilinear trabeculae, while the connective tissue stroma varies from delicate fibrillar to myxomatous areas. With the use of peracetic acid-aldehyde fuschin and trichrome staining, the results of the present study support the views of Hamner and Fullmer with the presence of greater amounts of oxytalan fibers

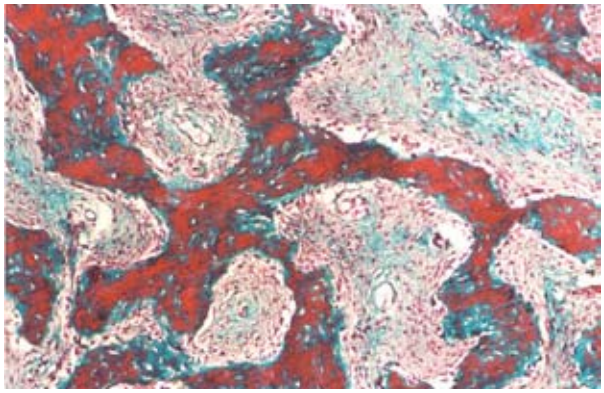

Fig. 6. *Fibrous dysplasia – collagen appears bluish-green, bone appears greenish-red and oxytalan fibers appear reddish-brown (Trichrome stain, x10).*

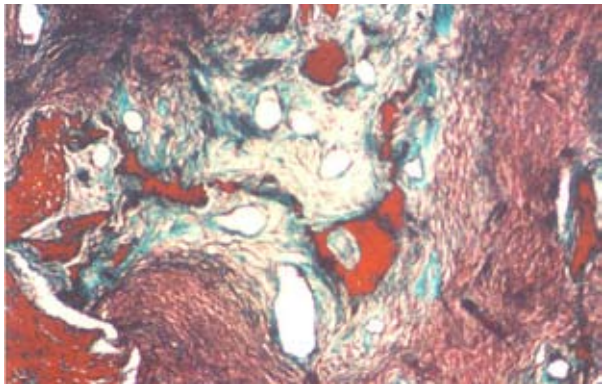

Fig. 7. *Ossifying fibroma – collagen appears bluish green, bone appears red and oxytalan fibers appear reddish-brown (Trichrome stain, x10).*

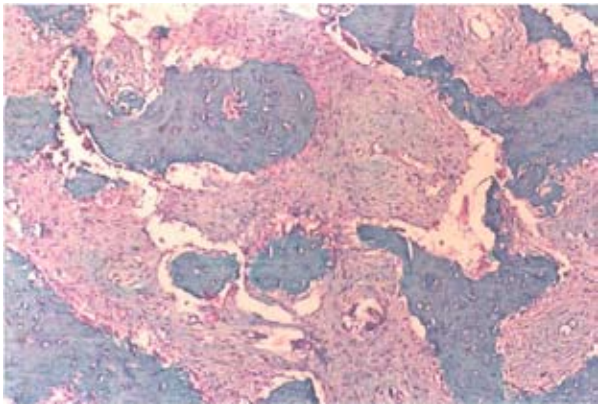

Fig. 8. *Fibrous dysplasia – collagen appears green, bone appears green and oxytalan fibers appear purple (modified Halmi stain, x10).*

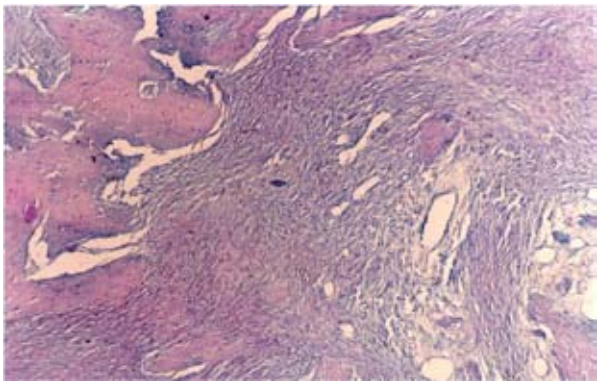

Fig. 9. *Ossifying fibroma – collagen appears green, bone appears purple and oxytalan fibers appear purple (modified Halmi stain, x10).*

in ossifying fibroma than fibrous dysplasia. Probably, the demonstration of the fibrous elements in both the disease entities by histochemical methods may be an additional aid to the pathologists in solving the thorny problem of diagnosis of these two fibro-osseous lesions, provided, the bony configuration in both is that of lamellated bone which may have led to an erroneous diagnosis of ossifying fibroma. This may also give a conclusive evidence of their origin.

Thus to conclude, though the ultimate diagnosis of fibrous dysplasia and ossifying fibroma depends on the correlation of clinical, radiographic and routine histopathologic examination, the differential stromal configuration observed with histochemical stains may serve as a marker in the diagnosis of fibrous dysplasia and ossifying fibroma in the absence of molecular evaluation, as well as an insight into their origin.

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