Case Report

Fibrous dysplasia or ossifying fibroma: diagnostic dilemma in the cranio facial region -a case report

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Abstract

Fibrous dysplasia and ossifying fibroma are common benign fibroosseous lesions. Differentiating fibrous dysplasia and ossifying fibroma in craniofacial bones needs detail clinical, radiological and histological examination as the treatment modalities for both the lesions differ. Presentation of the following case could clarify the overlap in the diagnosis of these pathological entities thereby helping in making a definitive diagnosis of these lesions for therapeutic considerations.

Key Words: Fibrous dysplasia, ossifying fibroma

Introduction

Fibrous dysplasia and ossifying fibroma are the most common Benign Fibro-osseous bone lesions (BFOLs)[1] which may be associated with significant cosmetic and functional disturbances[2]. These lesions demonstrate replacement of normal bone by fibrous connective tissue with an admixture of mineralized product including osteoid, mature bone, and/or cementum-like calcifications[1, 2].

Differentiating Fibrous dysplasia from Ossifying fibroma is not easy as there is no universally accepted criterion for distinguishing these lesions. Controversy in distinguishing one from another persisted and continues to persist. Nevertheless an emphasis on the diagnosis of these entities has been made on the basis of comprehensive clinical, radiological, intraoperative and histological findings[3]

Case report

A 51 year old male patient, agriculturist by occupation, came to the Department of Oral Medicine and Radiology at Manipal College of Dental Sciences, Manipal with the complaint of swelling on his upper right jaw for about a month and half. He was first made aware of the facial asymmetry by his local doctor about 15 years back. Following which there was a gradual increase in the size of the swelling to its present size. On extraoral examination diffuse swelling was seen approximately 1 x 1.5 cm on right maxillary region (Fig. 1a). There was no obliteration of nasolabial fold and the overlying skin was apparently normal. On palpation the lesion was bony hard in consistency. Intraorally, swelling on the right maxillary alveolar ridge was appreciated, approximately 4x3 cm in size extending from distal of 14 to mesial of 18, obliterating the buccal vestibule and extending lcm palatally (Fig.1 b). There were no apparent changes in the mucosa adjacent to the swelling. Lesion was bony hard in consistency with buccal and lingual cortical plate expansion and was fixed to the underlying structures.

Orthopantomogram, PNS and dentascan were carried out for further investigations. Orthopantomogram radiograph revealed well defined, homogenous radiopacity with respect to the right maxillary posterior region which was approximately 3x4 cm in size. Extending from mesial of 13 to distal of 18 and superiorly extending till middle of right maxillary sinus and inferiorly, till half of the crown of 17(Fig.2). PNS view revealed well defined radiopacity encroaching right maxillary sinus (Fig. 3). Dental scan on the Axial section of maxilla (Fig.4a) revealed radiopacity extending from 14 to 18 of size 4 x2 cm size with buccopalatal cortical plate expansion and area of irregular radiolucency with respect to 15 causing discontinuity in the buccal cortical plate outline. Coronal section of the maxilla (Fig.4b) revealed mixed area of

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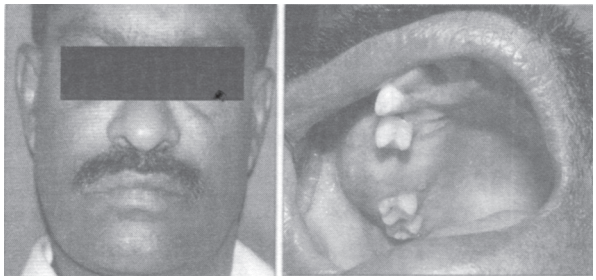

Fig. 1 (a) Facial asymmetry with diffuse swelling in middle one third of right side of the face (b) Large right posterior maxillary swelling with buccal and palatal cortical plate expansion

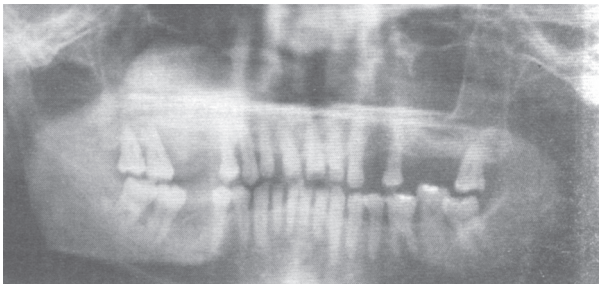

Fig. 2 - Orthopantomogram with dome shaped homogenous radioopacity over the corresponding right maxillary posterior region.

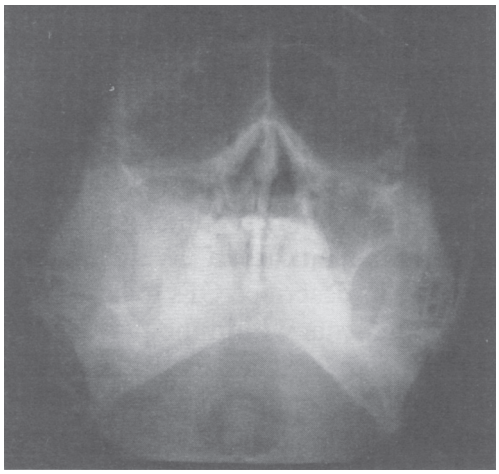

Fig. 3 — PNS view revealing well defined radiopacity encroaching right maxillary sinus.

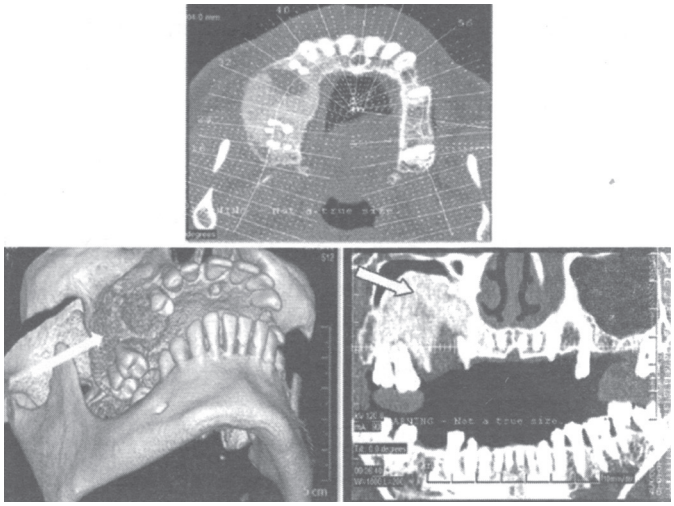

Fig. 4- (a) Dental scan on the Axial section of maxilla revealing radiopacity with buccopalatal cortical plate expansion and area of irregular radiolucency with respect to 15 causing discontinuity in the buccal cortical plate outline. (b) Coronal section revealing mixed area of radiopacity and radiolucency mesiodistally.

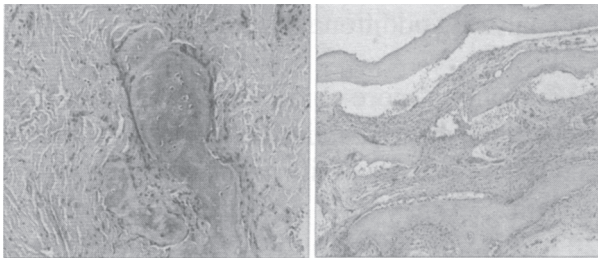

Fig. 5- (a) Photomicrograph showing irregular trabeculae of woven bone with osteocytes within the lacunae and absence of osteoblastic riming (b) Lamellated bones arranged in parallel arrays (x40)

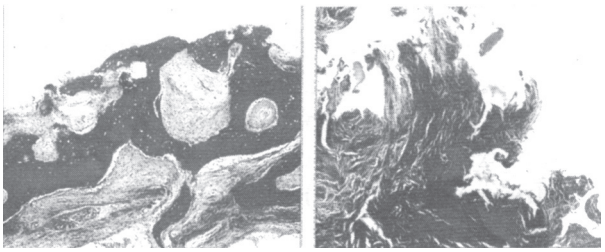

Fig. 6 -(a) Photomicrograph of Mature bone stained with Masson's Trichrome showing red stain (b) Immature bone stained with Masson's Trichrome showing green stain

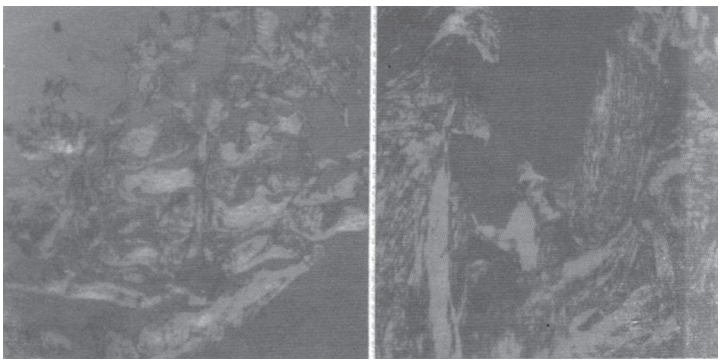

Fig. 7 - (a) Photomicrograph showing mature collagen stained with Picrosirius red showing bright red yellow birefringence (b) Immature collagen stained in Picrosirus red showing greenish birefringence.

radiopacity and radiolucency extending from the 14 to 18 region mesiodistally. The lesion extended from the alveolar ridge to the maxillary sinus approx 4 by 3 cm in size and areas of radiolucency was observed with respect to 15.

Clinical provisional diagnosis was given as Ossifying fibroma or Fibrous dysplasia and the patient was kept for follow up as he was not willing to undergo biopsy. Patient revisited after 2 months to Department of Oral Medicine and Radiology. There was no apparent change in the size on the lesion. Radiographic evaluation revealed slight increase in the radiopacity over the lesion. Curettage was done as the lesion was firmly fixed and was sent for histopathological examination.

Histological examination revealed areas of woven to lamellated boney trabaculae (Fig. 5a and b) with osteocytes within the lacunae. The trabaculae showed absence of osteoblastic rimming. The stroma was moderately cellular with minimal vascular spaces.

Furthermore histochemical evaluation was done using special stains like Masson Trichrome and Picrosirius. Masson Trichrome stain was used to evaluate the mineralised tissue and stromal elements. Lamellar mature bone showed parallel lamellations in trichrome stain which took up red stain (Fig. 6a) whereas immature woven bone was appreciated blending into fibrous stroma and took up green stain (Fig.6b). Similarly Picrosirius stain was used with polarising microscope for distinguishing mature from immature collagen. Mature bone showed bright red yellow birefringence (Fig 7a) whereas the immature woven bone showed greenish birefringence (Fig.7b). Based on the clinical, histological and histochemical findings, the diagnosis was more in favor of fibrous dysplasia, perhaps of long standing duration.

Discussion

Fibrous dysplasia (FD) is a sporadic benign skeletal disorder that can affect single bone (monostotic form), or multiple bones (polyostotic form). Although the exact cell of origin remains unclear, it seems that FD is derived from osteoprogenitor, fibroblast like cells[4]. It has been determined that both monoostotic and polyostotic FD have the same causal genesis, an activating, somatic mutation in the GNAS1 gene found on chromosome 20q13[5,6], that encodes the alpha subunit of the stimulatory G protein-coupled receptor, Gsa. The activating mutations ,occur post-zygotically, replacing the arginine residue amino acid with a cysteine or a histidine amino acid[7,8]. The mutations lead to constitutive activation of adenylyl cyclase, resulting in a persistent elevation of cyclic adenosine monophosphate. This, in turn, induces an alteration in the transcription and expression of several downstream target genes, including cfos, a proto-oncogene[9]. The systemic manifestations of the mutated Gsa protein coupled receptor complex include autonomous function in bone through parathyroid hormone receptor. The extent of the disease is related to the stage at which the post-zygotic mutation in Gsa had occurred, whether during embryonic development or postnatally[8].

Ossifying fibroma (OF) is considered to be true benign fibro-osseous neoplasm that develops mainly within the jawbones. Although the cell of origin remains unknown, Waldron and Giansanti in 1973[10] described OFs to have been derived from elements within the periodontal ligament cells. However, since similar appearing lesions arise in other cranial bones and much less commonly in the long bones, the exact origin of OFs remains unclear. A study by Sawyer et al.[11] in orbital OFs exhibited balanced translocations with recurring breakpoints at Xq26 and 2q33. Moreover, Dal CM et al.[12] also reported a mandibular OF with an interstitial deletion on chromosome 2 between q31-32 and q35-36. These findings are further needed to be confirmed by analyzing additional tumors.

OFs develop more commonly in females than males and have a peak incidence during the third and fourth decades of life and shows progressive growth[13]. FD has equal gender predilection about 20 to 25% of monostotic form affects the head and neck region and 40 to 60 % of polyostotic form affects the skull and facial bones[14]. The active growth of FD typically slows or ceases around the time of puberty or after skeletal maturation possibly because the burden of mutated cells in FD frequently declines with age, shifting the balance of transformed to normal cells towards predominance of normal cells, resulting in arrest of FD[15]. However, sporadic periods of regrowth have been reported in adulthood[16, 17] which is similar to our case report where in the patient was aware of the lesion since 15 years with slow increase in size of the lesion to its present size. This may be mainly attributed to the growth factors and hormonal changes, which can reactivate the lesion.[18] This nature of FD also firmly dispells the notion of FD as a simple hamartoma[17].

OFs are common in premolar-molar region of mandible whereas FD are diffuse hard swelling common in

maxilla[2] which further supports our case wherein the lesion was diffuse hard present in maxilla.

Radiographically OFs are cystic lesion (unicystic or multicystic) and mixed-density lesion while older lesion can be radiopaque with relatively smooth, well defined and mostly corticated borders[19]. FD radiographically depends on stage of development and amount of bony matrix within the lesion. It may appear well defined and radiolucent, whereas later lesions may appear largely sclerotic. Classic FD has a ground-glass or orange-peel appearance, with poorly discernible borders that appear to blend in with the surrounding, unaffected bone Where as in chronic cases, the lesion tends to become increasingly more radiopaque[20]. However Singer et al[18]. and Kharat et al.[21] reported FD with well defined borders in mandible and maxilla respectively, which is in accordance with our case. They attributed this to superimposition of the border of the expansile portion of the lesion present over the mandibles[18] which may also be acceptable in our case thus suggesting FD can also show well defined borders.

Histologically FD comprises irregular trabeculae of woven bone, blending into the surrounding normal bone and lying within a cellular fibrous stroma (Fig. 5a) with osteoblast progenitor cells resembling fibroblast. The bony trabecula are not connected to each other, and are not rimmed by osteoblasts. Early craniofacial FD is characterized by minimally mineralized deposits of woven bone with a continuum progressive lamellation of the woven bone trabeculae as FD become more mature (Fig. 5b) which is in contrast to FD of long bones where mature lamellar bone is not found. These differences between the mineralization of FD of long bones and of craniofacial membranous bones may be owing to the fact that these two embryologically distinct types of bones are under different inductive influences during development[22, 23]. In contrast to these finding of is a well-circumscribed, occasionally encapsulated mass which shells out in toto during surgical exploration[3] which often is a characteristic feature of OFs. OFs may show a variety of different microscopic patterns, depending on the stage of the lesion and the degree of calcification. It consists of thin, irregularly shaped trabeculae of woven bone; scattered trabeculae of lamellar bone; deposits of basophilic staining, round or ovoid, cellular or acellular calcified deposits that have been likened to cementum[24].

Depending on the clinical, radiological and most importantly histological features our case was more in favour of fibrous dysplasia of long standing duration. OF and FD often presents a diagnostic dilemma for both clinicians and pathologists because of their radiographic and histological similarity. Differentiation of these two lesions is critical because the treatment protocols are quite different. OF, although benign, must be enucleated due to its potential to recur. FD on the other hand is generally self-limiting and does not require treatment except for cosmetic reasons, pain, discomfort or impaired function. In FD the treatment, consisting of recontouring or resection, should be postponed until after cessation of skeletal growth, since early treatment may accelerate growth of the lesion[25].

Newer studies have been carried out by immunohistochemical markers like Osteocalcin for differentiating between the two lesions. Osteocalcin, is the most abundant noncollagenous protein distributed throughout normal bone and has been shown by gene knockout technology to be a negative regulator of bone formation[26, 27]. Toyosawa et al.[25] in their study showed abundance of osteocalcin in FD and its deficiency in OF, suggesting that the calcified material in FD is more similar to normal bone than that in OF. Thus indicating differences in bone formation and osteoblast differentiation between the two lesions. They also suggested PCR analysis with PNA for GNAS mutations at the Arg[20] codon to be a potentially useful method to differentiate fibrous dysplasia from ossifying fibroma[25].

Conclusion

Differentiating fibrous dysplasia and ossifying fibroma in craniofacial bones needs detail clinical, radiological and histological examination as the treatment modalities for.both the lesions differ. Newer immunohistochemical techniques and PCR analysis could be potentially useful method to differentiate these two entities.

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