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CASE ARTICLE

# Multifocal Polyostotic Craniofacial Fibrous Dysplasia

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**ABSTRACT**

*An extremely rare case of craniofacial fibrous dysplasia with multifocal involvement of bilateral maxilla and mandible in a 17 year old male patient is reported. The genetic basis, etiopathogenesis, progression, clinical-radiological features and treatment of fibrous dysplasia are reviewed and presented.*

***Keywords:*** *Fibro-osseous lesions [FOL], Skeletal Disorders, Polyostotic disease*

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## INTRODUCTION

The benign fibro-osseous lesions [FOL] of the jaws comprise and constitute a diverse, interesting, and challenging group of conditions with a striking common histological characteristic – substitution of normal bone by a tissue composed of collagen fibres and fibroblasts that contain varying amounts of mineralized substance, which may be bony or cementum-like in appearance.[1]

The fibro-osseous lesions of the craniofacial region includes: fibrous dysplasia, periapical cemento-osseous dysplasia, focal cemento-osseous dysplasia, florid cemento-osseous dysplasia, and cemento-ossfiying fibroma.[2]

Of these, FD is a congenital but non-inheritable benign, sporadic, developmental dysplastic, skeletal disorder that accounts for 7% of all benign bone tumors. It is described as a tumor-like condition that is characterized by replacement of normal bone with an excessive proliferation of fibrous connective tissue with irregular trabecular bone.[3, 4] Further, FD can affect one bone (monostotic form), or multiple bones (polyostotic form), or present as Jaffe-Lichtenstein Syndrome (JLS) comprising of polyostotic FD with cafe '-au-lait pigmented skin lesions and McCune-Albright syndrome (MAS) which also has the additional features of hyperfunctional endocrinopathies as precocious puberty, hyperthyroidism or acromegaly. The craniofacial bones are affected in about 10% of the cases of monostotic FD and in 50% to 100% cases of polyostotic FD. The term craniofacial FD is used when there is singular involvement of only the cranial and facial bones by the disease process.[3, 5, 6, 7]

## CASE REPORT

A 17 year old male patient reported to the department of craniofacial surgery in April 2014 with complains of a

progressively expansile mass of the face for the past 7 years, noticeable since 10 years of age. On clinical examination he presented with gross facial asymmetry involving bilateral maxilla and mandible left side > right side (**Figure 1**). On palpation, the swelling was bony hard in consistency with cortical expansion.

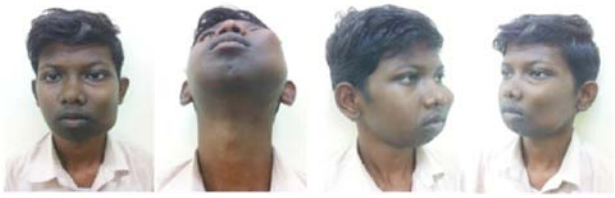

**Figure 1** (L to R) Frontal, Worm's view, right and left lateral view – demonstrating extensive bony expansion with gross facial asymmetry with left side involvement > right side

Although the clinical presentation was suggestive of involvement of the facial bones on the left side, a computed tomography image demonstrated panfacial involvement of bilateral maxilla and mandible. The extents of growth did not involve vital structures in the vicinity. There were no functional impairments despite extensive involvement of the facial skeleton (**Figure 2& 3**).

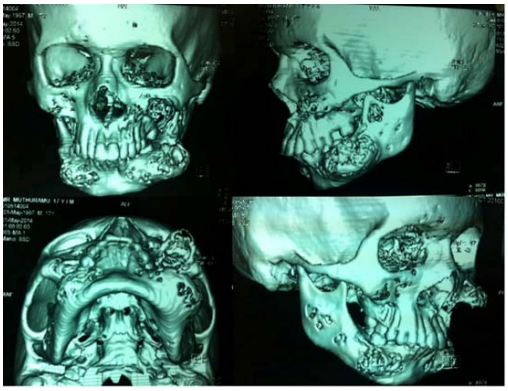

**Figure 2** Volume rendered 3D computed tomography images demonstrating panfacial involvement with multilocular expansile fibro-osseous lesions

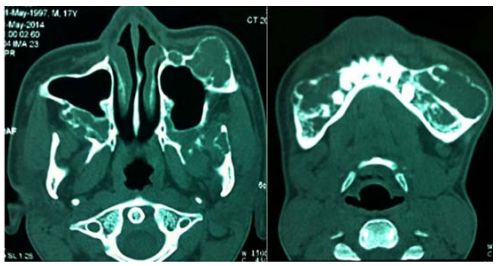

**Figure 3** Coronal sections demonstrating extent of involvement in the maxilla and mandible

A previous incision biopsy done in 2008 was suggestive of peripheral giant cell granuloma. Patient had not continued treatment then and presented to this facility as the growth was progressive. Following routine surgical workup and biochemical investigations which were under normal parameters, a trephine bone biopsy was done and specimen was sent for histopathological examination (HPE). The final HPE report was "*multifocal polyostotic fibrous dysplasia"*(**Figure 4**). Following HPE diagnosis, a staged surgical work up was formulated and it was decided upon to operate the left side first as it was cosmetically more disfiguring. The extent of bony expansion was not disfiguring on the right side, hence immediate surgery was deferred.

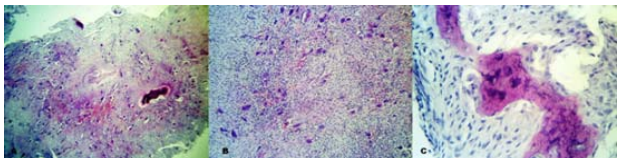

**Figure 4** (L to R): Representative areas of HPE sections demonstrating A: Cellular tumour comprised of proliferative spindle cells, giant cells and bony trabeculae; B. Spindle cells are arranged in pattern less manner admixed with numerous multinucleated giant cells; C. Metaplastic bone formation which is characteristic of fibrous dysplasia and appears irregular due to the dissection by surrounding spindle cells

Under general anesthesia, access to the lesion on the left maxilla was gained through a Weber-Fergusson incision and mandible through an Apron incision. Extensive cortical expansion of the involved bones and a thin overlying mucosa obviated the use of transoral approaches. The bony prominences were removed and the remaining bone was recontoured (**Figure 5**). The post operative period was uneventful and patient was discharged on sixth post operative day. He has been followed for a period of 1 year. There has been no clinical and radiological evidence of recurrence and soft tissue remodelling has also been adequate (**Figure 6** and **7**).

**Figure 5** 1st row (L to R) Marking for Weber-Fergusson incision, Exposed lesion, Recontoured bone; 2nd Row (L to R) Lesion exposed through a left Apron incision, Recontoured bone, Closure at both sites

**Figure 6** (L to R) At the time of presentation, 3rd post of month, 6th post op month and 1 year post operative period. Progressive soft tissue remodelling and restoration of facial symmetry is evident

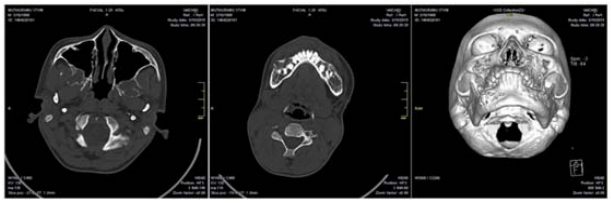

**Figure 7** (L to R) Post operative (1 year follow-up) multiplanar reconstruction (MPR) and volume rendered 3D reconstruction image series demonstrating disease free left maxilla and mandible region

## DISCUSSION

Fibro-Osseous lesions [FOL] are constituted by a group of lesions which are known to affect the jaws and the craniofacial bones and are regarded as very confusing area in diagnostic pathology.[7]. Most of these lesions are of unknown aetiology, while some lesions are believed to be neoplastic while others are related to metabolic disturbances.[8]

No universally accepted system of classification exists for these lesions, however concept of categorization has been widely used (**Table 1**).[9]

**Table 1** Classification schemes of Fibro-Osseous Lesions

| |
|---|
| Charles Waldron classification of the fibro-osseous lesions of the jaws (1985) |
| Working classification of fibro-osseous lesions by Mico M. Malek (1987) |
| Peiter J. Slootweg & Hellmuth Muller (1990) |
| WHO classification (1992) |
| Waldron modified classification of fibro-osseous lesions of jaws (1993) |
| Brannon & Fowler classification (2001) |
| WHO classification of fibro-osseous lesions of jaws (2005) |
| Paul m. Speight & Roman Carlos classification (2006) |
| Eversole classification (2008) |

Although various classification systems have gained acceptance and usage, Waldron's classification system is most recognized. The classification system of Waldron has suggested that the FOL originates from the periodontal ligament which contains multipotent cells which are known to differentiate into fibrous tissue cells, cementum and bone. From a clinical stand point the Modified Waldron classification of FOL (1993) is most relevant – **Table 2**.[9,10]

**Table 2** Modified Waldron's classification of fibrosseous lesions of the jaw (1993)

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|---|
| 1. Fibrous Dysplasia |
| 2. Cement-Osseous Dysplasia<br>a. Periapical Cement-Osseous Dysplasia<br>b. Focal Cement-Osseous Dysplasia<br>c. Florid Cement-Osseous Dysplasia |
| 3. Fibro-Osseous Neoplasm<br>a. Cementifying Fibroma<br>b. Ossifying Fibroma<br>c. Cement-Ossifying Fibroma |

FD was first described by von Recklinghausen in 1891 in a patient with skeletal deformities due to fibrotic bone changes and was termed "osteitis fibrosa generalisata". The disorder became known as "fibrous dysplasia" in 1938, when Lichtenstein introduced the term. The lesions of fibrous dysplasia were further subdivided by Schlumberger in 1946 as monostotic fibrous dysplasia when he described a single-bone involvement by the disease process.[4] When multiple bones are involved, it is termed polyostotic. In addition to these forms, Jones described hereditary familial form of localized FD, which is called Cherubism. McCune-Albright syndrome and Jaffe-Lichtenstein syndrome are the other variants of the disease.[3,4,11,12,13]

Although its actual incidence is not known, it accounts for between 2.5 and 10 percent of all bone tumors. Gender prevalence of FD is equal, although some authors suggest a female predilection.[3] The monostotic form is more common and affects the 20 to 30 year age group. Polyostotic FD has its onset mainly in children younger than 10 years of age the lesions grow with the child and stabilize after puberty and skeletal maturity. Although described as a non-familial, congenital bone disorder, it usually manifests before third decade of life.[1,5,6] Our case fell within the age group described.

The pathogenesis of FD has been theorized for many years, with causes attributed to trauma, developmental disturbances, and neurologic etiology. The genetic basis

of disease is now established and the various forms of FD occur as a result of postzygotic somatic activating mutation of the gene that encodes for GNAS 1 (guanine-nucleotide-binding protein, a-stimulating activity polypeptide 1) in the bone marrow cells, resulting in locally increased stimulatory activity of adenyl cyclase and cAMP.[4] This mutation leads to increased production of C-fos protein and interleukin-6 (IL-6) that result in classic dysplastic bone of FD. The severity of the condition depends on the postzygotic life and in which cells, mutation occurs. As the mutation takes place in a somatic cell rather than a germ cell, only the lineage from the affected somatic cell will express the abnormal GNAS 1 protein whereas the remainder of the cells will continue to develop normally. This phenomenon of variable expressivity is termed *"somatic mosaicism"* and is a characteristic genetic concept. The associated endocrinopathies are the result of constitutive activation of G protein coupled receptor by hormones acting through it including luteinizing hormone (LH), follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH) and growth hormone regulating hormone (GHRH), thereby manifesting as gonadotropin independent precocious puberty (GIPP).[3, 4, 5, 11]

Craniofacial FD typically presents during early childhood, at around 10 years of age and then progresses throughout adolescence. Craniofacial involvement in FD is seen in both monostotic and polyostotic forms. Craniofacial involvement occurs in about 30% of monostotic FD and typically affects the maxilla, mandible and rarely the calvarium. In the polyostotic form of the disease any cranial or facial bone can be affected by FD and the clinical features will depend upon the bone affected, site affected, extent, duration and nature of lesion.[1, 3, 4, 5, 9] Signs and symptoms of craniofacial FD are a gradual, initially painless enlargement of the involved bones manifesting as facial or cranial asymmetry and deformity. Other symptoms of craniofacial FD are result of constriction of cranial foramina or obliteration of any bony cavities. These include anosmia, orbital dystopia, diplopia, proptosis, blindness, epiphora, strabismus, facial paralysis, hearing loss, tinnitus, nasal obstruction, malocclusion and interference with mastication and speech.[4] In the present case, facial deformity predominated as the presenting complaint and there were no functional impairments.

The proportion of mineralized bone to fibrous tissue in the lesion determines the radiological features of craniofacial FD. Early lesions are usually radiolucent, either unilocular or multilocular and with ill-defined or well-defined borders. As the lesion matures, the lesions are characterized by a mixed radiolucent/ radiopaque appearance.[3] The density and trabecular pattern of FD lesions are variable. Rare cases of FD may appear to have granular internal septa, mimicking a multilocular appearance. The abundant abnormal and irregularly shaped trabeculae render a variable radiopaque pattern which may have a granular appearance (ground-glass appearance, resembling the small fragments of a shattered windshield), a pattern resembling surface of an orange peel (peau d'orange), a wispy arrangement (cotton wool), a swirling pattern similar to a fingerprint or as a very rare radiographic 'sunray' appearance.[13]In the present case, the CT image revealed a ground glass appearance of the affected areas. The other modalities for diagnosis and evaluation include magnetic resonance imaging (MRI), and radionuclide scans. In MRI, FD lesions are characterized by a decreased signal as well as sharply demarcated borders on both T1- and T2- weighted images.[5] Owing to the diffuse microscopic ossification in FD which allows increased dye uptake in affected areas, radionuclide scans like bone scintigraphy have high sensitivity but low specificity and are helpful in determining the activity and potential multicentricity of lesion. Single positron emission tomography (SPECT) has greater sensitivity in detecting FD involved areas in the bones.[5,6,8]

Treatment options can broadly be divided into 4 categories –observation, medical therapy, surgical remodelling, radical excision and reconstruction. Optic nerve decompression in cases of optic canal involvement can be classified as therapeutic or prophylactic. The procedure is performed in patients with decreasing visual acuity.[4,5]

Observation as a choice of treatment is indicated for patients with small asymptomatic lesions and those that are cosmetically acceptable. Medical therapy usually consists of treatment with bisphosphonates – intravenous pamidronate, oral alendronate, intravenous zoledronate.[3, 11]More recently intravenous neridronate has also been advocated in the treatment of FD.[14] The benefits of bisphosphonate therapy include reduced bone pain as result of suppressed osteoclastic activation and decrease in bone alkaline phosphatase (BAP) levels and other bone turnover markers (BTMs). Long term (>5 years) bisphosphonate therapy is associated with severe suppression of bone turnover (SSBT). Bisphosphonate

use is also associated with a poorly defined risk for the development of osteoradionecrosis of jaws.[11]

Surgery is the choice of treatment and is aimed at restoring function and aesthetics. The timing of surgery is usually delayed till puberty as it undermines the rationale that there is cessation of further lesion growth. Surgery usually comprises of contouring the bone, debulking and or surgical resection. The current treatment algorithm for surgical resection for the management of craniofacial FD by aggressive, radical surgery for resection of diseased bone was proposed by Chen and Noordhoft[15], and is accepted and followed universally (**Table 3**).

**Table 3** Chen and Noordhoft – Treatment Algorithm for Surgical Management of Craniofacial Fibrous Dysplasia

| | | |
|---|---|---|
| Zone 1 | Fronto-orbito-malar regions | Aesthetically critical zone. Reconstruction with simple bone grafting after resection |
| Zone 2 | Hair bearing scalp | Not of esthetic concern. Treatment is optional |
| Zone 3 | Central skull base including sphenoid, pterygoid, petrous temporal bone | Difficulty in surgical access. Observation is the choice of recommendation |
| Zone 4 | Maxilla and Mandible | Conservative management |

With the advent of microvascular surgery, free tissue transfer and dental implantology, definitive management of zone 4 lesions are now possible. Extensive lesions of the maxilla and mandible can be managed by radical resection; choice of reconstruction based on the nature, extent and involvement of the disease and staged oral and dental rehabilitation. In the present case, the lesions on the left maxilla and mandible were more extensive, cosmetically disfiguring than those on the right side, but with no effect on function and follow up after 1 year, post surgery and repeat CT scans demonstrated no obvious recurrence on the operated side and further growth on the right side.

## CONCLUSION

Although FD presents it as non-malignant, potentially self limiting disease, the resultant disfiguration and functional impairments often warrant a radical approach to the disease. Surgical planning, decision making and definitive treatment are patient based and vary depending on the clinical situation.

**Consent from the patient**: Consent has been taken

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