Review Article

# Craniofacial fibrous dysplasia - A review of current management techniques


## Abstract

Fibrous dysplasia is a pathologic condition of bone of unknown etiology with no apparent familial, hereditary or congenital basis. Lichtenstein first coined the term in 1938 and in 1942 he and Jaffe separated it from other fibro-osseous lesions. It is a bone tumor that, although benign, has the potential to cause significant cosmetic and functional disturbance, particularly in the craniofacial skeleton. Its management poses significant challenges to the surgeon. Craniofacial fibrous dysplasia is 1 of 3 types of fibrous dysplasia that can affect the bones of the craniofacial complex, including the mandible and maxilla. Fibrous dysplasia is a skeletal developmental disorder of the bone-forming mesenchyme that manifests as a defect in osteoblastic differentiation and maturation. It is a lesion of unknown etiology, uncertain pathogenesis, and diverse histopathology. Fibrous dysplasia represents about 2, 5% of all bone tumors and over 7% of all benign tumours. Over the years, we have gained a better understanding of its etiology, clinical behavior, and both surgical and non-surgical treatments.



**Key words:**
*Bisphosphonate, craniofacial fibrous dysplasia, pamidronate*


## Introduction

Fibrous dysplasia (FD) is a bone development anomaly characterized by hamartomatous proliferation of fibrous tissue within the medullary bone, with secondary bony metaplasia, producing immature, newly formed and weakly calcified bone, without maturation of the osteoblast which appears radiolucent on radiographs, with the classically described ground-glass appearance.[1] In 1937, McCune and Bruch first suggested that among all of the abnormalities of bone formation, this disorder should have its own place as a distinct clinical entity. The following year, Lichtenstein introduced the term "fibrous dysplasia".[2,3] The etiology of this abnormal growth process is related to a mutation in the gene that encodes the subunit of a stimulatory G protein (Gsα) located on chromosome 20. As a consequence of this mutation, there is a substitution of the cysteine or the histidine amino acids of the genomic DNA in the osteoblastic cells-by another amino acid, arginine. Consequently, the osteoblastic cells will elaborate a fibrous tissue in the bone marrow instead of normal bone. It is a benign bone disorder of an unknown etiology, uncertain pathogenesis and diverse histopathology. Fibrous dysplasia represents about 2.5% of all bone tumors and over 7% of all benign tumours.

Cranial or facial bones are affected approximately in 30% of the patients.[3,4] The average age of the patients with FD is 25, 8 years (from 5 to 67) without sex preference (46, 7% male) and usually manifests before the 3rd decade of life.[4,5] Fibrous dysplasia is described in terms of three major types: monostotic, involving a single bone; polyostotic, having multiple lesions involving multiple bones; and McCune Albright syndrome, a polyostotic form of fibrous dysplasia that also involves endocrine abnormalities. The monostotic form of fibrous dysplasia is the most common, comprising 70% of cases, most likely to quiesce at puberty. A typical monostotic lesion, usually presented unilateral, will involve the femur, tibia or ribs, with 25% occurring in the bones of the skull. Affection of the craniofacial bone is observed


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| **Website:** http://www.cysonline.org | Quick Response Code |
| **DOI:** 10.4103/2229-5186.98672 | |



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with 10% of the patients suffering from monostotic FD.[6,7] Twenty-five percent of fibrous dysplasia involves two or more bones. These lesions may be localized to one region of the body or they may be disseminated, involving virtually every bone. There is a female predilection in polyostotic fibrous dysplasia, and up to 50% may involve bones in the head and neck. These lesions are more likely to continue to progress even after puberty.

Deformity is progressive and by mass effect there may be impingement on other structures and functional impairment. These lesions tend to be structurally weak and are therefore prone to pathologic fracture. Alkaline phosphatase may be elevated in up to 30% of patients with polyostotic fibrous dysplasia, and a dramatic rise may herald malignant degeneration.[7] Malignant degeneration occurs in less than 1% of cases of fibrous dysplasia. Malignancies are almost exclusively osteosarcoma. For unknown reasons, monostotic and craniofacial lesions have the greatest potential for malignant degeneration. Pain, rapid growth of a lesion and a dramatic elevation of alkaline phosphatase may herald malignant transformation.[8]

## Diagnosis/Evaluation

The mere presence of fibrous dysplasia of the craniofacial region is not in itself an indication for treatment. Many small solitary lesions will remain static and asymptomatic for long periods. A marked or progressive deformity, pain or functional disabilities suggest the need for intervention. Aside from McCune-Albright syndrome, it is usually difficult to diagnose FD on clinical, radiographic or histological criteria alone; one must consider all three factors.[8] The plain radiological features of FD are non-specific and vary widely.[9] The typical appearance is that of radiolucent lytic lesions with a homogenous ground-glass appearance and ill-defined borders. Occasionally, the radiograph may reveal predominantly sclerotic lesions with or without accompanying lytic lesions.[9] Naturally, its nonspecific radiological appearance makes it difficult to differentiate from other conditions such as juvenile ossifying fibroma, chronic diffuse sclerosing osteomyelitis, osteoma, low grade osteosarcoma, osteoclastoma and fibrosarcoma and Paget's disease.[8,10] Computed tomography (CT) is a better radiological tool, especially for assessing the extent of the tumor in cases of suspected optic canal involvement.[11] While it is invaluable in pre-operative planning, it is also a superior diagnostic tool, although CT alone is insufficient to make a diagnosis of FD.[12] FD has characteristic appearances on CT [Figures 1-3] and consists of three varieties: ground-glass pattern (56%), homogeneously dense pattern (23%) and cystic variety (21%). Cystic variety is usually characterized by radiolucency surrounded by dense rim of bone seen in fibrous dysplasia occurring in mandible seldom seen in maxilla and other facial bones.[13] Various studies have suggested the use of magnetic resonance imaging (MRI) as a

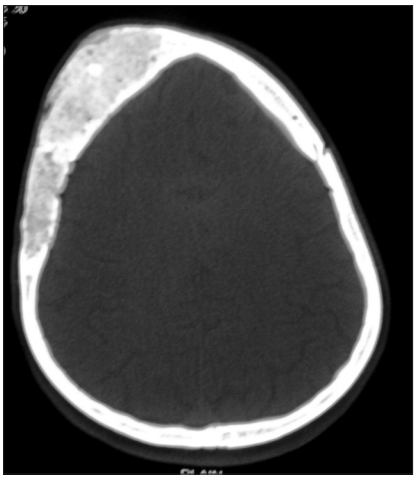

**Figure 1:** CT axial view showing ground glass appearance of the right temporal and frontal bones in a case of craniofacial fibrous dysplasia

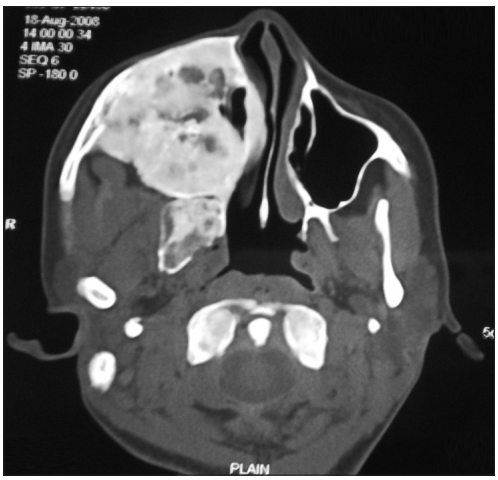


**Figure 2:** CT axial view showing dense homogenous pattern type of fibrous dysplasia affecting right maxilla and zygomatic bones with obliteration of right maxillary sinus

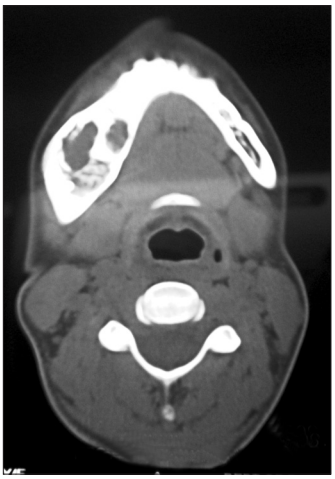

**Figure 3:** CT axial view showing dense cystic type of fibrous dysplasia affecting right side of the mandible

diagnostic tool for FD.[14,15] Lesions have been characterized by a decreased signal as well as sharply demarcated borders on both T1- and T2-weighted images. Some authors, however, have highlighted the potential for misdiagnosis with MRI.[16] The MRI characteristics of FD do not share the distinctive features seen on radiography or CT, and often resemble that of tumors. This is particularly so when the lesion shows intermediate signal intensities on T1-weighted images and high signal intensities on T2-weighted images, and enhances brilliantly after the injection of contrast material. The likelihood of correctly diagnosing FD by MRI is high only when the signal intensities on both T1- and T2-weighted images are low in spite of the injection of contrast material.[17] Radionuclide scans, such as bone scintigraphy, have some role in the diagnosis/evaluation of FD.[18]

Radionuclide scan has high sensitivity but low specificity. Single photon emission computed tomography (SPECT) has been reported to be more sensitive in detecting the areas involved in cases of FD.[19] Although the histology of FD is well-established, cytological descriptions are rare. One group reported on fine needle aspiration cytomorphology of FD; the smears contained blood, occasional osteoclastic multinucleated giant cells, and frequent C shaped fibrillary structures with dark central areas and lighter peripheries representing woven bone.[19,20] The role of fine needle aspiration cytology remains limited. There is some role for biochemical markers in the management of FD. Serum alkaline phosphatase and urinary hydroxyproline are examples of useful markers, and are used to monitor response in the nonsurgical treatment of the disease rather than for diagnosis.[19,20] The role of growth hormone as a predictor of the severity of the disease has also been recently reported, although the results are yet to be published. The frequency of malignant transformation of fibrous dysplasia is 0.4-1%. The interval from development to malignancy is usually takes years or decades. Most often, skull and facial bones undergo malignant change in monostotic disease, whereas femoral and facial bones undergo malignant change in polyostotic disease. Osteosarcoma and fibrosarcoma are the most common tumor where as chondrosarcomas occur less frequently. Radiographic features suggestive of malignant degeneration include rapid increase in the size of the lesion, change from a previously mineralized bony lesion to a lytic lesion along with clinical findings of increasing pain and enlarging soft tissue mass suggest malignant change.[20,21]

## Treatment

Medical treatment has a role in the management of craniofacial FD. Some authors have reported their experience with the use of steroids, mainly in the treatment of visual symptoms from optic nerve compression. One group reported one case of reversal of visual loss,[21] while others reported control of visual deterioration with the use of steroids.[22-24] Another line of medical treatment is the bisphosphonates, for example pamidronate. This group of drugs inhibits osteoclastic activity. Most experiences have been in patients with polyostotic FD or McCune-Albright Syndrome; there is limited data on patients with craniofacial FD and these experiences were mainly in children.[25] Bisphosphonates are generally safe and well-tolerated, although one reported side-effect is atypical fever.[25]

Unfortunately there are no objective methods to assess or predict the outcome of treatment, especially medical treatment. Subjective criteria have been suggested, such as a decrease in inflammatory symptoms like pain and swelling.[25] Serum alkaline phosphatase, a marker for bone turnover, is consistently reduced in patients treated with pamidronate, making it a good monitor of response to medical treatment.[26-28] The use of urinary hydroxyproline as a marker has also been suggested, although experience with it is more limited. Serial radiographs have been used to assess response but results are not consistent. One study demonstrated response to treatment by the filling of osteolytic lesions and/or cortical thickening,[27] while another showed no radiological response.[28] Local bone mineral density has been found be more consistent than serial X-rays in the monitoring of response to treatment.[28]

Surgical treatment of FD consists of either conservative shaving/contouring or radical excision with immediate reconstruction but treatment should be delayed until after skeletal maturity has been reached. Surgery is usually delayed until adolescence however, if the progression of the disease comprises neurological function, a decompressive procedure should be considered early in childhood to preserve normal function.[29] The choice of surgical option depends on several factors: site of involvement, rate of growth, aesthetic disturbance, functional disruption and patient preference, general health of the patient, surgeon's experience and the availability of a multi-disciplinary team (neurosurgeon, ophthalmologist, otolaryngologist and orthodontist).

Decompression of the optic nerve in cases of optic canal involvement can be classified as therapeutic or prophylactic. Optic nerve decompression has generally been advised, especially in those patients with decreasing visual acuity.[29,30] The value of therapeutic decompression has been questioned, especially in delayed cases. Studies have demonstrated that vision is less likely to return if the decompression is done more than one week after established blindness.[31-33] Decompression has been shown to have no value in cases of blindness of more than one month duration.[34,35] Prophylactic decompression is based on the belief that visual loss is directly related to optic canal stenosis and there have been encouraging reports on its value.[29,36] The procedure is generally safe, although it is associated with a steep learning curve and results are dependent on the experience of the surgeon performing the procedure. There seems to be a

recent shift in understanding of optic canal stenosis in FD and its relationship to visual loss. There have been reports of patients with encasement and narrowing of the canal yet without resultant visual loss.[37] Thus the relationship of canal stenosis to visual loss is not completely clear. In fact, visual loss has been proposed to be due to a primary or secondary mass lesion rather than optic canal stenosis. In light of these new findings, further studies are needed to define the value of prophylactic optic nerve decompression.

Reconstruction after excision is important in the management of craniofacial FD. The use of autologous tissues, namely grafts of calvarial bone and rib, is preferable. Split calvarial grafts are usually obtained from the frontal, temporal or parietal regions. As these bones have diploe between the inner and outer cortices they are easily split. The inner cortex is used as the graft while the outer cortex is placed back to its original position. Rigid fixation is achieved with mini or microplates. Rib grafts are also frequently used in a split fashion. One reconstructive technique is the "chainlink fence" technique, useful for the reconstruction of large defects especially in the fronto-orbital region, particularly when calvarial bone graft is not available.[38] Full-thickness rib grafts are useful for the reconstruction of the superior orbital rim as they are effective in re-establishing rim contour. Microvascular free flap reconstruction has a role, especially for lesions involving the mandible where segmental excision is necessary.[39]

## Conclusion

Isolated cases of fibrous dysplasia in craniofacial region are rare and can be difficult to differentiate from other benign and malignant bone disorders. For obtaining the definite diagnosis, treatment and further management of fibrous dysplasia is mandatory to be carried out imaging studies, histological and laboratory tests. Much progress has been made over the past decade, for example the identification of the genetic mutation linked to the etiology of the disease. This area still needs further exploration in order to establish the role of genetic manipulation in the management of the disease.

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**How to cite this article:** Guruprasad Y, Chauhan DS. Craniofacial fibrous dysplasia - A review of current management techniques. Chron Young Sci 2012;3:106-10.

**Source of Support:** Nil, **Conflict of Interest:** None declared