# SUCCESSFUL TREATMENT OF CRANIOFACIAL FIBROUS DYSPLASIA WITH BIS-PHOSPHONATE: A CASE REPORT

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**Abstract**

Fibrous dysplasia (FD) is a none-malignant skeletal disease which may affect single or multiple bones. These lesions usually involve long bones, craniofacial bones or ribs. FD has varied and broad clinical spectrum. As the disorder can be known as silent disease and be asymptomatic it can also cause severe pain, pathological fractures and deformities. In this case report we are presenting an 11-year old young girl with mandibular FD and her successfully treatment result with bisphosphonate. Different therapeutic approach was used for eliminating her symptoms (sever pain and swelling) but none were effective. Therefore, administration of intravenous bisphosphonate was initiated and resulted to target the major characteristics symptoms of FD and permanency of the treatment results remain to be seen in future. Based on our finding and other published reports, treatment of FD with bisphosphonate could be a suitable of FD and it should be considering in symptomatic cases.

**Kerwords:** Bisphosphonate, Craniofacial, Fibrous Dysplasia.

## Introduction

Fibrous dysplasia (FD) is a rare, benign and non-inherited bone condition, which normal bone and bone marrow space are replaced by fibrous tissue and abnormal bone (immature woven bone). FD is caused by missence somatic activating mutation of the GNAS gene. As a result, activation of adenylate cyclase will occur and consequently intracellular accumulation of cAMP will cause differentiation of abnormal osteoblast and production of dysplastic bone subsequently.[1-3]

FD may affect single skeletal site (monostotic) or multiple skeletal site(polyostotic) and may be associated with extra skeletal organs. The most common affected sites are the craniofacial bones, proximal part of femur and rib.[4] These patients commonly experience inflammation, bone deformities, pain and pathological fractures. Overgrowth Tendency in the craniofacial region has the potential to compress vital structures and cranial nerves. Therefore, Visual or hearing impairment could be presented when the disease is placed in the skull base or the maxilla.[5-6] Prevalence of FD is estimated to be around 1/30000. Women and men are equally affected.[7-8] Pain is the presenting symptom of the disease in many patients. Sever pain management requires the use of analgesics such as non-steroidal anti-inflammatory drugs.[9] Until recently, to a great extent treatment protocol of FD has been enclosed to surgery. Moreover, bisphosphonates were introduced for the treatment of FD by inhibiting osteolactic bone resorption. Also as a result of the treatment, reduction in biochemical markers of bone turnover and decrease of reactive bone pain is promising results from previous studies[10-11] The published data on the use of bisphosphonate is very limited. In this study the favorable bisphosphonate treatment of monostotic mandibular FD in an adolescent was presented.

## Case Report

The patient an 11-year old girl presented with swelling and pain of the right side of her face, specifically in the anterior right side of the lower jaw, following the use of orthodontics removable appliance which had lost its fitness after a week. She did not have any history of previous systemic disease in herself and her families. The pain and swelling was temporarily controlled by NSIADs (Ibuprofen 400mg q8hr) and antibiotic (Amoxicillin 500mg q8hr). At the same time, panoramic was ordered for further evaluation; it revealed normal view and no pathologic changes were found. After 2 months due to the continuity of swelling and pain, cone beam computerized tomography (CBCT) scan was recommended. CBCT scan showed a mixed tumor-like lesion with ill-defined border extended from right first molar to left first molar with periosteal reaction of the inferior border of the mandible while the cortex has been perforated in many places. [Figure 1,2]

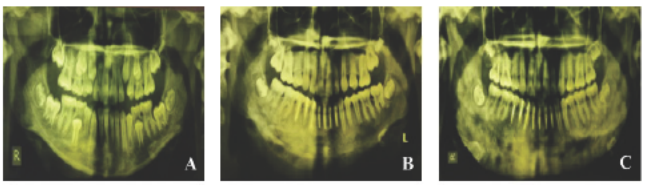


*Figure 1: Panoramic view of the patient disease course. A: normal appearance revealed in early stage . B: ill-defined ,mixed lesion .note the periosteal reaction of inferior border of the mandible. C:right after therapy of FD with Bisphosphonate. note the ground glass pattern of mandible.*

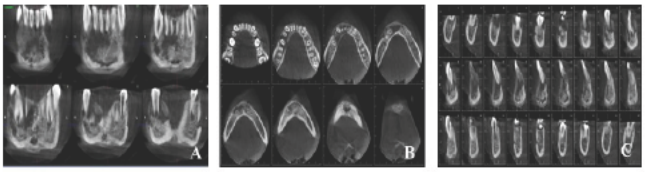


*Figure 2: CBCT images. A:coronal view shows the cotton wool appearance of the mandible .B, Axial view demonstrated expansion of buccal and lingual plate without expansion. C: Cross-sectional view.*

Finally, imaging studies were suggestive of fibrosseous, bone sarcomas and osteomyelitis. So, an incisional biopsy was made and the specimen was sent to the pathology service, and the diagnosis of fibrosseous was confirmed. In addition, bone scans significantly showed an increased activity in mandible, which was in favor of tumoural involvement of osteomyelitis, fibrous dysplasia. Involvement was limited to the mandible. [Figure 3]

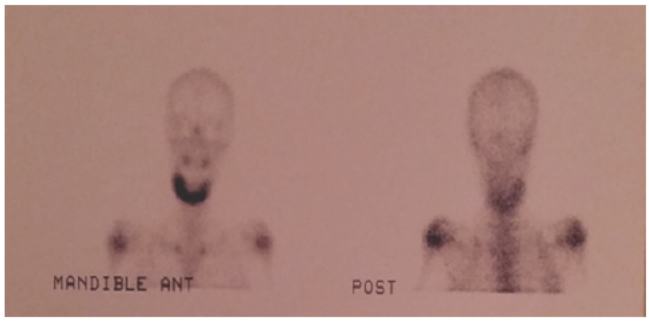


*Figure 3: Bone scan at baseline shows increase of tracer uptake in the mandible*

Perseverance of swelling and sever pain mislead the dentist into necrotic causative inflammation of vital tooth; therefore, root canal therapy for lower incisors, right canine and right first premolar was performed. Also apical root surgery was selected as minor surgery on incisors in order to reduce the symptoms. It was effective to reduce the pain only for a short period of time. Afterwards Injection of corticosteroid (Betamethasone Long acting 4mg/ml, IM) was started (once in a month, for four months) to reduce inflammation and pain. The patient blood chemistry and serum markers were assessed. High level of bone remodeling marker Alkaline phosphatase (ALP), erythrocyte sedimentation rate (ESR), and deficiency of vitamin D and calcium were detected; therefore, the patient received vitamin D (800 IU/day) and calcium (500 mg/day) supplements. After two months, progression of symptoms led to another biopsy and the diagnosis of fibrous dysplasia was confirmed. [Figure 4]

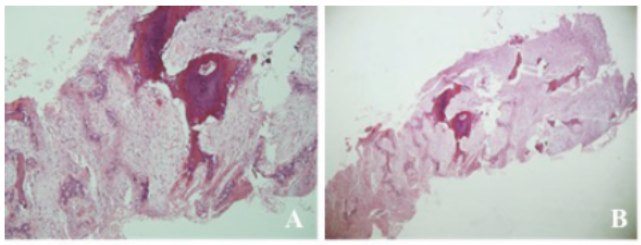


*Figure 4: Mostly reactive fibrotic tissure bearing foreign body type granulation and striated muscle fiber and few fragments of neoformed tissue composed of cellular fibrous tissue surrounding curvilinear bone trabeculae. the fibrous tissue is composed of plump spindle cells without cytologic atypia or mitotic figures. Bone trabecular are composed predominantly of woven bone.*

To relieve substantial, sever pain and inflammation, Celecoxib 100 mg (NSAID) was given every night for 2 years. Antibiotic therapy, root canal therapy, apical root surgery, corticosteroid therapy and the use of analgestics were different approaches to control the symptoms, but they failed to respond. A bone density specialist recommended therapy with Bisphosphonate regimen. After consulting with an oncologist, injection of intravenous zoledronic acid (Aclasta, 4cc every month for 2 times) was started. Surprisingly, after the first injection the pain and inflammation was suppressed, and the mandibular enlargement returned to normal size. It also decreased the ALP and ESR.

**Disscusion**

Fibrous dysplasia is a rare bone disease with varied and broad clinical spectrum. FD can be asymptomatic and can also cause bone deformity, sever pain and pathological fractures. Therapeutic modalities, medical or surgical treatments could be a strategy when FD is symptomatic. Surgical approach is usually recommended after the disease becomes stable and the symptoms are minor. However, in many cases with cosmetic deformity and facial asymmetry or functional impairment an earlier surgical intervention is required. Furthermore, the anatomy of craniofacial region with numerous vital structures placed in the involved area makes radical resection of FD almost impossible.[12-13]

Prescriptions of various medications such as NSAIDs and bisphosphonate have been used for patients complaining of bone pain. Intravenous bisphosphonates is to use when NSAIDs are not sufficient. The first used of bisphosphonate started in 1990s. Liens et. Al (1994) reported that an accelerated improvement in bone turn over markers and radiologic appearance was observed in their study after the medical treatment. Also, the pamidronate treatment reduced the bone pain. A prospective study on six patients with cranciofacial FD reported the use of bisphosphonate; as a result, all patients experienced pain relief and the disease were stabilized.[14-15]

In this case report typical symptoms of swelling and local pain were observed in the patient with monostatic FD of the mandible. A progressive course was administered until bisphosphonate treatment was initiated. The major characteristics of the disease were successfully targeted during the treatment including: a reduction in pain after the first infusion cycle, the termination of the soft tissue inflammation, normalization of the bone turn over and decrease in ALP and ESR of the blood; which all led to significant cosmetic improvement. The permanency of the treatment results remains to be seen in future.

There is still little known of the association of pain prevalence in skeletal sites and/or severity of FD, as well as treatment options in such patients. Bisphosphonate could relieve bone pain and other symptoms mentioned earlier in FD. Skeletal implication of childhood bisphosphonate treatment is not clearly known. Although osteonecrosis of the jaw is the main complication of the treatment in adults, but it has not been evident in children.

Therefore, long term effectiveness and complication of the treatment needs to be determined in further studies.

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