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Review Article

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Fibrous dysplasia: A rare bone disorder

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ABSTRACT

Fibrous dysplasia *is an abnormal bone growth where normal bone is replaced with fibrous bone tissue. Fibrous dysplasia causes abnormal growth or swelling of bone. Fibrous dysplasia can occur in any part of the skeleton but the bones of the skull, thigh, shin, ribs, upper arm and pelvis are most commonly affected. Fibrous dysplasia is very rare, and there is no known cure. Fibrous dysplasia is not a form of cancer. Most lesions are monostotic, asymptomatic and identified incidentally and can be treated with clinical observation and patient education. This disorder is usually diagnosed in childhood or early adulthood and can affect one or several bones. Males and females of any race are equally affected.*

Keywords: Fibrous Dysplasia, Monoostotic, Polyostotic

INTRODUCTION

Fibrous dysplasia is a bone disorder in which scar-like (fibrous) tissue develops in place of normal bone. As the bone grows, the softer, fibrous tissue expands, weakening the bone. Fibrous dysplasia can cause the affected bone to deform and become susceptible to fracture.

Fibrous dysplasia (FD) is a benign tumour-like congenital process, manifested as a defect in osteoblastic differentiation and maturation, with progressive replacement of normal bone with immature woven bone.

Most people with fibrous dysplasia are diagnosed during adolescence or early adulthood. Mild cases usually cause no signs or symptoms. More-serious cases of fibrous dysplasia may result in bone pain and deformity. Fibrous dysplasia of craniofacial bones is defined as "a benign, non-neoplastic intranedullary cellular proliferation of fibroblasts, with formation of irregular trabeculac of bone or ovoid calcifications that shows indistinct, non-encapsulated borders".

History:
As early as 1891, von Recklinghausen first described fibrous dysplasia of bones under the term 'Osteitisfibrosacystica'. Freund in 1934 named it as 'osteitisfibrosalocalizata/disseminata'. Jacobson in 1937 in his extensive review of jaw bone diseases described it as 'Fibrous Dystrophy' whereas Albright (1937) described it as Albright's syndrome, which is a triad of polyostotic fibrous dysplasia, cutaneous pigmentation and endocrine disturbances[1]. Lichtenstein in 1938 coined the tenn 'Fibrous Dysplasia of bone' and described it as a distinct entity of unknown etiology. Lichtenstein and Jaffe' in 1942, reported different clinical manifestations for fibrous dysplasia that is solitary (monostotic) and multiple (polyostotic) forms[2]. In 1958, Jaffe' suggested the term 'Fibro-osseous

Dysplasia' for fibrous dysplasia. The basic cause of fibrous dysplasia is unknown. There's no cure for fibrous dysplasia. Treatment focuses on relieving signs and symptoms[3].

Fibrous dysplasia can affect any bone, and can divide into four sub types (although there is some overlap):

- **Monoostotic** : Single bone
- **Polyostotic** : Multiple bones
- **Craniofacial fibrous dysplasia** : Skull and facial bones alone
- **Cherubism** : Mandible and maxilla alone (not true fibrous dysplasia)

Epidemiology[4]
Fibrous dysplasia is found predominantly in children and young adults, with ~ 75% of patients presenting before the age of 30 years (highest incidence between 3 and 15 years). There is no recognized gender predilection.

Although fibrous dysplasia is usually sporadic, a number of associations are well recognised:

- **McCune-Albright syndrome[5]**: In 2 - 3 % of cases with the polyostotic form
- Isolated endocrinopathy without the full McCune-Albright syndrome precocious puberty in girls
  - **Hyperthyroidism**
  - **Hyperparathyroidism : renal stones, calcinosis**
  - **Acromegaly**
  - **Diabetes mellitus**
  - **Cushing syndrome : osteoporosis, acne**
  - **Growth retardation**
- **Mazabraud syndrome[6]**: Soft-tissue myxomas (rare) ; typically multiple intramuscular lesions in vicinity of most severely affected bone

Clinical presentation[7]
The condition is often an incidental finding and is usually painless. Alternatively it may present due to bony expansion or remodelling. Morbidity may arise from compression and displacement of adjacent structures. This is particularly true in craniofacial fibrous dysplasia, where the content of the orbit or cranial nerves may be compressed.

Pathophysiology[8]
In fibrous dysplasia, the medullar cavity of bones is filled with fibrous tissue, causing the expansion of the areas of bone involved. The bony trabeculae are abnormally thin and irregular, and often likened to Chinese characters.

The cause of this transformation, in turn, is not completely known, however. Levels of the transcription factorC-fos are raised in fibrous dysplasia, leading to gene over-expression and tumor formation. It is not hereditary.

Histology[9]
- Fibrocellular matrix of immature collagen contains small irregularly shaped trabeculae of immature, inadequately mineralized bone.
- Trabeculae not rimmed by osteoblasts (differentiating feature from cemento-ossifying fibroma)
- cartilaginous islands present in 10% (differentiating feature from : chondrosarcoma)

Types and distribution Fibrous Dysplasia[10]
Monostotic form (involving only one bone)
This is by far the most common and accounts for 70 - 80% of cases. It is usually asymptomatic until 2nd - 3rd decade, but can be seen throughout adulthood. After puberty the disease becomes inactive, and monostotic form does not progress to polyostotic form.

- Ribs : 28% : most common
- Proximal femur : 23%
- Tibia

- Craniofacial bones : 10 - 25%
- Humerus

Polyostotic form
In the remaining 20 - 30% of cases multiple bones are involved. As expected this presents earlier, typically in childhood (mean age of 8 years) with 2/3^{rds} having become symptomatic by the age 10.

- often unilateral and monomelic : one limb
- Femur : 91 %
- Tibia : 81 %
- Pelvis : 78 %
- Foot : 73 %
- Ribs
- Skull + facial bones : 50 %
- upper extremities
- Lumbar spine : 14 %
- Clavicle : 10 %
- Cervical spine : 7 %

The cause of the gene mutation is not known. It is not inherited or passed on to the children of affected patients. No dietary or environmental cause is known. It occurs equally among males and females of all races.

Symptoms
As the abnormally formed fibrous tissue grows and expands, the involved area of bone becomes weaker. The weakened area of bone can become painful. Pain is more likely to occur in the weight bearing leg and pelvis bones. This type of pain generally begins as a dull ache that is made worse with activity and lessened with rest. It can progressively increase with time.

Sometimes, the bone breaks (fractures) through the weak area, causing sudden severe pain. This can happen after there has already been less severe pain for a time, or it may happen suddenly with no prior pain. The weakened area of bone can cause deformity of the bone over time. Deformity of the facial bones and bowing of the leg bones can be noticeable.

Severe deformity can lead to loss of vision or hearing when facial bones are involved. When the leg and pelvis bones are severely deformed, arthritis may develop in nearby joints.

Young patients with hormonal abnormalities may develop early puberty. This problem is more common in girls than boys. This is usually caused by over activity of the ovaries. Over activity may also occur in other glands of the body, including:

- The thyroid gland (causing anxiety, loss of weight, and abnormal sweating)
- The adrenal glands (causing weight gain, diabetes)
- The pituitary gland (causing milk production in women, gigantism, acromegaly)
- The parathyroid glands (causing high levels of calcium in the blood)

Pigmented skin lesions are often seen in patients with fibrous dysplasia and hormonal abnormalities. The elevated hormone levels normally associated with pregnancy may speed up the growth of fibrous dysplasia lesions, causing increased pain. Warning signs that an area of fibrous dysplasia may have become cancerous include increasing pain, particularly pain that wakes you up at night or does not go away with rest. The presence of a mass should always be investigated.

Tests and diagnosis[11]
If you have monostotic fibrous dysplasia, you may not know it until it's discovered incidentally on an X-ray for another condition. If you have signs and symptoms, your doctor will perform a physical examination and order X-

rays of the affected bones. On X-ray, fibrous dysplasia appears as an abnormal section of bone (lesion) that has the hazy appearance of ground glass.
In some cases, your doctor may order more tests to confirm the diagnosis or to determine the extent of the disorder. They include:

- **Imaging tests.** Computerized tomography (CT) or magnetic resonance imaging (MRI) scans may be used to determine how extensively your bones are affected.
- **Bone scan.** This test uses radioactive tracers, which are injected into your body. Your bones take up the tracers and emit radiation that's captured by a special camera, which produces a picture of your skeleton. Your doctor may order a bone scan to determine whether your fibrous dysplasia is monostotic or polyostotic.
- **Bone biopsy.** This test uses a hollow needle to remove a small piece of the affected bone for laboratory analysis. You'll receive local anesthetics to numb the area where the needle is inserted. In rare instances, an open biopsy — requiring general anesthesia and a surgical incision — may be necessary.

Treatments and drugs[12]
If in case of mild fibrous dysplasia that's discovered incidentally and individual not having signs or symptoms, the risk of developing deformity or fracturing of bone is low. A physician can monitor the condition with follow-up X-rays every six months. If there's no progression, no need of the treatment. If the signs and symptoms are developed, treatment may include medications or surgery.

Medications
Medications called bisphosphonates, including pamidronate (Aredia) and alendronate (Fosamax), are used to inhibit bone breakdown, preserve bone mass and even increase bone density in your spine and hip, reducing the risk of fractures. These medications are primarily used for adults to treat osteoporosis and increase bone density, but bisphosphonates may also reduce bone pain associated with fibrous dysplasia and, in some cases, improve bone formation. Little is known about the use of bisphosphonates for children and adolescents, but some studies indicate they may help relieve pain in children and adolescents with severe fibrous dysplasia.

Oral bisphosphonates are generally well tolerated, but may irritate gastrointestinal tract. These medications also take through a vein (intravenously). In case of serious kidney disease or low blood-calcium levels bisphosphonates can’t be prescribed.

Surgery is better option to:
- Correct a deformity
- Correct a difference in limb lengths
- Fix a fracture
- Remove an affected area of bone (lesion) that's causing you difficulty
- Relieve pressure on a nerve, particularly if the lesion is in your skull or face

Surgery may involve removing the bone lesion and replacing it with bone grafted from another part of your body or from bone tissue donated from a deceased donor. Surgeon may insert metal plates, rods or screws to stabilize the bone and the graft. Risks include infection, blood clots and bleeding. In addition, a bone graft may not last.

Complications
Besides bone fractures, severe fibrous dysplasia can lead to:
- **Bone deformity.** The weakened area of an affected bone can cause the bone to bend (bow). If spine is affected, it can develop scoliosis, an abnormal curving of the spine.
- **Vision and hearing loss.** The nerves to your eyes and ears may be surrounded by affected bone. Severe deformity of facial bones can lead to loss of vision and hearing, but it's a rare complication.
- **Arthritis.** If leg and pelvic bones are deformed, arthritis may form in the joints of those bones.
- **Cancer.** Rarely, an affected area of bone can become cancerous. This rare complication usually only affects people who have had prior radiation therapy.

Radiographic features[13]
Plain film

- ground-glass opacities
- may be completely lucent (cystic) or sclerotic
- well circumscribed lesions

Pelvis + rib

Ribs are the most common site of monostotic fibrous dysplasia. Fibrous dysplasia is the most common cause of a benign expansile lesion of a rib.

- bubbly cystic lesions
- fusiform enlargement of ribs
- protrusio acetabuli

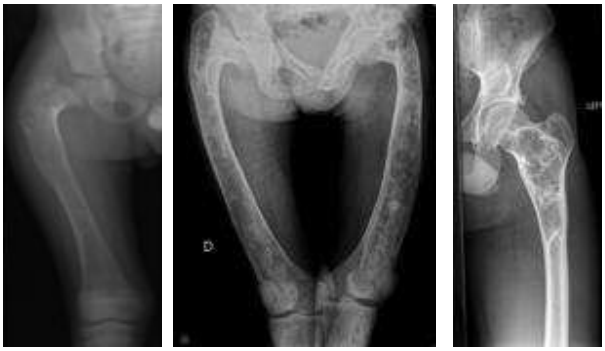
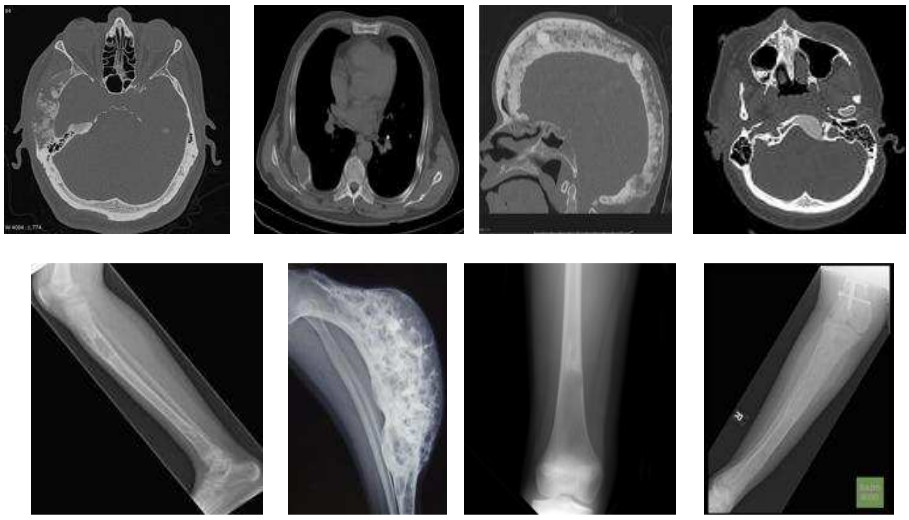


fig1: lesions occurs to pelvis and ribs in fibrous dysplasia

Extremities

- may lead to premature fusion of growth plates leading to short stature
- bowing deformities
- shepherd's crook deformity of femoral neck
- discrepant limb length
- Looser zones

CT



- ground-glass opacities : 56 % [4]
- homogeneously sclerotic : 23 %
- cystic : 21 %
- well-defined borders
- expansion of bone, with intact overlying bone
- endosteal scalloping may be seen [6]

MRI

MRI is not particularly useful in differentiating fibrous dysplasia from other entities as there is marked variability in the appearance of the bone lesions, and they can often resemble tumour or more aggressive lesions.

- **T1** - heterogeneous signal, usually intermediate
- **T2** - heterogeneous signal, usually low, but may have regions of higher signal

Nuclear Medicine

Demonstrates increased tracer uptake on Tc^{99} bone scans (lesions remain metabolically active into adulthood) :

Differential diagnosis

Due to the variability of appearance of fibrous dysplasia the potential differential is very long, but will be significantly influenced by the dominant pattern.

- **Paget's disease**

a) mosaic pattern bone histologically
b) radiographically may be similar
c) different demographics

- **Neurofibromatosis type I**

a) osseous lesions are rare
b) vertebral column is primary target
c) ribbon ribs
d) other features of the disease usually present

- **Osteofibrous dysplasia**

a) almost exclusively in tibia with anterior bowing
b) lesion begins in cortex
c) usually seen in children <10 years

- **Adamantinoma**

a) 80% seen in the tibia
b) may appear indistinguishable

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