Fibro-osseous Lesions

A group of lesions affecting the *craniofacial skeleton* and characterized microscopically by *fibrous stroma* containing various combinations of bones and/or cementum-like material fall under the term ***benign fibro-osseous lesions***. They include a wide variety of lesions of *developmental*, *dysplastic*, and *neoplastic* origins with different clinical and radiographic presentation & behavior. Because of the histologic similarities between these diverse diseases, proper diagnosis requires ***clinical findings***, ***radiographic features***, ***surgical notes*** and ***histopathologic correlation*** to establish a specific diagnosis. Commonly included among the fibro-osseous lesions of the jaw are the following:

1. Fibrous dysplasia.
2. Focal cemento-osseous dysplasia.
3. Periapical cemento-osseous dysplasia.
4. Ossifying fibroma.

The conditions mentioned above have different clinical courses and outcomes, hence different treatment modalities ranging from non to surgical excision. For this reason a specific diagnosis is critical.

Fibrous Dysplasia (FD):

FD is a skeletal anomaly in which normal bone is replaced and distorted by poorly organized & inadequately mineralized, immature, woven bone & fibrous connective tissue. The disease may affect a single bone (***monostotic***) or multiple bones (***polyostotic***). Polyostotic FD is less common, occurring in only 25% to 30% of cases. A few of these cases (≈3%) may be associated with skin pigmentation & endocrine abnormalities, a condition known as the ***McCune-Albright syndrome***, which is more common in females.

- **Etiology & Pathogenesis:**

The nature of this condition has not been firmly established. The name dysplasia was originally intended to indicate that the condition represented a dysplastic growth resulting from deranged mesenchymal cell activity or a defect in the control of

bone cell activity. Although FD has been considered as a developmental tumor-like condition; genetic studies, however, has provided evidence that it may be better classified as a neoplastic process. FD is a sporadic condition that results from a postzygotic mutation in the **GNAS1** (guanine nucleotide binding protein, α-stimulating activity polypeptide 1) gene.

Clinically FD may manifest as a localized process, as a condition involving multiple bones, or as multiple bone lesions in conjunction with cutaneous & endocrine abnormalities depending on the point in time during fetal or postnatal life that the mutation of GNAS1 occurs.

1. Mutation occurs in *early embryonic life* ⟶ mutation in one of undifferentiated stem cells ⟶ osteoblasts, melanocytes and endocrine cells ⟶ clinically presented as ***multiple bone lesions, cutaneous pigmentation*&*endocrine disturbances***.
2. Mutation occurring during *later stages of embryonic development of the skeletal system* ⟶ the mutated cells that participate in the skeleton formation ⟶ ***multiple bone involvements***.
3. Mutation during *postnatal life* ⟶ mutated cells confines to one site ⟶ FD of a ***single bone***.

- **Clinical Features of FD:**

The condition presents commonly an asymptomatic, slow enlargement of the involved bone. FD may involve a single bone or several bones concomitantly. Monostotic FD is the term used to describe the process in one bone. Polyostotic FD applies to cases in which more than one bone is involved.

- **McCune-Albright syndrome** consists of polyostotic FD, cutaneous melanotic pigmentations (*café-au-lait macules*) and endocrine abnormalities. The most commonly reported endocrine disorder consists of precocious sexual development in girls, acromegaly, hyperthyroidism, hyperparathyroidism, and hyperprolactinemia.
- **Jaffe-Lichtenstein syndrome** is characterized by multiple bone lesions of FD & skin pigmentations.

Monostotic FD is much more common than the polyostotic form, accounting for as many as 80% of cases.

Jaw involvement is common in this form of disease. Other bones that are commonly affected are the ribs & femur. FD occurs more often in the maxilla than in the mandible. Maxillary lesions may

extend to involve the maxillary sinus, zygoma, sphenoid bone and the floor of the orbit. This form of the disease, with the involvement of several adjacent bones, has been referred to as ***craniofacial FD***. The most common site of occurrence with mandibular involvement is the body portion.

Jaw involvement is usually slow & painless, typically a unilateral swelling. Teeth displacement may occur, with malocclusion and interference with tooth eruption, without tooth mobility.

The condition characteristically has its onset during the ***1st&2nddecade of life***.

Monostotic FD usually exhibits an equal sex distribution & the polyostotic form tends to occur more commonly in females.

- **Radiographic Findings:**

FD has a variable radiographic appearance that ranges from a radiolucent lesion to a uniformly radiopaque mass. Classical presentation is ***ground-glass*** effect, which results from the superimposition of poorly calcified bone trabeculae arranged in a disorganized pattern.

Radiographically, the lesions of FD are not well demarcated. The margins blend into the adjacent normal bone so that the limits of the lesion may be difficult to define.

- Involvement of the ***mandible*** results in:
  - Expansion of the lingual & buccal plates.
  - Bulging of the lower border.
  - Super displacement of the inferior alveolar canal.
  - Periapical (PA) radiographs: narrowing of the periodontal ligament (PDL) space with ill-defined Lamina dura.
- Involvement of the ***maxilla*** results in:
  - Displacement of the sinus floor superiorly.
  - Obliteration of the maxillary sinus.
  - Increased density of the bone of the skull.

*An important feature of FD is the poorly defined radiographic and clinical margins of the lesion that blend into the surrounding normal bone.

- **Lab Findings:**

Serum calcium, Phosphorus & Alkaline phosphatase are ***normal***in *monostotic FD*, but ***altered*** in *McCune-Albright syndrome*.

- **Histopathology:**

FD consists of a slight to moderate cellular fibrous connective tissue stroma that contains foci of irregularly shaped trabeculae of immature bone. The bone trabeculae assume irregular shapes linked to ***Chinese characters***and they do not display any functional orientation, without osteoblastic activity at the bone trabeculae margins.

- **Treatment & Prognosis:**

After a variable period of prepubertal growth, FD stabilizes, although a slow advance may be noted into adulthood.

Small lesions ⟶ No treatment

Large lesions ⟶ Cosmetic or functional deformity

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Surgical recontouring

Malignant transformation is a rare complication of FD (less than 1%), usually in the polyostotic type. Many of them (osteosarcoma) were treated by radiation.

Ossifying Fibroma:

OF is a benign neoplasm of bone that has the potential for excessive growth, bone destruction & recurrence.

Clinically & microscopically similar to cementifying fibroma, it is composed of a fibrous connective tissue stroma in which new bone is formed. OF is a true neoplasm with a significant growth potential. Recently, mutations in a tumor suppressor gene were identified.

- **Clinical Features:**

The epidemiology of Ossifying fibroma is unclear because many previous diagnosed cases were confused with focal cemento-osseous dysplasia (COD). For that reason what was thought to be OF, a common neoplasm, is now considered to be uncommon because most of the cases were in reality focal COD. tends to occur during the 3rd& 4th decades of life, in females more than in males. It is a slow growing asymptomatic & expansile lesion. OF may be seen in the jaw & craniofacial bones. Lesions in the jaw arise in the tooth-bearing region, mostly in the molar & premolar area. The tumor may cause expansion of the buccal and lingual cortical plates, however perforation is very rare. OF is mostly a solitary lesion, although multiple lesions have been reported.

- **Radiographic Findings of COF:**

Well circumscribed, sharply demarcated border is the most common presenting radiographic feature, although OF may present as relatively lucent or opaque depending on the density of the calcification present. Also they may be unilocular or

multilocular, mixed radiolucent-radiopaque image may be seen. The roots of the teeth present may be displaced & less commonly resorption is seen.

- **Histopathology:**

N.B. Cementifying fibroma, cemento-ossifying fibroma (COF), ossifying fibroma are terms used to describe the same condition, since the origin is the stem cells in the periodontal ligament which may give rise to both cementoblasts & osteoblasts forming both cementum & bone which cannot be differentiated on H&E stain. The last term (COF) is the one used by WHO classification.

COF is composed of fibrous connective tissue with well-differentiated spindle fibroblasts. Cellularity is uniform but may vary from one lesion to the next. Bone trabeculae or islands are evenly distributed throughout the fibrous stroma. The bone is immature & often surrounded by osteoblast (***osteoblast rimming***). Osteoblasts are infrequently seen.

- **Treatment & Prognosis:**

Surgical removal using ***curettage*** or ***enucleation***. The lesion can typically be separated easily from the surrounding bone. Recurrence is rare.

Juvenile Ossifying Fibroma:

Is a well circumscribed rapidly growing neoplasm lack the continuity with adjacent normal bone. Lesions are circumscribed radiolucencies in some cases contain central radio-opacities (Ground glass) opacification may be observed. Those are present within a sinus may appear radiodense and create a clouding that could be confused with sinusitis. Two different neoplasm have been reported: (1) **Trabecular** and (2) **Psammomatoid**. The latter neoplasm occur more than the trabecular type in a ratio of approximately 4:1

- **Histopathology:**

Both patterns are nonencapsulated but well demarcated from the surrounding bone. Tumors consist of cellular fibrous connective tissue with variants areas of loose and other are so cellular, mitotic figures are found but rare,

areas of hemorrhage and small clusters of multinucleated giant cells are usually seen.

The trabecular type shows irregular strands of highly cellular osteoid encasing plump osteocytes. These starnds are lined by plump osteoblast and in other areas by giant cells.

In psammomatoid pattern concentric lamellated and spherical ossicles that have basophilic centers with peripheral eosinophilic osteoid rims.

Cemento-osseous Dysplasia (COD):

The term COD refers to a disease process of the jaws for which the precise etiology is unknown.

COD includes:

- Periapical COD.
- Focal COD.
- Florid COD.

All the 3 disease processes have the same features, only distinguished on the basis of the extent of involvement of the affected portions of the jaw.

1.Periapical COD:

Represents a reactive or dysplastic process rather than a neoplastic one. It may represent an unusual response of periapical bone & cementum to some undetermined local factor.

- When not associated with a tooth apex ⟶ ***Focal COD***.

- **<u>Clinical Features:</u>**

A common phenomenon, that occurs at the apex of vital teeth. A biopsy is unnecessary because the condition is usually diagnosed by clinical & radiographic features. Females are affected more than males. PACOD occurs in females at middle age (around 40 years) & rarely before the age 20. The mandible, especially the anterior periapical region, is far more commonly affected than other areas. More often, the apices of two or more teeth are affected.

- The condition appears 1st as a *periapical lucency* that is continuous with the periodontal ligament space. *To be differentiated from* ***Periapical granuloma*** ⟶ ***<u>vitality test</u>***.

- As the condition progresses, the lucent lesion develops into a mixed or mottled pattern because of bone repair.
- The final stage appears as a solid, opaque mass that is surrounded by a thin, lucent ring (after months – years).

2.Florid COD:

The FCOD is an exuberant[1] form of PACOD. FCOD represents the severe end of the spectrum of this unusual process. The patient is asymptomatic except when complication of osteomyelitis occurs. Females are more commonly affected (**black women**); between 25-60 years of age. The condition is typically bilateral & may affect all four quadrants.

Radiographically, FCOD appears as diffuse radiopaque masses throughout the alveolar segment of the jaw. A ***ground-glass*** or cyst-like appearance may also be seen.

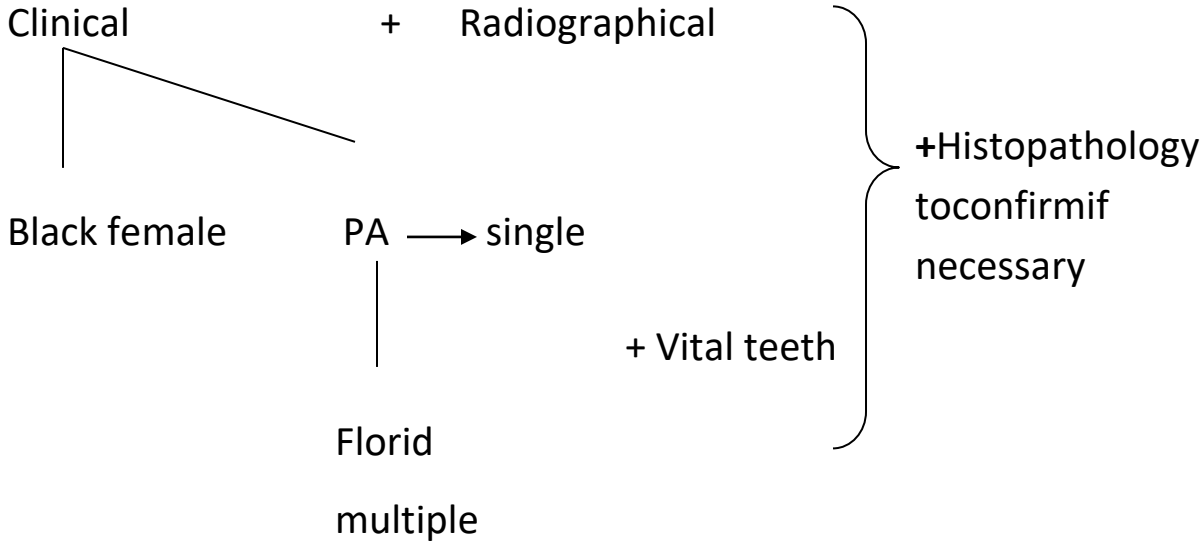
[1]Exuberant: excessive in size or extent.

- **Histopathology of COD:**

All 3 types show a mixture of benign fibrous tissue, bone, and cementum. The calcified tissue is arranged in trabeculae, spicules or larger irregular masses. Numerous small blood vessels & free hemorrhage is typically noted throughout the lesion. The proportion of the mesenchymal component to the mineralized material is variable depending on the stage and from area to area in the same lesion.

Lucent stage	***Mature radiopaque***
Less bone trabeculae	Solid sclerotic masses of bone or cementum

- **Diagnosis:**



Treatment: No treatment.

FCOD → sclerotic stage → vascularity → prone to ***necrosis*** & ***osteomyelitis*** → instruction for good oral hygiene to prevent infection.