Inherited & Developmental Disorder of Bone

Patients with inherited or developmental disorders of bone are infrequently seen in dental practice, partly because the disorders are uncommon and partly because jaw involvement may only be a minor feature or be absent altogether.

Fibro-osseous lesions

The term fibro-osseous lesion is used to describe a variety of disorders which, histologically, are characterized by the replacement of normal bone by cellular fibrous tissue within which islands and trabeculae of metaplastic bone develop.

Fibro-osseous lesions:

1. ***Non neoplastic lesions***
   - **Fibrous dysplasia**
     - -Monostotic
     - -Polyostotic
     - -Craniofacial Fibrous dysplasia.
   - **Cemento-osseous dysplasia**
   - -Periapical Cemento-osseous dysplasia(P.cemental dysplasia)
   - -Florid cemento-osseous dysplasia
   - -Focal cemento-osseous dysplasia
2. ***Fibro-osseous neoplasms***
   - **Ossifying/ cemento-ossifying fibroma**

Fibrous dysplasia of bone

Fibrous dysplasia of bone may involve one or several bones in the body, and the terms monostotic and polyostotic are applied to these different forms of the disease.

Monostotic fibrous dysplasia

Monostotic fibrous dysplasia is much more common than polyostotic forms virtually any bone may be involved but the lesion arises most

frequently in a limb bone, rib, or skull bone, particularly the jaws. Jaw lesions are more common in the maxilla than mandible.
The majority of patients with monostotic fibrous dysplasia present in childhood or adolescence, but occasionally the disease is not diagnosed until adult life.
In either jaw the first sign of the disease is a gradually increasing painless swelling which is not well circumscribed and which causes a gradually increasing facial asymmetry. The enlargement is usually smooth, often fusiform in outline, and is more pronounced buccally than lingually or palatally.

When the maxilla is involved there is usually increased prominence of the cheek and buccal expansion distal to the canine, which may extend to involve the tuberosity. The canine fossa is obliterated. Maxillary lesions commonly extend locally to involve the sinus, zygomatic process, and floor of orbit, and the orbital contents may be displaced.
In some cases where growth is more rapid and extensive there may be marked swelling of the cheek with exophthalmos and proptosis.

Mandibular lesions occur most frequently in the molar and premolar regions and if the lower border is involved there may be an obvious protruberance an increase in depth of the jaw. In either jaw there may be some malalignment, tipping, or displacement of teeth and in children any teeth involved by the lesion may fail to erupt.

Radiographically

The jaw lesions are variable in appearance .The lesions may resemble cyst-like radiolucencies containing faint bony trabeculae but as the degree of trabeculation increases they become mottled and eventually opaque, the many delicate trabeculae giving a ground-glass or orange-peel-stippling effect on intraoral radiographs.

Polyostotic fibrous dysplasia

Polyostotic fibrous dysplasia is two to three times as common in females as males and the distribution of lesions is very variable. They frequently occur in the bones of one limb, especially the lower, but the skull, vertebrae, ribs, and pelvis are also often involved. There is a tendency for the lesions to arise segmentally and to be localized in one limb or on one side of the body. Patients with severe polyostotic disease are usually diagnosed in childhood

because of the associated bony deformities and pathological fractures. The disorder may be accompanied by patchy melanin pigmentation of the skin *(cafe-au-lait* spots). The polyostotic form may also present as **McCune-Albright syndrome** in which the bone lesions are accompanied by skin pigmentation, precocious puberty in females, and occasionally other endocrine abnormalities and premature skeletal maturation.
Pigmentation of the oral mucosa has also been reported. The syndrome is very uncommon. A similar syndrome in males may occur without precocious puberty.
Jaffes Syndrome: it consists of polyostotic fibrous dysplasia + skin pigmentation.

Craniofacial Fibrous dysplasia

It is a rare condition affect facial & cranial bones and the most common site of occurrence is the body of mandible, it is a polyostotic only. This lesion is asymptomatic and cause mature deformity of bone which may lead to malocclusion of the teeth. Jaw involvement is usually slow and painless, typically a unilateral swelling. The condition characteristically has its onset during 1st and 2nd decade of life.

Pathology:

Microscopically; the fibrous dysplasia shows replacement of normal bone by fibrous tissue containing islands and trabeculae of metaplastic bone.
The fibrous tissue may be richly cellular and show a whorled pattern or consist mainly of thick, interlacing collagen bundles. Typically, the newly formed trabeculae of bone are delicate and of irregular shape resembling Chinese characters, and consist of immature, coarse-fibred woven bone.
In jaw lesions the trabeculae may be thicker and blunter than in long bones, and spheroidal areas of calcification resembling cementum may also be present. Osteoblastic and osteoclastic activity may be seen in relationship to some trabeculae and collections of osteoclast-like cells may also be present in the fibrous tissue at some distance from the bone, although these are seldom prominent.
At the margins of the lesion the lesional bone fuses with that of the surrounding normal bone and it is this feature in particular which distinguishes the lesion from ossifying fibroma.

Etiology & behavior

The nature of fibrous dysplasia has not firmly established. The disorder is generally regarded as a developmental defect but 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.

. The natural history of the lesions, most of which expand during the period of active skeletal growth and become inactive in adult life. A genetic defect involving Gs-alpha proteins appears to underlie this process.

A few cases of malignant transformation of fibrous dysplasia have been reported, usually to fibrosarcoma, some of which have followed radiotherapy.

The majority of cases are treated by conservative surgical removal of sufficient amount of the lesion to reduce deformity.

Cemento-osseous dysplasia

COD are benign fibro-osseous lesions of the jaws closely associated with the apices of teeth and containing amorphous spherical calcifications thought to resemble an aberrant form of cementum; lesions are usually without signs or symptoms.

Periapical cemental dysplasia(periapical fibrous dysplasia)

This condition arises most frequently in the incisor region of the mandible in females(female to male ratio is about 10:1) over the age of 30 years and often involves several teeth. Nearly 70% of cases affect blacks. It is usually symptomless and is discovered as an incidental finding on routine radiographs. The disease closely resembles fibrous dysplasia of bone and is sometimes referred to as periapical fibrous dysplasia. Initially, there is a replacement of bone by cellular fibrous tissue around the apices of the involved teeth resulting in ill-defined radiolucent areas which must be distinguished from periapical granulomas.

1st stage there is radiolucency around the root called (osteolytic stage).
2nd stage is radiolucent with radio-opacity and called (cementoblastic stage)
3rd stage is radio-opaque called (mature stage).

Periapical cemental dysplasia is of unknown aetiology; chronic inflammation is not implicated and the involved teeth remain vital. As the lesions mature cementum-like tissue and trabeculae of bone are deposited in the fibrous tissue resulting in increasing radiopacity.

Histopathology

The histologic appearance changes with the stage of maturation. The **osteolytic stage** consists primarily of cellular connective tissue replacing the normal trabecular bone with calcified structures . The **cementoblastic stage** has the same connective tissue component, but displays a mixture of spherical calcifications and deposits of osteoid and mineralized bone. These calcified and mineralized structures are surrounded by osteoblasts containing osteocytes . The **matured stage** is composed almost entirely of coalesced spherical calcifications and sclerotic mineralized bone with little connective tissue.

No **treatment** is required.

Florid cemento-osseous dysplasia(gigantiform cementoma)

The lesions of florid cemento-osseous dysplasia are often multiple and symmetrically distributed in the jaws, although **solitary** lesions may occur such a lesion has been designated as *focal cemento-osseous dysplasia*.

Florid cemento-osseous dysplasia arises most frequently in middle-aged Negro females and there may be a family history. The usual complaint is of a painless swelling, slowly increasing in size.

Radiographs show poorly demarcated, dense, and lobular radiopaque masses, and cyst-like radiolucency may be seen.

Histologically, is composed of cellular connective tissue containing many small and large spherical calcifications and large nodules of dense bone. Many blood vessels and hemorrhage are seen in the lesion.

lesion is not treated unless the dense bone nodules become secondarily infected and produce osteomyelitis in the area.

Ossifying /Cemento-ossifying fibroma

The cemento-ossifying fibroma now encompasses lesions previously designated as ossifying or as cementifying fibromas. A cemento-ossifying fibroma can be defined as a well-demarcated or rarely encapsulated benign neoplasm consisting of fibrous tissue containing varying amounts of metaplastic bone and mineralized masses resembling cementum. Its demarcated nature is an important feature distinguishing it from fibrous dysplasia. . Recently, mutations in a tumor suppressor gene were identified.

Clinically, it presents as a slowly enlarging and progressive swelling most often in the premolar-molar region of the mandible, and can occur over a wide age-range. Some authors have reported a definite female predilection.

Radiologically:

The appearances vary with the stage of development of the lesion. Initially there is a well-demarcated radiolucent area within which, as the lesion matures; varying amounts of calcified tissue(radioopacities) are deposited.

Histologically:

The lesion is well circumscribed. It consists of cellular fibrous tissue containing trabeculae of bone and, rather characteristically, numerous spherical deposits or rounded masses of homogeneous acellular calcified material resembling cementum. In these respects it is indistinguishable from fibrous dysplasia. Clinical and radiographic features are important in establishing the diagnosis.

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

The majority of ossifying fibromas are slow growing but some, mainly in children and adolescents, show rapid growth. Two patterns of juvenile ossifying fibroma: (1) trabecular and (2) psammomatoid.

Among lesions involving the craniofacial skeleton, the number of psammomatoid cases reported exceeds the number of trabecular cases reported by a ratio of approximately 4:1.

Radiographically, In early lesions the area may be radiolucent, becoming more radiopaque as more bone is formed. A mature lesion contains abnormal bone that produces a "ground glass" or "orange peel" pattern on radiographs.

Histologically, They are characterized by richly cellular, mitotically active fibrous tissue with trabeculae of immature looking woven bone and must be distinguished from osteosarcomas.

In contrast to the more usual type of cemento-ossifying fibroma above, which has a negligible recurrence rate, juvenile ossifying fibroma has a recurrence rate of about 30-60%.