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原文作者姓名：	Liviu Feller, Neil H Wood, Razia AG Khammissa, Johan Lemmer and Erich J Raubenheimer
通訊作者學校：	Department of Periodontology and Oral Medicine, Department of Oral Pathology, School of Dentistry, Faculty of Health Sciences, University of Limpopo(Medunsa Campus), Pretoria, South Africa
報告者姓名(組別)：	侯政廷 L 組
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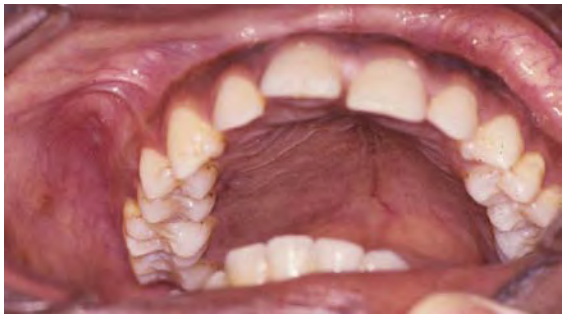
內文：

Introduction of FD

- Fibrous dysplasia (FD) is a sporadic benign skeletal disorder
  - monostotic form
    - 20~30 years age group
  - polyostotic form
    - mainly in children(<10 years), the lesions grow with the child, stabilize after puberty.
  - The ratio of occurrence of polyostotic to monostotic FD ----3:7
  - Jaffe-Lichtenstein syndrome (JLS)
    - Polystotic FD + café-au-lait pigment
  - McCune-Albright syndrome (MAS)
    - Polystotic FD + café-au-lait pigment + hyperfunctional endocrinopathies
- Gender prevalence ---equal
- Signs and symptoms
  - Bone pain, pathological fractures and bone deformities
  - Serum alkaline phosphatase (ALP) ----occasionally elevated
  - Persons with extensive polyostotic FD ---hypophosphatemia, hyperphosphaturia and osteomalacia
- Malignant transformation ---rare
- The **craniofacial bones** are affected
  - Monostotic FD—10%
  - Polyostotic FD— 50~100%
- **Craniofacial FD**(only the cranial and facial bones are affected by FD)
  - Monostotic craniofacial FD—10%~29%
  - Polyostotic craniofacial FD—71~91%
- FD of the jaws
  - Maxilla > mandible
  - Female > male
- Any cranial or facial bone can be affected by FD and the clinical associated features will depend upon the bone or bones affected.
  - Signs and symptoms
    - Facial pain, headache, cranial asymmetry, facial deformity, tooth displacement, and visual or auditory impairment

The aetiology of FD

- FD is a genetic non-inherited condition caused by missense mutation in the gene GNAS1 on chromosome 20, that encodes the alpha subunit of the stimulatory G protein-coupled receptor, Gsα.
- The activating mutations occur post-zygotically
- The mutation
  - selezctively inhibits GTPase activity, resulting in constitutive stimulation of AMP-protein kinase A intracellular signal transduction pathways.
- The extent of the FD is related to the stage at which the post-zygotic mutation in Gsα had occurred, whether during embryonic development or postnatally.
- Polyostotic FD can affect bones derived from mesoderm or neural crest, and is associated with pregastrulation mutation.
- The same process associated with multiple organ manifestations of Gsα mutation is referred to as McCune-Albright syndrome.
  - mutated pluripotential cell →mutated clone of cells →affecting bones and multiple organs.
- Monostotic FD and polyostotic FD without either craniofacial skeletal or extraskeletal organ involvement can develop from a post-gastrulation mutation.
- But since polyostotic FD nearly always involves craniofacial bones, it is reasonable to assume that the monostotic FD is the only form of FD that can develop post-gastrulation.
- The postnatal manifestation of FD
  - is not a reflection of the stage of development when the mutation occurred
  - but indicates the time that the dynamic equilibrium between mutated and normal osteogenic cells in the mosaic fibrous dysplastic bone favoured the mutated cells.
- Possible factors influencing the dominance of mutated over normal cells include growth factors and hormones ,and it is probable that there is a 'critical mass' of mutated cells necessary for the development of FD.
- In fibrous dysplastic bone, the increased expression of cAMP by the mutated lesional cells is associated with abnormal osteoblast differentiation and formation of defective bone.

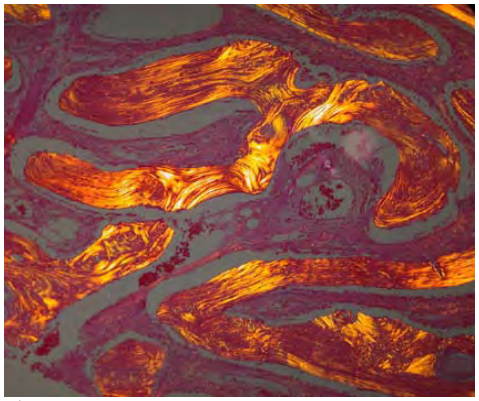
The skeletal lesions of FD

- Focal lesions of FD are somatic mosaics, and the severity and extent of the bony lesions are a function of the ratio between the mutated cells and the normal osteoblasts.
- The mutated cells are
  - Poorly differentiated, functionally impaired osteoblasts with an increased proliferation rate.
  - Capable of producing extracellular matrix and woven bone. However the woven bone is abnormal in organization and in composition.

- The bone matrix in fibrous dysplastic lesions is deficient in osteopontin and in bone sialoprotein (BSP), compared to normal bone.
- Fibrous dysplastic bone lesions demonstrate a deficit in mineralization that can be defined as localized osteomalacia.
- The unmineralized woven bone in long bones at sites where FD develops never matures into lamellar bone; and the local 'normal' mineralized bone adjacent to the lesion shows a relatively low mineral concentration.
- In addition to the osteomalacic changes, fibrous dysplastic bone shows increased osteoclastic activity, and markers of bone resorption may be elevated in some affected persons.
- The mutated stromal cells of FD express high levels of IL-6 owing to the inherited cellular excess of cAMP. The increased levels of IL-6 stimulate osteoclastogenesis that contributes to the bone resorption at the site of FD.
  - Thus the fibrous dysplastic bone is characterized by increased bone resorption and poor mineralization.
- FD and bone lesions caused by hyperparathyroidism are similar in nature, and are generated by the intracellular downstream effect of the activation of the parathyroid hormone (PTH) G protein-coupled receptor of osteogenic cells.
- While in hyperparathyroidism PTH receptor is over stimulated by excess PTH, in FD the same receptor is inherently active owing to the mutation in the α subunit of the G protein.
  - The end result in both FD- and in hyperparathyroidism-associated bony lesions is an increase in osteoclastogenesis resulting in bone resorption.
    - Tunnelling bone resorption
    - But tunnelling resorption is not evident in persons with FD that do not have parathyroidism.

Radiological features and microscopic features of FD

- Radiological feature
  - Diverse
  - Dependent upon the proportion of mineralized bone to fibrous tissue in the lesion.
  - Early FD of craniofacial bones
    - radiolucent with either ill defined or well defined borders, and may be unilocular or multilocular.
  - Mature lesion
    - The bony defects acquire a mixed radiolucent/radiopaque appearance, and established FD exhibits mottled radiopaque patterns often described as resembling ground glass, orange peel or fingerprints, with ill defined borders blending into the normal adjacent bone
- Microscopically
  - Irregular trabeculae of woven bone, blending into the surrounding normal bone and lying within a cellular fibrous stroma with osteoblast progenitor cells resembling fibroblasts.
  - Chinese script writing



- Early craniofacial FD
- Characterized by minimally mineralized deposits of woven bone with a continuum progressive lamellation of the woven bone trabeculae as FD becomes more mature in contrast to FD lesions in long bones where mature lamellar bone is not found.

Treatment of FD

- There is **no cure** for FD, and the existing guidelines for treatment are not universally accepted.
- Surgical intervention
  - Is required when important structures are in danger of compression
  - a conservative surgical approach will often require more than one intervention to control the clinical signs and symptoms.
- Intravenous bisphosphonate therapy
  - relief of bone pain and reduction of osteoclastic activity.

Conclusion

- Fibrous dysplastic lesional cells are committed osteogenic precursor cells with impaired capacity to differentiate into normal functioning osteoblasts. The defects in osteoblast differentiation are associated with Gsα mutation of both neural crest and mesoderm-derived osteogenic cells and may thus affect any part of the osteogenic compartment.

題號	**題目**
1	下列何者為 Fibrous dysplasia 於顯微鏡下或 X 光觀察中不會觀察到之構造？ (A) Chinese scrip writing (B) Woven bone (C) Ground-glass appearance (D) Codman's triangle
答案(D)	出處：Oral and Maxillofacial Pathology, 3rd edition
題號	**題目**
2	下列何種 syndrome 有合併內分泌疾病？ (A) Jaffe-Lichtenstein syndrome (B) MeCune-Albright syndrome (C) Mezabraud syndrome (D) Neurofibromatosis
答案(B)	出處：Oral and Maxillofacial Pathology, 3rd edition