Fibrous Dysplasia & Cherubism: Craniofacial and Dental Implications

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Commonly Asked Questions:

- How is craniofacial FD/Cherubism diagnosed?
- When and How do the bone lesions show up?
- Where are most lesions located in the craniofacial skeleton?
- Will more lesions develop?
- What functional problems can occur?
  - Blindness?
  - Hearing loss?
  - Dental problems?
- How do you treat craniofacial FD/Cherubism?
Craniofacial Anatomy
Prevalence - FD

- Monostotic FD is reported to be most common
  - Case reports are inconclusive
  - None of the patients in these studies had thorough skeletal/endocrine screening to determine full extent of disease

- Most common locations are craniofacial bones, proximal femur, and ribs

**Monostotic (MFD)** = One bone or region of bony involvement

**Polyostotic (PFD)** = More than one bone/region involved

**McCune-Albright Syndrome (MAS)** = FD + skin + endocrine abnormalities
Where are most lesions located?

- In MFD, the zygomatico-maxillary complex (ZMC) most commonly involved.

- In PFD and MAS, the craniofacial region is involved in 90% of the cases and the anterior cranial base is involved in over 95% of cases.

- 84% of patients with craniofacial FD have jaw lesions.
  - 31% have FD lesions in both jaws.
    - Maxilla > Mandible

Akintoye et al., OOOO, 2003
Daramola et al. OOO, 1976
Prevalence - Cherubism

- Rare, hereditary, benign bone disease with an autosomal dominant inheritance
  - Most cases from mutation in SH3BP2 gene on chromosome 4p16.3
  - Can affect different generations
  - Isolated non-familial cases have been reported

- **Bilateral** expansion of the upper and/or lower jaw
  - Becomes noticeable in early childhood (ages 2-7) and grows progressively until puberty
  - Lesions regress, fill with bone & remodel until ~age 30

Papadaki, Orphanet 2012
Prevalence - Cherubism

- Lower jaw more commonly affected

Classification

- Quiescent – older individuals, lack of growth
- Non-aggressive - teenagers
- Aggressive – younger children
  - Large, rapidly growing
  - May cause tooth displacement, root resorption, perforation of bone cortex (lining)
  - Affects normal eruption of teeth, occlusion and function of dento-alveolar complex

- Symptoms range from undetectable to gross deformity of the jaws, airway, vision or hearing impairment
How do lesions show up?

- **Signs and Symptoms:**
  - Incidental findings on x-rays
  - Asymmetry of face: eyes, forehead, cheeks, nose, jaws
    - Teeth typically NOT displaced n FD
  - Functional changes:
    - Vision loss/visual disturbances
    - Hearing loss
  - Nasal congestion
  - Epiphora (overflowing of tears)
  - Headaches/bone pain
  - Paresthesia (numbness)
  - Seizures (very rare)
How is a diagnosis made?

- **History and physical exam**
  - Cherubism: Family History
  - Asymmetry & Swelling – most common complaints in facial skeleton

- **Radiographs**
  - Computed tomogram (CT)
  - Bone scan
  - Dental x-rays

- **Genetic Testing**
  - Gsα mutation in affected tissue (FD)
  - SH3BP2 gene (Cherubism)

- **Lab values (i.e growth hormone levels)**

- **+/− Biopsy**
Giant Cell Lesions: What are they?

- Bengin primary bone tumors containing multinucleated giant cells and many blood vessels

- FD & Cherubism are “cousins” of the same disease process
  - Gross pathology specimens appear almost identical
  - Radiographically and histologically similar
Craniofacial Fibrous Dysplasia

- Degree of facial deformity varies
  - MAS most severely affected, particularly when associated with untreated/inadequately treated growth hormone excess
Cherubism/Giant Cell Lesion
Plain X-rays

Fibrous Dysplasia
No involvement
Plain X-rays: Panorex

Cherubism

No involvement

FD
Computed Tomography (CT)

- Axial/transverse plane
- Bone windows

Fibrous Dysplasia  No Involvement
Bone Scan

Monostotic
Fibrous Dysplasia
Craniofacial Fibrous Dysplasia on CT

- Obliteration of normal architecture and landmarks
  - Cortex of bone remains intact

- Variable radiographic appearance
  - Lytic/Lucent
  - Ground glass/mixed
  - Sclerotic
  - Cystic component

- Not uniform

- Appearance changes over time
Cherubism on CT
When do FD lesions present?

- CF-FD lesions are earliest to occur, but can remain “silent” until deformity or growth occurs.
- 90% of FD lesions were present prior to age 15.
  - 90% of all CF-FD lesions detectable on bone scan by age 3.4.
  - No new CF-FD lesions reported beyond the age of 10.

Hart, JBMR, 2007
How do FD lesions progress?

4y 9m

15y

Uninvolved
Will more FD lesions develop?

- More new lesions are not likely to develop

- Lesions can expand and may change over time
  - Radiographic changes
    - Suggests changes in the activity of the abnormal bone-forming cells as a function of age
    - Most dramatic change occurs in the second decade (11-20 yrs)
      - Patients undergoing growth and hormonal changes
  - Become associated with rapid growing lesions
    - i.e. aneurysmal bone cysts
  - Extremely rare transformation to malignancy, <1%
  - Growth Hormone excess can exacerbate
What functional problems can occur?

- Vision loss/Visual disturbance
- Hearing Loss
- Dental problems
- Numbness
Fibrous Dysplasia and Vision Loss

- Polyostotic fibrous dysplasia: frequent anterior cranial base involvement
  - Proximity of FD to optic nerve
  - Sporadic case reports of vision loss
  - Most commonly reported neurologic symptom is vision loss (Sassin & Rosenberg, 1968)

- Assumption: FD around the optic nerve inevitably leads to blindness → prophylactic optic nerve decompression is necessary
Fibrous Dysplasia and Vision Loss

- Statistically significant narrowing of the optic canal occurs.

- Majority (94.7%) of patients had normal eye exams:
  - 2 of 38 (5.3%) had an abnormal exam.

- Prophylactic optic nerve decompression is not recommended based on radiographic findings alone since these findings DO NOT correlate with vision loss.

- FD is NOT a progressive condition which results in inevitable blindness.

Lee JS et al, NEJM, 2002
Dental Problems

- Because of often complex co-morbidities, dental aspects are frequently overlooked
  - Variable presentations cause some dental practitioners to delay or avoid dental procedures

- Patients can receive various dental therapies (restorations, root canals, extractions) without exacerbating lesions

- Increased rate of cavities
  - May require more frequent hygiene visits, electric toothbrush, application topical fluoride

- Medication-induced osteonecrosis of the jaws (ONJ)
  - Very rare despite higher doses

Akintoye, S. et al, OOOO, 2013
Dental Anomalies in FD Patients

Attrition
Retained tooth
Taurodontism
Enamel hypomineralization
Enamel hypoplasia
Displacement
Oligodontia
Rotation

Patients with dental anomaly (%)
Dental Problems in Cherubism

- While development and tooth eruption appear to be normal in FD, they are significantly affected in Cherubism.

- Impact on development and eruption varies depending on the time of onset and severity of the expansile lesions.
  - Arrangement of primary teeth can be disturbed.
  - Disruption of permanent dentition can include:
    - absent teeth (mostly molars)
    - abnormally shaped teeth/rudimentary development
    - partially resorbed roots
    - delayed and ectopically erupting teeth

Papadaki, Orphanet 2012
Dental Problems in Cherubism

- Tooth extraction may be needed in cases with teeth “floating” in cherubism lesions, or if they are impacted.

- In severe instances, children may require prostheses which need adjustment with growth.
  - Can improve function and aesthetics.
Orthodontic Therapy

- The majority of patients with jaw FD have malocclusion (disorganized arrangement of the teeth)

- Dental malocclusion/crowding
  - Orthodontic treatment can be performed in FD/Cherubism patients
  - Orthodontic therapy may take longer in FD bone
  - Relapse may be more common because teeth tend to return to their initial position

- ? Delay ortho until skeletal maturity – not always necessary in FD, but this should be the rule in Cherubism
Dental Implants

- Bone healing and integration of the implants occurs
  - May be slower and the quality of bone is thin

- Reported case of 32 yo female w/MAS:
  - Successful integration and loading of dental implants in maxilla and mandible occurred
  - Maxillo-mandibular lesions had been quiescent for 3 years
  - Dental implants were at least 15 mm in length
  - Functional after 5 years

- Literature is limited - unclear risk of implant failure

- Recommend that implant(s) placed after skeletal maturity AND once growth of the FD lesion has subsided

How is CF-FD Treated?

- Management depends on age/skeletal maturity and clinical findings
  - Lesions can be characterized as:
    - Quiescent (stable with no growth)
    - Non-aggressive (slow growing)
    - Aggressive (rapid growth +/- pain, paresthesia, etc.)

- Monitor, observation and close follow-up
  - Clinical assessment, including photographs
  - Sensory nerve testing
  - Maxillofacial CT – depending on clinical findings

- Medical management – bone pain
How is CF-FD Treated?

- **Indications for surgery:**
  - Biopsy if diagnosis is questionable
  - Concern for aggressive growth/atypical or unusual behavior

- **Surgical options:**
  - “Contouring” – should be done after growth has stopped
  - Resection and reconstruction – if lesion can be completely removed or if there is concern for associated disease/malignancy
  - Orthognathic surgery – correct malocclusion or facial/dental asymmetry
    - No documented contraindication if lesions are quiescent
    - Bone healing is normal
How is CF-FD Treated?

- *However, there is evidence that lesions can regrow after surgery and even become aggressive*

- We cannot predict or prevent regrowth

- Surgery is not typically indicated for cosmetic purposes
  - Dependent on psychosocial situation
How is CF-FD Treated?

Photos c/o Dr. Kaban, MGH
How is CF-FD Treated?
How is Cherubism Treated?

- Management varies based on the extent, aggressiveness and clinical behaviour

- Conservative treatment is the most common form of treatment, as it is self-limiting
  - UNLESS, the lesion is causing serious disfigurement and expansion
  - Concern for secondary process/unusual behavior
  - Psychosocial reasons

- Medical treatment
  - Interferon
  - Calcitonin
  - Anti-inflammatory agents?
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