July 19: Odontogenic Cysts

**July 19: Odontogenic Cysts, Tumors, and Related Jaw Lesions**

**Preceptor: Stewart**

1. (DL) Review the classification of jaw cysts

Odontogenic cysts are defined as epithelial-lined structures derived from odontogenic epithelium. The following classification system is a modification of the World Health Organization classification, which divides cysts based on etiology.

   A. Developmental (Odontogenic)
      1. **Follicular cyst** (dentinigerous cyst): develops within the normal dental follicle surrounding an unerupted tooth.
      2. **Odontogenic keratocyst**: the odontogenic keratocyst (OKC) is the most important of the odontogenic cysts. This cyst may have any clinical appearance; it is a great mimic. Unlike other cysts, they are aggressive and can be difficult to remove. They can grow rapidly. Frequently recur.
      3. **Eruption cyst**: develops from dental lamina overlying erupting tooth. Often bursts spontaneously.
      4. **Gingival cyst of infants**: Gingival cysts of newborns generally occur in multiples but occasionally occur as solitary nodules. They are located on the alveolar ridges of newborns or young infants. They originate from remnants of the dental lamina and are located in the corium below the surface epithelium.
      5. **Gingival cyst of adults**: Gingival cysts of the adult are found only in soft tissue in the lower premolar areas. These cysts present as tense, fluctuant, vesicular, or bullous lesions. Histologically, they look like lateral periodontal cysts, and they probably represent the same lesion when found in soft tissue.
      6. **Developmental lateral periodontal cyst**: pathogenesis not known. May develop from rests of Malassez, or rest cells of the dental lamina trapped within bone after eruption of the tooth.

   B. Developmental (Nonodontogenic)
      1. Nasopalatine duct cyst
      2. Midpalatal cyst of infants
      3. Nasolabial cyst
      4. Globulomaxillary cyst, median mandibular cyst, and median alveolar cyst

   C. Inflammatory
      1. **Radicular cyst**
         a. **periapical cyst** (radicular cyst): most common odontogenic cyst. Usual etiology is tooth infection leading to necrosis of the pulp. Toxins exit the apex of the tooth inflammation that stimulates the Malassez epithelial rests in the periodontal ligament, resulting in the formation of a periapical granuloma that may be infected or sterile. The epithelium undergoes necrosis due to lack of blood supply, and the granuloma becomes a cyst.
         b. **inflammatory lateral periodontal cyst**: lateral to tooth

   D. Nonepithelial
      1. **Idiopathic bone cavity** (traumatic, solitary, hemorrhagic bone cyst): Thought to originate from intramedullary hemorrhage caused by trauma. Degeneration of the clot leaves an empty bone cavity. Restricted venous drainage leads to increasing edema, which causes continued resorption of trabeculae and expansion of the lesion. Expansion of the lesion tends to stop when cortical bone is reached.
      2. **Aneurysmal bone cyst** neither a cyst nor an aneurysm. Exact etiology and pathogenesis unknown. One theory is that alterations in local hemodynamics lead to venous engorgement, resorption, and replacement with connective tissue and osteoid.
      3. **Stafne’s mandibular lingual cortical defect**: inclusion of aberrant salivary gland tissue within or, more commonly, adjacent to the lingual surface of the body of the mandible within a deep and well-circumscribed depression.
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2) Review the classification for odontogenic tumors

<table>
<thead>
<tr>
<th>Epithelial</th>
<th>Clinical</th>
<th>Histology</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>ameloblastoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) peripheral</td>
<td>Age: 30-50 y, M &gt; F</td>
<td>similar to basal cell carcinoma, not invasive</td>
<td>most common tumor</td>
</tr>
<tr>
<td></td>
<td>Loc: soft tissue outside alveolar bone, mandible twice as often as maxilla</td>
<td></td>
<td>Age &lt; 30, unusual in age &gt; 30</td>
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<tr>
<td></td>
<td>Sx: asymptomatic OR painless swelling, loose teeth, malocclusion, or nasal obstruction</td>
<td></td>
<td>can be locally invasive</td>
</tr>
<tr>
<td></td>
<td>Sx: asymptomatic</td>
<td>located within wall of cyst</td>
<td>associated with impacted tooth or dentigerous cyst</td>
</tr>
<tr>
<td></td>
<td>Sx: asymptomatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2) central unicystic</td>
<td>Age: 10-20 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Loc: 90% in mandible</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sx: asymptomatic</td>
<td></td>
<td></td>
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<tr>
<td>3) central solid/multicystic</td>
<td>Age: 20-30 y</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Loc: 80% in mandible, usually molar region</td>
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<td></td>
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<tr>
<td></td>
<td>Sx: rarely painful</td>
<td></td>
<td></td>
</tr>
<tr>
<td>calcifying epithelial</td>
<td>Age: wide range</td>
<td></td>
<td>(Gorlin's cyst), can be extrasosseus</td>
</tr>
<tr>
<td>odontogenic</td>
<td>Loc: mandibular premolar region</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sx: painless</td>
<td></td>
<td></td>
</tr>
<tr>
<td>adenomatoid odontogenic</td>
<td>Age: &lt; 20 y, 2/3 in women</td>
<td>encapsulated, cystic structure, ductlike arrangement</td>
<td>(adenoameloblastoma), late disturbance in odontogenesis</td>
</tr>
<tr>
<td>tumor</td>
<td>Loc: 2/3 in anterior maxilla</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sx: painless swelling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>calcifying odontogenic</td>
<td>Age: wide range</td>
<td>epithelial lining with pale eosinophilic cells and &quot;ghost cells&quot;</td>
<td>(Gorlin's cyst), can be extrasosseus</td>
</tr>
<tr>
<td>cyst</td>
<td>Loc: mandibular premolar region</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sx: painless</td>
<td></td>
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</tbody>
</table>

| Mesenchymal                 |                                   |                                     |                                            |
| odontogenic fibroma         | Age: children, adolescents, young adults | collagen fibers and fibroblasts | rare, resembles dental follicle, slow expansile growth |
|                             | Loc: mandible                     |                                     |                                            |
|                             | Sx: rare pain                     |                                     |                                            |
| odontogenic myxoma          | Age: 10-20 y                      | few cells, prominent mucoid intercellular substance, stellate/spindle-shaped cells | slow expansile growth                     |
|                             | Loc: mandible > maxilla           |                                     |                                            |
| cementomas                  | Age: black woman > 20 y           | cementoblasts, cemental tissue, fibrous connective tissue | (periapical cementoosseous dysplasia) |
|                             | Loc: mandibular incisor root apices multiple lesions |                                     |                                            |
|                             | Sx: asymptomatic                  |                                     |                                            |

| Mixed                       |                                   |                                     |                                            |
| ameloblastic fibroma        | Age: <10 y, Mean age: 14.6 y      | islands of epithelial cells in nests and cords; occasional stellate reticulum-like tissue, no calcification | slow-growing, uncommon                     |
|                             | Loc: molar region of mandible     |                                     |                                            |
|                             | Sx: rare pain                     |                                     |                                            |
| ameloblastic odontoma       | Age: any age, more freq in children | great variety of cells in complex distribution, resemble tooth germ | extremely rare                             |
|                             | Loc: mandible > maxilla           |                                     |                                            |
|                             | Sx: mild pain, delayed eruption of teeth |                                     |                                            |

3. (DR) Discuss basal cell nevus syndrome.

Nevus basal cell syndrome (aka Gorlin’s syndrome)
- Rare: incidence 1:60,000
- Autosomal dominant, caused by mutation of tumor suppressor PTCH
- Five major characteristics:
  1. Neviod basal cell carcinomas of skin
  2. Multiple odontogenic keratocysts (OKCs)
  3. Congenital skeletal abnormalities (bifid ribs, hypertelorism, frontal bossing)
  4. Ectopic calcifications (falx cerebri)
  5. Palmar or plantar pits

- Also can be associated with benign ovarian and cardiac fibromas, as well as cleft lip/palate
- Tend to be multiple OKCs that are benign but locally aggressive and have high recurrence rate
- Treatment of OKCs usually by enucleation and application of Carnoy’s solution (ETOH, chloroform, acetic acid)
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4. (JLev) Why are radiographs important in the workup of jaw cysts and odontogenic tumors? Describe some pathognomonic appearances of these lesions.

Radiologic appearance of jaw cysts and odontogenic tumors varies considerably. The common lack of physical findings and the development of most of these lesions within the confines of the bone make radiologic investigation and interpretation uniquely important. Radiographs are also important in treatment planning for surgical removal. They can evaluate encroachment on vital structures, extent into soft tissue, size of the lesion, and requirements for reconstruction. Radiography allows for creation of a radiologic differential diagnosis. Modalities include intraoral (e.g. occlusional, peri-apical, bitewing), extraoral (e.g. panoramic, lateral oblique, water’s), and CT.

**PATHOGENOMONIC APPEARANCES**

**Osteosarcoma of the mandible**: sunburst appearance, radiating periosteal new bone

**Chondrosarcoma of the mandible**: soft tissue mass with amorphous “popcorn” calcifications

**Ameloblastoma**: displaced surrounding structures, with multiple loculations and a honeycomb appearance

**Cemento-ossifying fibroma**: well-circumscribed lesion with a dense core and lucent rim; the core enlarges and rim diminishes with maturation

5. (DJ) Name the two most common cystic lesions of the jaw.

I. **Radicular (periapical) cysts** – the most common type of jaw cysts (65-70%) which are inflammatory in nature and can occur around the root of any nonvital tooth (due to dental caries entering the tooth pulp, trauma, or surgical devitalization). They derive their epithelial lining from proliferation of odontogenic epithelium within the periodontal ligament.

   - **Pathogenesis**: cyst develops as a result of dental pulp inflammation that progresses to the periapical area through the apical foramen of the tooth or through a lateral root canal.
   - **Clinical findings**: small radicular cysts usually do not become acutely infected and are frequently asymptomatic. Larger cysts may produce expansion of bone, displacement of tooth roots, and crepitus when palpating the expanded alveolar plate. Radiographic appearance is that of cystic lesion around the end of the root (most commonly the maxillary anterior teeth). Histopathologic exam will reveal a thin, non-keratinized cyst lining.
   - **Complications**: loss of supportive alveolar bone and the loss of teeth
   - **Treatment**: endodontic therapy for small cysts (i.e. <5mm), endodontic therapy plus periapical surgery and cyst enucleation for larger lesions, or if the tooth is not restorable, tooth extraction combined with cyst enucleation. Prognosis is excellent and recurrences are rare.

II. **Dentigerous (follicular) cysts** – second most common type of jaw cysts (15-18%) which are associated with the cementoenamel junction at the crown of impacted and unerupted teeth. The epithelial lining is derived from proliferation of reduced enamel epithelium. These lesions are well-defined, radiolucent, sometimes expansile lesions that are slow growing and benign. The lower 3rd molars and upper canines are most commonly involved.

   - **Pathogenesis**: cyst develops subsequent to an accumulation of fluid between the remnants of the enamel organ and the contiguous tooth crown
   - **Clinical findings**: Initially asymptomatic; may cause intraoral or extraoral swelling later or become infected causing pain. Radiographic appearance is that of a well-delineated lesion associated with and unerupted tooth. Aspiration of light, straw colored fluid is characteristic. Histopathologic exam will reveal a thin, non-keratinized cyst lining.
   - **Complications**: bony destruction, infection, weakening of the jaw, displacement of teeth, resorption of adjacent tooth roots, encroachment on the maxillary sinus floor, and deflection of the inferior alveolar canal. Transformation into an ameloblastoma is also possible. Dysplasia or carcinomatous transformation is rare.
   - **Treatment**: Enucleation of the cyst and removal of the associated tooth is the treatment of choice. Even large bony cavities can regenerate bone of several months. For extremely large defects may use primary bone grafting. Prognosis is generally excellent and recurrence rate is very low.
6. (KY) Why is an odontogenic keratocyst often difficult to diagnose? Why is its differentiation from other types of cysts important?

Odontogenic keratocysts are often difficult to diagnose because they may occur in many clinical situations, may be asymptomatic until gradual expansion is noted or secondary infection occurs, may be identified in a variety of anatomic locations, and may have several radiographic variations. Also, the diagnosis of an odontogenic keratocyst is mainly a histologic one.

Differentiation of odontogenic keratocyst from other types of odontogenic cysts is important because of its high recurrence rate. Recurrence rates from 10-60% have been reported. Large difference in rate of recurrence may be related to inconsistencies in reporting of data and inadequate follow-up, these lesions take many years to recur.

The high incidence of recurrence is possibly due to several factors:
1) Some lesions are multilocular, making them difficult to remove.
2) The cyst lining is thin and friable, making it easy to leave behind fragments during enucleation.
3) Odontogenic cysts have been shown to have higher mitotic rates, which may make any residual epithelium more likely to proliferate.
4) These lesions tend to perforate cortical bone more frequently, cystic epithelium may be located in soft tissue from where it is more difficult to completely excise.
5) These lesions are often mistaken for benign cysts and are treated less aggressively.

Presentations:
- It may appear as a follicular cyst associated with the crown of an unerupted tooth.
- It may also appear to be associated with the root of a tooth as a radicular cyst.
- Thirdly, it may occur by itself as a primordial cyst, which is a cyst that arises where there is no apparent tooth formation associated.

Clinical features:
- Peak incidence is in the second and third decades, rare in those younger than age 10.
- Anatomically the mandible is affected more frequently than the maxilla, with 75% of the lesion occurring there.
- Third molar and ramus areas are most frequently affected.

Radiographic features:
- Approximately 50% of these cysts have a unilocular appearance, but multilocular appearance can occur.
- May be follicular or radicular.
- Well-circumscribed with sclerotic border.

Histologic Criteria:
- Thin, stratified squamous epithelium that is a uniform 6-8 cells thick.
- Prominent columnar or cuboidal basal cell layer with dense nuclear staining.
- Corrugated surface layer of parakeratin or orthokeratin.
- Thin connective tissue wall.

Treatment:
- Enucleation and curettage.
- If lesion is large, decompression with subsequent enucleation is advantageous.

7. (SR) Ossifying fibroma vs. fibrous dysplasia?

**Fibrous Dysplasia:**
Not a true neoplasm -- it is a genetically based tumor-like condition where normal medullary bone is replaced with fibrous connective tissue. Usually a sporadic mutation of α-subunit of G-protein signal transduction.

Monostotic (one bone) is most common than polyostotic (multiple bones).
McCune-Albright: polyostotic fibrous dysplasia, cafe-au-lait skin macules, endocrinopathies
Slow-growing asymptomatic, produces bony hard swelling. Can be self-limiting, can displace teeth and cause malocclusion.

**Expands cortices but does not displace inferior alveolar canal.**
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Margins not well demarcated. Early lesions radiolucent, later lesions radiopaque. "Ground-glass" appearance as medullary bone is replaced with trabecular bone. Histopathology: irregularly shaped trabecular bone in fibrous connective tissue. Abnormal bone coalescing with normal surrounding tissue. Treatment/Prognosis: Surgery only for disfigurement/CN dysfunction 2/2 compressive lesions. Recontouring of bone more common than resection. Wait until lesion matures. Reports of sarcoma transformation; Recurrence more likely if treated during active growth phase of lesion vs. after maturity.

Ossifying Fibroma: True benign tumors of mesenchyme with strong predilection for tooth-bearing sections of jaw. Slow growing, expansile. Typically woman in 20-30s. Early lesions radiolucent, more opaque as lesion matures. Can expand the cortices and displace adjacent structures. In mandible, usually are midbody inferior edge and expand down and out from the mandible. Histopathology: dense cellular fibrous tissue with variable calcified trabecular osteoid/bone/spherical cementumlike structures. Well circumscribed, does not diffusely infiltrated adjacent tissues. Treatment/Prognosis: Enucleation/Curettage if early vs. Resection if larger (5mm margin). Recurrence rare. Juvenile ossifying fibroma is aggressive and rare and presents more in maxilla.

8. (TL) How do developmental non-odontogenic cysts form?

Non-Odontogenic Cysts (Fissural cysts) and development
- Fissural cysts are not related to teeth but to fusions of upper jaw bones.

Nasolabial (Nasoalveolar) Cysts
- Most common in adults 40-60 with 3:1 female predominance
- Cyst epithelium derived from remnants of nasolacrimal duct.
- Symptoms: Physical exam reveals dark-blue mass in anterolateral nasal floor and vestibule often extending into sublabial sulcus. Can causes swelling in lateral aspect of upper lip may elevate nasal vestibule and cause nasal alar flaring +obliteration of nasolabial fold. Generally painless unless infected.
- Imaging: no radiographic sign
- Histopath: cyst lined by psuedostratified columnar epithelium –cilia/goblet cells
- Treatment: transoral surgical excision via sublabial approach
- Prognosis: excellent, rare recurrence. If left untreated, long standing pressure may result in erosion of nasal floor or premaxilla.

Nasopalatine Cysts
- Symptoms: May present with well-defined oval mass by anterior nasal spine vs. palatal swelling. Complain of salty taste.
- Cyst epithelium derived from embryonic remnant of nasopalantine duct
- Treatment: If <7 mm may follow clinically and radiographically. Larger cysts treated with enucleation via a palatal flap.
- Imaging:well-defined unilocular radiolucency is middle of maxilla
- Prognosis: excellent. Recurrence is rare.

Globomaxillary Cysts: some say doesn’t exist
- Inclusion cysts that develop at fusion between maxillary process and globular portion of median nasal process
- Imaging: Large radiolucency between the lateral incisor and cuspid. Tends to cause divergence of the roots.
- Lies within the bone unlike nasoalveolar cysts which arise from soft tissue overlying the bone
- Result in complete dehiscence of palate and separation of canine and lateral incisor teeth
- Histopath: cyst lined by stratified squamous or respiratory epithelium
- Treatment: enucleation
- Imaging: pear-shaped lucency causing divergence of tooth roots
Median Palantine Cysts

- Uncommon. Only true fusion cyst. Arises from entrapped epithelial rests along line of fusion of palatal and maxillary processes.
- Located at midline of hard palate and maxilla
- Symptoms: midpalatal swelling. Asymptomatic
- Imaging: well-circumscribed radiolucency with sclerotic border in midline of hard palate posterior to incisive canal
- Treatment: Access via full-thickness palatal flap. Can cure with curettage or enucleation with low-reccurrence risk.

9. (CY) Describe the characteristics of ameloblastoma of the mandible? How would you manage this patient? Is there a potential for metastasis?

Ameloblastoma:
- Benign epithelial odontogenic tumor
- Can be extremely locally aggressive and infiltrative
- Occur in individuals aged 20-40 years
- Posterior mandible is the most common location; only 20% of lesions are found in the maxilla
- Males = females
- Presentation: incidental finding on x-ray or as painless bony expansion
- Radiographic findings: expansile multilocular radiolucency in the area of the lower third molar, but they may be found anywhere in the jaw
- Classification
  - Peripheral (extraosseous) – from alveolar mucosa
  - Central (intraosseus)
  - unicystic: younger population (adolescents to 20s), well-circumscribed radiolucency associated with the crown of an unerupted tooth, located with the wall of a cyst
  - Multicystic or solid
    - Metastasis can occur although very rare, case reports of metastasis to LNs, lungs, orbit, intracranial malignant ameloblastoma

Treatment
- Must be monitored radiographically throughout their lifetime
- 1-cm clear margins are considered the standard with block or segmental resection, depending on the relationship of the lesion to the inferior cortical border.
- The single exception = unicystic ameloblastoma
  - Believed that this lesion is encapsulated and can be removed with enucleation/curettage procedures alone.
- For peripheral ameloblastoma, a more conservative excision with close clinical follow-up is the standard of care.