PathMD™: Board Review Letter

Author: Philip Ferguson, M.D. **Odontogenic Lesions – Part 1** Volume 1, Number 17

Embryology Questions

1. Which of the following embryologic elements is responsible for the formation of dentin?

    B. Odontoblasts

Answer: B. Odontoblasts differentiate from the mesenchyme of the dental papilla and make dentin. Ameloblasts are on the outer surface and produce the enamel of the tooth. (Sadler, T.W. *Langman's Medical Embryology*. 7th Ed. Williams & Wilkens, 1995. pp 341-343)

2. Tomes' fibers, which are 200μm long unmyelinated nerve fibers, are found in which of the following tooth associated structures, and are responsible for sensation?

    A. Dentin

Answer: A. Odontoblasts, which are neural crest in origin, are responsible for the formation of dentin. As these cells deposit the dentin, they leave small processes (Tomes' fibers) within small dental tubules. In normal teeth, enamel covers the dentin and prevents sensitivity. However, if one has a receding gum line, the dentin (and therefore unmyelinated nerve fibers) is exposed causing very sensitive teeth. (Sternberg, S.S. *Histology for Pathologists*. 2nd Ed. Lippincott-Raven, 1997. pp. 367-390)

Cystic Lesions

3. Cysts that occur at the junctions of developing structures in the head and neck are called:

    E. Fissural cyst

Answer: E. Fissural cysts occur at the junctions of developing structures in the head and neck. As tissue elements come together in fetal development sometimes small epithelial fragments get trapped, and later develop into fissural cysts. These cysts do not have a unique histologic appearance, and therefore can only be diagnosed with clinical-radiological correlation. Interestingly they are named according to their location, such as globulomaxillary or nasolabial cysts. (www.pathologyoutlines.com/mandiblemaxilla.html)

4. All of the following are needed to accurately classify an odontogenic cyst EXCEPT:

    E. Patient age

Answer: E. The age of the patient is not very helpful because cystic lesions can often occur in a wide range of ages. It is vital though to know the information in answers A-D. Many cysts in the jaw look the same, and the only way to classify them is by location and association with other structures. It is vital that the entire cyst be submitted for histology because if there is significant inflammation it may mask the findings of an odontogenic keratocyst. The characteristic features may only be present focally.

5. This cyst develops from epithelial rests of Malassez after tooth development, has a non-keratinized squamous epithelial lining, and is located at the root of a non-vital tooth. The best diagnosis is:

    A. Radicular cyst

Answer: A. This is a classic description of a radicular (periapical) cyst. They may be related to bacterial infections or other offensive agents. The association with the root of a non-vital tooth is required for specific diagnosis. (Rosai J. *Rosai and Ackerman's Surgical Pathology*. 9th Ed. Mosby, 2004. pp. 279-299 and Kumar V, et al. *Robbins and Cotran Pathologic Basis of Disease.* 7th ed. 1999. p. 782)

6. This lesion is characterized by thin layer of para-keratinized stratified squamous epithelium with a corrugated appearance and a prominent palisaded basal layer. The best diagnosis is:

    B. Odontogenic keratocyst

Answer: B. This is the classic description of an odontogenic keratocyst. It cannot be under emphasized how important it is to make this diagnosis histologically, and to submit all of the tissue for histologic examination.

7. Which of the following tumors is characterized by sheets of hyperchromatic, pleomorphic cells with foci of mineralization. These islands and sheets of cells are dispersed throughout a nonspecific fibrous stroma. Foci of eosinophilic material c/w amyloid by congo red staining are also found with this tumor. The best diagnosis is:

    A. Calcifying (epithelial) odontogenic tumor

Answer: A. These features are characteristic of a Pindborg tumor, which is also known as a calcifying (epithelial) odontogenic tumor. (Robinson, R.A. & Vincent, S.D. *Surgical Pathology of Odontogenic Neoplasms and Cysts: Histologic Features with Clinical and Radiographic Correlations*. Short Course #33, 2005 Annual Meeting, San Antonio, TX United States and Canadian Academy of Pathology, and Rosai J. *Rosai and Ackerman's Surgical Pathology*. 9th Ed. Mosby, 2004. pp. 279-299)

8. All of the following are specific patterns of an ameloblastoma EXCEPT:

    E. All of the above are correct

Answer: E. All of the answers are patterns of ameloblastomas. The follicular pattern is the most common, and what most people think of as the classic appearance. In addition to the patterns listed in the answers, there are desmoplastic and basal cell patterns. (Rosai J. *Rosai and Ackerman's Surgical Pathology*. 9th Ed. Mosby, 2004. pp. 279-299)

<u>Unknown Cases – Website</u>

9. This lesion arose in a 25 y/o male, and was associated with an embedded tooth. Based on the images for Case #1 on the website for this question set, the best diagnosis is:

    E. Calcifying Odontogenic Tumor

Answer: E. Calcifying (Epithelial) Odontogenic Tumor (Pindborg tumor) is an unusual and characteristic lesion composed of sheets of hyperchromatic, pleomorphic cells with foci of mineralization. They have an unusual bimodal age distribution with peaks in the 20's and 40's, and are usually associated with an embedded tooth. Microscopically, islands and sheets of epithelial cells are dispersed throughout a nonspecific fibrous stroma. The epithelial cells often are polygonal and show pleomorphism and hyperchromasia. The boarders are well defined, and intercellular bridges are present between epithelial cells. Some tumors show a prominent clear cell component. Foci of eosinophilic material c/w amyloid by Congo Red staining are also found with the tumor. Hybrids between this tumor and adenomatoid odontogenic tumor have been described. (Robinson, R.A. & Vincent, S.D. *Surgical Pathology of Odontogenic Neoplasms and Cysts: Histologic Features with Clinical and Radiographic Correlations*. Short Course #33, 2005 Annual Meeting, San Antonio, TX United States and Canadian Academy of Pathology. Kumar V, et al. *Robbins and Cotran Pathologic Basis of Disease.* 7th ed. 1999. p. 782.)

10. A cystic lesion is found in a 27 y/o female. Based on the images for Case #2 on the website for this question set, the best diagnosis is:

    D. Calcifying odontogenic cyst

Answer: D. The **Calcifying Odontogenic Cyst (a.k.a. Gorlin cyst)** is an unusual lesion because it can take on an appearance from a thin epithelial lined cyst to a complex focally solid tumor-like mass. Microscopically, cystic lesions will be lined (at least focally) by stratified squamous epithelium with a well-defined basal layer of cuboidal to columnar cells, which may resemble ameloblasts! The epithelial lining may appear stellate or fusiform suggesting stellate reticulum. Ghost cells (similar to those in a pilomatricoma) are found individually or in sheets, which are important in differentiating the lesion from an ameloblastoma. Foci of mineralization with a dentin or cementum appearance are often present. Treatment is with conservative surgery, and has a low recurrence rate.

- When COCs are predominately solid and tumor-like, it has been proposed that they be classified separately to reflect their increased propensity to recur and be destructive. If the lesion is solid and contains foci of ghost cells and dentin, then the term odontogenic ghost cell tumor is recommended. If the lesion is solid, contains COC features, and features of another odontogenic tumor (other than odontoma), then the term of the odontogenic tumor "with COC features" should be used.
- Rare reports of carcinoma have occurred within an odontogenic ghost cell tumor or typical calcifying odontogenic cyst. This diagnosis is based on nuclear morphology with pleomorphism, mitoses, and atypia being present. Invasion may also be helpful. The preferred term is odontogenic ghost cell carcinoma.

(, T.J. *Clinicopathologic Spectrum of the So-Called Calcifying Odontogenic Cysts*. The American Journal of Surgical Pathology, Vol. 27, No. 3, pp. 372-384. 2003. Rosai J. *Rosai and Ackerman's Surgical Pathology*. 9th Ed. Mosby, 2004. pp. 279-299.)

11. A cystic lesion arises in a 32 y/o male. Based on the images for Case #3 on the website for this question set, the best diagnosis is:

    B. Odontogenic Keratocyst

Answer: B. Odontogenic keratocyst is important to differentiate because it can have an aggressive course. There is evidence these may be neoplastic due to frequent loss of heterozygosity of p16, p53, PTCH, and MCC. They occur most often in men between 10 and 40 years old in the posterior mandible. The cyst lining contains a thin layer of ortho-keratinized or para-keratinized stratified squamous epithelium (corrugated appearance) with a prominent palisaded basal layer. The epithelium is 6-10 layers thick without rete ridge formation, unless inflammation is present. Treatment requires complete excision. Multiple OKCs should prompt an evaluation for nevoid basal cell nevus syndrome (Gorlin syndrome), which is associated with mutations in the tumor suppressor gene PTCH.[6]

It is important to communicate whether the cyst lining is orthokeratinized or parakeratinized because this may affect treatment. Parakeratinized OKCs have a 20-50% chance of recurrence with simple curettage, and surgeons will use chemical cautery in this situation. Many dentists feel the high recurrence rate is due to the "wet tissue paper" consistency of the lesion when curetting, which makes it extremely difficult to excise the entire lesion. Orthokeratinized cysts do not have a propensity to recur. Close long term follow-up is necessary for these patients, in contrast with other odontogenic cysts. (Agaram, N.P., et al. *Molecular analysis to demonstrate that odontogenic keratocysts are neoplastic* Arch Pathol Lab Med. 2004 Mar;128(3):313-7. Dr. Steven D. Vincient, College of Medicine and Denistry, University of Iowa. Personal Communication, March, 2005. Rosai J. *Rosai and Ackerman's Surgical Pathology*. 9th Ed. Mosby, 2004. pp. 279-299.)

12. A 30 y/o male presents with an odontogenic lesion. Based on the findings in the images associated with Case #4 on the website for this question set, the best diagnosis is:

    A. Giant Cell Granuloma

Answer: A. Inflammatory lesions can by solid or cystic. They often arise from untreated dental caries. Some have prominent giant cells: the most common being a **central giant cell granuloma** (a.k.a. giant cell reparative granuloma). The cause is unknown, but may be secondary to slow, minute, recurrent hemorrhages. It is an intraosseous lesion that is often associated with trauma. There are numerous osteoclast-like giant cells near hemorrhagic areas, cellular vascular stroma, new bone formation at the edge of the lesion, frequent mitoses, and no necrosis. Patients are usually children or young adults. Treatment is with curettage and they may recur.

If there is a central giant cell granuloma, then there must be a **peripheral giant cell granuloma**. These are *extra-osseous* and resemble pyogenic granulomas. The age distribution is a little older (average = 30 y/o), and there is often a history of trauma, irritation or infection.

Another example of an inflammatory lesion is the **dental granuloma**. This is also referred to as localized osteitis, and consists of histiocytes and chronic inflammatory cells surrounded by dense fibrous tissue. It doesn't really fit into the peripheral or central giant cell granuloma category because of a different histologic picture. If or when a dental granuloma undergoes cystic degeneration, it is referred to as a *periapical or radicular cyst*. (Robinson, R.A. & Vincent, S.D. *Surgical Pathology of Odontogenic Neoplasms and Cysts: Histologic Features with Clinical and Radiographic Correlations*. Short Course #33, 2005 Annual Meeting, San Antonio, TX United States and Canadian Academy of Pathology.)

13. A 30 y/o male presents with a cystic odontogenic lesion. Based on the findings in the images associated with Case #5 on the website for this question set, the best diagnosis is:

    B. Unicystic ameloblastoma

Answer: B. **Unicystic ameloblastomas** (15% of all ameloblastomas) must be unilocular **and** have a single cyst lining of ameloblastoma! Specifically, if ameloblastic epithelial islands are found infiltrating the surrounding fibrous wall (some call this the mural variant), the lesion should not be classified as a unicystic ameloblastoma (treatment and clinical course are different). Ameloblastic features include: (1) palisading of basal cells with polarization of the nuclei to the distal ends of the cells, (2) hyperchromasia of the basal cell nuclei, (3) vacuolization of the cytoplasm of the basal cells, and (4) spinous cells showing a loose, fusiform configuration similar to the stratum spinosum of a developing tooth. Some portions of the lesion may not show these features, and secondary inflammation (focally present in most lesions) will disrupt the diagnostic features. Some authors subcategorize these into on of several histologic variants: luminal, intraluminal, and mural. The luminal variant is the classical unicystic ameloblastoma morphology without any projections of tissue into or out of the cystic structure. The term intraluminal is applied when portions of epithelium extend into the lumen, and the mural variant is when ameloblastic epithelium extends into the surrounding fibrous wall. When the epithelium invades the fibrous wall, the lesion behaves like a solid classical ameloblastoma (and should be diagnosed as such). Don't diagnose a mural variant of a unicystic ameloblastoma. (Robinson, R.A. & Vincent, S.D. *Surgical Pathology of Odontogenic Neoplasms and Cysts: Histologic Features with Clinical and Radiographic Correlations*. Short Course #33, 2005 Annual Meeting, San Antonio, TX United States and Canadian Academy of Pathology. Rosai J. *Rosai and Ackerman's Surgical Pathology*. 9th Ed. Mosby, 2004. pp. 279-299.)

14. A 12 year old male presented to a dental office with an asymptomatic swelling of the right posterior mandible. He was referred to an oral surgeon, and representative images of the histology are presented in Case #6 on the website associated with this question set. Based on the findings, the best diagnosis is:

    C. Juvenile ossifying fibroma

Answer: C. Juvenile ossifying fibroma.

- **Fibrous dysplasia** is characterized by C-shaped or Chinese figure-like trabeculae or immature/woven bone within a proliferating fibroblastic stroma. Usually, there is no osteoblastic rimming and rare osteoclasts. It can be monostotic or polystotic. *Please review McCune Albright syndrome.* Most importantly, radiology shows an irregular border compared to a smooth well demarcated borders of ossifying or cementifying fibromas.
- **Ossifying fibroma** (fibrous osteoma) has trabecular or spherical islands of bone uniform throughout the lesion, prominent osteoblastic rimming, and variable stromal cellularity. Patients are usually 20-40 y/o.
    - **Juvenile ossifying fibroma** comes up in this differential, but has a more aggressive clinical behavior and more cellular stroma. The trabeculae / psammomatous bodies are irregularly distributed. Patients are usually 5-15 y/o (younger than typical ossifying fibroma patients).
- **Cementifying fibroma** usually occurs in patients over 40 y/o and contains cellular fibrous connective tissue with multiple round to oval psammoma-like calcifications resembling cement. If a lesion has portions that look more like cement and other areas that have a trabecular appearance, then it can be classified as a **cemento-ossifying fibroma**.
- **Ameloblastic fibroma** – please refer to the section on odontomas below.
- **Desmoplastic Fibroma** is identical to an extra osseous desmoid tumor. Simplistically, it is an ossifying fibroma or fibrous dysplasia without the bony component. Many sections should be taken to exclude this possibility. This lesion is basically intraosseous fibromatosis.
- **Odontogenic fibroma** consists of a mass of interwoven cellular fibrous connective tissue that contains scattered nests or strands of odontogenic epithelium. Myxoid foci; calcifications; or osteoid, cementoid, or dysplastic areas are sometimes seen.

(www.emedicine.com. www.pathologyoutlines.com/mandiblemaxilla.html. Rosai J. *Rosai and Ackerman's Surgical Pathology*. 9th Ed. Mosby, 2004. pp. 279-299. Robinson, R.A. & Vincent, S.D. *Surgical Pathology of Odontogenic Neoplasms and Cysts: Histologic Features with Clinical and Radiographic Correlations*. Short Course #33, 2005 Annual Meeting, San Antonio, TX United States and Canadian Academy of Pathology.)

