

Embryology questions

1. Which of the following embryologic elements is responsible for the formation of the enamel on the surface of the tooth?

C. Ameloblasts

Answer: C. 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. The periodontal ligament anchors the tooth to the bone socket of the jaw and maxilla. Which of the following embryological elements is responsible for the formation of periodontal ligament?

D. Mesenchymal cells outside the tooth

Answer: D. The mesenchymal cells outside the tooth are responsible for the formation of cementum, which covers dentin below the gum line, and the periodontal ligament, which anchors the tooth to the bone. (Sternberg, S.S. *Histology for Pathologists*. 2nd Ed. Lippincott-Raven, 1997. pp. 367-390)

3. Gorlin syndrome (nevoid basal cell nevus syndrome) is associated with which of the following:

A. Multiple odontogenic keratocysts

Answer: A. Multiple odontogenic keratocysts is associated with Gorlin syndrome. This should not be confused with a Gorlin cyst, which is a calcifying (epithelial) odontogenic cyst. (Kumar V, et al. *Robbins and Cotran Pathologic Basis of Disease*. 7th ed. 1999. p. 782 and Agaram, N.P., et al. *Molecular analysis to demonstrate that odontogenic keratocysts are neoplastic* Arch Pathol Lab Med. 2004 Mar;128(3):313-7)

4. This cystic lesion is characterized by a stratified squamous epithelium (at least partially), a well defined basal layer of cuboidal to columnar cells (may resemble ameloblasts), and ghost cells (similar to a pilomatricoma). The best answer is:

C. Calcifying odontogenic cyst

Answer: C. This describes a calcifying odontogenic cyst, which is also known as a Gorlin's cyst. Do not confuse this with Gorlin's syndrome, which is associated with multiple odontogenic keratocysts. Additionally, there can be focally solid tumor-like areas, and as the name implies, calcification. (Li, 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 and Rosai J. *Rosai and Ackerman's Surgical Pathology*. 9th Ed. Mosby, 2004. pp. 279-299)

5. A unicystic ameloblastoma is characterized by all of the following EXCEPT:

E. Infiltrating ameloblastic epithelial islands into the surrounding fibrous wall

Answer: E. A unicystic ameloblastoma has an excellent prognosis and is characterized by answers A-D. It must by definition be unicystic (don't overlook). If the lesion otherwise looks like a unicystic ameloblastoma, but has ameloblastic epithelial islands infiltrating the fibrous wall, it is best characterized as an ameloblastoma. (Kumar V, et al. *Robbins and Cotran Pathologic Basis of Disease*. 7th ed. 1999. p. 782)

Solid Tumors

6. This lesion usually occurs in children or young adults, is often associated with trauma, and may be secondary to slow, minute, recurrent hemorrhages. The most likely diagnosis is:

E. Giant cell granuloma

Answer: E. A giant cell (reparative) granuloma is characterized by the description above. In addition, there are usually numerous osteoclast like giant cells near the hemorrhagic areas, vascular cellular stroma, new bone formation at the edge of the lesion, frequent mitoses, and no necrosis. (Rosai J. *Rosai and Ackerman's Surgical Pathology*. 9th Ed. Mosby, 2004. pp. 279-299)

7. Which of the following lesions is associated with McCune Albright Syndrome:

A. Fibrous dysplasia

Answer: A. Fibrous dysplasia combined with endocrine abnormalities is characteristic of McCune Albright Syndrome.

8. This lesion is characterized by a poorly differentiated conglomeration of dentin, cementum, and enamel. There are usually found in the first two decades of life. The best diagnosis is:

C. Complex odontoma

Answer: C. A complex odontoma is a poorly differentiated lesion and consists of a conglomeration of dentin, cementum, and enamel. They are usually found in the first two decades of life. After conservative excision recurrence is almost unheard of for either complex or compound odontomas. (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 Kumar V, et al. *Robbins and Cotran Pathologic Basis of Disease*. 7th ed. 1999. p. 782)

9. Which of the following lesions is known as a Pindborg tumor?

A. Calcifying (epithelial) odontogenic tumor

Answer: A. A calcifying (epithelial) odontogenic tumor is also known as a Pindborg tumor.

Website Image Cases

10. (Case #1) A 31 /o male had a destructive jaw lesion which was surgically removed. Representative images from the case are shown. Based on the findings, which of the following is the best diagnosis?

D. Ameloblastic Carcinoma

Answer: D. Ameloblastic Carcinoma

- **Malignant ameloblastoma** – have the same benign histopathologic features of ameloblastoma but metastasizes (usually after many years). The lung is the most common site, and cervical lymph nodes may be involved. This diagnosis can not be made prospectively.
- **Ameloblastic carcinoma** – this lesion shows cytologic features of malignancy (increased mitoses, increased N:C ratio). This diagnosis can be made prospectively, but fortunately is very rare.

(Rosai J. *Rosai and Ackerman's Surgical Pathology*. 9th Ed. Mosby, 2004. pp. 279-299.)

11. (Case #2) A 28 y/o female presents with a cystic jaw lesion. The cyst is curetted and representative images are shown. Based on the findings, which of the following is the best diagnosis.?

C. Odontogenic Keratocyst

Answer: C. Odontogenic Keratocyst

- **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.

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.

- 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 dentinoid, 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.

Glandular odontogenic cysts are relatively recently described. They were included in the non-stratified squamous cyst lesion category in the past. Sialo-odontogenic cyst and mucoepidermoid cyst are terms that have also been used. This is a pretty rare lesion with no specific radiologic features from other cysts of the jaw. Histologically, the lesion has a non-keratinized squamous lining with the superficial layer often being cuboidal or columnar. Cilia may be present, and mucus-containing cells are usually present. No evidence of keratinization or stellate reticulum is present! The most important differential diagnosis is with mucoepidermoid carcinoma.

(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. Li, 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. 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.)

12. (Case #3) A 30 y/o patient is found to have a solid jaw lesion. Surgical excision is performed, and representative images are shown for review. Based on the findings, which of the following is the best diagnosis?

D. Ameloblastic Fibroma

Answer: D. Ameloblastic Fibroma

- **Ameloblastic odontoma (ameloblastic fibro-odontoma or odonto-ameloblastoma)** Some consider this lesion as an early developmental stage of odontoma, and others define this tumor as an ameloblastic fibroma that also produces enamel and dentin. Most patients are young (average age = 10 y/o). This tumor rarely occurs in adults. Histologically, they show islands and cords or ovoid, cuboidal, and columnar odontogenic epithelium in a myxoid background in addition to mineralized enamel, dentin, and cementum. These lesions are not thought to be related to ameloblastomas, have a benign course, and rarely recur.
 - **Ameloblastic fibroma** is composed of strands and buds of epithelial cells within the cellular connective tissue. In contrast to ameloblastomas, a stellate reticulum is rarely present. Dentin, enamel, and cementum are absent, which differentiates it from an ameloblastic odontoma (by some authors).
 - **Ameloblastic fibrosarcoma** is an extremely rare occurrence in an ameloblastic fibroma, and is characterized by pleomorphic atypical fibrous cells with frequent mitotic activity. Even with this, they recur locally (may cause death) but do not metastasize.

(Rosai J. *Rosai and Ackerman's Surgical Pathology*. 9th Ed. Mosby, 2004. pp. 279-299.)

13. (Case #4) A 30 y/o patient is found to have a solid jaw lesion. Surgical excision is performed, and representative images are shown for review. Based on the findings, which of the following is the best diagnosis?

A. Ameloblastoma

Answer: A. Ameloblastoma

Ameloblastoma (solid intraosseous type) is a neoplasm that recapitulates ameloblastic development, and may arise from the lining of an odontogenic cyst. They can also arise in the soft tissue (peripheral) or the basal layer of the gingiva. Three main clinical types: (1) solid, (2) unicystic [discussed earlier], and (3) peripheral. Unicystic and peripheral have better clinical outcomes after conservative management. Sometimes “follicular” used interchangeably with “solid type” ameloblastomas. In addition to the mandible and maxilla, they may involve the maxillary sinus and nasal cavity.

Radiographically, they may appear similar to other cysts or odontogenic tumors, but when the lesions become larger they may show a “soap bubble” appearance. **THIS IS ON THE BOARDS!** Microscopically, there are six morphologic subtypes, but it is most critical for the pathologist to recognize them as ameloblastomas because the subtype has no bearing on the prognosis.

The specific patterns are:

1. Follicular pattern – most common variant. Epithelium is arranged with a peripheral column of cells resembling *ameloblasts* with the nucleus away from the basal layer pointing inward to the epithelial proliferation. These cells also show vacuolization. The central portions of epithelial nests look like *stellate reticulum* cells. Cyst formation is common.
2. Plexiform cell pattern – second most common variant. Long plexiform or anastomosing columns and sheets of cuboidal to columnar cells with little to no stellate reticulum differentiation.
3. Granular cell pattern – shows eosinophilic granules in the cytoplasm of tumor cells that are central within the epithelial islands. The peripheral columnar and cuboidal cells retain their reverse polarity and basal vacuolization.
4. Acanthomatous pattern – large areas of squamous metaplasia and keratin formation. The big differential here is with squamous cell carcinoma. The lack of nuclear atypia and peripheral columnar cell arrangement should help differentiate the two lesions.

5. Desmoplastic pattern – small nests of tumor cells within a sclerotic/densely collagenized background. This is a rare variant and found more often in the anterior segments of the mandible. Unfortunately, the islands of ameloblastic epithelium show less peripheral palisading, and may look more squamous. Additional sections may be required to make the diagnosis.
6. Basal cell pattern – the least common variant. Nests of basaloid cells with peripheral cuboidal to columnar cells are seen. Little to no stellate reticulum is seen. Thought to represent a basal cell carcinoma for many years.

Ameloblastomas like to infiltrate cancellous bone (difficult to infiltrate compact bone). Even after enblock resections, 10-15% may recur. Some surgeons advocate a 1 cm margin past the radiologic limits of the tumor. Other variations on the ameloblastoma theme:

- **Unicystic ameloblastoma** – discussed earlier.
- **Peripheral ameloblastoma** – histopathologically the same (including the variants) as an intraosseous / solid ameloblastoma, but arises in the soft tissue and gingiva. Since they do not infiltrate bone, simple excision is curative.
- **Malignant ameloblastoma** – have the same benign histopathologic features of ameloblastoma but metastasizes (usually after many years). The lung is the most common site, and cervical lymph nodes may be involved.⁵ This diagnosis can not be made prospectively.
- **Ameloblastic carcinoma** – this lesion shows cytologic features of malignancy (increased mitoses, increased N:C ratio). This diagnosis can be made prospectively, but fortunately is very rare.

(Rosai J. *Rosai and Ackerman's Surgical Pathology*. 9th Ed. Mosby, 2004. pp. 279-299.)

14. (Case #5) A 30 y/o patient is found to have a solid jaw lesion. Surgical excision is performed, and representative images are shown for review. Based on the findings, which of the following is the best diagnosis?

A. Ameloblastoma

Answer: A. Ameloblastoma. This represents the basal cell pattern of an ameloblastoma. Please refer to the previous question's explanation for more details.

15. (Case #6) A 30 y/o patient is found to have a solid jaw lesion. Surgical excision is performed, and representative images are shown for review. Based on the findings, which of the following is the best diagnosis?

A. Clear Cell Odontogenic Carcinoma

Answer: A. Clear Cell Odontogenic Carcinoma

Clear cell odontogenic carcinoma may be confused with a Pindborg tumor. This lesion is a low grade malignancy (up to 80% recurrence rate) and occasionally metastasizes to the lungs or local lymph nodes. Histologically, it is composed of glycogen containing clear cells with distinct membranes and small basaloid cells. Nests with palisading of peripheral cells containing hyaline deposits suggestive of osteoid or dentinoid are variably present. Rare mitosis, minimal pleomorphism, and no/minimal stellate reticulum are found. This tumor commonly has perineural invasion.

Adenomatoid Odontogenic Tumor (Adenoameloblastoma or ameloblastic adenomatoid tumor) appears to be derived from the enamel producing epithelium. Microscopically, it is composed of mostly epithelial cells that are spindle shaped, which form rosettes or whorled masses in a scanty fibrous background.⁵ There are duct-like structures lined by ameloblastic like cells (polarization is in the wrong direction). The spindled areas may also be confused with stellate reticulum of an ameloblastoma. Foci of amyloid and varying amounts of dentin or cementum may also be found.⁴ The gland or duct-like spaces are probably the most helpful morphologic aspect to diagnose this tumor. Particularly, if one has not seen a lot of ameloblastomas, these can easily be mistaken for the polarized cells and stellate reticulum of an 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.)

Notes for question set:¹

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