ORAL PATHOLOGY

LECTURE # : 13
DOCTOR : NAME
DONE BY : NAME
CORRECTED BY : NAME
DAY & DATE : 4/12/2016

PRICE :

ABC Books
مكتبة تلاع العلي
شارع الجامعة الأردنية – جسر كلية الزراعة
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Malignant tumors:

A. Odontogenic carcinomas

There are two malignant types of ameloblastoma
- Malignant ameloblastoma.
- Ameloblastic carcinoma.

Other types of odontogenic carcinomas:

- Primary intraosseous squamous cell carcinoma.
  This is a lesion inside the bone showing features of squamous cell carcinoma.

- Malignant variant of other epithelial tumors.
  Clear-cell odontogenic carcinoma.
- Malignant change in odontogenic cysts.

B. Odontogenic sarcomas

- Ameloblastic Fibrosarcoma
- Ameloblastic fibro-odontosarcoma

- Tumors of debatable origin

- Melanotic neuroectodermal tumor of infancy
- Congenital gingival granular cell tumor (congenital epulis)

recall: there is a granular cell tumor that affects the tongue.

✓ Ameloblastoma

- Most important
- It is the most common odontogenic tumor.
  Recall: most common oral tumor is SCC.
- Benign but locally aggressive - local invasion -
- Local invasion indicates a high recurrence rate and more difficult surgery where safety margins need to be considered.
Clinically

- Most commonly occurs in the 4th and 5th decade in life (middle-aged), but can also occur at any other age.
  - No gender variations.
  - Most common site is the posterior mandible -like keratocyst-.
  - Slowly and gradually growing over time.
  - If not dealt with, it might perforate the bone and extend into soft tissue; making the management more difficult in locating the margins.

  - Displacement, resorption, impaction of nearby tooth might occur.
  - Might affect occlusion.

  - Even in very severe cases, ulceration of the skin will not happen since it’s not malignant.

Radiographic image

- Mostly shows multilocular, soap bubble appearance.
  - Root resorption.
  - May find impacted teeth.

  - In some cases it might appear unilocular
  - This case might be confused with cystic lesions, but biopsy verifies ameloblastoma.

  - The solution is resection and grafting.
  - Since it is invasive as we mentioned we take safety margins and therefore part of the mandible is also removed.

Grossly

- It is not solid
  - Cystic spaces containing fluid material.

  - It consists of more than one cyst that’s why it appears multilocular on the radiograph.

Histologically

- Many patterns but mainly two

  - Follicular pattern
- Islands or follicles of epithelium against fibrous connective tissue stroma.
- Periphery of these islands differs from their centre; periphery contains columnar or occasionally cuboidal cells and the center contains angular cells.
Recall: in teeth development the enamel organ also showed this pattern where in the periphery we find columnar cells and in the centre we find angular or stellate reticulum.
- At a closer look at the columnar cells, the nucleus is seen away from the basement membrane, and this is known as **reversed polarity**.
- These columnar cells with reversed polarity resemble ameloblasts.

- Degeneration of the angular cells in the centre causes the formation of **cystic spaces**.

- Then these cystic spaces soon grow causing the previously seen gross appearance.

Note: the beginning of cystic spaces starts in the stellate reticulum like cells region in the follicles causing multilocular spaces.

- In some cases stellate reticulum do not undergo degeneration but undergo transformation into other type of cells such as squamous cells and form keratin.
- The centre shows squamous cells
- This type of ameloblastoma is known as **acanthomatous** type of ameloblastoma. *(Acanthomatous pattern)*
- Keratin may be seen inside of the tumor.

- Some may show granular cell pattern as that seen in granular cell tumors.

![Granular cell variant](image)

- The other type is the **plexiform pattern**

![Fishnet arrangement of epithelium](image)

- The arrangement differs slightly but the cell content is the same.
- **Fishnet** arrangement of epithelium.
- Same cell layers; periphery contains columnar or cuboidal cells and the centre contains angular / stellate cells.
- Cystic changes do not occur inside of the follicles, but in the surrounding connective tissue between the cells (difference from the follicular pattern).

- Rare variants of ameloblastoma are the desmoplastic variant and the basal cell variant.

Pathogenesis of ameloblastoma:

- Since it resembles the enamel organ it is thought to be a result from the remnants of the dental lamina.
- Are not ameloblasts; if they were fully maturated ameloblasts they would have stimulated adjacent tissues to form dentine (note: dentine forms before enamel).
- Therefore, they are Preameloblasts.

Behavior

1. It is locally invasive causing destruction and perforation of bone. 
   Also causes displacement of teeth.

2. Acanthomatous pattern shows less recurrence rate, while other types have high recurrence rate.

3. Pulmonary metastasis, how can this happen if it’s benign?

   Explanation: since it is locally invasive, recurrence is high thus surgery is performed more than once for the same tumor; as a result during surgery some parts may be aspirated to the lung and cause the same focus of tumor (aspiration during surgery). 
   This condition is known as malignant ameloblastoma - It is not a malignant tumor -

Unicystic ameloblastoma

Clinically

- It only contain one cystic space.

- We have to differentiate between this type and the multicystic type.
  Note: the multicystic type is sometimes called solid tumor, although it is not really solid.
- **Unicystic ameloblastoma** is confused with and sometimes treated as if it’s a cyst since:
  - It occurs in younger patients
  - Its’ site is in the posterior mandible -the same as the keratocyst-
  - appears unilocular in the radiograph.
  - Might be found surrounding an impacted tooth.

*all these resemble cystic lesion such as the radicular cyst, keratocyst or dentigerous cyst.

**Histologically**

- We will find ameloblast like tissue, and it has three different types of proliferation:
  1. **luminal**: found only in the lining.
  2. **Intraluminal**: proliferation moves inwards.
    - It is a good type since the mass can be entirely removed in surgery.
  3. **Mural**: this is the worst type. Ameloblast like tissue proliferates towards the capsule.
    - It might invade surrounding structures; therefore some parts might be left behind in surgery causing a high recurrence rate/it has the highest recurrence rate.

- Histological section shows dense fibrous connective tissue capsule, surrounding solitary fluid filled lumen.

Histological sections help us differentiate Unicystic ameloblastoma from cysts.
Important points that help us differentiate:
- In keratocyst we find pseudocolumnar parakeratinized epithelium.
- Ameloblast like cells with reversed polarity and stellate reticulum are features of ameloblastoma.

When a histological section indicates the mural type, pathologist must inform the surgeon to take a safety margin; in order to prevent the recurrence of this lesion.

**Peripheral ameloblastoma**

Solid and unicystic ameloblastoma occur inside the bone while peripheral ameloblastoma occurs in soft tissue/gingiva.

**Clinically**

- **Peripheral ameloblastoma** is a solid, firm sessile nodule that might be confused with bony or benign connective tissue tumors (e.g., neuroma, schwannoma).

**Origin**

- There are different theories regarding the origin; it is either originating from the basal oral epithelium or from the remnants of dental lamina.

**Histologically**

- Similar to intraosseous appearance seen before; can show follicular pattern, plexiform pattern and etc.

**Prognosis**

- It is less aggressive than the intraosseous type.

*Note: If peripheral ameloblastoma is large, it might compress bone.*
**Squamous Odontogenic tumour**

- **Clinically**:
  - Young adults
  - Anterior to molars
  - Painless swelling, ± Tenderness & loosening of associated teeth
  - Origin: rest cells of malassez (odontogenic epithelium)

- Radiograph: it's like a severe periodontal disease or lateral periodontal cyst.

Unilocular, semilunar radiolucency (could be triangular in shape sometimes) present between the roots of the teeth.

As the calcification increases the radio-opacity increases inside the tumor.
  - When you take a biopsy you could notice that it's a solid tissue.

- **Hist**:
  - Elongated and rounded islands of normal appearing stratified squamous epithelium.
  - Surrounded by fibrous tissue trauma
  - Inside the epithelial islands, Keratin, microcysts spaces, calcified structures could be found.

**Calcifying epithelial odontogenic tumour (Pindborg tumour)**

- **Clinically**:
  - Rare (less than 1% of these tumors)
  - Mainly occur in Adults
  - Slowly enlarging painless mass (as its benign)
  - 2/3 of the cases are found in the Mandible, in the molar & premolar region
  - Its mainly a central tumor (within the bone) but in some cases, its formed inside the gingiva so it's called peripheral Calcifying epithelial odontogenic tumour.

- **Prognosis**:

It’s a benign but locally invasive/infiltrative neoplasm like the ameloblastoma, but it has a lower recurrence rate (less than 20%).

- **In radiograph**: [Image]
- It can’t be differentiated easily (irregular radiolucent area)
- Can be multilocular or unilocular
- Radio-opaque bodies are seen within the lesion due to calcification process (the calcifications increase with time)
- Can be associated with unerupted teeth
- The border is well defined as it’s a benign lesion

- Differential diagnosis (odontogenic keratocyst, ameloblastoma, CEOT, and other tumors).

- As the lesion progresses, the calcifications increase and that gives the appearance of driven snow to the lesion (old lesions appear radio-opaque not radiolucent as the new lesions).
- Associated with impacted teeth
- So the presence of a radio-opacity will exclude the ameloblastoma and the keratocyst from the diagnosis

- **Histologically:**
  - Unlike the ameloblastoma, this tumor is formed by sheets of large polyhedral epithelial cells with abundant eosinophilic cytoplasm and prominent intercellular bridges (connections between the cells)
  - It contains features that could be misleading (looks like a malignancy):
    - (Pleomorphism, multinucleation, hyperchromatism) of the nuclei
  - Inside the lesion we could find amorphous amyloid-like material deposited from epithelial cells, the presence of the amyloid can be confirmed by the histopathologist by using the "congo red stain," this lesion is +ve for this stain so this test is a good diagnostic tool for this tumor.
  - The amyloid-like material can be calcified forming spherical calcifications (by time the no. of calcifications inside the lesion increases)

**Adenomatoid odontogenic tumour**

Benign tumor

- Clinically:
- Start at the 2nd decade of life (young patients mainly children)

- On radiograph it may be misdiagnosed as a dentigerous cyst as in this age many teeth could still be impacted (like the canines)

- The difference between this tumour and the dentigerous cyst, is that its extended below the CEJ surrounding the crown and part of the root.

- Its an intraosseous tumor, its rarely to be extraosseous

- Radiograph:

  Unilocular radiolucency containing a tooth

  Some parts of the lesion could be calcified (Faint flecks of radio-opacities are found inside the lesion) and this can help to differentiate it from the dentigerous cyst.

  Differential diagnosis; include the dentigerous cyst and keratocyst in addition to this tumor.

- Prognosis:

  Considered as a hamartoma so it’s a very benign lesion and has no recurrence possibility.

Histopathology:

1. Surrounded by thick, fibrous connective tissue wall

2. Could be solid or cystic

3. Islands/Whorls with central spaces surrounded by columnar epithelium called rosette, or ducts-like structures, the presence of ducts-like structures give this lesion its name (adeno)

4. Homogenous eosinophilic material that could be calcified.

**Ameloblastic fibroma/fibrodentinoma/fibro-odontoma:**

- Contains both epithelial (ameloblastic) + mesenchymal (fibroma) tissues

- Both components are neoplastic.

- We have to differentiate between this tumor and the ameloblastoma!

- Young patients
- Slowly growing, painless mass

- Mainly found in the mandible (in the molars area)

Radiograph:

- uni/multilocular radiolucency

- associated with unerupted teeth so the differential diagnosis should include the keratocyst and the dentigerous cyst

Note: we should always send a biopsy to the lab in these cases even if it looks as a benign lesion!

Histology:

- It’s not a cystic lesion (solid tissue)

- Thin strands & cords of odontogenic epithelium

- Loose cellular fibromyxoid connective tissue (looks like the dental papilla or the immature pulp tissue)

- The stellate reticulum is less abundant unlike the ameloblastoma (which has stellate reticulum in the center and its epithelium is surrounded by fibrous tissue) where as in this lesion the epithelium is surrounded by cellular tissue.

- Peripheral layer of cuboidal or columnar cells enclosing Stellate Reticulum which is like what’s found in the ameloblastoma

- This tumor is different than the ameloblastoma in (the prognosis, the surrounding tissue, the abundance of stellate reticulum)

- As Ameloblastic fibroma contains dental pulp like structures + ameloblasts, formation of dentin like material could happen so its then called Ameloblastic Fibrodentinoma.

- Sometimes, the process continues to form enamel, dentin and cementum forming an odontome complex or compound forms, so its called ameloblastic fibro-odontoma

- Prognosis: all types of this tumor are not aggressive, the local recurrence rate is low, and it’s not an invasive tumor.
Odontoamblasticoma

- This tumor is basically like an ameloblastoma which contain an odontoma
- Its behavior is like the ameloblastoma (invasive and has high local recurrence rate) so its more dangerous than the ameloblastic fibro-odontoma.

Calcifying cystic odontogenic tumour/cyst

The Solid form of it: Dentinogenic Ghost cell tumour

Clinically:
- Usually the patients are < 40 years old
- Occur in the anterior region
- Slowly enlarging painless swelling
- 25% extraosseous

Prognosis:
The soild form is more aggressive than the cystic form.

Radiograph:
✓ Well defined uni/multilocular radiolucency containing radiopaque flecks
✓ May be associated with unerupted teeth

So the differential diagnosis of tumors that contain radio-opacity and radiolucency include many tumors

The radiolucent margin around the lesion (fibrous connective tissue around it) indicate that the lesion is benign.

So the radiograph is a good diagnostic tool to determine if the lesion is benign or malignant depending on the margins, whether it was well or poor defined.

Histopathology:
( this lesion is easy to be diagnosed depending on the histopathological features of it)
✓ Cystic cavity that’s lined by basal ameloblast-like Cells & Stellate Reticulum

Unlike the unicystic ameloblastoma, this lesion contain inside the stellate reticulum ghost cells ghost cells: large epithelial cells that contain keratin
Dentine or odontome could be formed within this lesion.

*note that the odontome could be associated with many odontogenic tumors*

Prognosis:
- The solid form is more aggressive than the cystic form

**Odontogenic fibroma & myxoma**

- This tumor is mesenchymal in origin (Periodontal ligament, Dental follicle, Dental papilla) and it's usually associated with a tooth or replacing a missing tooth.
- The myxoma is infiltrative and has a higher recurrence rate than the fibroma.
- We studied the fibroma in the CT (the fibroepithelial polyp) before, but here the fibroma is present within the bone (Odontogenic fibroma) or a myxoid tissue (Odontogenic myxoma).

- **Odontogenic fibroma:**

  Clinically:
  - Slowly enlarging, painless benign tumor
  - Appear mainly in the mandible and could be present in the gingiva rarely (extraosseous)

  Radiograph:
  Well defined radiolucency, uni/multilocular

  Histopathology:
  - Fibrous connective tissue (collagen & spindle-shaped fibroblasts)
  - Strands of odontogenic epithelium (like rest cells of Malassez) could be found inside the CT
  - Calcifications could be found also

  If extraosseous; the presence of the odontogenic epithelium and the calcifications indicate that the lesion is peripheral odontogenic fibroma rather than fibrous epulis

- **Odontogenic myxoma:**

  Clinically:
  - More common compared with fibroma
  - Could be present either in mandible or maxilla.
Slowly enlarging, painless (but the growth rate is higher than the fibroma)

Tooth displacement could happen

Radiograph:
- Well defined multilocular radiolucency, “soap bubble” or (tennis racket) appearance,
- Could cause resorption for the adjacent root

Histologically:
- Mucoid material surrounded by thin fibers so it’s easy to be ruptured, so it can’t be removed by inoculation, safety margins should be taken to ensure the complete removal of this tumor
- Angular cells with long anastomosing processes
- No capsule present so this lesion is infiltrative inside the bone

Mixed tumours of both fibroma and myxoma can be found and its named according to the dominant tissue as Fibromyxoma or myxofibroma

Prognosis:
The presence of the myxoid tissue makes the prognosis worse than the fibroma as it has high recurrence rate (25%)
Treatment: surgical extraction and removing of the tooth (using a flap), simple extraction could cause fracture of the tooth or incomplete removal of the tumor.

- **Radiograph:**
  - Well defined radio-opaque mass in the late stage, but in the first stages it could appear as radiolucent mass. (with time the radio-opacity increases)
  - Thin radiolucent margin surrounding the lesion (benign)
  - Attached to the roots of a tooth (continuous with the periodontal ligament)
  - Resorption of related roots could happen

- **Histopathology:**
  - Capsule (fibrous connective tissue)
  - Mass of calcified material (Cementum with many reversal lines)
  - Spaces that represent Peripheral zone of un-mineralized tissue containing cementoblasts

Now we'll take about the Malignant odontogenic tumours:

**Malignant ameloblastoma:**
- Typical histology of benign ameloblastoma but it undergone aspiration to the lung leading to pulmonary ameloblastoma with the same histopathological features of the ameloblastoma in the mandible, it occur mainly with the lesions that was removed surgically more than one time
- Its an aspiration process not true metastasis which occur through the blood/lymph.

**Ameloblastic Carcinoma:**
• Ameloblastoma that contain follicles, surrounded by columnar cells, has stellate cells at the center but contains features of malignancy:

Hyperchromatism, polymorphism, high mitotic activity, invasion to the surrounding tissues.

Could spread to the lymph nodes.

**Primary intraosseous squamous cell Carcinoma**

Originated from the odontogenic epithelium of the mucosa

Signs of malignancy are present within the lesion.

**Clear Cell Odontogenic Carcinoma:**

Rare tumor

Malignant tumor that infiltrate to the lymph nodes

**Histopathology:** large cells with clear cytoplasm that looks like the histopathological image of renal cell carcinoma

the patient should be examined for assurance that he doesn’t have renal cell carcinoma

**Malignant change in odontogenic cysts:**

• Clinically & Radiographically a Cyst exist

• **Histopathology:** part of the cyst contains malignant features

• **Pathogenesis:**
  _ Carcinoma change in a cyst
  _ Cystic degeneration in a Carcinoma
  _ Carcinoma invading the cyst

**Odontogenic Sarcomas:**

• E.g: Ameloblastic Fibrosarcoma

• Fibrosarcoma tissue and Non-neoplastic odontogenic epithelium
Tumours of debatable origin:

**Congenital gingival granular cell tumor (Congenital epulis):**

(The typical Granular cell tumour usually develop in the tongue and it consists of large, closely packed granular cells and the surface epithelium show hyperplasia so it could be misdiagnosed as SCC)

- **Origin:** unknown

- **Clinically:** same as the granular cell tumor in the tongue but it appear in a Newborn’s gingiva

Anterior maxilla

Mainly female newborn

Pedunculated swelling from crest of alveolar ridge

Up to several cms in size

- **Hist:**

Looks like the granular cell tumor but it has Atrophy of overlying epithelium rather than hyperplasia

Diagnosis: S100 –ve unlike the GCT which is S100 +ve

Treatment: local excision

**Melanotic neuroectodermal tumour of infancy**

- **Origin:** neural crest

- **Clinically:**

< 6 months newborn

brown or black pigmented swelling come from inside the maxilla mainly occur in Anterior Maxilla but can occur in Extra-oral sites: (brain, skull, testis)
• **Radiograph:** radiolucent area with tooth buds displacement

• **Histopathology:**

  Two cell types (the first type looks like the melanocyte and the second type looks like lymphocyte) with dense fibrous CT stroma

The presence of the melanocyte like cells give the lesion its name and it helps in the diagnosis