Bone Pathology

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OPTH 727

Bone Pathology

- Why is it important to study bone pathology?
  - Our profession (as you know) deals extensively with bone. There is no other medical specialty (besides orthopedics) that deals with bone as much as we do. Therefore, all of the diseases described in the following slides are important. Yes, some of them are rare… yes, some you may never see… but if any medical professional needs to know them, it is us.

Please know the entire slide

Bone Fracture

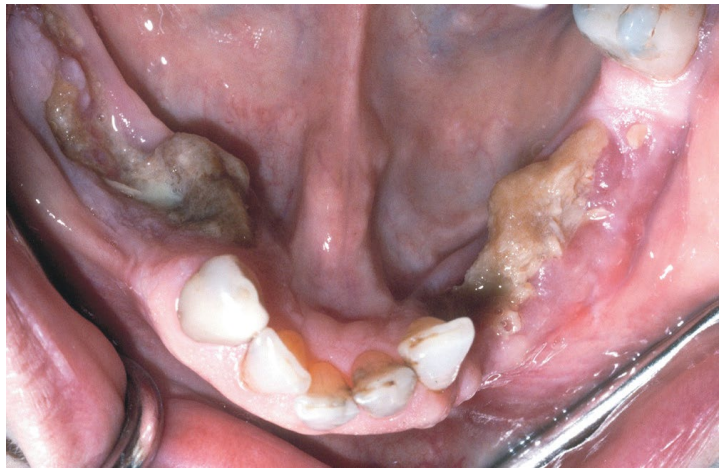
- By far, the most common bone “pathology” is a fracture (break in the continuity of bone).
- Fracture may be partial or complete.
- Pain and swelling are the most common symptoms of fracture
- Fracture is most commonly due to trauma, i.e. you break your leg while skiing. Usually a substantial amount of force is required to cause fracture.
- Fracture may also occur either spontaneously or with very minor trauma to bones already weakened by disease. In these cases, the fracture is known as **pathological fracture**. Often times, pathological fracture is the first sign of an underlying bone disease.
  - Most of the diseases described in the subsequent slides lead to weakening of bones- and therefore, affected patients are more susceptible to fracture (pathological fracture).

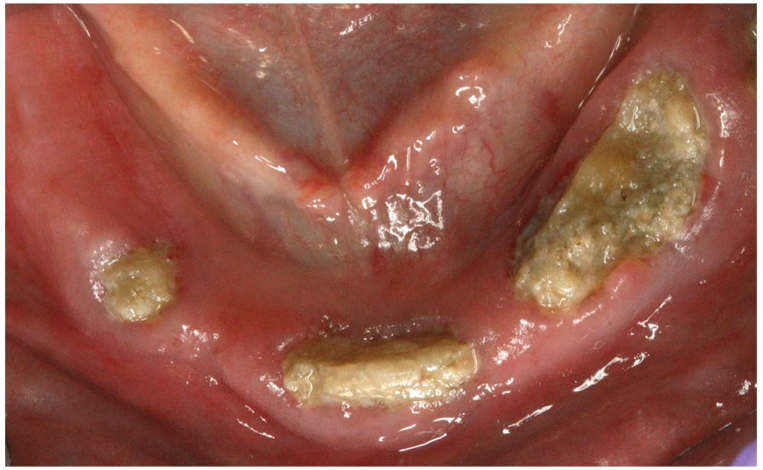
Osteoporosis

Please know the entire slide

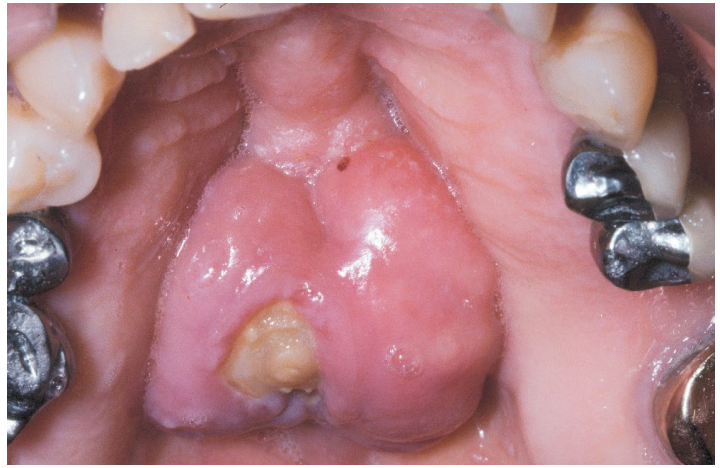
- Very common condition that results in reduced bone density
  - Reduced bone density makes patient susceptible to pathological fracture
  - The term "osteoporosis" is really more of a sign than a disease itself (similar to anemia, remember?)
    - Many diseases/conditions may cause osteoporosis. Hormone disturbances, malnutrition, metastatic disease, other systemic diseases)
- One common cause is lower levels of sex hormones (particularly estrogen) in old age
  - Therefore, osteoporosis most often affects the elderly
  - Females more often affected then males –
    - Due to a severe reduction of estrogens post menopause
- In general, osteoporosis occurs when the body either makes too little bone (dysfunction of osteoblasts) or there is too much bone resorption (overactivity of osteoclasts). Sometimes there is a combination of both.
  - Osteoclast inhibitors, (usually bisphosphonate drugs, which you will learn a lot about in dental school) are often used to treat osteoporosis. Bisphosphonate drugs are also used to treat some cancers (at much higher doses)
    - A side effect of these bisphosphonate drugs is MRONJ (medication related osteonecrosis of the jaw)
      - Note: most cases of MRONJ are the result of the much higher dose of bisphosphonate drugs that are used to treat cancer not osteoporosis)

Examples of MRONJ





Following bisphosphonate treatment cancer



Following bisphosphonate treatment for osteoporosis

A few examples of MRONJ (you will learn a lot about this in the next few years).
You can see the exposed, necrotic bone in the jaw following medication (usually bisphosphonates).
Also, you may appreciate the greater severity in cancer cases vs osteoporosis cases, because bisphosphonate dose is much higher in treating cancer. The exposed, necrotic bone may get infected and result in osteomyelitis.

Osteoradionecrosis (ORN)

- Exposed, non-vital bone following radiation (cancer therapy)
  - Many head and neck cancers are treated partly by radiation
  - Far more common in mandible than maxilla

- Presents similarly to MRONJ
  - Exposed, non-vital bone
- Radiation therapy leads to reduction of blood supply and ischemia of bone.
  - Bone may become further necrotic following tooth extraction in a patient who has received radiation therapy
    - For this reason, questionable teeth are extracted/treated prior to radiation therapy
    - Bone can become necrotic even in the absence of extraction or dental treatment
    - Radiation therapy also leads to salivary gland hypofunction and increased caries risk

Note: bone ischemia/necrosis may occur due to a number of factors. Medications and radiation therapy are two such causes. Osteomyelitis, tumors, and pathological fracture may also produce bone ischemia/necrosis.

Please know the entire slide

Osteomyelitis

- Osteomyelitis is a general term used to indicate infection of bone.
  - Many types of osteomyelitis exist.
    - Some are mild cases
    - Some are severe.
    - Some are acute infections containing pus… some are chronic infections
  - The most serious cases involve the medulla of the bone

- Osteomyelitis is often associated with some systemic disease
  - Immune compromise
  - Serious infection from another part of body that spreads to bone (via septicemia), e.g. tuberculosis.
- Osteomyelitis may also result from direct access of bacteria through an open wound
  - Could be a fracture (pathological or traumatic fracture) or other bone injury
  - The jaws are unique because they house teeth… teeth provide an open access from the oral cavity (filled with bacteria) to the bone.
    - Osteomyelitis is still uncommon in the jaw… but probably more common in the jaw than most other bones because of the proximity/communication with the oral cavity (due to diseased teeth or following tooth extraction)

Osteogenesis Imperfecta

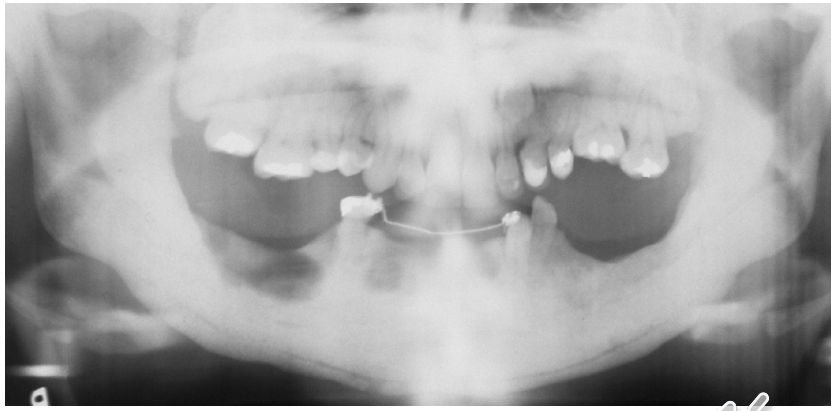
You've studied this disease before, and will do it again.

- Diverse group of genetic diseases all characterized (in general) by osteopenia and bone fragility
  - Rare. ~1:10,000
  - Numerous different mutations in many different genes all cause a similar clinical presentation
    - Most cases exhibit mutations in Type I collagen genes, COL1A1 or COL1A2
  - Large diversity in clinical severity
- Clinical features
  - Depending on severity… multiple bone fractures, growth impairment, bone deformities, hyperextensive joints
    - May see facial deformities
  - In some cases, blue sclera and hearing deficits may be seen
  - Dental alterations may be present
    - Dental alterations, if present, will resemble what is seen in dentinogenesis imperfecta.
      - Opalescent teeth, pulpal obliteration,

Osteopetrosis

Please know the entire slide

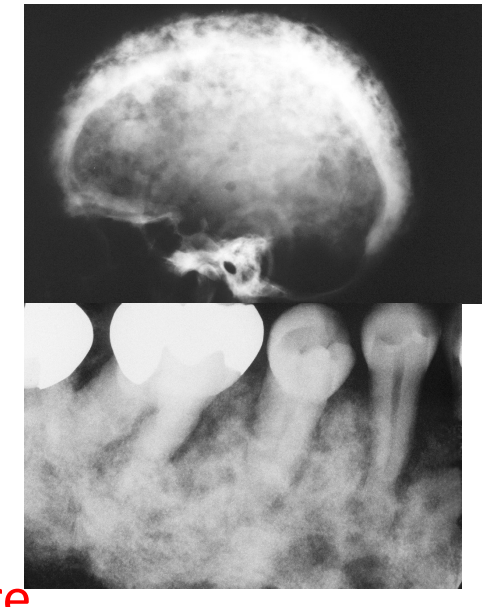
- Rare group of hereditary skeletal disorders characterized by markedly increased bone density
- Increased bone density does not lead to stronger bones… it leads to bones more susceptible to pathologic fracture.
  - Q: Why? A: Normally, the stronger bone cortex and spongy medulla allow for greater resistance to traumatic force. In osteopetrosis, marrow spaces fill with bone, this actually makes the bone weaker/ and more susceptible to fracture.
  -
- General characteristics:
  - Numerous types of disease with spectrum
  - Some clinical features
    - Reduced hematopoiesis because bone grows into marrow spaces
    - Increased fractures and osteomyelitis
  - Mutations in one of several genes cause disease



Pagets Disease of Bone (osteitis deformans)

- Abnormal, haphazard deposition of bone
  - Results in skeletal distortion and weakening

- Cause is unknown
  - In some cases, a genetic cause has been identified, but in most cases, no genetic cause is identified.
- Who is affected?
  - Primarily people of Anglo-Saxon descent
    - High rates in UK, New Zealand, Australia
    - About one percent of people in USA are affected
  - Disease is adult onset, usually over 40
- Clinical and radiographic features:
  - Cotton wool appearance of bone radiographically
  - Bone pain
  - Bones become thickened, enlarged, weakened and susceptible to fracture
  - Pelvis, femur, lumbar vertebrae, and skull most often affected
    - Jaws affected 17% of cases
  - Laboratory testing: elevated serum alkaline phosphatase levels



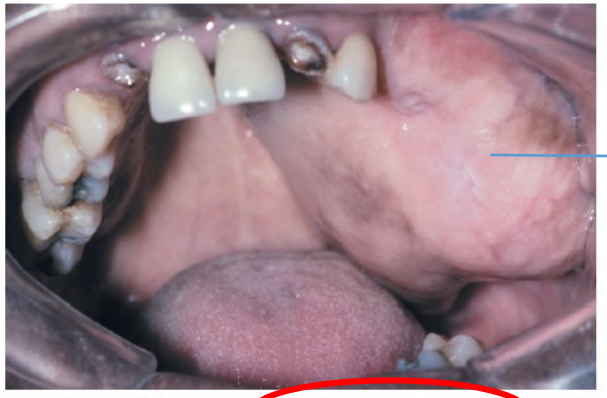
Fibro-osseous lesions

- Diverse group of processes that are characterized by replacement of normal bone by a mixture of fibrous connective tissue that is partially calcified.

- Three entities that affect the jaws exist. (will be discussed extensively in oral pathology)
  - Fibrous dysplasia- discussed on next page
  - Cemento-osseous dysplasia
    - Somewhat common condition
    - Found in tooth bearing areas of jaws
  - Ossifying fibroma
    - Potentially aggressive tumor of jaws
      - Obviously, not all cases are aggressive

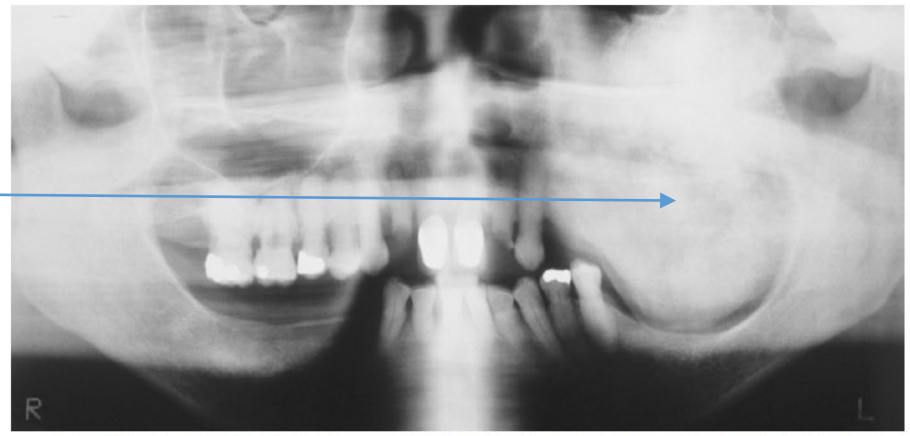
Fibrous dysplasia

- Developmental tumor-like condition
  - Caused by genetic mutation of GNAS gene
    - Mutations are usually sporadic and post-zygotic (therefore, would you expect this disease to be inherited from parents?)
- Normal bone is replaced by a mixture of fibrous connective tissue and immature bone.
  - Many different bones may be affected, craniofacial bones, ribs, femur, tibia
  - Growths may present in childhood and continue in adulthood
  - The growth replaces the normal bone continues growing and produces enlargement (swelling) and a “ground glass” radiographic appearance.



• **Fig. 14-31 Fibrous Dysplasia.** Expansile mass of the left maxilla in a 45-year-old woman. This lesion was known to have been present for at least 20 years.

The intraoral swelling on the left presents like this on a panoramic radiograph



• **Fig. 14-32 Fibrous Dysplasia.** Panoramic radiograph of the patient shown in Fig. 14-31. A diffuse “ground-glass” radiopacity is evident. (Courtesy of Dr. Richard Brock.)

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Fibrous dysplasia (FD), continued

- A patient with fibrous dysplasia may involve one bone (monostotic) or several bones (polyostotic)
- The polyostotic types are more rare and more severe
  - Polyostotic types may be associated with some multi-organ syndromes
    - Jaffe-Lichenstein syndrome
      - Polyostotic FD and café-au-lait pigmentations
    - McCune-Albright syndrome
      - Polyostotic FD and multiple endocrinopathies

(do you remember another syndrome that has café-au-lait pigmentations on the skin?)

(do you remember another syndrome that has multiple endocrinopathies?

Primary bone neoplasms – a few considerations that you should definitely know.

While it is not a "hard and fast" rule: primary bone tumors often affect the long bones (femur, tibia, etc.). They affect these bones more often than other bones i.e. jaws… Why? The long bones grow for the longest period of time (through adolescence) and therefore cells in the long bones are mitotically active for a longer duration of time. As we have learned, the more mitotically active a cell type is, the greater chance there is of developing a neoplasm that originates from that cell. This is why most tumors and most cancerous tumors in the body (in general) are carcinomas… i.e. originate from epithelium (because epithelium has the highest cell turnover). As we have discussed, carcinomas are far more common than sarcomas. A malignancy of bone origin is an osteosarcoma. A malignancy of cartilaginous origin is chondrosarcoma

Another consideration… in general, tumors are a characteristic of adulthood. Bone (and cartilage) tumors often present in childhood and adolescence (as well as adulthood). This is because that is the age at which the hard tissues grow. So, why then don't carcinomas present in childhood as well as adulthood? After all, the carcinomas that you have learned about, GI, lung, oral, etc originate from cells that have a high turnover throughout life (respiratory and GI epithelium). Why wouldn't there be a high incidence of these carcinomas in childhood as well. The reason that these carcinomas almost always present in adults is that because many of these cancers are due to repeated injury or exposure to toxic agents, or endocrine activation.

Finally, even benign tumors (and cysts) of bone may be destructive and debilitating. Obviously, malignant tumors are more dangerous, because they are typically faster growing, infiltrative and have the ability to spread (metastasize) to other parts of the body. Benign tumors are dangerous because they may significantly weaken the bone and lead to easy fracture (pathological fracture).

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Primary bone neoplasms – the entities

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- Osteoma
  - Proliferation of mature, lamellar bone.
  - Tori are examples of osteomas
  - Common. Not destructive. Some argue whether these are real neoplasms.
  - Radio-opaque
- Osteoblastoma, also called osteoid osteoma
  - Benign neoplasm of osteoblasts. May be destructive, but still benign.
  - Radiolucent or mixed radioopaque/radiolucent
- Osteosarcoma
  - Malignant neoplasm of osteoblastic origin.
- Chrondrosarcoma
  - Malignant neoplasm of chondroblastic origin
- Chondroma
  - Benign neoplasm of cartilageonous origin.
  - **Sinovial chondromatosis** (what does the suffix –osis mean?)
    - Numerous benign cartilagenous tumors deposit in joints. Usually, this is the elbow, knee, hip and shoulder. TMJ may also be affected, but more rarely.
- Ewing Sarcoma
  - Rare, aggressive, malignant tumor of mesenchymal stem cell origin
  - Mostly children and adolescents

Story time… back in the 80s, there was a popular TV show “Dallas”. It was too racy for kids so my mom wouldn’t let me watch it. Anyway, the main character was a guy named JR Ewing who was a nasty SOB: a conniving, cheating sociopath. JR Ewing was a nasty human just like Ewing Sarcoma is a very nasty cancer.

Odontogenic tumors and cysts

- The jaws are unique bones for two reasons
  - 1) Jaws are the only bones that have other organs growing within them (teeth)
  - 2) the teeth are exposed to the scary, outside world rife with bad things trying to harm us (i.e. bacteria). A compromise in tooth structure provides a direct conduit for bacteria to reach the bone.

- For these reasons, jaws have several unique pathological entities
  - As mentioned earlier – they are far more susceptible to infection/inflammation

  - There are unique lesions (tumors and cysts) that are derived from the tooth organ (you remember from oral histology all of those cells that produce tooth structure?) You will know more about these than you will ever care to (in Oral Path classes in third year).

Odontogenic cysts and tumors

- Some of the (epithelial) cells that produce teeth do not go away when teeth are completed.

- Remnant epithelial cells may proliferate and cystify producing jaw cysts (remember, a cyst is an epithelial lined, fluid filled cavity)
  - **Odontogenic keratocyst** (a more aggressive odontogenic cyst)
  - **Radicular cyst** – inflammation from a necrotic tooth pulp travels to bone and causes cystification of the remnant epithelial cells
  - **Dentigerous cyst** – a common cyst always associated with an impacted tooth. When a tooth is impacted, the tooth organ is less likely to resolve. Epithelial cells are more likely to be present and cystify.

- Remnant epithelial cells can also grow as a solid tumor
  - **Ameloblastoma** – is most common odontogenic tumor.

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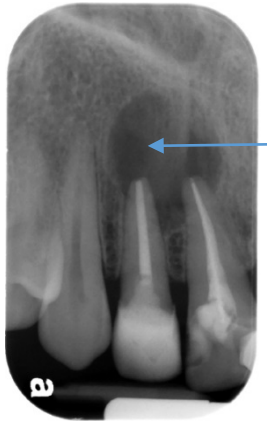
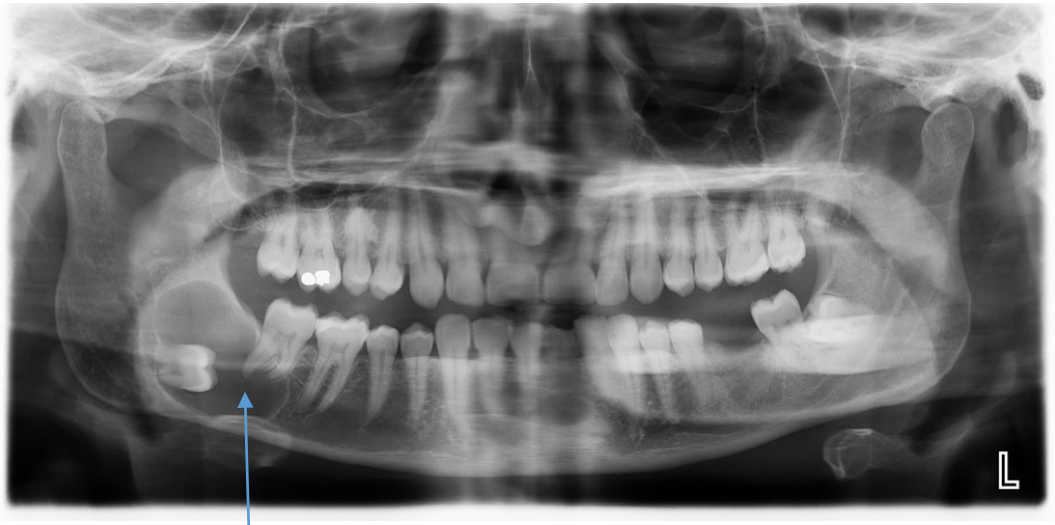
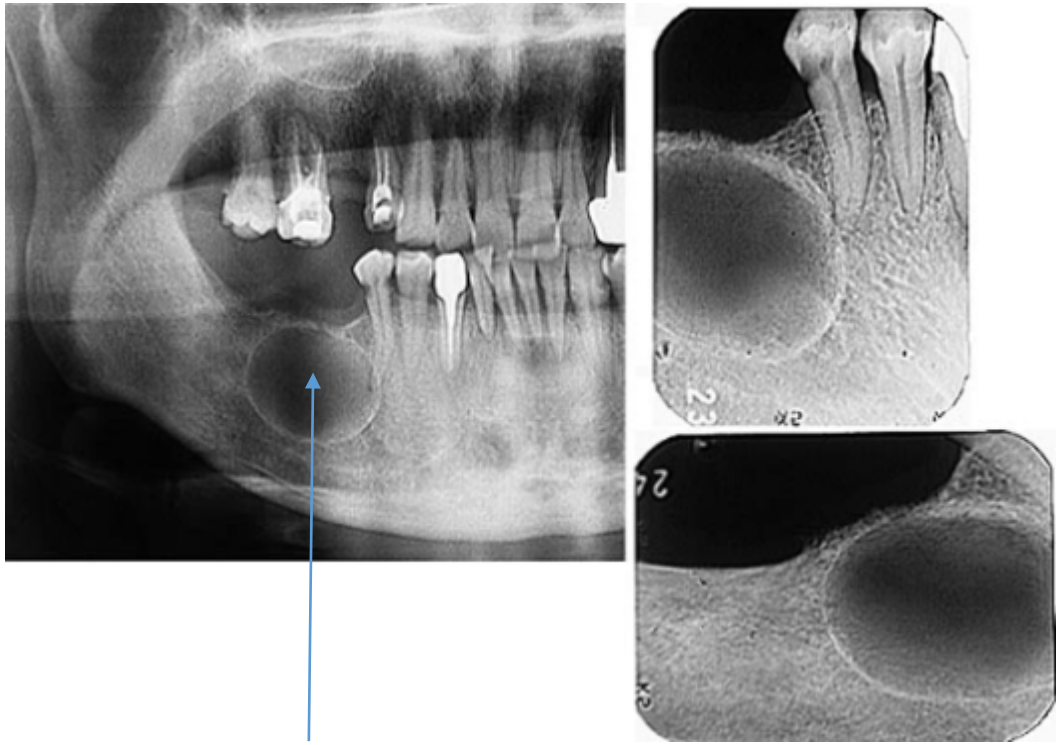


A cyst that is apical to a diseased tooth pulp is most likely a radicular cyst but could be other entities.



Jaw lesion around an impacted tooth is most likely a dentigerous cyst but could be other entities as well (ameloblastoma or odontogenic keratocyst).



The above lesion could be an odontogenic keratocyst or Ameloblastoma

Metastatic disease to bone

- Metastatic disease is the most common form of cancer affecting bone
- Vertebrae, ribs, pelvis and skull are most common sites of metastasis
- Jaw metastases are rare (but they definitely occur)
  - Posterior mandible is most common site of metastatic disease in jaws
  - As with other bone cancers, pain, dysthesia and/or swelling are most common symptoms.
- Q: Which cancers most often metastasize to the jaw?
  - A: As we have learned, the most common (non-skin) cancers are breast, lung, thyroid, colon, prostate and kidney cancers. (A useful mneumonic is "BLT with a Cold Kosher Pickle). These will be the most common cancers to metastasize to the jaw.
    - Non-melanoma skin cancers are, by far, the most common cancers overall but they have very low metastatic potential.

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Arthritis

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- By definition: inflammation of the joints and subsequent destruction of cartilage
- Symptoms: pain, reduced range of motion, and stiffness
- Any joint may be affected.

- Several types
  - Osteoarthritis- overwhelmingly the most common
    - This is the main type of arthritis that affects tens of millions of people
    - Aging, abnormal loading of joints, crystal deposition, constant wear and tear
    - Pain/dysfunction is usually constant
  - Rheumatoid arthritis
    - Caused by autoantibodies against antigens within the joint spaces
    - Serological testing (for autoantibodies) is key for making diagnosis
    - Rheumatoid arthritis may be seen concurrently with Lupus, Scleroderma, Rheumatic Fever
  - Psoriatic arthritis
    - An arthritis found in patients with psoriasis (red patches of skin topped with silvery scales)
    - This is also thought to be autoimmune, but diagnosis based on concurrent skin lesions, not serology.
  - Gout
    - A particular type of arthritis in which uric acid crystals deposit in joints
    - Produce episodic, severe pain
      - Redness, swelling and pain most often on big toe
      - Joint discomfort may last a few days to a few weeks
    - Dietary factors and systemic diseases contribute to propensity for gout

Vitamin D deficiency

- Fortification of milk and cereal with vitamin D has made deficiency rare in the United States.
- In young children/infants… Vitamin D deficiency produces rickets.
  - Growth impairment
  - Bowing of long bones (of legs) occurs due to loading of weak bones
  - Hypomineralzation of teeth
  - Weak overall bone structure- susceptible to pathological fracture
- In adults… Vitamin D deficiency produces osteomalacia
  - Weak overall bone structure- susceptible to pathological fracture
  - No tooth abnormalities… dentition has already been developed

Vitamin D-Resistant (independent)Rickets

- Rare condition producing similar symptoms as Vit D dependent rickets
  - Growth impairment, bowed long bones
  - Vitamin D independent rickets does not have tooth abnormalities.
- X-linked DOMINANT trait (not a lot of these)
  - Males more severely affected, but females also affected
  - Mutation in a zinc metalloproteinase gene

- In addition to the above… there is another genetic disease called Vitamin D -dependent rickets
  - Disease is due to lack of 1alpha-hydroxylase that converts vitamin D to its active form.
  - Autosomal recessive.
  - Symptoms are similar to rickets (see previous page)

Supplementation with vitamin D, will NOT mitigate symptoms of Vitamin D-Resistant Rickets

Hypophosphatasia

- Rare metabolic bone disease
  - Many types, variable severity
- Characterized by deficiency of alkaline phosphatase
- One of the first presenting signs of the disease is premature loss of the primary teeth.
  - Tooth loss is caused by a lack of cementum on the root surfaces
- Clinical manifestations similar to rickets
  - Growth impairment
  - Bowing of bones
  - Weak bones due to poor mineralization of skeleton