Giant cell lesions of bone

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Giant cell lesions include a group of lesions of markedly identical histopathological features, although they vary in their clinical behavior.

These lesions include:

1- Brown tumor of hyperparathyroidism
2- Giant cell granuloma (Central & Peripheral)
3- Giant cell tumor (Osteoclastoma)
4- Aneurysmal bone cyst
5- Cherubisim

Hyperparathyroidism

- Excess production of parathyroid hormone (PTH) results in the condition known as **hyperparathyroidism.** PTH normally is produced by the parathyroid glands in response to a decrease in serum calcium levels.

- **Hyperparathyroidism may be:**
  - **Primary Hyperparathyroidism:** is characterized by uncontrolled production of PTH, usually as a result of a parathyroid adenoma (80% to 90% of cases) or parathyroid hyperplasia (10% to 15% of cases).
    Rarely (approximately 1% of cases), a parathyroid carcinoma may be the cause of primary hyperparathyroidism.

  - **Secondary Hyperparathyroidism:** develops when PTH is continuously produced in response to chronic low levels of serum calcium, a situation usually associated with chronic renal disease.
    The kidney processes vitamin D, which is necessary for calcium absorption from the gut. Therefore, in a patient with chronic renal disease, active vitamin D is not produced and less calcium is absorbed from the gut, resulting in lowered serum calcium levels.

Clinical Features

- Most patients with primary hyperparathyroidism are older than **60** years of age.

- Women have this condition two to four times more often than men
  (greater in menoposal women).

- Early symptoms include, fatigue, weakness, arrhythmias, polyuria, bone & joint pain, headache, abdominal pain & kidney stones (because of elevated serum calcium levels).

Radiographic features

- **In the jaw bones**, there is an osteoporotic appearance of both mandible & maxilla reflecting a generalized resorption, overall cortical thinning, loss of lamina dura surrounding the roots of the teeth.

- With persistent disease, other osseous lesions develop, such as the so-called **brown tumor** of hyperparathyroidism. These lesions appear radiographically as well demarcated unilocular or multilocular radiolucencies.
They commonly affect the mandible, clavicles, ribs, and pelvis.
They may be solitary but are often multiple, and long-standing lesions may produce significant cortical expansion.

- The most severe skeletal manifestation of chronic hyperparathyroidism has been called **osteitis fibrosa cystica,** a condition that develops from a significant bone demineralization with fibrous replacement producing radiographic changes that appears as a cyst..

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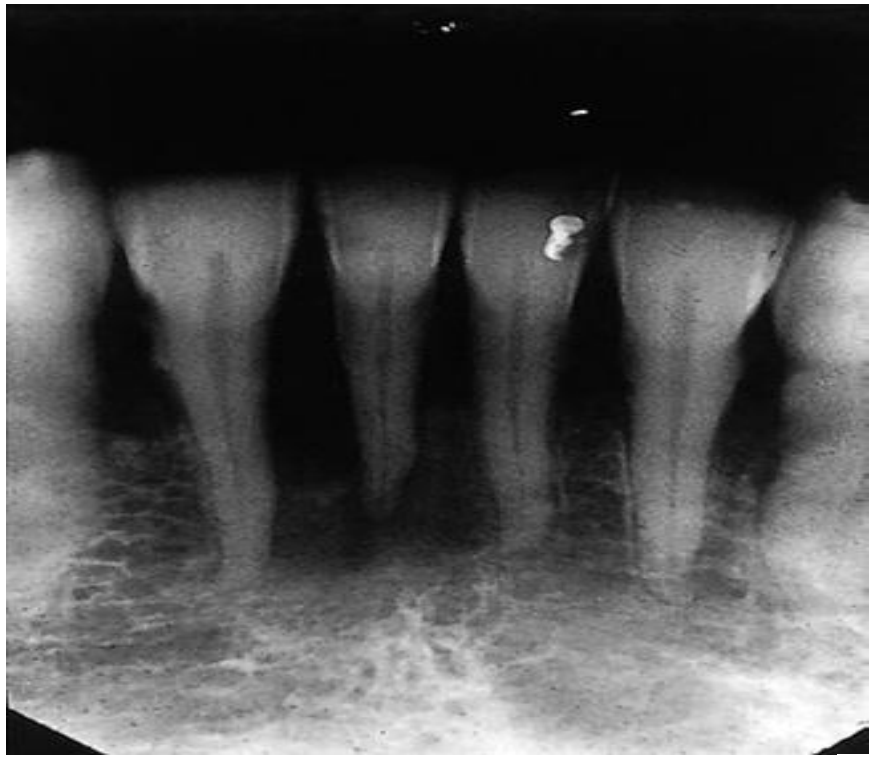
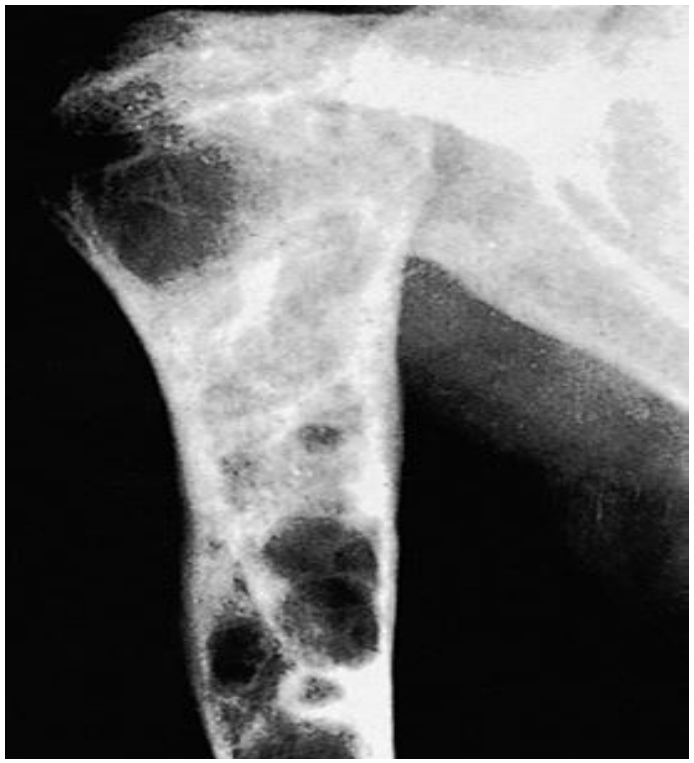
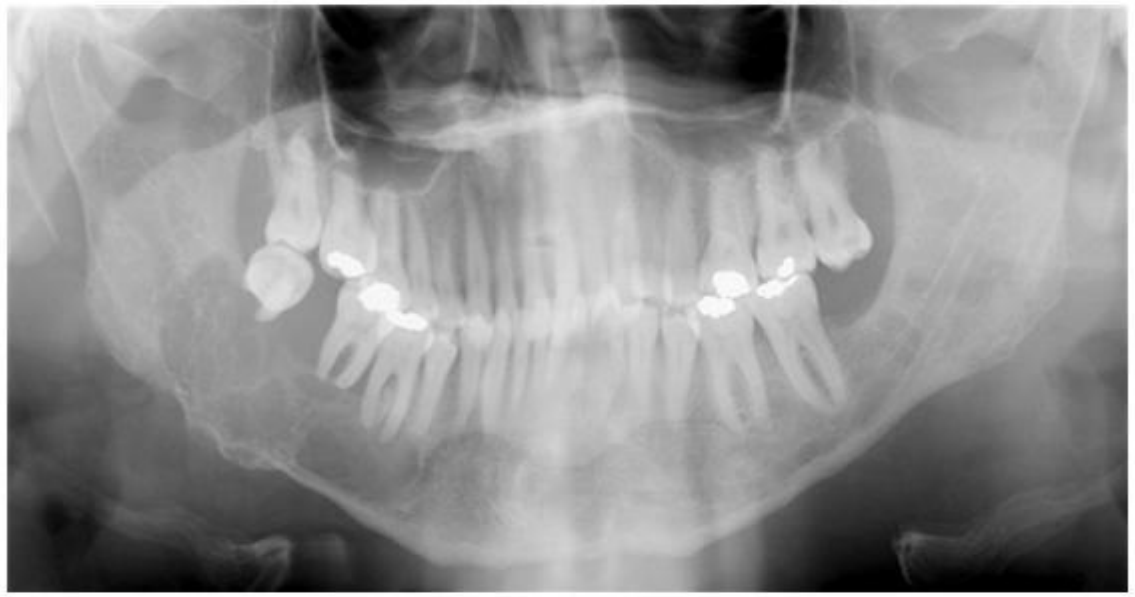




Hyperparathyroidism.
A periapical view reveals the relative radiolucency of the bone. There is loss of lamina dura around the roots, loss of trabeculae centrally and coarsening of the trabecular pattern elsewhere.



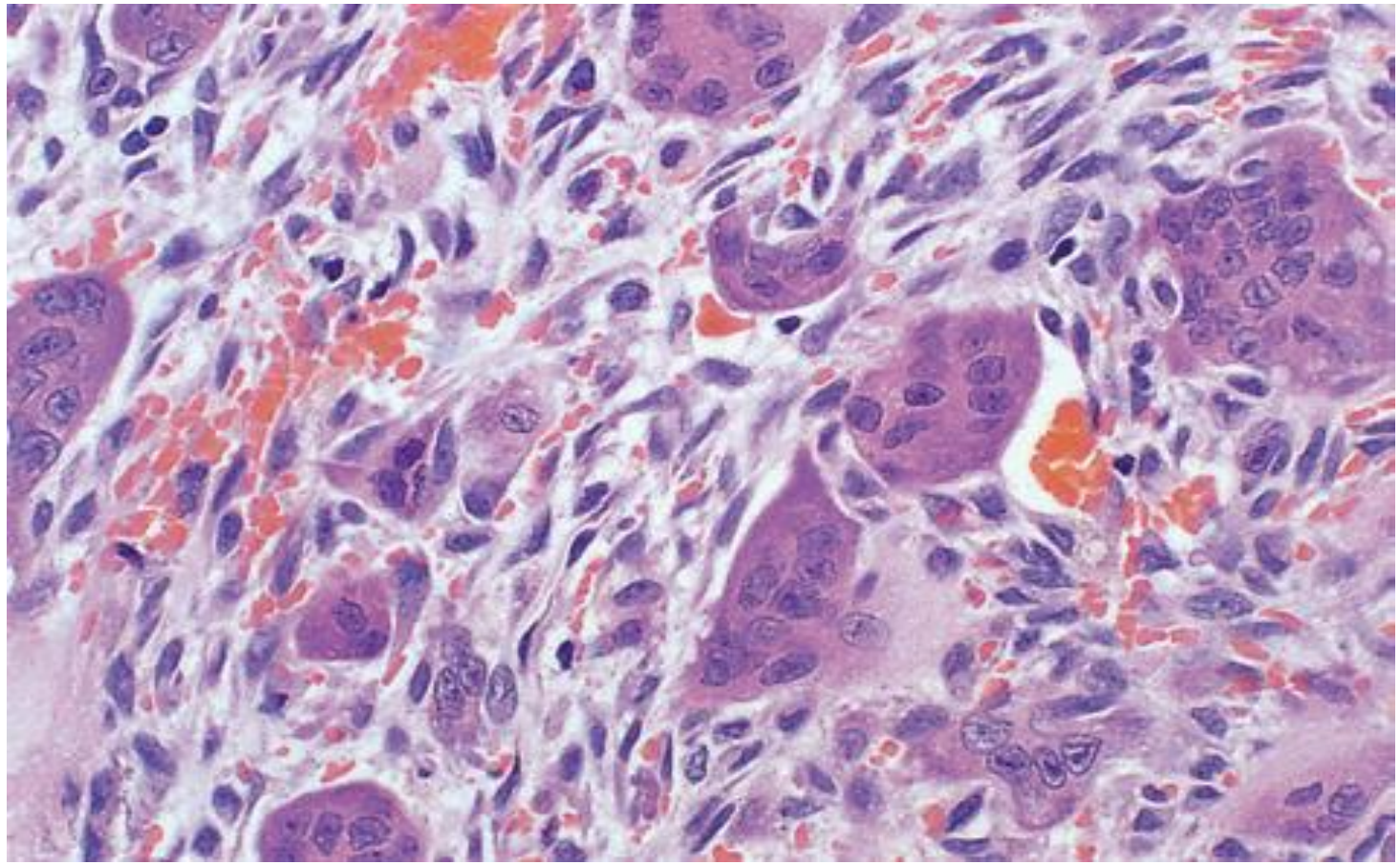
Histological Features

- The brown tumor of hyperparathyroidism characterized by a proliferation of exceedingly vascular granulation tissue, which serves as a background for numerous multinucleated osteoclast-type giant cells .

- Some lesions may also show a proliferative response characterized by a parallel arrangement of spicules of woven bone set in a cellular fibroblastic background with variable numbers of multinucleated giant cells.

- Accumulation of hemosiderin & extravasated RBC. As a result the tissue may appear dark reddish- brown accounting for the term **(Brown tumor).**

- This lesion is histopathologically identical to central giant cell granuloma of the jaws.



Hyperparathyroidism.
Multinucleate osteoclast-like giant cells are lying in a haemorrhagic fibrous tissue. The appearances are indistinguishable from giant cell granuloma histologically.

Diagnosis

Brown tumor of hyperparathyroidism is clinically, radiographically, & histopathologically is similar to **Central giant cell granuloma**, therefore, a bone chemistry profile should reveal **elevation** of serum PTH & calcium, with **a decrease** of phosphorous.

Treatment and prognosis

After diagnosis of hyperparathyroidism, the patient should be referred :

- to a surgeon for excision of the hyperplastic parathyroid tissue or the parathyroid gland tumor (to reduce **PTH** level to normal) In case of primary hyperparathyroidism.

- or for a renal function evaluation in case of secondary hyperparathyroidism.

The jaw lesions should resolve after treatment.

Central giant cell granuloma

- The **central giant cell granuloma** is an intraosseous lesion of unknown etiology.

-There is much debate regarding whether this entity represents a reactive process or a benign neoplasm.

- In the past, it was hypothesized to represent a reparative response to trauma-induced hemorrhage,___ hence, its former designation **giant cell reparative granuloma.**

- Most oral and maxillofacial pathologists today prefer the term **giant cell granuloma** & dropped the term " reparative ".

- In fact, some demonstrate locally aggressive behavior similar to that of a benign neoplasm.

Clinical Features

- Central giant cell granulomas of the jaws occur over a broad age range (2 to 80 years), although more than **60%** of cases occur before age **30** .

- There is a **female** predilection.

- Approximately **70%** of cases arise in the mandible.

- Lesions are more common in the anterior portions of the jaws, and mandibular lesions frequently cross the midline.

- Most CGCG of the jaws are asymptomatic, discovered either during routine radiographic examination or as a result of painless expansion of the affected bone.

- Aminority of cases , may be associated with pain, paresthesia, or perforation of the cortical plate, occasionally resulting in ulceration of the mucosal surface by the underlying lesion.

- **Based on the clinical & radiographic features, central giant cell granulomas of the jaws may be divided into two categories:**

1. **Nonaggressive lesions** comprise most cases. They are relatively small, exhibit few or no symptoms, grow slowly, and do not cause cortical perforation or root resorption of teeth involved in the lesion.

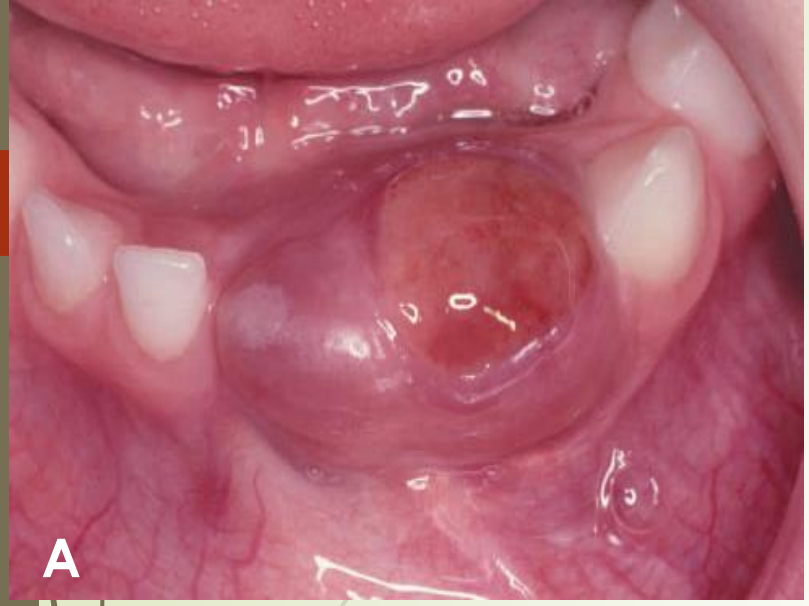
2. **Aggressive lesions** are characterized by pain, rapid growth, cortical perforation & root resorption. They show marked tendency to recure after treatment, compared to nonaggressive type.

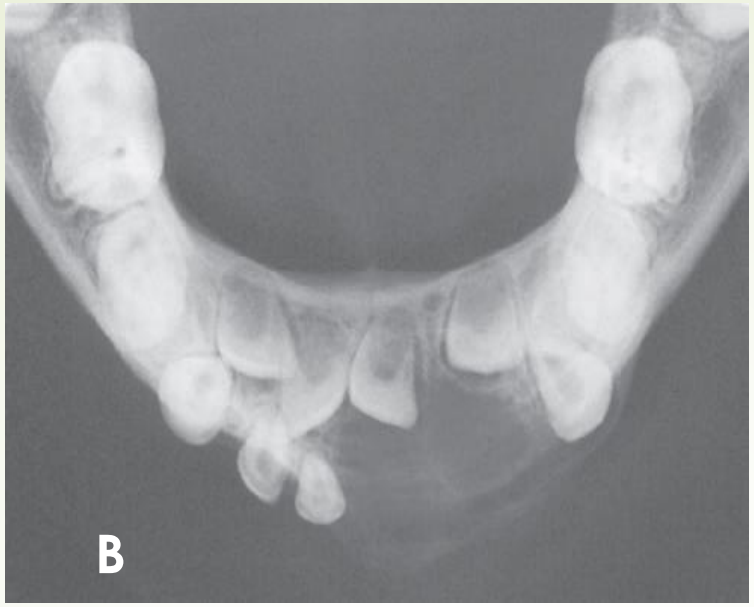
Radiographic features

- The central giant cell granuloma appears as a unilocular or multilocular radiolucency with well-delineated but generally non-corticated borders.

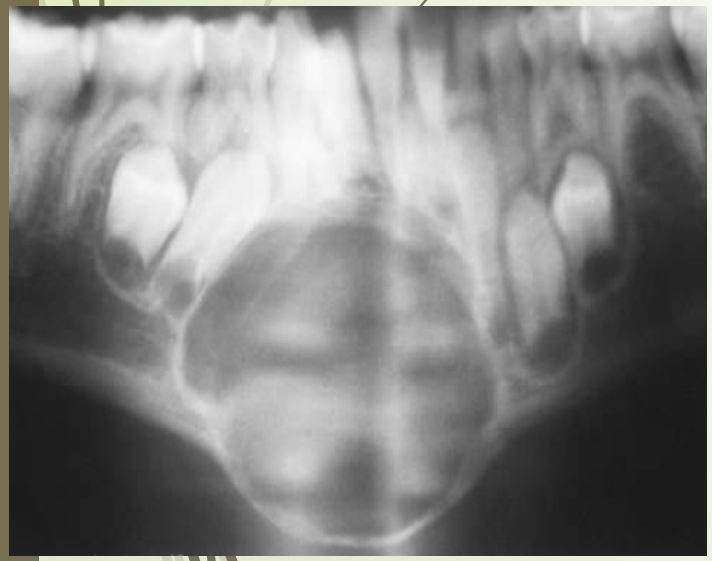
- The lesion may vary from a 5 mm incidental radiographic finding to a destructive lesion greater than 10 cm in size.

- The radiographic findings are not specifically diagnostic. Small unilocular lesions may be confused with periapical granulomas or cysts, and multilocular lesions may appear similar to ameloblastomas or other multilocular lesions.

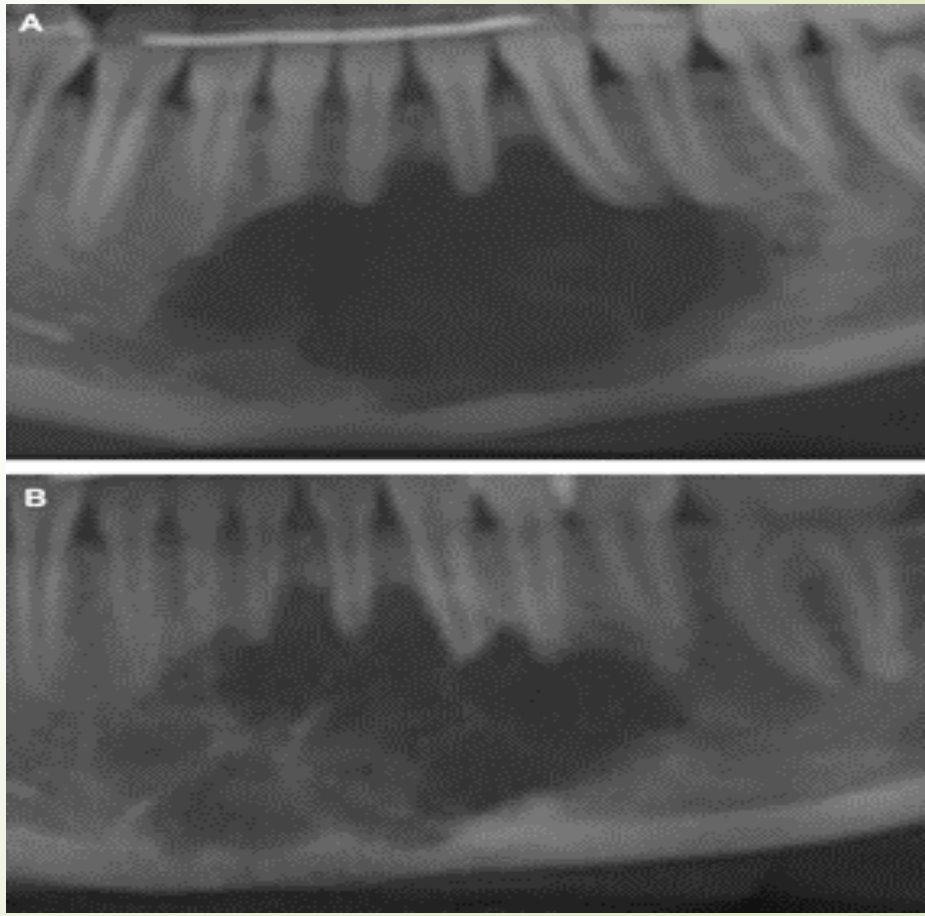




A, blue-purple, ulcerated mass is present on the anterior alveolar ridge of this 4-year-old white boy. **B**, The occlusal radiograph shows a radiolucent lesion with cortical expansion.



Central Giant Cell Granuloma. Panoramic radiograph showing a large, expansile radiolucent lesion in the anterior mandible. (Courtesy of Dr. Gregory R. Erena.)



Histopathologic features

- Microscopically, giant cell lesions of the jaws exhibit few to many multinucleated giant cells in a background of ovoid to spindle-shaped mononuclear stromal cells.

- There is evidence that these giant cells represents osteoclasts, although others suggest the cells may be aligned more closely with macrophages.

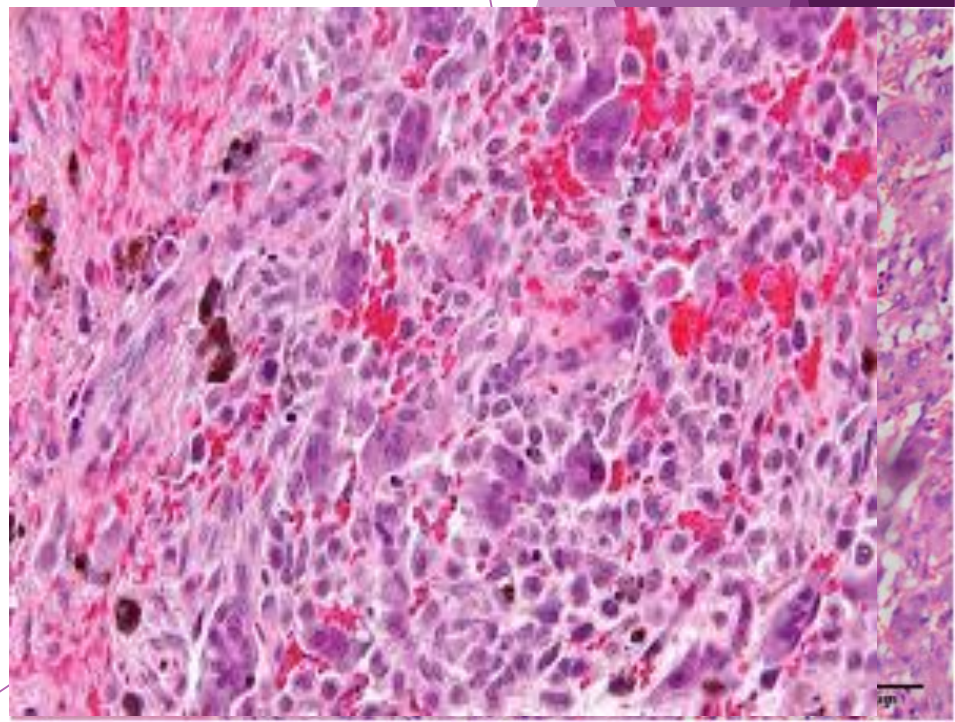
- The giant cells may be aggregated focally in the lesional tissue or may be present diffusely throughout the lesion. These cells vary considerably in size and shape from case to case. Some are small and irregular in shape with only a few nuclei, whereas others are large and round with 20 or more nuclei.

- The stroma may be loosely arranged and edematous or more cellular.

- Erythrocyte extravasation and hemosiderin deposition are often prominent.

- Older lesions may show considerable fibrosis of the stroma.

- Foci of newly formed bone & osteoid formation may be present.



Treatment and prognosis

- Central giant cell granulomas of the jaws usually are treated by thorough curettage.

- Most studies indicate a recurrence rate of about 20%. Recurrent lesions may require further curettage, although some aggressive lesions require more radical surgery for cure.

- Alternative treatments include intralesional **corticosteroid** injections, subcutaneous **calcitonin**, subcutaneous **interferon alpha-2a**.

- In spite of the potential for recurrence, the long-term prognosis is good.

Peripheral giant cell granuloma

- The **peripheral giant cell granuloma** is a relatively common tumor-like growth of the oral cavity. It probably does not represent a true neoplasm but rather is a reactive lesion caused by local irritation or trauma.

- The peripheral giant cell granuloma bears a close microscopic resemblance to the **central giant cell granuloma** and some pathologists believe that it may represent a soft tissue counterpart of this intraosseous lesion.

Clinical features

- The peripheral giant cell granuloma occurs exclusively on the gingiva or edentulous alveolar ridge, presenting as a red or red-blue nodular mass.

- Most lesions are smaller than 2 cm in diameter, although larger ones are seen occasionally.

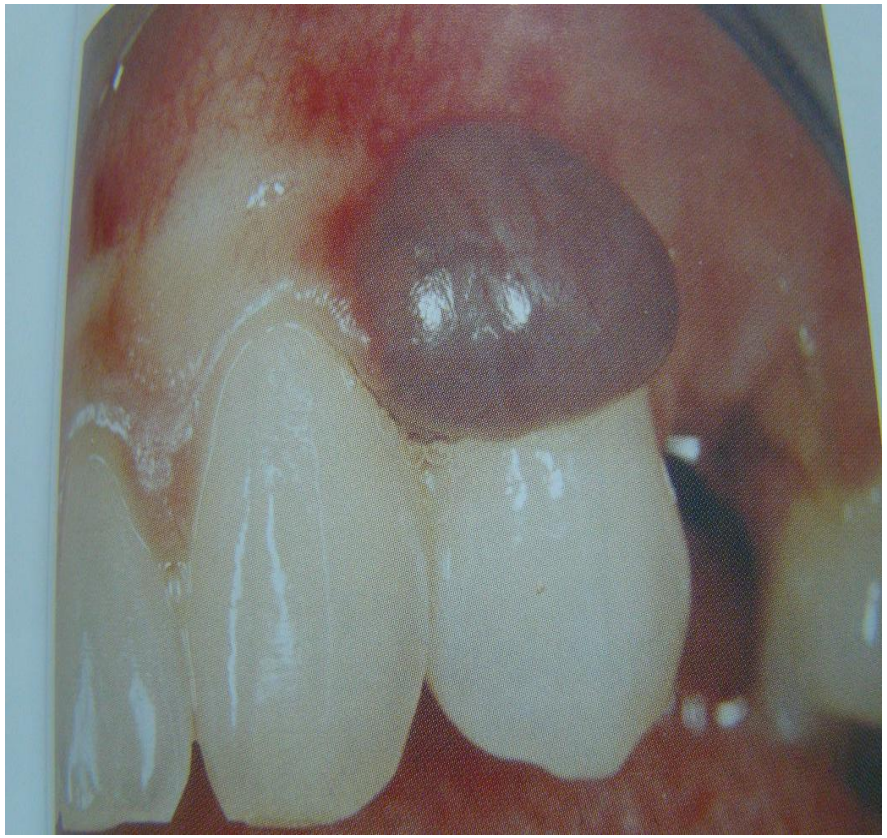
- The lesion can be sessile or pedunculated and may or may not be ulcerated.

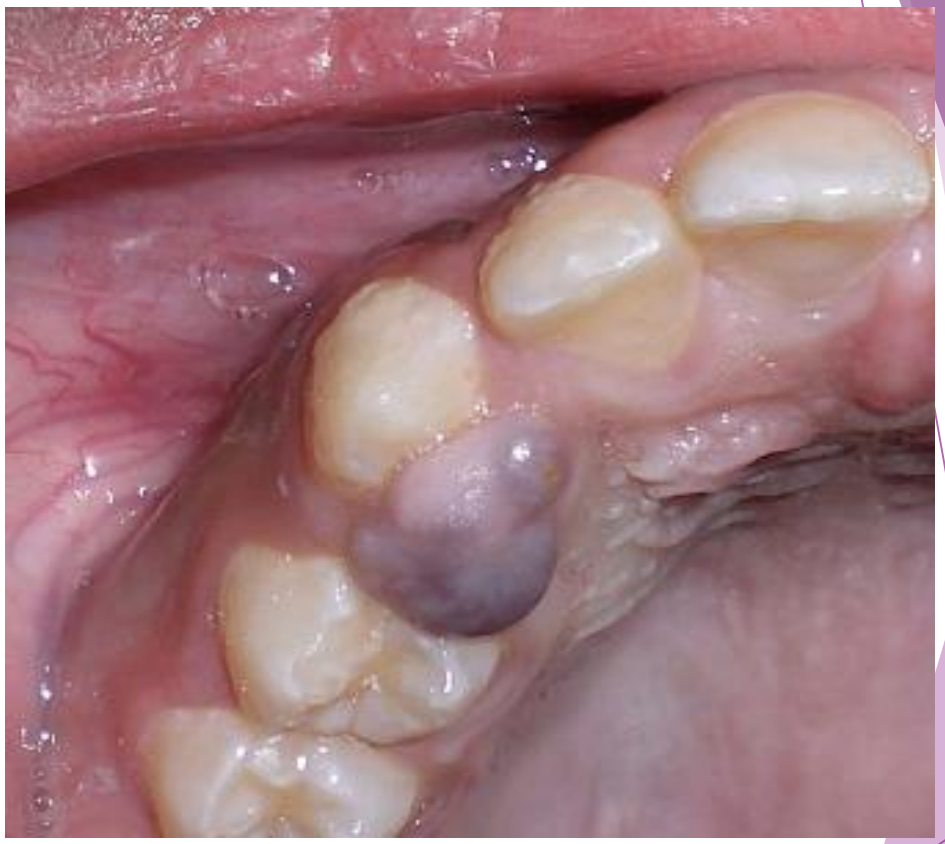
- The clinical appearance is similar to the more common pyogenic granuloma of the gingiva although the peripheral giant cell granuloma often is more blue-purple compared with the bright red of a typical pyogenic granuloma.

- Peripheral giant cell granulomas can develop at almost any age, especially during the first through sixth decades of life.

- Approximately 52% to 60% of cases occur in females. It may develop in either the anterior or posterior regions of the gingiva or alveolar mucosa, and the mandible is affected slightly more often than the maxilla.

X-ray: Nothing, however large lesion produce superficial erosion of cortical plate





Histologic features

- **Proliferation of multinucleated giant cells with a back ground of ovoid & spindle-shaped mesenchymal cells in a fibrous C.T stroma.**
- **Abundant hemorrhage is characteristically seen throughout the mass with hemosiderin deposit at the periphery of the lesion.**
- **Surface ulceration may be seen with chronic inflammatory cells infiltrate.**
- **Sometime , reactive new bone formation may be seen.**

Treatment

Surgical excision done to the underlying bone

Giant cell tumor

- A true neoplasm that arise most commonly in the epiphysis of long bone. These tumors exhibit a wide spectrum of biologic behavior from benign to malignant.

- The relationship between this lesion & CGCG is controversial. Mostly it is regarded as distinct from CGCG, acknowledging the very **rare** occurrence of this tumor within the jaw, & a **higher rate of recurrence**, in addition there is a **malignant changes** up to **10%** of cases. (concerning the lesions in the jaw bones)

- It is most often seen in **3rd & 4th** decades of life.

- Lesions exhibit slow growth and boney expansion, or they produce rapid growth, pain or paresthesia.

- **Radiologically,** the giant cell tumor produces a radiolucent image.

- **Surgical excision is the treatment of choice with great tendency to recur after treatment than CGCG.**

Histopathologically

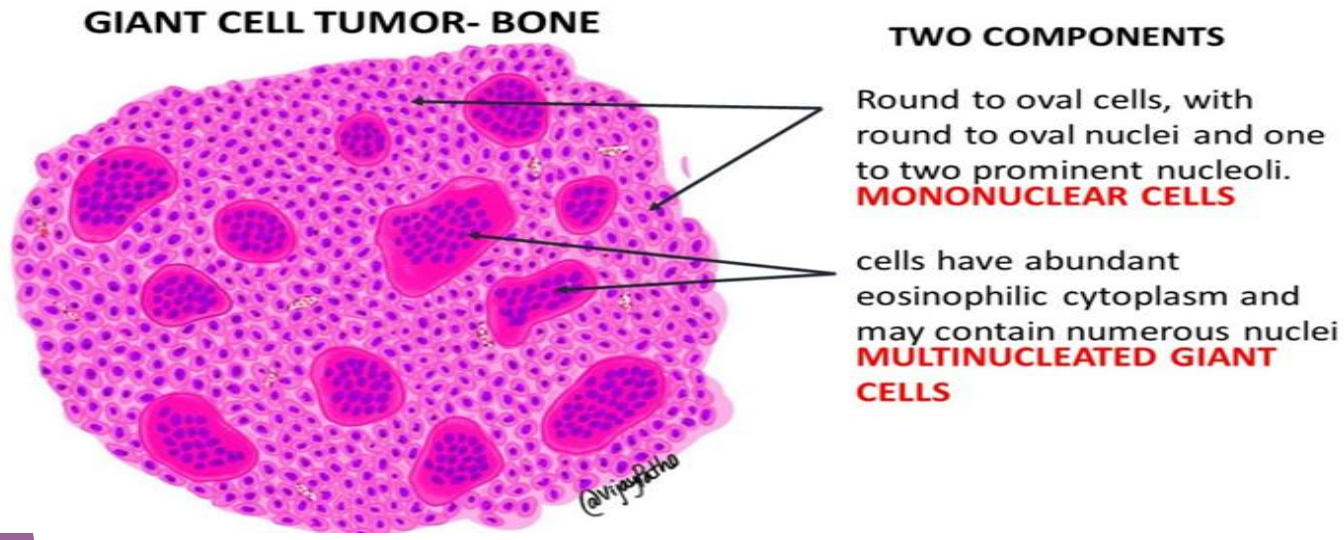
- Presence of numerous multinucleated giant cells dispersed evenly among mononuclear fibroblast.

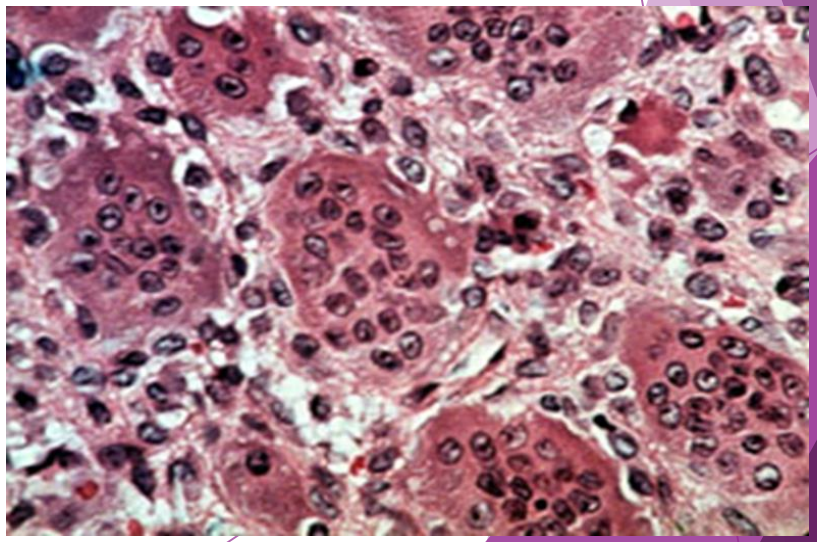
- Stromal cellularity is usually prominent with minimal collagen production.

- Giant cells are usually larger and contain more nuclei than corresponding cells in CGCG.

- Giant cell tumors may contain inflammatory cells and areas of necrosis.

- Osteoid formation is noted less than CGCG.





Aneurysmal bone cyst

- The **aneurysmal bone cyst** is an intraosseous accumulation of variable-sized, blood-filled spaces surrounded by cellular fibrous connective tissue and reactive woven bone.

- Because the lesion lacks an epithelial lining, it represents a pseudocyst rather than a true cyst.

Clinically

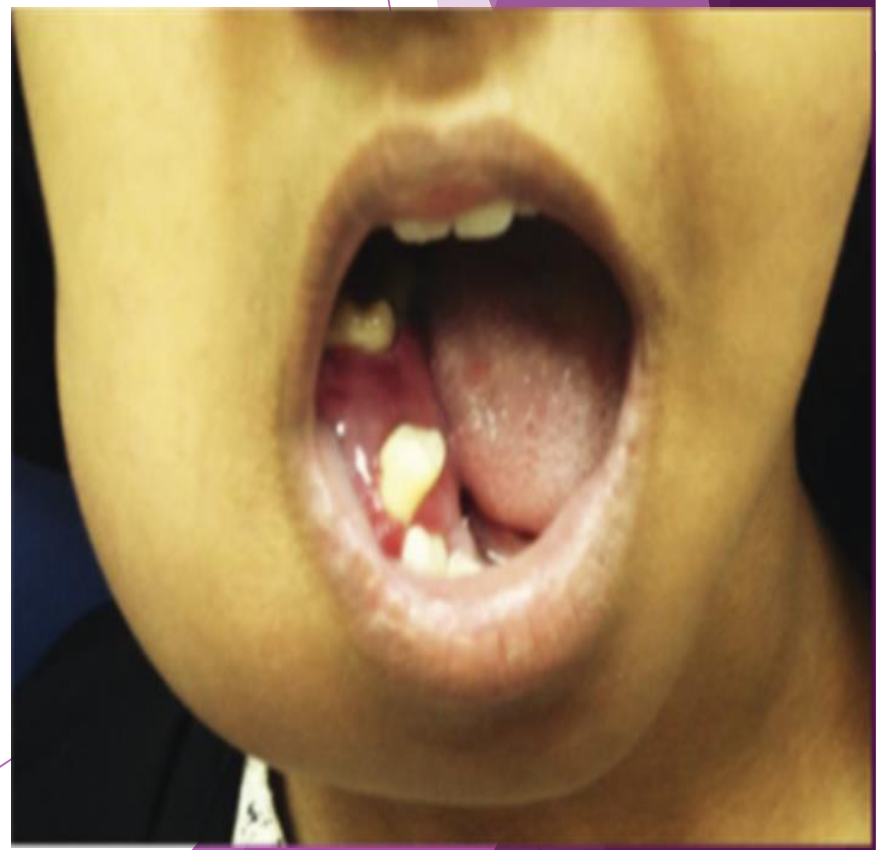
- Aneurysmal bone cysts arise primarily in the long bones or vertebrae **Rare** in jaws .

- Arise in **posterior part** of the body or at angle of the mandible.

- Mostly affect children and young adult **(10- 20 years**).

- **No significant** sex predilection.

- Appear as a firm swelling that developed rapidly causing facial deformity and may be associated with pain.



Radiographically

Radiographic examination shows a unilocular or multilocular radiolucency with a characteristics ballooned-out appearance due to gross cortical expansion & thinning.

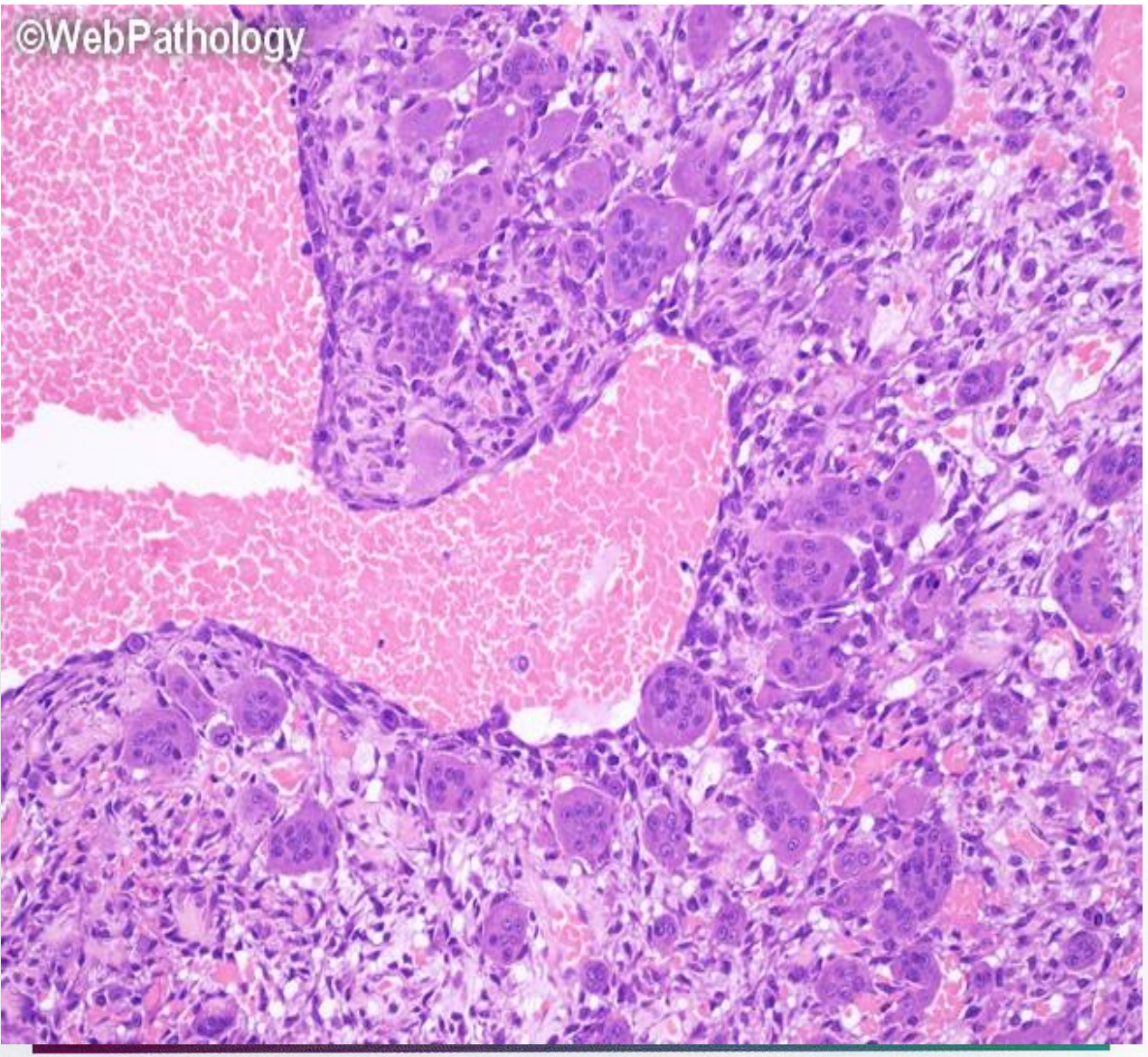
[=expansile soap –bubble radiolucency]

Histopathology

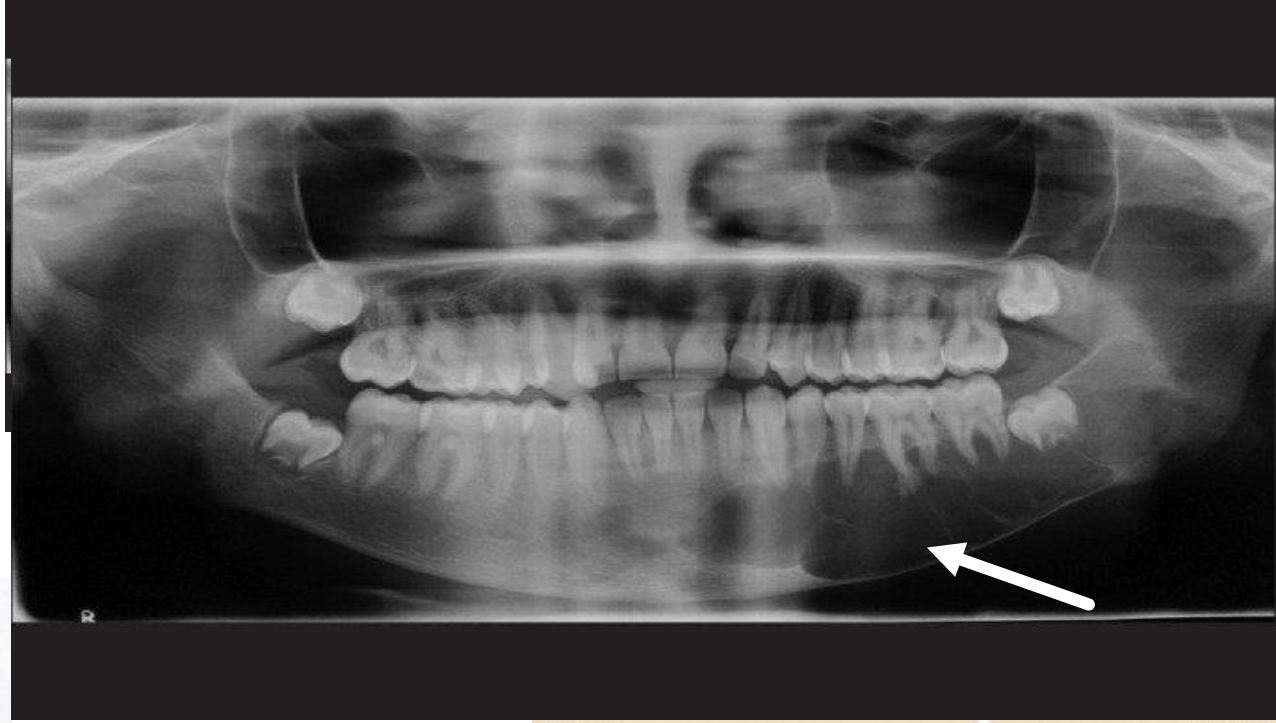
Lesion composed of numerous, non – endothelial lined blood filled spaces of varying size separated by cellular fibrous tissue containing multinucleated giant cells, trabeculae of osteoid & woven bone, & evidence of old & recent hemorrhage.

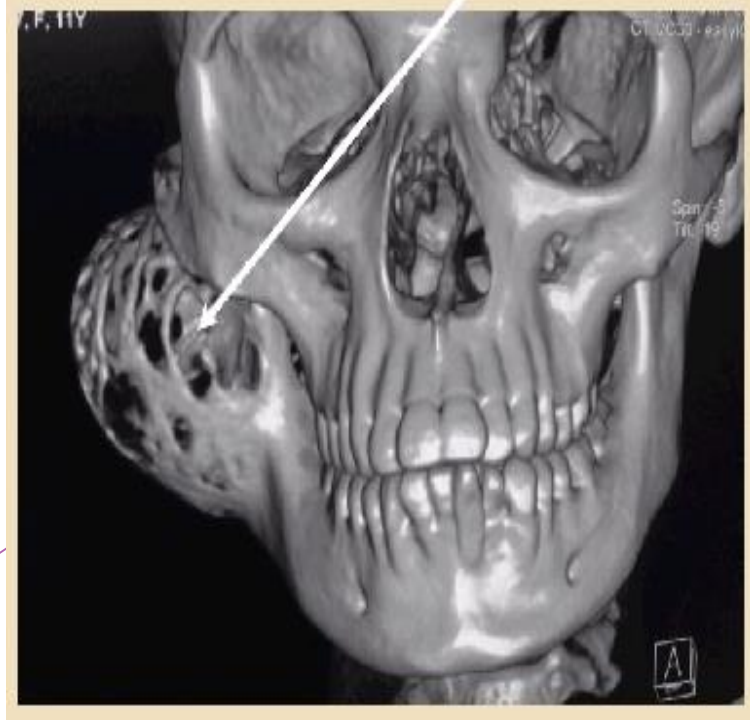
Pathogenesis

The etiopathogenesis is poorly understood. Traditionally, the aneurysmal bone cyst has been considered a reactive lesion. Many authors have theorized that a traumatic event, vascular malformation, or neoplasm may disrupt normal osseous hemodynamics, resulting in an enlarging area of hemorrhage and osteolysis.



Aneurysmal bone cyst. Photomicrograph showing a blood-filled space surrounded by fibroblastic connective tissue. Scattered multinucleated giant cells are seen adjacent to the vascular space.





Treatment

- Curettage and enucleation(sometimes with cryosurgery)
- Recurrence rate –8% -60%
- The higher rate due to incomplete removal of the lesion
- However, good long-term prognosis

Thank you