

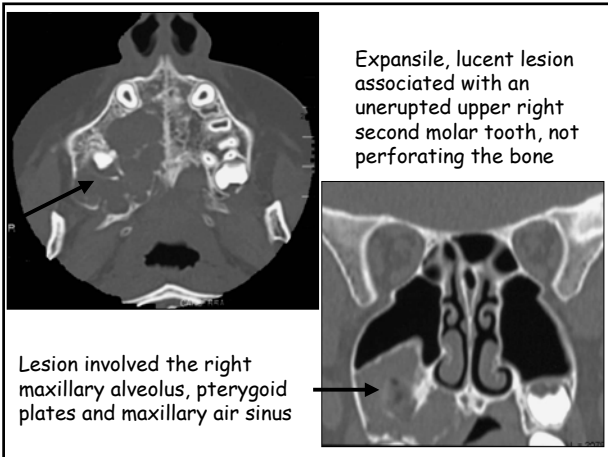
# Central Giant Cell Granuloma

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## Case presentation

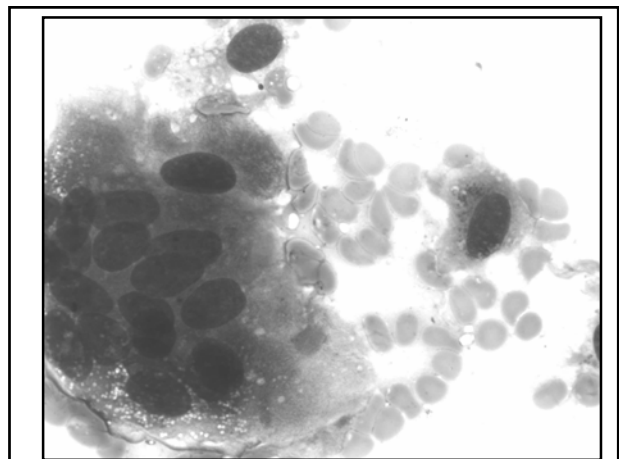
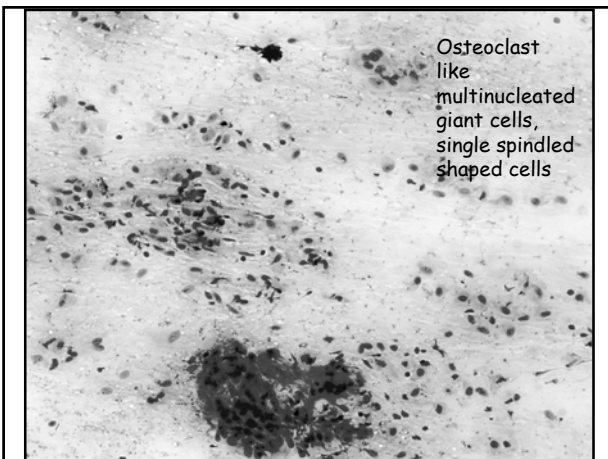
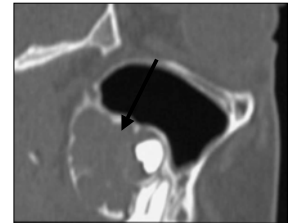
- ✦ James, 15 year old boy
- ✦ Presented with a < 6 month history of a rapidly growing right sided palatal mass and loose teeth
- ✦ No pain
- ✦ CT scan of Maxilla



## Case presentation

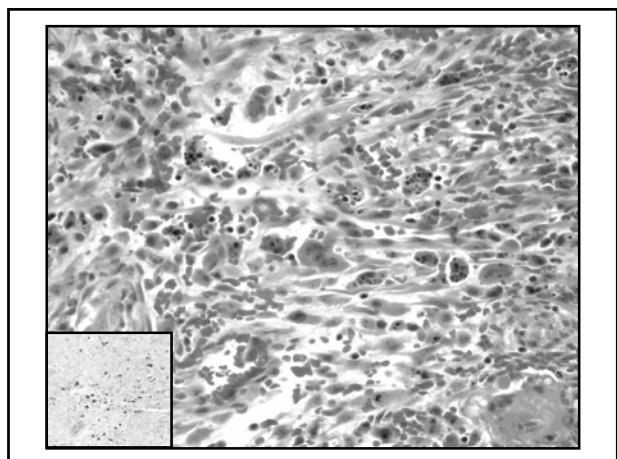
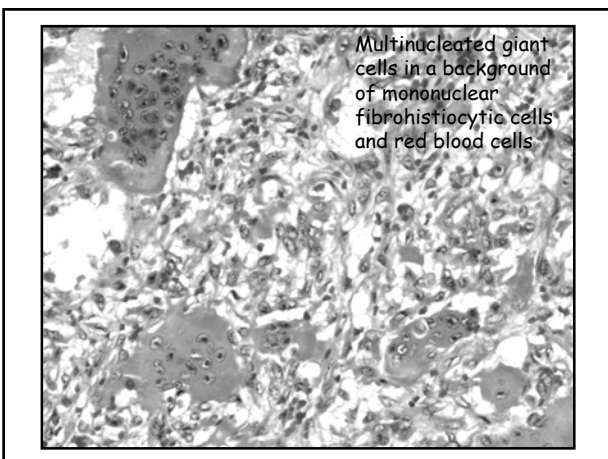
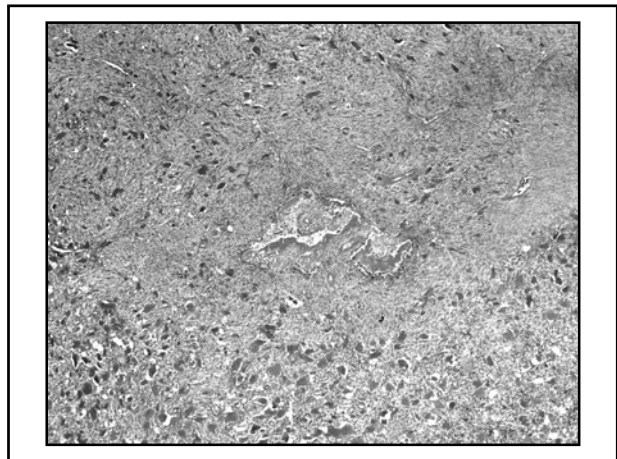
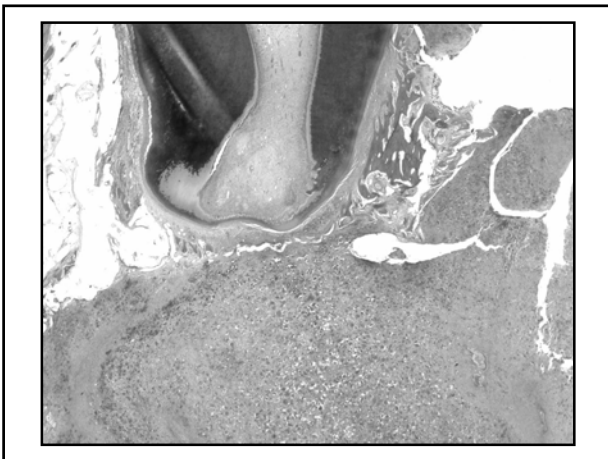
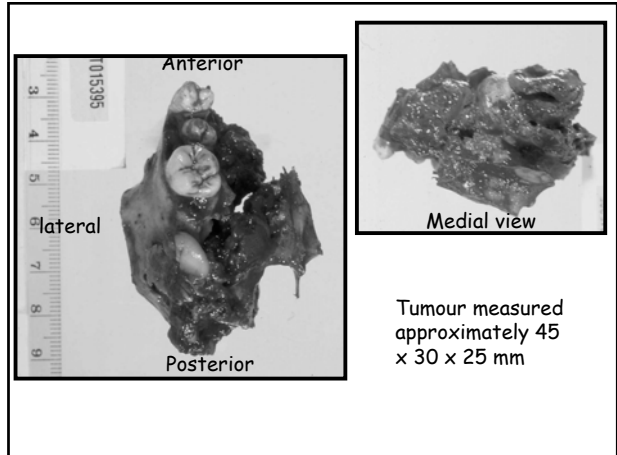
- ✦ Differential diagnosis on CT:

dentigerous cyst  
or  
ameloblastoma



## Case presentation

- ✦ FNAC - central giant cell granuloma - confirmed on incisional biopsy
- ✦ Referred to Sydney oral surgeon for second option in relation to management, including non surgical options
- ✦ Right partial maxillectomy rather than curettage was recommended due to the location and size of the tumour

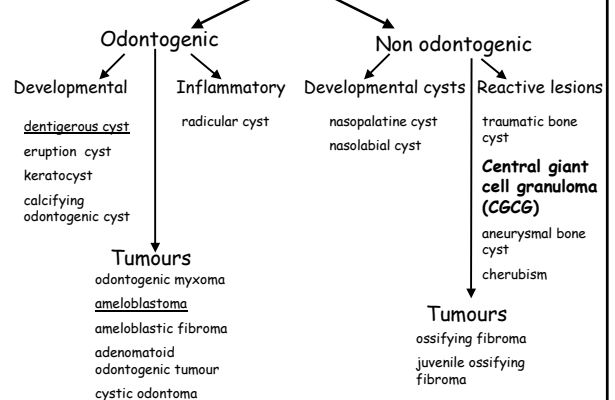


## Case presentation

### Follow - up

- Well - 5 years
- No recurrence
- Reconstructive surgery

## Radiolucent cyst-like lesions in the jaw



## Central Giant Cell Granuloma

✚ **Synonyms:** Central giant cell reparative granuloma; central giant cell lesion (WHO)

### Pathogenesis:

- Unknown
- Intraosseous neoplastic-like, reactive proliferation
- ? due to recurrent slow, minute haemorrhages; sometimes associated with trauma

✚ **Prevalence:** 7% of all benign lesions of the jaw

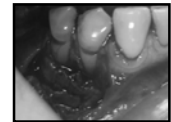
## Central Giant Cell Granuloma

✚ **Age:** 11- 30 years (>60% of patients < 30 yr age)

✚ **Sex:** Women > men = 2-3 : 1 (hormonal?)

✚ **Site and size:** In bone

- Mandible (anterior) > maxilla = 2-3 : 1
- Most lesions develop anterior to first molars, where deciduous teeth are found
- Often crosses the midline
- Size is variable

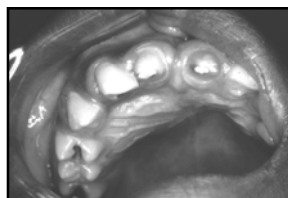


<http://instruct.uwo.ca/anatomy/636/clinical%20cases/granuloma/gallery/>

## Central Giant Cell Granuloma

### Presentation:

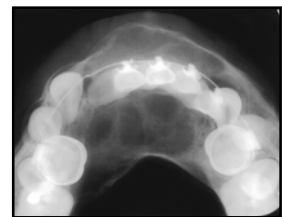
- Typically experience painless swelling
- Palpation may elicit tenderness
- Frequently expansion of bone and displacement of teeth
- Slow-growing - asymptomatic swelling
- Rapid-growing - pain, loose dentition (high rate of recurrence)



## Central Giant Cell Granuloma

### Radiology:

- Varies
- Early lesions -usually small, unilocular areas of lucency
- Later, multilocular lucency (60%) with wispy internal septa and osseous expansion
- If slow growth - well-defined borders
- If rapid growth - irregular borders
- May have resorption / movement of teeth and penetration of jaw cortex

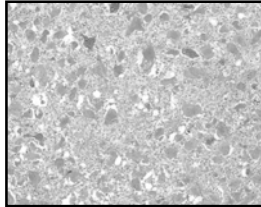


<http://radiographics.rsna.org/cgi/content/full/19/5/1107>

## Central Giant Cell Granuloma

### Pathology:

- Numerous osteoclast-like giant cells, unevenly dispersed throughout a fibrovascular stroma
- Frequent mitotic figures; rare necrosis
- Hemorrhagic areas
- Small foci of reactive woven bone



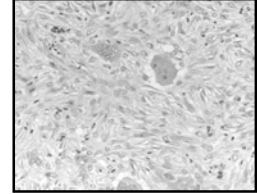
## Central Giant Cell Granuloma

### Immunohistochemistry:

- CD68, vimentin (giant cells); ER negative
- Vimentin, actin (stroma)

### Electron microscopy:

- Fibroblasts
- Myofibroblasts
- Histiocytes



### Genetics:

- Carinci F et al (Italy) 2005: Genetic profiling of central giant cell granuloma of the jaws
- ??associations Noonan syndrome and neurofibromatosis

## Central Giant Cell Granuloma

### Differential Diagnosis:

#### Child:

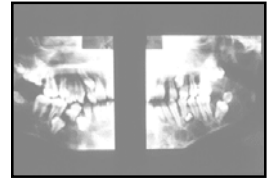
- Cherubism

#### Adult:

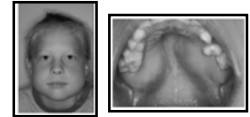
- Hyperparathyroidism
- ? Giant cell tumor (osteoclastoma)

## Cherubism

- Rare
- Autosomal dominant, variable expression (caused by mutations in the c-Abl-binding protein SH3BP2 on gene 4p16.3)
- M > F. Onset 6 month-7 years
- Symmetrical enlargement of the alveolar ridge ("chubby cheeks")
- Bilateral, expansile, multilocular radiolucent areas of mandible, occasional involvement of maxilla
- Identical pathology *CGCG* - may see cuff-like perivascular collagenous deposits
- Resolves in time (25-30 yr)



<http://www.dent.ohio-state.edu/OralPath/parish.htm>



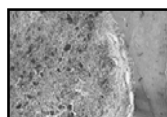
<http://www.ncbi.nlm.nih.gov/entrez/disposim.cgi?id=118400>  
<http://web1.umkc.edu/dentistry/practitioner/assets/BoneDiseases.pdf>

## Hyperparathyroidism (Brown tumours)

- Adults
- Primary (adenoma) or secondary (renal failure)
- Similar histology and radiology *CGCG*
- Generalized demineralization of the medullary bones of the jaw
- Raised serum parathyroid hormone
- Hypercalcemia
- Hypophosphatemia

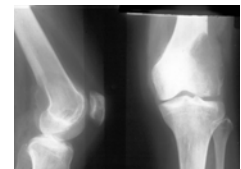


<http://www.dental.mu.edu/oralpath/lesions/hyperparathyroidism/hyperparathyroidism.htm>

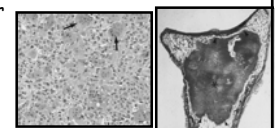


## Giant cell tumor (osteoclastoma)

- ? Does not occur in the jaw
- Usually near end of long bone e.g. near a knee joint
- Cause unknown, some cases linked to Paget's disease
- Most occur when skeletal bone growth is complete (20-40 yr)
- M=F
- Painful, fast growing
- Radiology - lytic and subarticular
- Less osteoid and haemorrhage, even distribution of giant cells
- Can recur, 5-10% metastasize



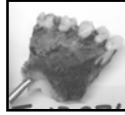
<http://myweb.lsbu.ac.uk/~dir1/museum/margaret/451-3182-3320340.jpg>



## Central Giant Cell Granuloma

### Treatment

- Individualized treatment depending on characteristics and location of tumor



### ⚡ Surgical:

- Curettage - recurrence 10-20% > maxilla
- Extraction if unerupted tooth involved
- Block resection (if aggressive lesion)

### ⚡ Non-surgical:

- Radiation - out of favor (risk of sarcoma)
- Systemic Calcitonin therapy
- Intralesional Glucocorticosteroids
- Subcutaneous interferon alpha-2a



## Central Giant Cell Granuloma

### ⚡ Systemic Calcitonin

- 1993 (Harris, London)
- Giant cell granulomas are rich in calcitonin receptors
- Calcitonin inhibits osteoclast activity
- Subcutaneous injection daily or nasal spray for about 1 year
- Arrest the growth of lesion, until spontaneous healing (19 to 21 months)
- Side effects: nausea, dizziness, vomiting, headaches, diarrhea
- Pathology: 6 months after treatment - absence of giant cells and uniform cellular stroma

## Central Giant Cell Granuloma

### ⚡ Intralesional glucocorticosteroids

- 1998 (Jacoway, North Carolina)
- Steroids cause decrease in secreted level of lysosomal proteases from osteoclasts (eg:TRAP, cathepsin B) which are responsible for bone resorption
- Administer weekly or biweekly for least 6 weeks - 3 months
- Growth arrest of tumour, sometimes resolution
- Problem: difficult to inject as lesion resolves

## Central Giant Cell Granuloma

### ⚡ Subcutaneous interferon alpha-2a

- 1999 (Kaban, Boston)
- Inhibits angiogenesis by suppressing over expression basic fibroblast growth factor (bFGF)
- Raised bFGF in urine
- Dose of 1.1 - 6.16 million units/m<sup>2</sup> daily, 1 year
- Growth arrest of tumour, urinary bFGF levels return to normal
- Side effects: fever, flu-like symptoms, lethargy, postnasal drip, skin rash, hair loss, mild neutropenia

## Central Giant Cell Granuloma

### Non-surgical treatments

#### ⚡ Advantages:

- Less invasive
- Low cost
- Low risk
- Still able to treat lesion surgically if required

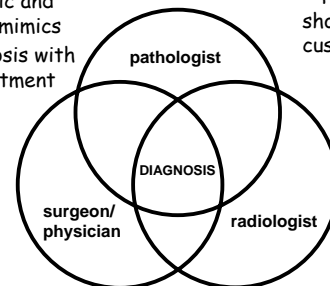
#### ⚡ Disadvantages:

- Long treatment duration
- Side effects
- Lack of long term studies

## Central Giant Cell Granuloma

- Troublesome lesion
- Radiographic and pathological mimics  
→ misdiagnosis with delayed treatment

- Treatment should be customised



Modified from IAP 2004 F Bonar

## Acknowledgements

✦ Patient, James McElehinney and his family

✦ Dr Peter Vickers

✦ Dr Sanjiv Jain

✦ A/Prof Ross O'Neil

✦ Mrs Fiona Guymer



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