Central Giant Cell Granuloma

Jane Dahlstrom
Anatomical Pathologist
The Canberra Hospital

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

Expansile, lucent lesion associated with an unerupted upper right second molar tooth, not perforating the bone

Lesion involved the right maxillary alveolus, pterygoid plates and maxillary air sinus

Differential diagnosis on CT:
dentigerous cyst or ameloblastoma

Osteoclast like multinucleated giant cells, single spindled-shaped cells
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

Tumour measured approximately 45 x 30 x 25 mm

Matured giant cells in a background of mononuclear fibrohistiocytic cells and red blood cells.
Case presentation

Follow-up
- Well - 5 years
- No recurrence
- Reconstructive surgery

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

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)

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

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

Central Giant Cell Granuloma

Radiolucent cyst-like lesions in the jaw

Developmental odontogenic
- dentigerous cyst
- eruption cyst
- odontogenic cyst

Developmental inflammatory odontogenic cyst
- radicular cyst
- nasopalatine cyst

Reactive lesions
- traumatic bone cyst
cerubism

Tumours
- odontogenic myxoma
- ameloblastoma
- ameloblastic fibroma
- adenomatoid odontogenic tumour
cystic odontoma

Tumours
- ossifying fibroma
- juvenile ossifying fibroma

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**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

**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 CCGC - may see cuff-like perivascular collagenous deposits
- Resolves in time (25-30 yr)

Hyperparathyroidism (Brown tumours)

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

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
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

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

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

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/m² 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

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
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References