Giant cell tumour (osteoclastoma)

Definition
A benign locally aggressive tumour made up of multinucleated giant cells, occurring in the epiphysis of long bones.

A primary malignant GCT exists when a frankly sarcomatous lesion is contiguous with a typical benign GCT.

Secondary malignant GCT results when a sarcoma develops at the site of a previously treated benign GCT.

History
First described in 1940 by Jaffe, Lichtenstein and Portis.

Epidemiology
4% of all primary bone tumours but more common in Chinese.
Females>males (in contrast to most other bone tumours which have a male predominance).
Multicentric in less than 1%
Malignant in 3-10%. Patients with malignant change are slightly older.
Usually occurs after closure of physes and before 40; the peak occurrence is in the third decade. Very unusual before 20 and after 55.

Aetiology
No known risk factors.
The exact cell of origin of these tumours is still unknown; it could be that the mononuclear cells are of histiocytic origin and the giant cells result from their fusion.
Irradiation of benign osteoclastomas may precipitate malignancy.

Localisation
Most are found in the distal femur, proximal tibia, proximal humerus and distal radius. Another common site is the sacrum where the differential diagnosis is with chordoma.
They can also be found in the tubular bones of the hands and the feet.
If found in the vertebrae they involve the body.

Clinical
Pain and swelling are the usual complaints
A hard mass is found in more than 80%
Pathological fracture occurs in 10-15%.
Systemic complaints are uncommon.

Investigations
Radiology
Plain XR
Radiolucent area situated eccentrically at the end of a long bone, running right up to the subchondral bone plate.
There may be a “soap bubble” appearance with thin strands of bone crossing the lucent area; these correspond to bone ridges on the wall.
The cortex is typically expanded and thinned and may be focally destroyed.
The lesion may be well or poorly marginated; Stalley emphasises the lack of reaction of cancellous bone in GCTs.
Periosteal reaction is usually absent. There is no matrix calcification.

CT
The tumour is solid and has similar signal characteristics to muscle.
Septae may be demonstrated but these are not as prominent as in ABC

MRI
T1 – low intensity. T2 – high intensity

Staging
CT scan, MRI.

Should rule out hyperparathyroidism; brown tumours may look identical. Check the serum calcium, phosphate and PTH before diagnosing a GCT.
A radiological classification has been proposed…

Type I	Quiescent
Type II	Active
Type III	Aggressive

…but is thought by some authorities to be misleading and not useful.

Pathology
Gross
The tumour tissue is characteristically soft, friable and dark brown – "chocolate brown".
The tumour nearly always extends to the articular cartilage but does not invade or perforate it.
The periosteum is rarely breached.

Histopathology
Giant cells are scattered uniformly throughout the lesion.
The background consists of mononuclear cells. Sometimes it may be hard to work out where the giant cells stop and the mononuclear background begins.
Mitotic figures are commonly found in the mononuclear cells.
Spindle cell proliferation may dominate the appearance.
Giant cell tumours do not generally produce matrix, except when extending into soft tissue.
Infarct like necrosis is frequently found.
Jaffe and Lichtenstein described a grading system but this was abandoned because it was found to have no prognostic significance.
A secondary reactive proliferation of fibrous tissue may occur and ABC may become superimposed.

Differential diagnosis
Aneurysmal bone cyst
Brown tumour (beware multicentric tumours!)
Giant cell reparative granuloma
Chondroblastoma (epiphyseal tumour)
Giant cell rich osteosarcoma

Management
Low-grade lesions may be curetted out with margins cleared with 5% phenol, CO_2 laser, cement or liquid nitrogen. Both phenol and nitrogen can burn skin if inadvertently spilled. The free radicals released by the cement and the heat of polymerization may give a zone of necrosis of 2-3mm. Liquid nitrogen leads to a zone of necrosis with a depth of one to two centimetres, but this greater depth is hard to control and has a high risk of fracture (e.g. 6 fractures in 12 patients in one study). Phenol gives a depth of necrosis of 1-2mm.

The resultant defect is filled with bone chips or cement. The use of cement has some advantages; any new lucent line around the cement indicates tumour recurrence, and the patient can start weight bearing sooner. The small risk of transplanting the tumour while taking bone graft is removed. One potential downside of cement use is damage to adjacent cartilage.

Tumours in expendable bones are excised en bloc.

Radiotherapy is used in cases where the tumour is inaccessible or its resection would result in excessive morbidity (in practice this is usually the axial skeleton). Radiotherapy has been associated with malignant change. Originally orthovoltage treatment with approximately 250kilovolts peak was used and this was associated with malignant change in up to a third of patients; now megavoltage radiotherapy, giving a cumulative dose of 50-60 G is used and may be less dangerous. Recent studies looking at megavoltage therapy have shown rates of recurrence of from 7-26%, and rates of malignant change of 3% at 10 years.

Chemotherapy appears to have no role in the management of this tumour.

Prognosis
Histological grading not useful in predicting outcome.

For followup the affected region should be XR every 6 months for 3 years and then yearly after that; there should be a yearly CXR.

Low-grade lesions have a recurrence rate of 5-10% with modern techniques. Recurrence usually occurs within the first 2 years but cases have been reported of recurrences at 19 to 30 years and long term follow up is required. Late recurrences are more likely to be malignant.

Between 8 and 22% of recurrent GCTs become malignant. Each recurrence increases the risk of malignant change.

Pulmonary mets occur in 3% of patients, at a mean time of around 4 years post diagnosis. Pulmonary mets or local extension in unresectable tumours may result in the patient's death. The metastasis may arise from *benign* giant cell tumours. There can be good results from excision of pulmonary metastases; a 1998 JBJSB study (Siebenrock) showed no evidence of disease in 11 or 12 patients after metastasectomy.