Case study

Mr L, an Asian man aged 48 years, presented to his family doctor with a 3 month history of pain and swelling of his left wrist. He described the pain as ‘dull and gnawing’, which escalated to a sharp and shooting sensation radiating to his third and fourth fingers. Pain was worsened by movement and only mildly relieved by rest. He rated the wrist pain as 5/10 severity 3 months ago, and the current pain as 8/10 severity, despite regular paracetamol and ibuprofen at maximum doses. Often the pain kept him awake at night. There was no anaesthesia or paraesthesia, but he had noticed increasing weakness of the lateral three fingers. Over the past 4 weeks, he had also noticed a swelling of the affected wrist, which felt ‘hot’ at times. The pain started when he twisted his wrist while carrying hand luggage 3 months ago. He initially used a hot pack to relieve the pain, with limited benefit. He started taking analgesia 4 weeks before his visit to his family doctor. However, the unresolved pain and increasing agony in dressing and turning the steering wheel of his vehicle, eventually alerted him to seek medical advice.

Mr L exercised regularly and had never smoked cigarettes. He took no regular medications and had no known allergies. His mother had a history of colon cancer. One of his maternal aunts suffered from severe rheumatoid arthritis, and one maternal uncle had severe plaque psoriasis.

On examination, there was a firm swollen deformity over the distal radius, which was tender on palpation (Figure 1a and 1b). There were no associated skin changes. Pain was elicited on hyperextension of the fingers and also on deep palpation of the volar aspect of the wrist. Power of the flexor muscles of the left forearm was reduced to 3/5 on a Medical Research Council (MRC) scale for muscle strength.

Question 1
What are the differential diagnoses?

Question 2
What initial investigation would you consider?

Question 3
A plain X-ray of the wrist was ordered and results are shown in Figure 2. What are the possible diagnoses and what other tests would you consider?

Question 4
What is the management and prognosis?
Answer 1
Differential diagnoses include tendon sprain, rheumatoid arthritis, gouty arthritis, mal-union of fractured distal radius, osteoarthritis, metabolic bone disease, soft tissue tumours and bone tumours (benign and malignant). As the firm swelling arose from the distal radius and not the radio-carpal joint, the diagnoses of osteoarthritis, rheumatoid arthritis and gouty arthritis are less likely. Due to the solitary nature of the lesion and lack of other systemic symptoms, metabolic bone diseases (e.g. Paget and hyperparathyroidism) are considered less likely. In view of the history of a relatively minor twisting injury without violent trauma, tendon sprain or tendinitis are more probable diagnoses than a radial fracture.

Important red flag features that should alert the general practitioner to consider more sinister diagnoses include:
- unresolved pain over a 3 month period
- increased pain severity
- nocturnal pain waking the patient from sleep
- noticeable mass over the distal radius.

Answer 2
Plain X-ray of the wrist to confirm or exclude possible bone tumours.

Answer 3
Plain X-ray of the left wrist revealed a 4 x 3 cm osteolytic lesion destroying much of the distal radius, extending to the subchondral bone with minimally displaced fracturing. Differential diagnoses include giant cell tumour, aneurysmal bone cyst or more aggressive bone tumours.

Magnetic resonance imaging (MRI) of the wrist would help to delineate the boundary of the tumour mass and evaluate possible invasion of the carpal bones, wrist joint or the carpal tunnel. This is particularly relevant as the patient already had signs of carpel tunnel syndrome. A radionuclide bone scintigraphy is also needed to exclude possible metastatic disease. Finally, a tissue biopsy is the gold standard for the definitive diagnosis.

Answer 4
Giant cell tumour of bone (GCTB) is a locally aggressive tumour, which is typically benign. It affects young adults aged 20–40 years with a male:female ratio of 1:1.5.1–3 Asian populations have a higher incidence than Caucasian populations. In China, GCTB accounts for 20% of all primary bone tumours4,5 as opposed to 4–8% of all primary bone tumours worldwide.2

Chronic pain unrelated to weight bearing, with warmth and palpable swelling, is the classic clinical presentation of GCTB. The extremities of long bones are most commonly affected. The three most common sites affected are distal femur, proximal tibia and distal radius in descending order of prevalence.5,6 The distal radius accounts for 8–13% of all cases.6,7 Morphologically, GCTB lesions often arise from the epiphysis and grow from an off-centred position toward the metaphysis.3 Due to its rapid expansile nature, it may be haemorrhagic and cystic with fluid levels.

Giant cell tumour of bone are predominantly benign, but 2–9% have been reported to be malignant8–10 and metastasise to areas including the lymph nodes, lungs, skin, calf muscles and pelvis, with a preponderance to the lungs.10–12 The prognosis for pulmonary metastases is variable; early detection may allow surgical resection and survival.10,11,13,14 p53 gene mutations and previous radiotherapy are associated with malignant forms of GCTB.8,15,16

The goals of GCTB management are to minimise local recurrence and maximise joint preservation.15 In general, local recurrence rate after curettage and cement is higher than with wide local excision.7,17 However, wide local excision has a higher risk of loss of functionality.

Curettage of tumour is the initial treatment of choice, but when used alone, the local recurrence rate at all sites can be as high as 56–99%,6,18,19 with a 25–31% risk for lesions involving the distal end of the radius.7,20,21 Hence, additional steps have been employed to reduce local recurrence rate such as extended curettage with high speed burrs.22,23 Recent studies also support the use of ‘aggressive curettage’ where the lesional cavity is treated with adjuvant chemicals (phenol, alcohol or liquid nitrogen) or generous diathermy to eradicate possible tumour cells and hence further reduce the local recurrence rate.19,24

Typically, local recurrence occurs 12–18 months after surgery and rarely beyond 3 years. Hence, regular follow up with a thorough physical examination and plain X-rays every 3–4 months in the first 3 years is necessary.6 Should the tumour recur locally, surgical treatment options include repeat extensive curettage,19 wide local bone resection with bone graft,19 endoprosthesis18 or arthrodesis.25,26 Radiotherapy is also a possible non-surgical option for recurrent, incompletely resected, or unresectable lesions.27,28 Recently, Denosumab, a monoclonal antibody against the RANK ligand, has shown promise in a phase 2 clinical trial for recalcitrant GCTB.29,30

Case conclusion
Initial X-rays could not exclude erosion of the tumour through the bone cortex or extension of the tumour into adjacent soft tissue. Further investigations were performed: MRI of the wrist revealed multiple fluid levels in a 5 x 3 cm expansile mass eroding into the cortex of the distal radius; computed tomography of the chest did not detect any metastatic lesions; and bone scintigraphy of the whole body showed increased flow, pool and intense osteoblastic activity in the distal left radius, with no activity in other parts of the body.

In view of the generally benign nature of GCTB and a lack of distant tumour spread, intra-lesional removal of tumour with bone cement was offered as the preferred management over en bloc bone resection, in order to preserve maximum functionality of the wrist.6,31,32 Mr L was promptly scheduled for a curative excision biopsy. On-table frozen section confirmed

Figure 2. Plain X-ray of the patient’s left wrist
the diagnosis of giant cell tumour, and the lesion was radically curettaged with generous diathermy to the inner surfaces of the cavity. The lesional space was then packed with polymethylmethacrylate bone cement (Figure 3).

With physiotherapy, the patient recovered 95% of left wrist function when reviewed at 6 months. A second stage operation for plate-and-screw arthrodesis of the wrist would ensure adequate weightbearing capability.

**Summary**

Giant cell tumour of the bone is an uncommon and typically benign tumour, which is locally aggressive and which has a higher incidence among Asian people. Clinical presentations of GCTB are typically non-diagnostic, and may include chronic pain and swelling of a joint. Presentations can easily mimic musculoskeletal pain and tendon injuries, as presented in this case.

The red flags in this case included unresolving pain, increasing severity of pain, nocturnal pain and noticeable mass over the site of pain, which prompted further investigation leading to the final diagnosis.

Surgical removal in the form of curettage with local adjuvants is the preferred initial treatment for maximum preservation of joint function. Follow up every 3–6 months with clinical examination and plain X-ray is necessary for 3 years post-operatively.

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**References**


**Figure 3. Intra-operative X-ray of the wrist showing curettage of the GCTB and packing with PMMA bone cement**

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