Case Report

A case of thoracic giant cell tumor of bone and discussion of radiological features and current management practices

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A B S T R A C T

Giant cell tumor of bone (GCTB) is a rare condition with distinct radiological features that aid diagnosis. We present the case of an adult female patient, with locally invasive GCTB and review important radiological and management principles. Specific radiological features include locally aggressive, lytic radiolucent lesions, which can demonstrate cortical thinning and expansile remodeling of bone and typically involve the epiphysis and metaphysis. Management is primarily surgical, and denosumab has a role in the advanced setting.

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Case

We present the case of a 31-year-old Polish lady who presented to the Emergency Department with a 10-month history of progressively worsening thoracic pain. This pain radiated laterally, and she had associated parathesia. On examination, she was in significant distress due to pain. She was afebrile, her pulse was 93 bpm; oxygen saturation on room air 99%; respiratory rate 16; blood pressure 122/85. Full clinical examination did not reveal a cause for her symptoms. Her laboratory investigations were normal. She had no significant personal or family medical history. A thoracic x-ray demonstrated a radiolucent T8 vertebral body. (Fig. 1)

A noncontrast computed tomography (CT) thoracic spine demonstrated an expansile soft tissue mass within the T8 vertebral body extending into the pedicles bilaterally. There was associated cortical destruction, and the mass abutted the right posterior pleura and extended into the right anterior spinal canal. There was a lack of matrix mineralization (Fig. 2).

Magnetic resonance imaging spine demonstrated diffusely abnormal marrow signal within the T8 vertebral body with a solid and cystic mass lesion extending into the pedicles bilaterally; worse on the left. The solid component displayed mild postcontrast enhancement. The spine at other levels was normal, and there was no evidence of metastatic disease (Figs. 3-5). Possible differentials included a plasmacytoma,
Langerhans cell histiocytosis, metastatic lesion, giant cell tumor, chordoma, chondroblastoma or lymphoma. She had a CT guided core biopsy of T8. Histology from this sample revealed a giant cell tumor of bone (GCTB) with surrounding reactive and regenerative changes of surrounding bone (Fig. 6). Numerous multinucleated giant cells were present but no necrosis and only occasional mitoses. This process infiltrated the bone, but there was no atypia present (Fig. 2). Radiological features were consistent with a grade 3 lesion as per the Campanacci grading system for GCTB [1].

The patient underwent an anterior T8 corpectomy, spinal decompression, and fusion without complication. Subsequently, she proceeded to a posterior stabilization of T8 (Fig. 7). Final histology demonstrated a well-circumscribed GCTB with negative margins. The case was reviewed at the Oncology Multidisciplinary Team Meeting. The decision was made to proceed with active surveillance and not for adjuvant therapy because of the limited evidence for benefit. The patient is currently doing well 18 months from her initial diagnosis.

**Discussion**

GCTB is a rare, locally aggressive tumor, which accounts for 5% of primary bone tumors. It rarely manifests in an immature skeleton and usually occurs in patients with closed physes [4–6] between the ages of 20-40 years; typically effecting females slightly more frequently than males [1]. GCTBs typically occur within the epiphysiometaphyseal region of long bones and are eccentric in location [5,16–20]. Lesions, typically demonstrate geographic bone lysis, are usually associated with a narrow zone of transition, abut the articular margin, and lack a surrounding sclerotic rim [4]. Involvement of the vertebra is uncommon, and the most common sites of GCBT are around the knee: distal femur and proximal tibia (50%-65%) followed by the distal radius (10%-12%) and sacrum (4%-9%) [1]. Metastases are rare occurring in 1% of cases [2,3].

X-ray and CT imaging can demonstrate well the locally aggressive processes associated with GCBT. Plain radiographs typically demonstrate a radiolucent lesion with a sharply defined, nonsclerotic border [21]. There is no periosteal response [4–6], unless fractured. Pathologic fractures are
identified in up to 10% of patients. There may be aggressive features such as cortical thinning, expansile remodeling, and a wide transition zone (Fig. 3) [5,16–19]. GCBTs typically demonstrate prominent trabeculation and a loculated appearance [4]; however, this has been thought to actually represent pseudotrabeculation because of prominent osseous ridges caused by endosteal scalloping [22]. CT is superior to plain radiography in the detection of cortical thinning, pathologic fractures, periosteal reaction, the degree of osseous expansile remodeling, and lack of matrix mineralization [23,24].

Magnetic resonance imaging is helpful in demonstrating whether there is extension through the articular surface, as well as marrow and soft tissue changes (Figs. 4 and 5). The solid component of giant cell bone tumors typically demonstrates intermediate signal intensity on T1-weighted images and hypointense signal on T2-weighted images because of the presence of collagen within fibrous components and because of hemosiderin deposition within the tumor [21]. Imaging post IV gadolinium administration can help differentiate between solid and cystic portions of the tumor and can aid image-guided targeted biopsy of the solid component of the lesion [21]. Fluid-fluid levels may be identified within the tumor and can be due to the presence of an aneurysmal bone cyst or due to intralesional hemorrhage [25,26]. GCBT is the most common lesion to be associated with secondary aneurysmal bone cysts, present in 19%-39% of cases [4,5,17,27], and it has been reported that the presence of secondary aneurysmal bone cysts are associated with an increased risk of local tumor recurrence [27,28].

The differential diagnosis for a possible case of spinal GCBT includes a metastasis, plasmacytoma, chordoma, chondroblastoma, or sarcoma (eg telangiectatic osteosarcoma) [5,16,17].

Surgery is the preferred treatment for GCTB, with lower recurrence rates after en bloc resection. The options for surgery include intralesional curettage, marginal excision, wide local excision, or en bloc resection. It depends where and how extensive the tumor is. En bloc resection is considered where there is extensive cortex destruction (as in this case) or if it is impossible to salvage the joint [7,8]. The rate of recurrence is 10%-20% and will often occur locally. Other options for local control include curettage and application of intralesional heat, freezing or ablative agents, for example, phenols [3].

GCTB contain stromal cells, monocytes, and osteoclast-like giant cells [9]. The osteoclasts cause the damaging osteolysis that results in the morbidity associated with GCTB [9]. Osteoclast differentiation and recruitment depends on several factors; including receptor activator of nuclear factor kappa B
ligand (RANKL). RANKL is highly expressed on the stromal cells in the GCTB, resulting in osteoclast recruitment and activation [9,10]. Therefore, this and the other molecules that mediate this process can be targeted with molecular therapy.

Denosumab is a human monoclonal antibody that specifically inhibits RANKL, and therefore inhibits osteoclast-driven bone destruction [2]. An important phase II study by Thomas et al showed 30 of 35 patients with recurrent or surgically unresectable disease demonstrated a tumor response when given denosumab [1]. This confirms that targeting RANKL signaling is a valuable strategy in treating GCTB.

Following on from this, Chawla et al carried out another Phase II trial to evaluate the safety and efficacy of denosumab [11]. The authors found that denosumab had an acceptable safety profile and was an effective treatment for GCTB. Their results showed that treatment with denosumab could reduce the morbidity of planned surgery or eliminate the need for surgery [11]. Median follow-up was 1 year, so further long-term data is required.

Owing to the low rate of associated adverse effects and demonstrated high rate of tumor control, denosumab has been approved by the European Medicines Agency as treatment for patients with unresectable GCTB or when surgical resection is likely to result in severe morbidity.

There is weak evidence that bisphosphonate use in GCTB may improve symptoms and local disease control [12]. A case-control study by Tse et al [13] demonstrated a reduced rate of tumor recurrence after using bisphosphonates as adjuvant therapy to intralesional curettage or excision. However, bisphosphonate use in the adjuvant setting has not been approved, and the role of these drugs is not clear.

Interferon (IFN) or pegylated interferon is included as a treatment option in the NCCN guidelines for GCTB that are unresectable or metastatic at presentation. GCTB has been found to have overexpression of angiogenic growth factors, and so IFN is used to target this. The evidence for its efficacy is anecdotal. Given that IFN is poorly tolerated, other treatment options may be preferable in this setting [14,15].

In conclusion, although GCTB is rare, there are distinct radiological features associated, which can aid diagnosis. Severe morbidity can occur due to its locally destructive effects. Management is primarily surgical. Denosumab has demonstrated tumor control in unresectable disease; however, its efficacy in the adjuvant setting is under investigation at present.

**Learning points**

- GCTs rarely occur within the vertebrae above the sacrum.
- Imaging (CT) useful to target biopsy to the solid portion.
- Surgery can be curative.
- Key points in making radiological diagnosis of GCT of bone:
  - occur in patients with closed physes within epiphysio-metaphyseal region of long bones;
  - narrow zone of transition;
  - abut the articular surface;
  - eccentric in location;
  - lack sclerotic rim;
  - may be associated with a secondary aneurysmal bone cyst.

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