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Case Report

Giant cell tumor of a rib following denosumab treatment

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ABSTRACT

Giant cell tumor (GCT) of the bone is an aggressive lytic lesion, commonly treated with surgery. Denosumab is a relatively recently introduced osteoclast activation inhibitor used for neoadjuvant therapy of GCT. Here we report the case of a GCT of a rib undergoing extensive osteosclerosis on computed tomography imaging following treatment with denosumab.

1. Case presentation

A 33-year-old Chinese female was diagnosed with a giant cell tumor (GCT) of a rib. Initial imaging included computed tomography of the chest which showed a 5.4 cm expansile, homogenous, lytic lesion involving anterior aspect of the left eighth rib (Fig. 1). The decision by the multidisciplinary treating team for neoadjuvant treatment with denosumab was taken in an attempt to try and shrink the tumor prior to resection. Computed tomography of the chest performed 8 weeks later, following therapy with three doses of denosumab demonstrated size stability of the tumor, and its marked peripheral osteosclerosis (Fig. 2). The patient has subsequently undergone en bloc resection of the tumor.

2. Discussion

GCT of the bone is a locally aggressive lytic lesion commonly involving epiphyses and metaphyses of long bones. Typical age of patients at diagnosis is between 20 and 40 years [1]. GCTs are usually treated surgically; however, the rate of their local postoperative recurrence is high. GCT metastases are rare, and usually involve the lungs [1].

Histologically, GCT is composed of aggregates of mononuclear cells with scattered macrophages and multinucleated osteoclast-like giant cells [2]. The mononuclear cells express high levels of receptor activator of nuclear factor kappa-B ligand (RANKL). The latter binds to RANK, a receptor expressed on the surface of the osteoclast-like giant cells and their

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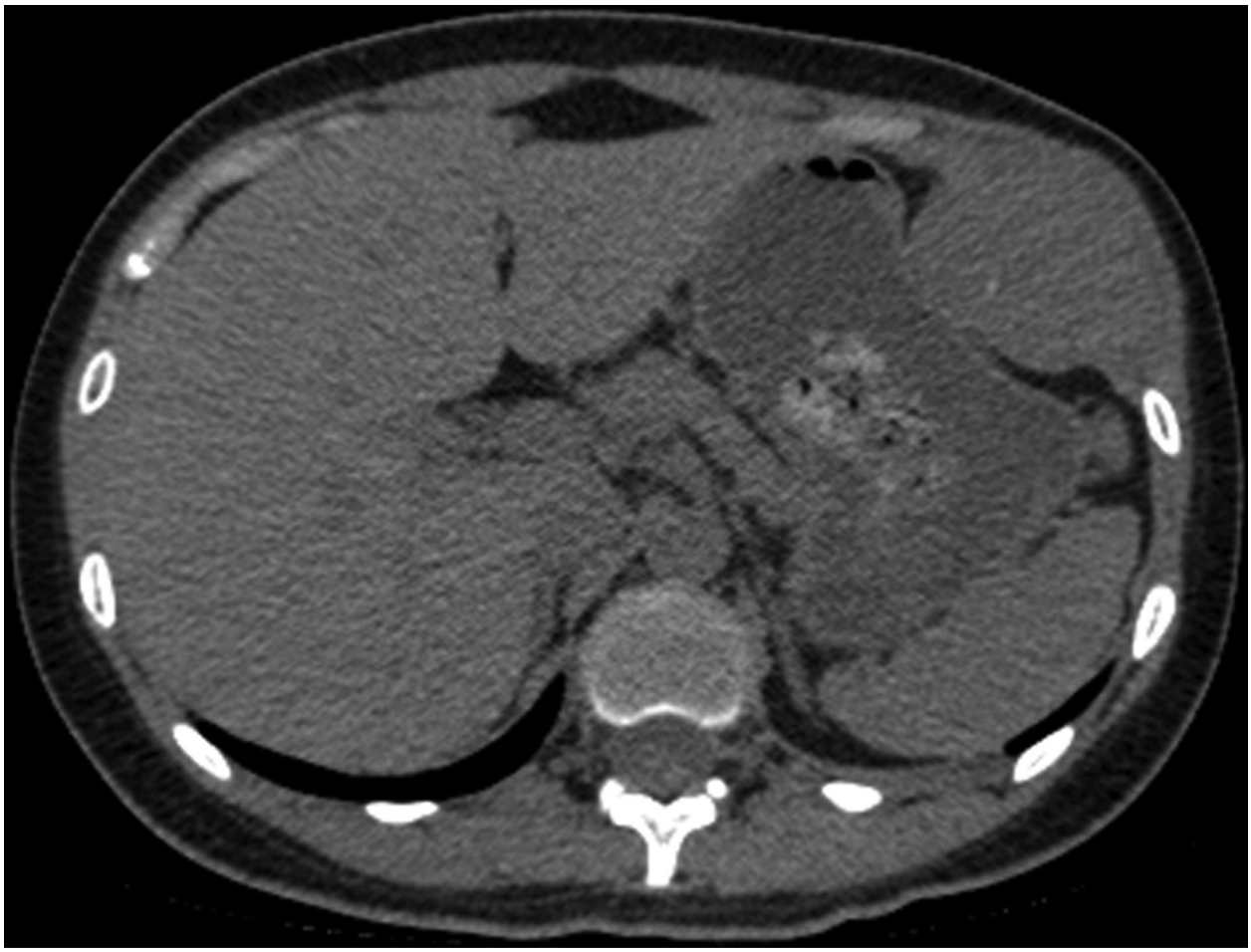

Fig. 1 – Computed tomography of the chest performed prior to treatment demonstrates a 5.4 cm expansile lytic lesion of the left eighth anterior rib.

precursors, resulting in their activation and proliferation, which in turn leads to bone resorption [2].

Denosumab is a human monoclonal antibody, which is a RANKL inhibitor. As such, denosumab specifically inhibits normal and tumor-associated bone lysis by preventing RANKL-mediated formation and activation of multinucleated osteoclasts or giant cells from RANK-positive mononuclear preosteoclasts and macrophages [2]. Denosumab has been shown to impede activation and proliferation of osteoclasts in GCT, and is currently used as a neoadjuvant therapy agent in its treatment [2]. A number of clinical studies have demonstrated benefits of denosumab in treatment of GCT, which include subjective clinical improvement as reported by the patients, and surgical down-staging resulting in reduced need for morbid surgery [3]. Nevertheless, several controversies concerning denosumab therapy still remain. Thus, on one hand, denosumab treatment reconstitutes subchondral and cortical bone around the GCT, which allows for easier resection [3]. On the other hand, some surgeons report that denosumab treatment-induced new osseous matrix and thickened cortical bone impede the surgeon's ability to reliably delineate the true extent of the tumor, which could lead to increased risk of local recurrence [3]. Additionally, it is not completely clear whether denosumab treatment may lead to increased risk of GCT malignant transformation or give rise to new malignancies. The latter concern stems from the postulation that RANKL plays an important role in lymphocytes differentiation and dendritic cell survival, therefore its inhibition by denosumab could lead to immunosuppression and, as a result, an increased risk of neoplasia [3].

Reports of radiological changes occurring in GCT following denosumab treatment are scarce [4,5]. As our case illustrates, denosumab may cause marked osteosclerosis and osteogenesis in the originally homogenously lytic GCT. This should not be misinterpreted as tumor progression or transformation into a more aggressive type of malignancy, such as chondrosarcoma or osteosarcoma, but instead as a positive therapeutic response [4].

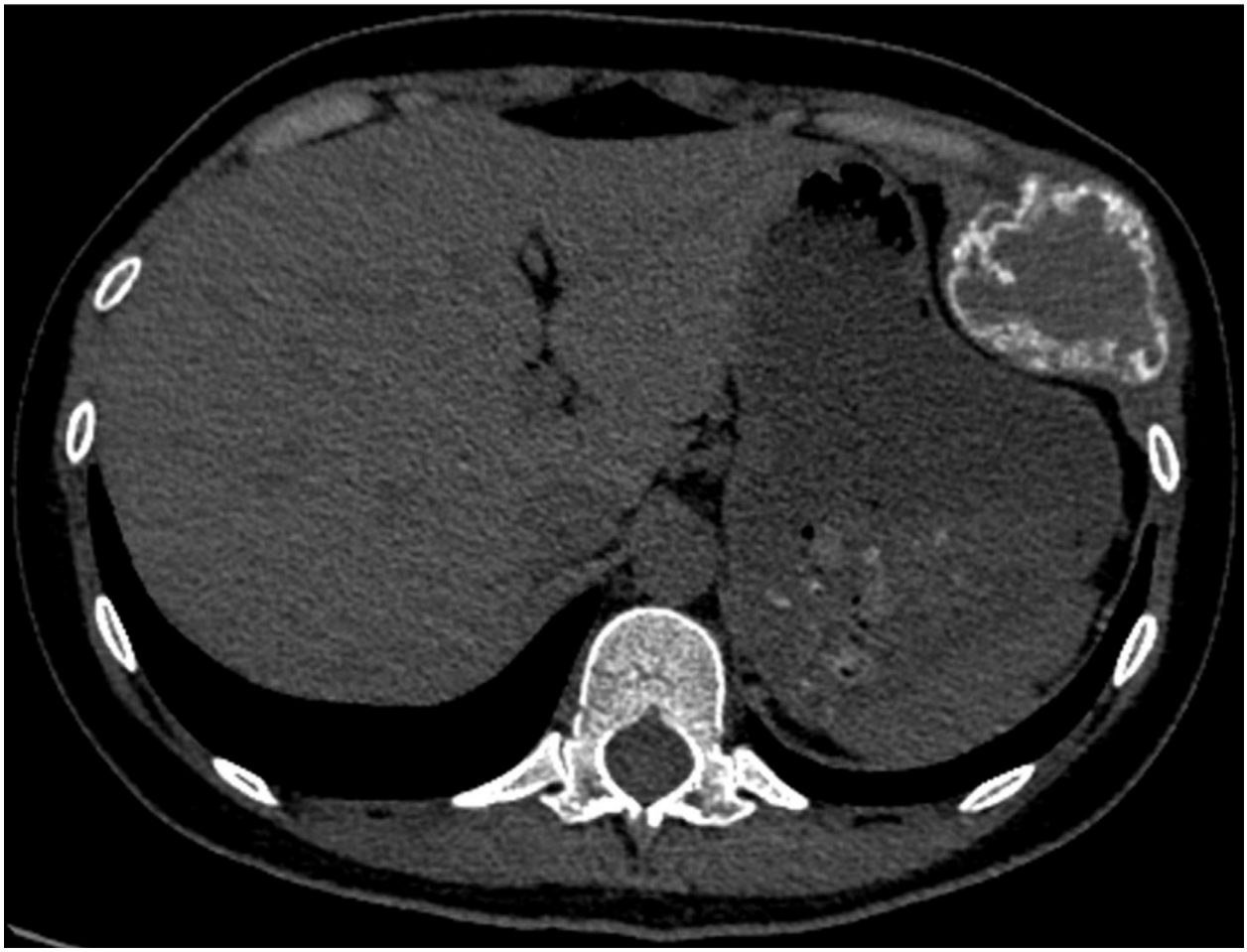

Fig. 2. Computed tomography – (CT) of the chest performed eight weeks after the original CT, following treatment with three doses of denosumab demonstrates stable size but extensive peripheral osteosclerosis of the rib lesion.

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