Clinical Case Reports

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CASE REPORT

Use of denosumab in recurrent chondroblastoma of the squamous temporal bone: a case report

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Key Clinical Message

Chondroblastoma is a rare, benign bone tumor that represents 1–2% of all primary bone tumors. Denosumab, a monoclonal antibody, has been demonstrated to inhibit the growth of giant cell tumors. We report a case of recurrent chondroblastoma of the squamous temporal bone that is currently suppressed with denosumab.

Keywords

Bone tumor, chondroblastoma, denosumab, giant cell tumor.

Introduction

Chondroblastoma is a rare, benign bone tumor that represents 1–2% of all primary bone tumors and approximately 5% of benign bone tumors [1, 2]. It most commonly occurs in the femur, humerus, and tibia [3–5] but has also been described in flat bones such as the scapula, patella, sternum, and the bones of the skull.

While the tumor is characterized by the presence of compact areas of chondroblasts, microscopic examination also readily demonstrates an abundance of osteoclast-type giant cells. These giant cells have been examined in depth in relation to giant cell tumor of bone. There is evidence that these cells are responsible for the osteolytic nature of these tumors due to their osteoclastic nature [6, 7].

Denosumab, a monoclonal antibody that targets the receptor activator of NF-κB ligand (RANKL) responsible for the recruitment and activation of giant cells, has been demonstrated to inhibit the growth of giant cell tumors [8]. Yuang et al. [8] found that RANKL was also expressed in chondroblastoma and theorized that this was responsible for the aggressive nature of the tumor.

To our knowledge, denosumab has not been used for the treatment or prevention of recurrence of chondroblastoma. We report a case of recurrent chondroblastoma of the squamous temporal bone that is currently suppressed with denosumab.

Case Report

A 64-year-old gentleman presented to our service with a chondroblastoma of the squamous temporal bone. He had no significant past medical history.

In June 2011, he presented to an ear, nose, and throat surgeon with a painful swelling around his right temporomandibular joint, which had been present for 3 weeks with only pain prior to this for 2 months. A computerized tomography scan of the area demonstrated a lobulated, solid mass measuring 33 × 25 × 24 mm within the squamous portion of the temporal bone. Surrounding edema was noted in the overlying temporalis muscle,

extending into the surrounding lateral pterygoid and adjacent temporomandibular joint on magnetic resonance imaging (Fig. 1).

Biopsy of the lesion demonstrated a giant cell-rich neoplasm, which was supported by the radiographic findings. A histological diagnosis of chondroblastoma was made. The gentleman subsequently underwent a resection of the tumor, with histopathology demonstrating there to be contaminated margins.

Ten months following resection, the patient developed nocturnal pain in the right side of the jaw. MRI and CT demonstrated an expansile soft tissue mass in the greater sphenoid wing, representing the anteroinferior margin of the previous resection (Fig. 2). He underwent a repeat resection with pathology reconfirming the diagnosis of chondroblastoma (Fig. 3) and demonstrating tumor present at the margins of the specimen.

Following a review of the literature and discussion with the patient's treating medical oncologist, the decision was made to commence the patient on denosumab therapy to prevent recurrence of the tumor. Therapy was commenced with denosumab 120 mg subcutaneously once per month.

The patient underwent treatment with denosumab from August 2012 to December 2013. During this time, follow-up scans did not demonstrate any local recurrence of the tumor. In December 2013, treatment was ceased. On repeat MRI imaging in December 2014, a 19-mm recurrent tumor was found at the site of prior resection.

Repeat resection of the tumor was performed in February 2015 with histopathology demonstrating clear surgical margins.

Denosumab was recommenced in February 2015, and as of January 2016, repeat imaging has not demonstrated any recurrence of the malignancy. While undergoing denosumab therapy, the patient did not experience any known adverse effects of the medication.

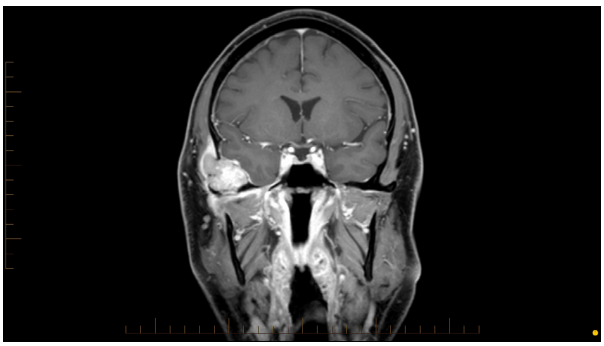

Figure 1. Postgadolinium magnetic resonance imaging demonstrating an expansile mass on the inferolateral surface of the right squamous temporal bone.

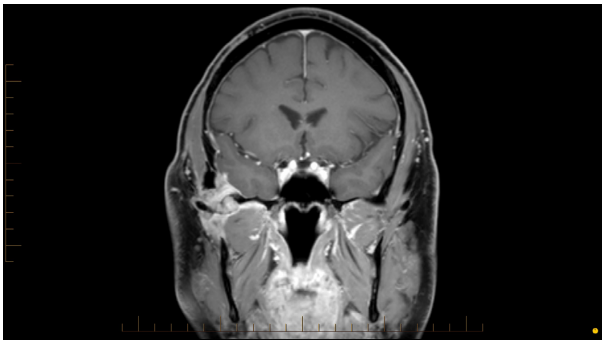

Figure 2. Postgadolinium magnetic resonance imaging demonstrating a lobulated mass at the inferomedial border of the previous resection.

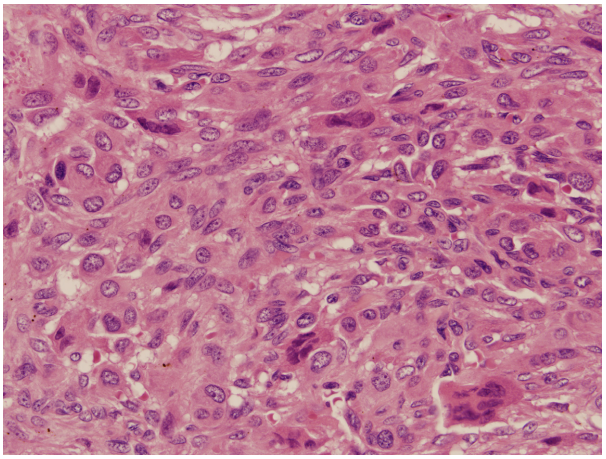

Figure 3. Histological features consistent with chondroblastoma. Hematoxylin + Eosin stain. 400× Magnification.

Discussion

The exact histogenesis of chondroblastoma is still unknown. Romeo et al. [9] demonstrated that the cartilage-signaling molecules Indian Hedgehog/parathyroid hormone-related protein and fibroblast growth factor were both active in the disease suggesting that the tumor is of mesenchymal cell origin that is committed to chondrogenesis via active growth plate signaling pathways.

The current mainstay of treatment for chondroblastoma is surgical resection with no widely accepted methods for the prevention of recurrence. Radiotherapy has been described in case reports for the prevention of recurrence, but it is not currently accepted as the standard of care. Hence, a treatment modality that can minimize recurrence risk is needed.

In a 2003 paper, Huang et al. [10] demonstrated that RANKL was expressed in chondroblastoma tumor cells; however, it was not expressed in chondrosarcoma. RANKL is critical in the recruitment of osteoclastic giant

cells and has been extensively studied in relation to giant cell tumors. Interim results of phase 2 studies [11, 12] have demonstrated that the human monoclonal antibody that targets RANKL, denosumab, may be a safe and effective treatment that slows the progression of giant cell tumors of bone, which typically are very aggressively lytic. As the agent is not tumoricidal, prolonged treatment with denosumab to prevent bone lysis would likely be required to prevent recurrence.

There have been no studies or trials that have looked at the responsiveness of chondroblastoma to denosumab. We believe that this is the first reported case in which it has been used for the prevention of recurrence of chondroblastoma. The patient described initially had recurrence of his tumor within 10 months after initial resection. During the 16 months that the patient was on denosumab, there was no identifiable tumor recurrence and it was not until the agent was ceased that there was return of the tumor. The decision to cease treatment with the agent was made by the treating physician due to lack on recurrence on follow-up scans and the patient due to significant out-of-pocket expense incurred with off-label use of the medication.

While a single case is insufficient to draw any definite conclusions, we believe that this patient's disease free period following intralesional resection and in the context of a previous quickly recurrent tumor suggests that denosumab may be a potential therapy for chondroblastoma and may warrant further study.

Conflict of Interest

None declared.

Authorship

DW: contributed to the initial conception of the article, drafting of the article, and final approval of the article. NC: contributed to the data collection, interpretation, and drafting of the article.

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