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CASE REPORT

Giant Cell Tumor of Cervical Spine Presenting as Acute Asphyxia

Successful Surgical Resection After Down-Staging With Denosumab

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Study Design. Case report and literature review.

Objective. To describe treatment of a unique case of acute airway obstruction by a large C7 giant cell tumor (GCT) with preoperative denosumab followed by surgical resection, and review the literature on this rare entity.

Summary of Background Data. Standard treatment for GCTs includes surgical resection or curettage and packing. Large lesions in the spine may require preoperative therapy with denosumab, a human monoclonal antibody to RANKL, to facilitate surgery. It is highly unusual for GCT arising in cervical spine to present with acute asphyxia (requiring tracheostomy).

Methods. We report a patient with large C7 GCT that caused tracheal compression with almost complete airway obstruction requiring emergency intubation.

Results. The tumor responded to subcutaneously administered denosumab with marked decrease in size and relief of symptoms. Increased tumor mineralization in response to therapy facilitated subsequent successful surgical tumor resection. The patient remains symptom-free 2 years after surgery without tumor recurrence.

Conclusion. Denosumab can shrink the size of large GCTs, providing symptom relief before surgery and facilitate tumor resection.

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Level of Evidence: 5

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Giant cell tumor (GCT) of bone is a benign tumor that most often involves the long bones. Spinal disease is rare, and mostly involves the sacrum.[1,2] We report the case of a young woman with a large GCT of C7 that caused marked tracheal narrowing with acute asphyxia. Therapy with denosumab resulted in dramatic decrease in tumor size, which relieved airway obstruction, and increased tumor mineralization, which facilitated resection.

CASE REPORT

A 20-year-old woman presented to an outside emergency center with acute dyspnea requiring intubation after being treated as asthma for due progressive shortness of breath and wheezing for the last 4 months. Computed tomography (CT) showed a large expansile lytic lesion involving the C7 vertebra (Figure 1A) with a soft tissue component that resulted in anterior tracheal displacement and marked tracheal narrowing. Magnetic resonance imaging showed a heterogeneously enhancing, large, lobulated mass arising from a severely compressed C7 that measured 10.0 × 9.0 × 7.5 cm (craniocaudal × transverse × anteroposterior) and resulted in spinal canal stenosis due to C7 retropulsion (Figure 1B and C).

The endotracheal tube was exchanged for a tracheotomy because of continued dyspnea, and the patient was transferred to our hospital. Review of outside biopsy material at our institution confirmed GCT (Figure 2A and B).

As the large tumor was deemed inoperable, the patient was treated with three cycles of subcutaneous denosumab. Follow-up CT showed diminished tumor size (now 6.2 × 6.3 × 6.8 cm), and increased tumor mineralization (Figure 3A). Magnetic resonance imaging showed markedly decreased

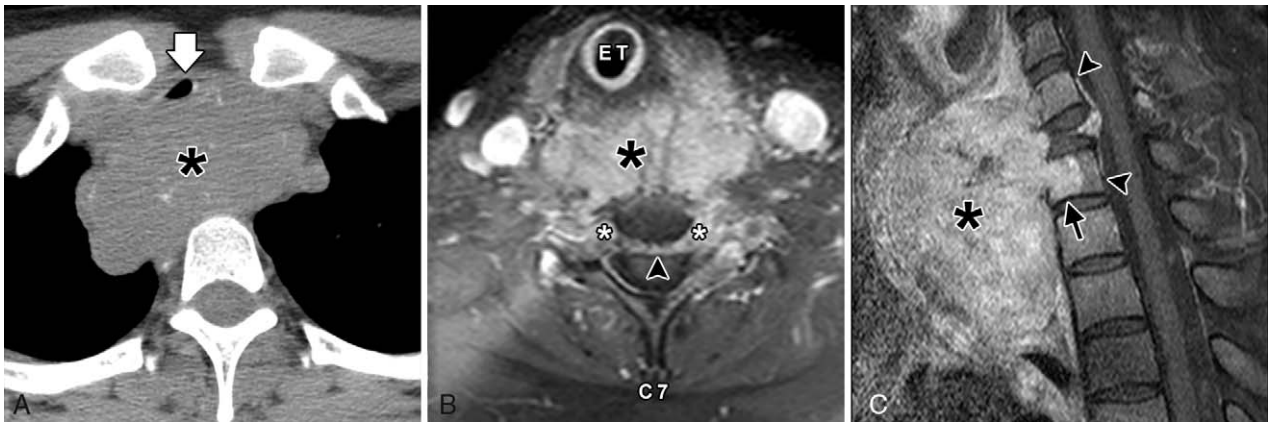

Figure 1. (**A**) Axial CT image shows a large soft tissue mass (*) compressing the traches (white arrow). (**B**) Axial contrast-enhanced MRI with fat suppression at the level of C7 shows a heterogeneously enhancing mass with prevertebral (black *), bilateral neural foraminal (white *), and epidural (black arrowhead) components. An endotracheal tube (ET) is in place. (**C**) Sagittal contrast-enhanced MRI with fat suppression shows the full craniocaudal epidural extent of disease (black arrowheads), severe compression fracture of C7 with retropulsion into the spinal canal, and secondary involvement of the T1 vertebral body (black arrow) by the soft tissue mass (*). CT indicates computed tomography; MRI, magnetic resonance imaging.

tumor enhancement with nonenhancing areas corresponding to mineralization on CT (Figure 3B and C). The tracheal compression and displacement had resolved.

A two-stage resection of the tumor consisted of initial anterior C7-T1 intralesional corpectomy and titanium cage reconstruction, followed by C7-T1 partial laminectomy and posterior element resection with anterior C6-T2 and posterior C4-T4 stabilization (Figure 4A–D). Histological examination of the resected tumor showed no residual GCT. The patient remains symptom-free with good range of neck motion, and without radiologic evidence of tumor recurrence 2 years after surgery.

DISCUSSION

Cervical GCTs are rare and invariably symptomatic.[1–3] Small cervical GCTs can be treated with curettage and packing, with lesions confined to anterior vertebral body sometimes requiring anterior stabilization.[4,5] Curettage has been associated with high recurrence rates ranging from 30% to 50%.[4] Thus, excision of the tumor with wide

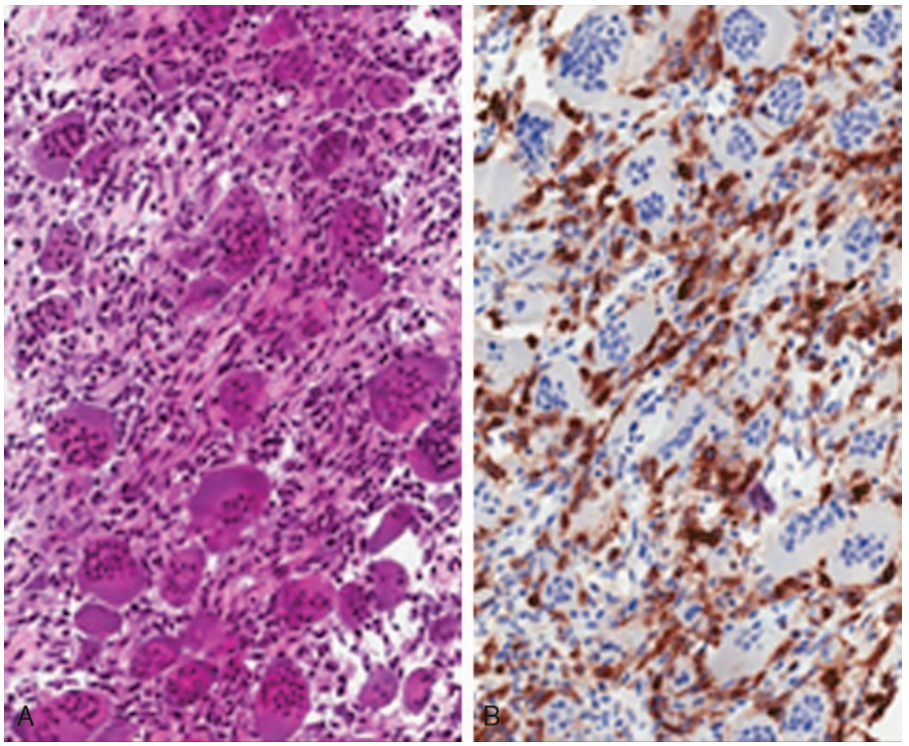

Figure 2. Light microscopic appearance of C7 giant cell tumor with numerous multinucleated giant cells in background of mononuclear stromal cells (**A**). Immunohistochemical staining with anti-RANKL antibody highlights mononuclear cell component, but not osteoclasts, thus confirming the diagnosis (**B**). RANKL indicates receptor activator of nuclear factor kappa-β ligand.

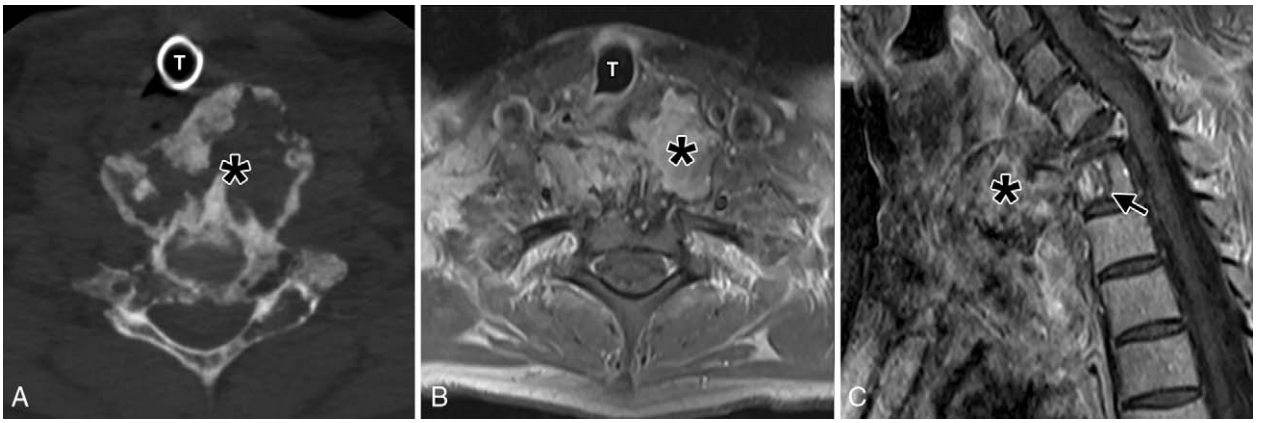

Figure 3. Follow-up imaging after treatment with subcutaneous denosumab. (**A**) Axial CT image shows marked decrease in size and increased mineralization of the GCT (asterisk). The shrunken tumor with well-defined corticated borders no longer compresses and displaces trachea. A tracheostomy tube (T) is in place; however, there is no compression of displacement of the trachea. (**B**) Axial postcontrast MRI at the level of T1 shows decrease in size of the mass (*) with mineralization resulting in decreased signal peripherally T1WI. A tracheostomy tube (T) is in place. (**C**) Sagittal MRI shows resolution of the epidural disease, but persistent spinal canal narrowing due to C7 retropulsion. The prevertebral soft tissue mass (*) has decreased enhancement compared with the pretherapy MRI (Figure 1). CT indicates computed tomography; GCT, giant cell tumor; MRI, magnetic resonance imaging.

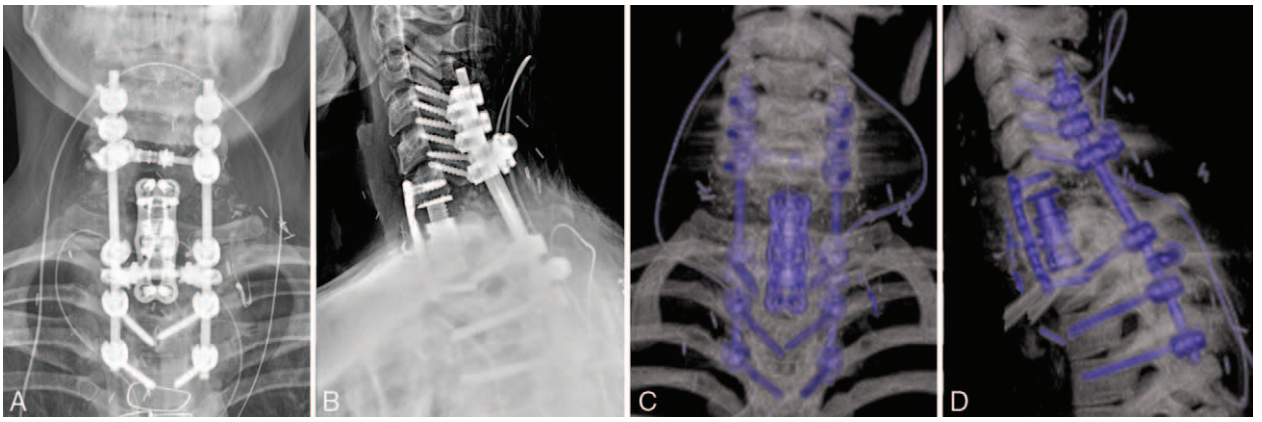

Figure 4. Postoperative imaging showing the operative construct after anterior C7-T1 intralesional corpectomy and titanium cage reconstruction, followed by C7-T1 partial laminectomy and posterior element resection with anterior C6-T2 and posterior C4-T4 stabilization. Anteroposterior (**A**) and lateral (**B**) radiographs and volume-rendered frontal (**C**) and lateral (**D**) projections from CT.

margins is preferred. Two-stage surgery is often required with combined anterior and posterior excision supplemented by anterior and posterior fusion.[4–10]

When resection with wide margins is not possible without the risk of neurological deficit and spinal instability,[4,11,12] alternative or neoadjuvant therapies can be helpful. Serial arterial tumor embolization and treatment with alpha interferon can be curative in some cases.[4,13,14] Bisphosphonates have been advocated in locally aggressive or inoperable GCTs.[15–17] The role of radiation is controversial[3–5,12,18] due to the risk of sarcomatous transformation in 10% of patients, with radiotherapy reserved for unresectable or partially resected GCT, and in patients with local recurrence.[3,5] A high tumor recurrence rate, however, has been reported when radiotherapy is used alone for treatment.[15]

Denosumab is a human monoclonal antibody against the receptor activator of nuclear factor kappa-β ligand (RANKL), which promotes osteoclastic activity.[19–21] By disrupting the Rank-RANKL interaction, denosumab inhibits osteoclast-mediated bone destruction. In a recent Phase 2 clinical trial, 96% of the patients with unresectable GCTs responded favorably to the agent; 90% of the patients, who had planned to have major surgery, but instead had received denosumab, either avoided surgery or had less morbid surgery.[19,21,22] In most cases, the drug not only reduces tumor size, but promotes new bone formation,[4,11,22–25] as exemplified in our patient (Figure 3). Neoadjuvant downstaging of unresectable GCTs before surgical resection of spinal GCTs with denosumab has previously been reported.[11,24]

CONCLUSION

We have described a unique case of large C7 GCT with almost complete airway occlusion, requiring emergent intubation and tracheostomy. Denosumab resulted in decreased

tumor size, relieving tracheal compression, and increased mineralization facilitated subsequent tumor resection.

➢ Key Points

- ❑ GCT of cervical spine presenting as acute asphyxia is rare.
- ❑ Therapy with denosumab can result in shrinkage and increased mineralization of the tumor.
- ❑ This can facilitate surgical resection.

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