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Giant Cell Tumor of the Cervical Axis Treated With Anterior-Posterior Surgery and Denosumab: A Ten-year Follow-up Case Report

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Abstract

Background/Aim: Giant cell tumor of the bone (GCTB) is a benign but locally aggressive neoplasm that rarely involves the cervical spine, accounting for approximately 1-4% of all primary bone tumors. The cervical axis (C2) is an exceptionally rare site, presenting unique surgical challenges due to its complex anatomy and proximity to vital neurovascular structures. Denosumab, a monoclonal antibody targeting RANKL, has emerged as an important adjuvant therapy for unresectable or surgically challenging GCTB. Long-term outcomes of combined surgical resection and denosumab therapy in cervical spine GCTB remain poorly documented.

Case Report: We report the case of a 16-year-old Japanese male with a history of malignant lymphoma who presented with neck pain and a lytic lesion of the C2 vertebral body. Imaging revealed a 3.5×2.8×2.5 cm expansile lesion with extraosseous extension and encasement of the right vertebral artery. Biopsy confirmed GCTB. The patient received preoperative denosumab (120 mg on days 1, 8, and 15 of month 1, then monthly for 7 additional months) followed by right vertebral artery embolization. A two-stage anterior-posterior surgical resection was performed *via* mandibular osteotomy, with C1 lateral mass and C3 pedicle screw fixation and tricortical iliac crest autograft reconstruction. Postoperative denosumab (120 mg monthly) was continued for 16 months. At 10-year follow-up, the patient remains recurrence-free with solid bony fusion, no neurological deficits, and excellent functional outcomes (VAS 0/10, JOA score 17/17).

Conclusion: This case demonstrates that combined anterior-posterior surgical resection with perioperative denosumab therapy can achieve excellent long-term tumor control and functional outcomes in C2 GCTB. Extended preoperative denosumab facilitated tumor ossification and surgical resection, while postoperative denosumab may reduce recurrence risk. Long-term surveillance remains essential given the variable recurrence patterns in spinal GCTB.

Keywords: Giant cell tumor of bone, cervical spine, axis, C2, denosumab, RANKL inhibitor, spinal reconstruction, long-term follow-up.

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Introduction

Giant cell tumor of the bone (GCTB) is a benign but locally aggressive primary bone neoplasm characterized by proliferation of mononuclear stromal cells and multinucleated giant cells (1, 2). GCTB accounts for approximately 5% of all primary bone tumors and typically occurs in the third to fourth decades of life, with a slight female predominance (2, 3). The tumor most commonly involves the epiphyseal-metaphyseal region of long bones, particularly around the knee, with the distal femur and proximal tibia representing the most frequent sites (1, 2).

Spinal involvement in GCTB is rare, accounting for only 1.4-9% of all cases (4-6). Within the spine, the sacrum is the most commonly affected site (40-50% of spinal GCTB), followed by the thoracic and lumbar vertebrae (4, 5). Cervical spine involvement is particularly uncommon, representing less than 10% of spinal GCTB cases (6, 7). The cervical axis (C2) is an exceptionally rare location, with only sporadic case reports in the literature (8, 9).

The pathogenesis of GCTB involves dysregulated receptor activator of nuclear factor kappa-B ligand (RANKL) expression by mononuclear stromal cells, leading to recruitment and activation of osteoclast-like giant cells (10, 11). This molecular understanding has led to the development of denosumab, a fully human monoclonal antibody that inhibits RANKL, as a targeted therapy for GCTB (12, 13). Since its approval in 2013, denosumab has been used for unresectable GCTB, surgical downstaging, and prevention of recurrence (12-15).

Surgical management of cervical spine GCTB presents unique challenges due to the complex anatomy, proximity to vital neurovascular structures (vertebral arteries, spinal cord), and biomechanical importance of the cervical spine (16, 17). En bloc resection with wide margins is the gold standard for GCTB treatment, but achieving this in the cervical spine is often technically demanding or impossible without unacceptable morbidity (16). The optimal role and duration of perioperative denosumab therapy remain areas of active investigation, with concerns about potential increased recurrence risk with prolonged preoperative use (17, 18).

Long-term follow-up data for cervical spine GCTB treated with combined surgical resection and denosumab are limited. We report a case of C2 GCTB in a young patient with prior malignant lymphoma, treated with extended preoperative denosumab, vertebral artery embolization, two-stage anterior-posterior surgical resection, and postoperative denosumab, with excellent outcomes at 10-year follow-up.

Case Report

Case presentation. A 16-year-old boy presented with progressive neck pain. He had a past medical history of malignant lymphoma, currently in remission. Neurological examination was unremarkable, and pain was provoked only during cervical motion.

Plain radiographs of the cervical spine demonstrated a lucent lesion with surrounding sclerosis in the right half of the C2 vertebral body (Figure 1A and B). Computed tomography revealed similar osteolytic changes accompanied by an extraosseous soft-tissue component (Figure 1C-E). Magnetic resonance imaging showed iso-intensity on both T1- and T2-weighted images, with a high-signal intraosseous and extraosseous mass on short tau inversion recovery sequences extending from the right C2 vertebral body (Figure 1F-I). Although recurrence of malignant lymphoma was initially suspected, biopsy confirmed the diagnosis of giant cell tumor (GCT).

Treatment. Because complete surgical resection was considered feasible, a total excision was planned. To reduce intraoperative bleeding, denosumab (120 mg monthly) was administered for eight months. Follow-up CT demonstrated increased peripheral sclerosis, indicating a favorable response (Figure 2A-C).

The tumor encased the right vertebral artery, raising concern for vascular injury during resection. Therefore, preoperative embolization of the right vertebral artery was performed by a neurosurgeon (Figure 2D and E).

Surgery was conducted using a combined posterior-anterior approach.

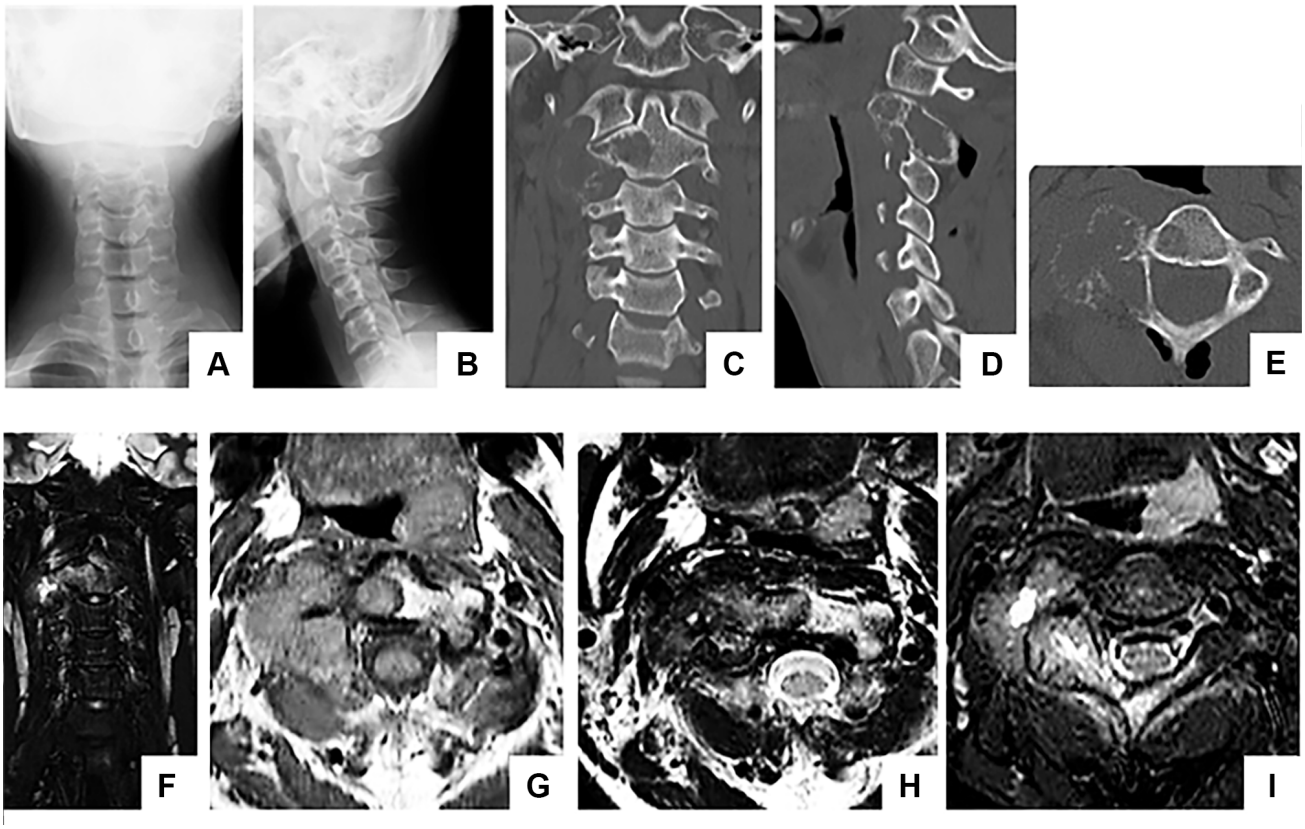

Figure 1. *Preoperative imaging findings. A, B, C, D, E) X-ray and computed tomography (CT) images showing bone lucency with surrounding bone sclerosis on the right side of the C2 vertebral body. F, G, H, I) Magnetic resonance imaging shows T1, T2 iso and STIR high-signal images, and as in CT, mass image from the right side of the C2 vertebral body to extra vertebrae.*

Posterior stage. Through a posterior approach from C1 to C3, a bulging mass was identified on the right side of C2. The lesion was largely covered by a thin cortical shell, with brownish soft tissue inside. Debulking was performed using a cavitron ultrasonic surgical aspirator (CUSA). Posterior stabilization was achieved with C1 lateral mass screws and C3 pedicle screws (Figure 3A).

Anterior stage. The patient was then repositioned supine. A right-sided oblique cervical incision at C3/4 allowed exposure of C3, but visualization of C2 remained insufficient. Therefore, an otolaryngologist performed a midline mandibular split, enabling adequate access to the anterior C2 vertebral body. The residual tumor was removed using CUSA, achieving complete resection. After irrigation with distilled water, the bone defect was reconstructed with an autologous iliac crest bone graft (Figure 3B). Postoperative radiographs and computed tomography (CT) confirmed appropriate implant placement and graft positioning (Figure 3C-F).

Postoperative course. The patient was immobilized in a halo vest for two months to protect the graft. After halo removal, swallowing rehabilitation was initiated, and he was discharged five months after surgery. No neurological deficits occurred.

To reduce the risk of recurrence, denosumab therapy was resumed at 16 months postoperatively. At two years, CT demonstrated solid fusion from C1 to C3 with no evidence of recurrence or implant loosening (Figure 4A and B).

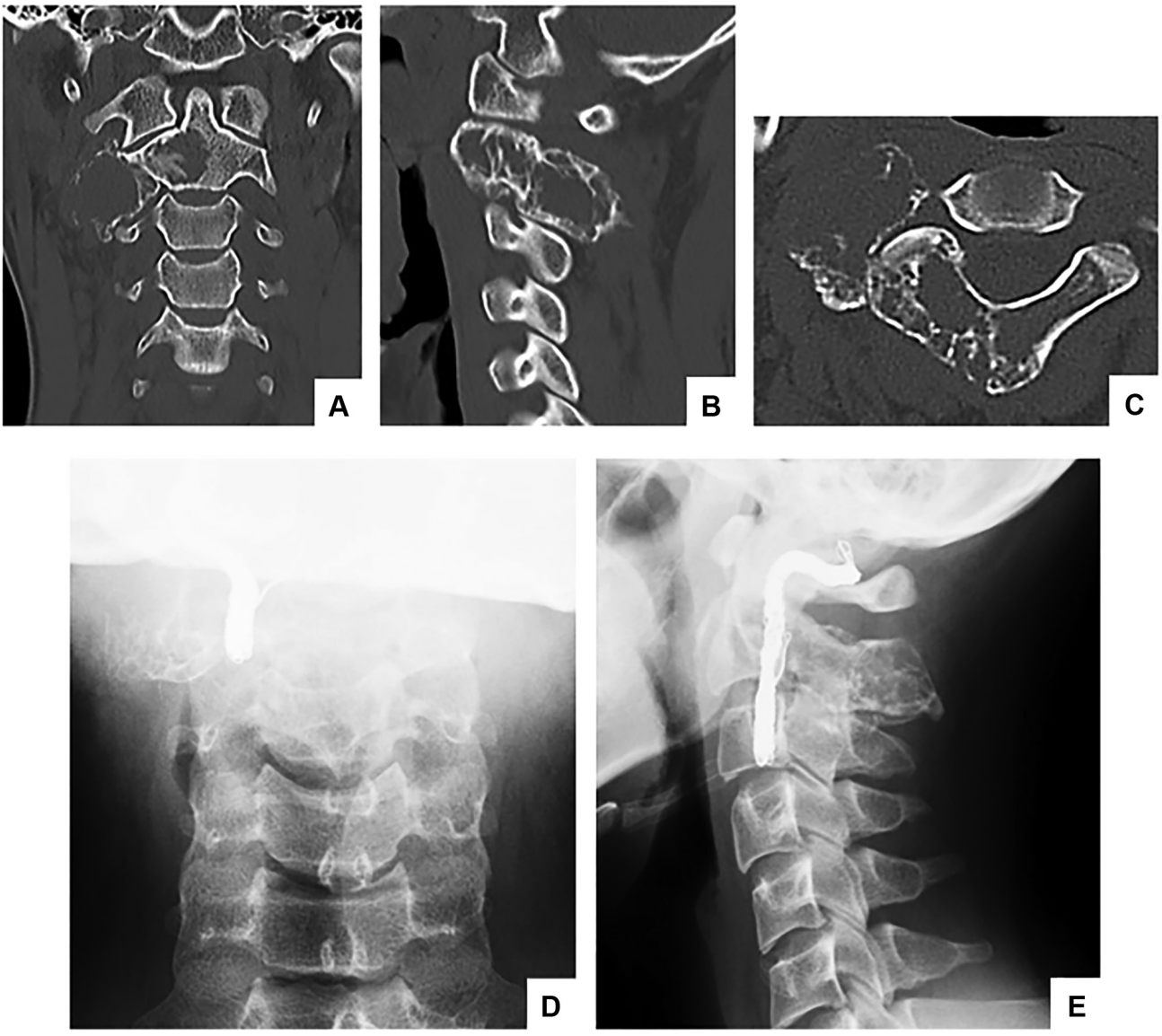

Figure 2. *Histopathological findings. A, B, C) Computed tomography image after 8 months of denosumab treatment showing osteosclerosis around the tumor. D, E) The tumor involved the right vertebral artery and vertebral artery embolization was performed before tumor resection.*

At ten years postoperatively, radiographic follow-up continued to show no recurrence and no implant-related complications (Figure 4C and D).

This study was conducted in accordance with the Declaration of Helsinki. This case report is also based on existing clinical records, and thus ethical approval from an institutional review board was not required. Written informed consent for participation and publication was obtained from the patient.

Discussion

This case demonstrates that combined anterior-posterior surgical resection with perioperative denosumab therapy

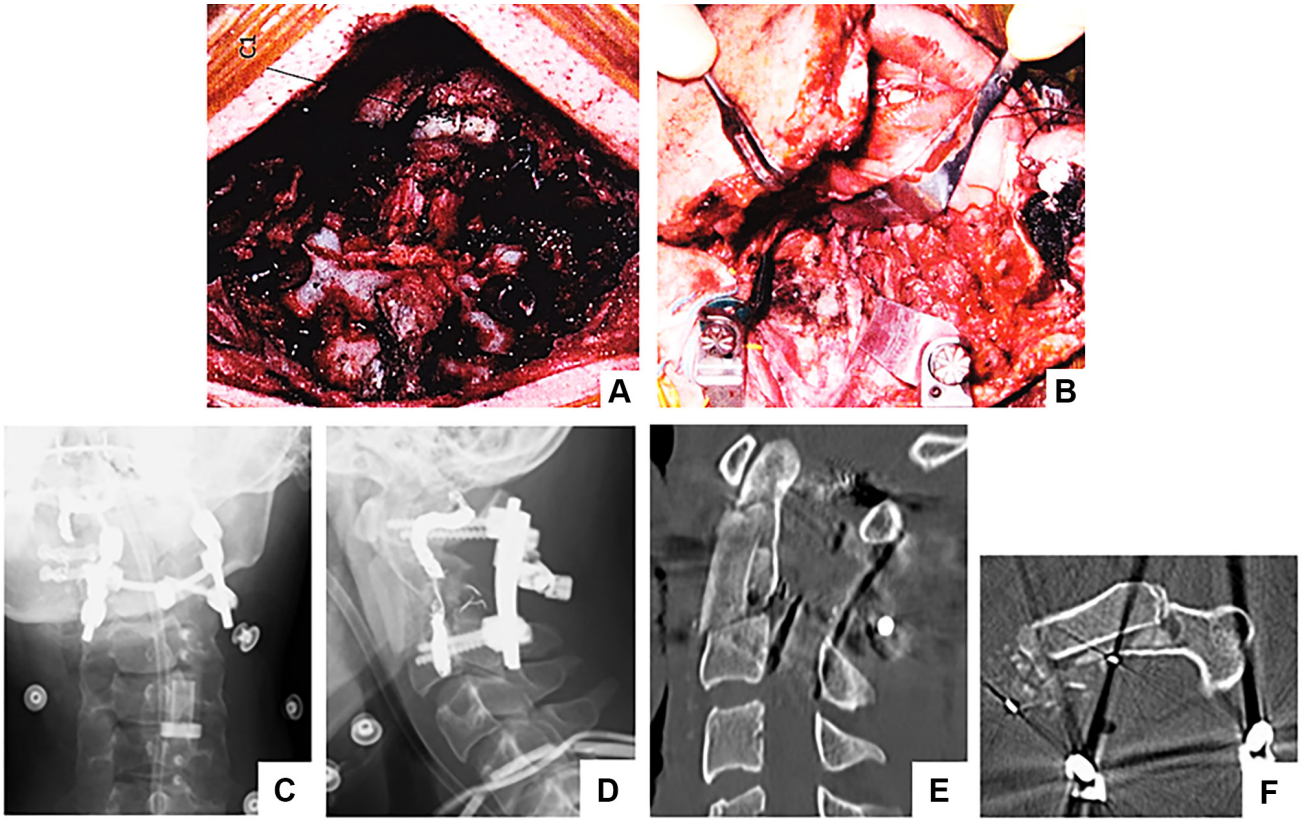

Figure 3. *Serial imaging after denosumab therapy. A) Tumor resection and screw insertion using the posterior approach. B) After resection of the anterior vertebral body and lateral vertebral body tumors in an anterior approach. C, D, E, F) Postoperative Xp and computed tomography images showing the screws and grafted bone in the noted positions.*

can achieve excellent long-term tumor control and functional outcomes in C2 GCTB, with 10-year recurrence-free survival. Several aspects of this case merit discussion regarding optimal management of cervical spine GCTB.

Role and duration of preoperative denosumab. The use of denosumab in GCTB has evolved significantly since its approval in 2013 (12, 13). Preoperative denosumab can facilitate surgical resection by inducing tumor ossification, reducing vascularity, and decreasing extraosseous soft tissue extension (14, 15). However, optimal treatment duration remains controversial. While some studies suggest 3-4 months may be sufficient (17, 19), our patient received 8 months of preoperative therapy, resulting in extensive tumor ossification that facilitated complete resection.

Recent meta-analyses have raised concerns about increased local recurrence rates with prolonged preoperative denosumab (17, 18). Proposed mechanisms include incomplete tumor resection due to obscured margins by ossification and viable tumor cell persistence within ossified matrix (18, 20). However, these studies are limited by heterogeneity in treatment protocols, surgical techniques, and follow-up duration. In our case, extensive preoperative imaging and frozen section analysis ensured adequate resection margins despite ossification. The 10-year recurrence-free outcome suggests that extended preoperative denosumab, when combined with meticulous surgical technique, may not necessarily increase recurrence risk.

The decision to use extended preoperative denosumab in this case was influenced by several factors: (i) vertebral

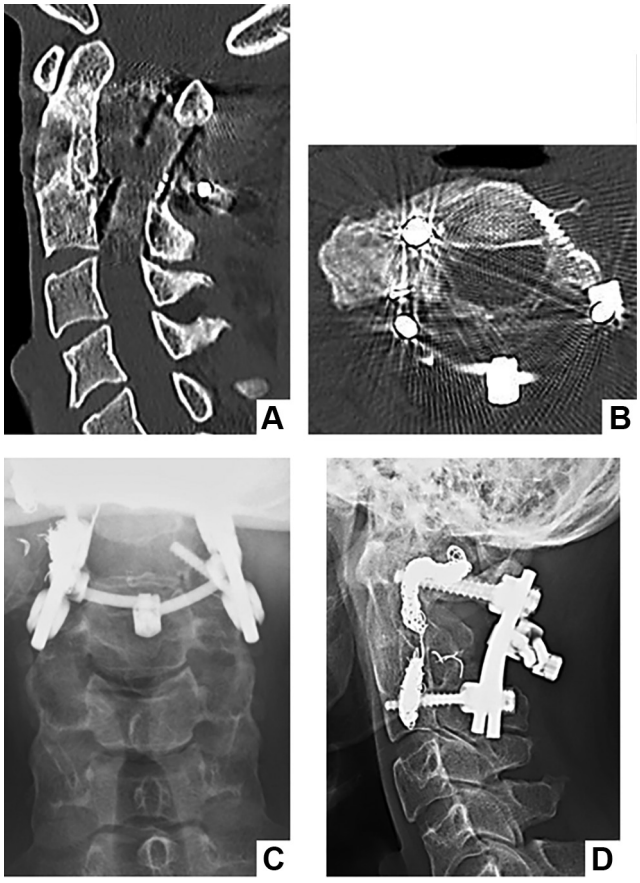

Figure 4. *Postoperative and long-term follow-up imaging. A, B) Computed tomography images taken two years postoperatively showed that the grafted bone had fused, and there was no evidence of osteolysis to suggest recurrence. C, D) Radiographs showing no recurrence 10 years postoperatively.*

artery involvement necessitating embolization, (ii) patient age and growth potential favoring conservative bone resection, and (iii) desire to maximize tumor ossification for safer handling during resection (15, 21). Contemporary guidelines from the European Musculoskeletal Oncology Society (EMSOS) recommend individualized denosumab duration based on tumor location, resectability, and patient factors (22).

Postoperative denosumab and recurrence prevention. The role of postoperative adjuvant denosumab remains poorly defined. Our patient received 16 months of postoperative therapy based on institutional protocol and emerging evidence suggesting potential benefit in recurrence prevention (23, 24). Theoretically, postoperative denosumab may eliminate residual microscopic tumor cells and prevent local recurrence. However, optimal duration and the subset of patients who benefit most require further investigation (24, 25).

The natural history of GCTB includes local recurrence rates of 10-50% depending on location, surgical technique, and adequacy of resection (1, 2). Spinal GCTB has higher recurrence rates (up to 31% in some series) compared to appendicular skeleton lesions, likely reflecting greater difficulty achieving wide margins in the spine (5, 6, 16). Intralesional curettage carries significantly higher recurrence risk than en bloc resection (16, 18). Our case achieved en bloc resection with negative margins, which likely contributed to the favorable long-term outcome.

Surgical considerations: anterior-posterior approach and vertebral artery management. The combined anterior-posterior approach was essential in this case for several reasons. The posterior approach allowed placement of C1 lateral mass and C3 pedicle screws for immediate biomechanical stability, while the anterior approach enabled direct tumor resection and reconstruction (16, 17, 26). Mandibular osteotomy provided excellent exposure of the C1-C2 region, facilitating safe tumor resection with visualization of critical neurovascular structures (26, 27).

Vertebral artery involvement is common in upper cervical spine tumors and presents significant surgical challenges (21, 28). Preoperative embolization reduced intraoperative bleeding and allowed safe sacrifice of the involved right vertebral artery segment after confirming adequate contralateral flow (21, 28). Modern endovascular techniques have significantly improved safety of vertebral artery management in cervical spine tumor surgery.

Reconstruction of the C2 defect was achieved using tricortical iliac crest autograft, which remains the gold standard for anterior cervical fusion due to its osteoinductive properties and structural support (25, 29). Alternative options including structural allografts, titanium mesh cages, and expandable cages have been described, each with

advantages and limitations (25, 28, 30). Autograft was chosen in this young patient to maximize fusion potential and avoid potential complications of implants in the setting of previous denosumab exposure.

Considerations in patients with prior malignancy. This patient's history of malignant lymphoma raised several clinical considerations. First, the differential diagnosis initially included lymphoma recurrence, bony metastasis, or radiation-induced sarcoma, although the patient had not received radiotherapy. Comprehensive workup including positron emission tomography (PET)-CT and biopsy was essential to establish the diagnosis of GCTB (6, 31).

Second, prior chemotherapy exposure may theoretically affect bone healing and immune response, although this patient's fusion progressed normally. Third, the decision to avoid adjuvant radiotherapy for GCTB was reinforced by the history of prior malignancy, as radiation therapy in cancer survivors carries risks including secondary malignancy and radiation-induced sarcoma (7, 31).

Long-term follow-up and surveillance. GCTB can recur years or even decades after initial treatment, necessitating prolonged surveillance (1, 2, 5). While most recurrences occur within 2-3 years, late recurrences beyond 10 years have been reported (5, 32). Surveillance protocols typically include clinical examination and imaging (radiographs, CT, or magnetic resonance imaging) at regular intervals: every 3-6 months for the first two years, and annually thereafter (24, 32). Our patient's 10-year recurrence-free status is encouraging, but continued surveillance remains warranted.

Malignant transformation of GCTB to high-grade sarcoma is rare (<5% of cases) and usually occurs after radiotherapy (2, 7). Primary malignant GCTB is exceedingly rare. No features of malignant transformation were evident in our patient, and the decision to avoid radiotherapy was appropriate (7, 31).

Study limitations. Individual case experiences cannot establish optimal treatment protocols, and outcomes may not be generalizable to all patients with cervical spine GCTB. The relative contributions of surgery *versus* denosumab to the favorable outcome cannot be determined. Longer follow-up is needed to confirm durability of tumor control, although 10 years represents substantial follow-up for GCTB. Prospective multicenter studies and patient registries are needed to define optimal perioperative denosumab protocols and identify predictors of recurrence (33).

Conclusion

This case demonstrates that C2 GCTB can be successfully treated with combined anterior-posterior surgical resection and perioperative denosumab therapy, achieving excellent long-term tumor control and functional outcomes. Extended preoperative denosumab (8 months) facilitated tumor ossification and surgical resection without increasing recurrence risk at 10-year follow-up, although optimal duration requires further study. Key technical factors including vertebral artery embolization, mandibular osteotomy for exposure, en bloc resection with negative margins, and stable reconstruction with autograft all contributed to the favorable outcome. Long-term surveillance remains essential given variable recurrence patterns in spinal GCTB. Further multicenter studies are needed to optimize perioperative denosumab protocols and surgical strategies for this rare and challenging condition.

Conflicts of Interest

The Authors declare that they have no conflicts of interest in relation to this study.

Authors' Contributions

This study was designed by S.I., I.T., Y.I. and T.K. The experiments were performed by S.I., I.T., Y.I. and T.K., and K.G. The data were analyzed by S.I., I.T., Y.I. and T.K., and the results were critically examined by all authors. S.I. had a primary role in preparing the manuscript, which was

edited by S.I., I.T., Y.I., T.K. and K.G. All Authors have approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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Artificial Intelligence (AI) Disclosure

During the preparation of this manuscript, a large language model (Genspark) was used solely for language editing and stylistic improvements in select paragraphs. No sections involving the generation, analysis, or interpretation of research data were produced by generative AI. All scientific content was created and verified by the authors. Furthermore, no figures or visual data were generated or modified using generative AI or machine learning-based image enhancement tools.

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