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Multimodal Management of Combined Posterior and Anterior Surgical Approach and Postoperative Pharmacological Therapy for Giant Cell Tumor of the Cervical Spine Encasing the Vertebral Artery: A Technical Case Report

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Abstract

Giant cell tumor (GCT) of bone is essentially benign but locally aggressive, and the rate of local recurrence is high when the resection is not enough. En bloc resection is recommended as an ideal solution for GCT to decrease the risk of local recurrence, but it remains challenging for cervical GCT. In this technical case report, we present a case of extensively infiltrating GCT of the cervical spine completely encasing the vertebral artery (VA) on one side. The tumor was distributed to layers A-D, sectors 3-8 based on the Weinstein-Boriani-Biagini staging. Combined posterior and anterior surgical approach for the cervical spine was successfully performed and followed by postoperative adjuvant pharmacological therapy. This kind of multimodal management may be one of the solutions for advanced cervical GCT.

Keywords: bisphosphonate, giant cell tumor, cervical spine, denosumab, vertebral artery

Introduction

Giant cell tumor (GCT) of bone is a benign tumor classified as an intermediate type based on the World Health Organization classification. However, it presents locally aggressive behavior and has a high rate of local recurrence. The incidence in the spine is not high, varying between 1.4% and 9.4%.[1-3] The most common spinal location of GCT is the sacrum, and the incidence in the cervical spine is quite low. Complete en bloc resection is the ideal treatment, but it is sometimes impossible for surgeons to perform radical resection of cervical GCT while preserving vascular and neural functions.[2] Herein, we demonstrate a safe solution using combined posterior and anterior surgical approach and postoperative adjuvant pharmacological therapy for extensively infiltrating GCT of the cervical spine completely encasing the vertebral artery (VA) on one side.

Case Report

History and radiological diagnosis

A 72-year-old woman with a 2-month history of severe neck pain was referred to our hospital. Her neurological findings on her first visit were normal, except for severe neck pain. Plain lateral cervical radiographs showed an osteolytic lesion within the C3 vertebra body (Fig. 1A). Computed tomography (CT) scan revealed an osteolytic lesion of the C3 vertebral body (Fig. 1B). Magnetic resonance imaging (MRI) showed a tumor formation in the C3 vertebral

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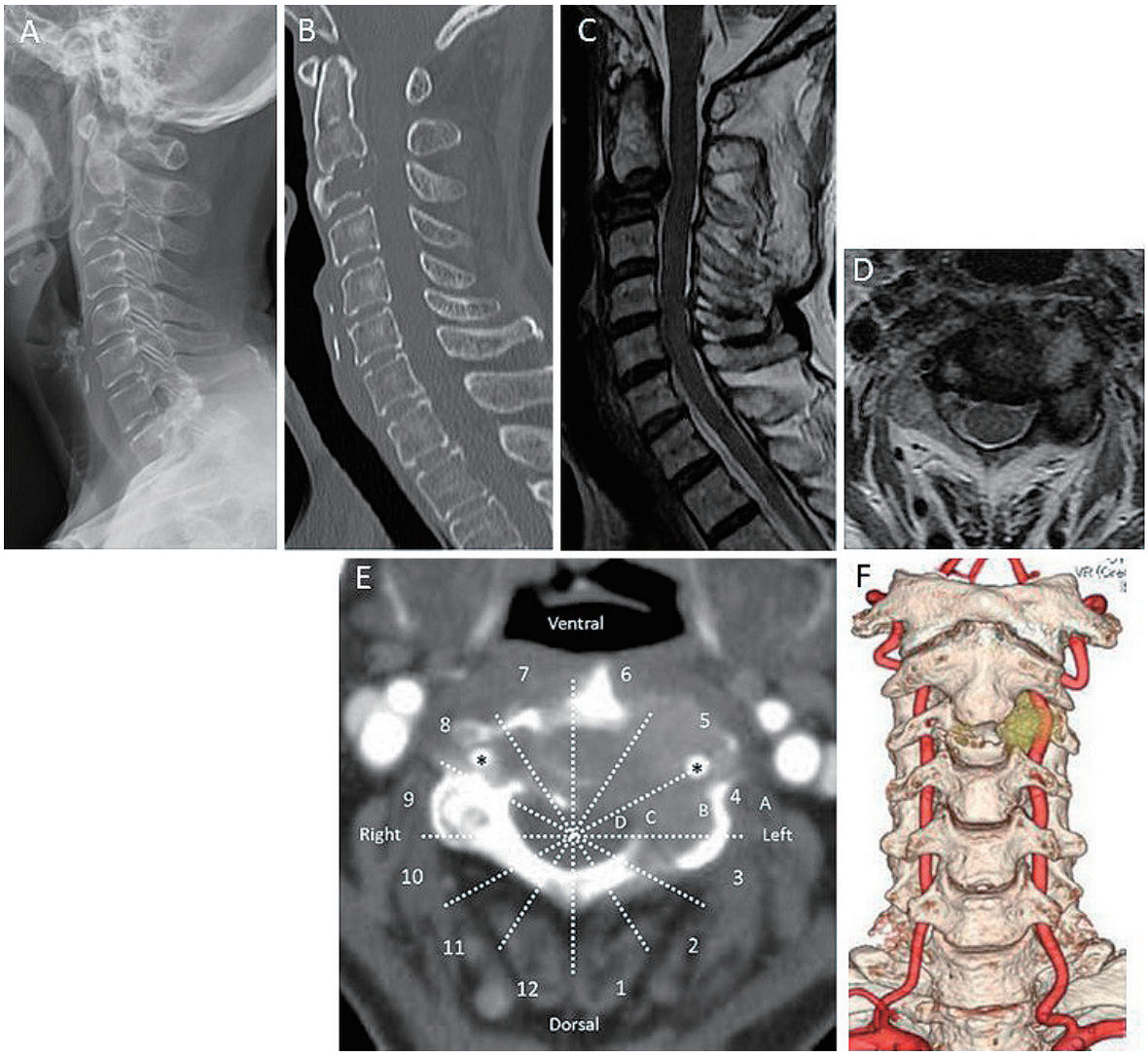

Fig. 1 Preoperative images of the cervical spine. A, B: Preoperative plain X-ray and computed tomography (CT) showing the osteolytic lesion of the C3 vertebral body. C, D: Preoperative T2-weighted magnetic resonance imaging (MRI) showed a tumor formation in the C3 vertebral body with minimal compression to the spinal cord. E, F: Preoperative CT with contrast showing the osteolytic lesion of the C3 vertebral body completely encasing the vertebral artery on the left side. The tumor was distributed to layers A–D, sectors 3–8 based on the Weinstein–Boriani–Biagini staging. Zone A begins at the junction of the osseous spine and the surrounding soft tissues, Zone B involves the bone superficially, Zone C involves the bone closer to the spinal canal, and Zone D begins at the junction of the osseous extent of the spinal canal and the epidural space. Please note the vertebral artery (*).

body with minimal compression of the spinal cord (Fig. 1 C, D). The VA on the left side was completely encased by the tumor on the contrast CT and MRI (Fig. 1D-F). Systemic examination showed no evidence of metastatic tumor. The tumor was distributed to layers A-D, sectors 3-8 based on the Weinstein-Boriani-Biagini staging (Fig. 1E), a classification devised for the oncological treatment of primary spinal tumors.[4]

Surgery

Combined posterior and anterior surgical approach for the cervical spine was scheduled (Fig. 2A, B). Posterior fixation of C2-C5 with C3 laminectomy was first performed (Fig. 2A). Partial tumor removal was attempted from the lateral mass and pedicle of the C3 on the left side. The tumor was soft and could be removed piece by piece. Bleeding from the tumor was noted (Fig. 2C), but hemostasis by the coagulation was not difficult. The operative time was 4 hours and the estimated blood loss during the surgery was 130 mL. Intraoperative rapid pathological examination of the tumor suggested GCT. The second stage of the anterior cervical surgery was performed 1 week later (Fig. 2B). En bloc resection of the tumor was not intended in the anterior surgery. Subtotal resection of the tumor combined with postoperative adjuvant therapy was planned before surgery. A vertebral occlusion test or endovascular therapy

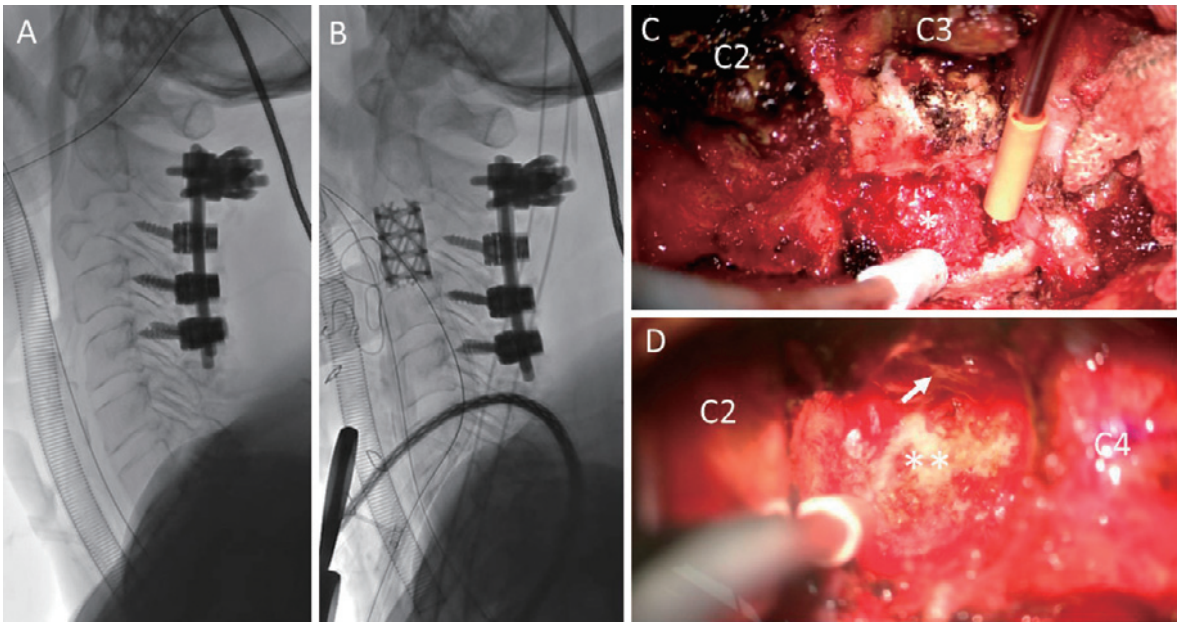

Fig. 2 Intraoperative images and photographs of the cervical spine. A: Lateral fluoroscopic image during the first posterior approach showing posterior stabilization from C2 to C5. B: Lateral fluoroscopic image during the second anterior approach showing anterior reconstruction of the C3 vertebral body. C: Photograph showing the tumor surface (*) after removing the posterior wall of the C3 lateral mass on the left side in the first surgery of the posterior approach. D: Photograph showing the posterior longitudinal ligament (**) after completion of subtotal removal of the tumor in the second surgery of the anterior approach. The tumor around the left vertebral artery (→) was left behind.

to the tumor was not performed. C3 anterior corpectomy and tumor removal were carefully carried out. The C2/3 and C3/4 disc spaces were first dissected and then the C3 vertebral body was removed. The inside of the C3 vertebral body was filled with a soft tumor. Tumor removal was performed posteriorly until the posterior longitudinal ligament was exposed, but the tumor around the left VA was partially removed using intralesional curettage (Fig. 2D). There was no strong adhesion between the tumor and the surrounding tissue. The bone around the tumor was only removed to a safe extent. After completion of subtotal removal of the tumor, anterior fixation using a mesh cage of the C3 vertebral body was successfully achieved without any vascular or neural complications (Fig. 3A). The operative time was 2 hours and 47 minutes and the estimated blood loss during the surgery was 50 mL. A histopathological examination confirmed the diagnosis of GCT (Fig. 3B).

Postoperative course

Improvement of the neck pain was noted early after the surgery. Postoperative pharmacological treatment using denosumab (Ranmark, Daiichi Sankyo Do., Tokyo, Japan) was safely started. Subcutaneous injection of 120 mg denosumab was administered once a month with careful consideration of the risk of adverse events associated with denosumab use. Cervical CT obtained 3 months after surgery showed partial ossification at the level of the C3 vertebral body (Fig. 3C). Postoperative pharmacological treatment was further changed from denosumab to bisphosphonate. The patient was doing well without any adverse events. Cervical MRI and CT obtained 6 months after surgery demonstrated no local recurrence and stable condition of the cervical spine (Fig. 3D, E).

Discussion

GCT of bone is benign but locally aggressive, and the rate of local recurrence would be high when the resection is not enough.[1,5] En bloc resection is recommended as an ideal solution for GCT to decrease the risk of local recurrence, especially in young patients, but it remains challenging for cervical GCT.[2] The morbidity or functional deterioration associated with surgery is one of the major concerns. In cases in which cervical GCT completely encases the VA, VA rupture may occur during surgery if complete or en bloc resection of GCT is attempted. In young patients, complete curative surgery with or without sacrifice or reconstruction of the VA on the tumor side should be considered. Junming et al. reported unilateral VA rupture during excision in two cases of cervical GCT.[2] Preoperative embolization of the VA may be the solution for safe and total resection of GCT of the cervical spine encasing the VA. Gille et al. described a recurrent case of cervical GCT.[6] The authors suggested that complete resection of malignant cervical vertebrae is possible if both VAs can be successfully occluded, permitting complete removal of the

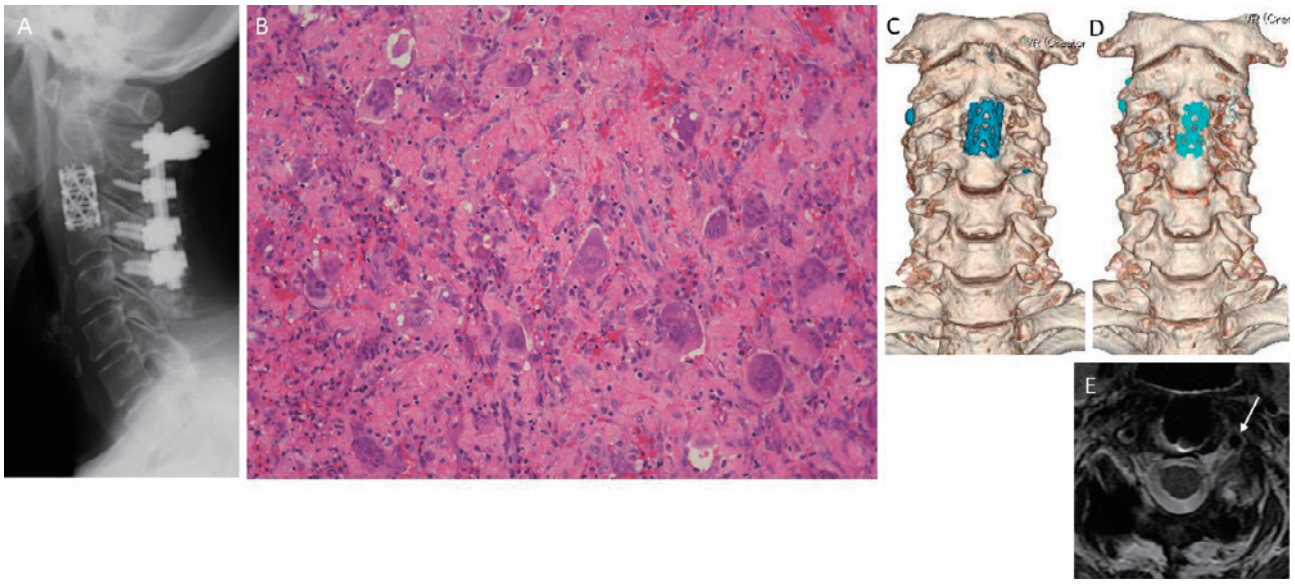

Fig. 3 A: Postoperative plain X-ray showing reconstruction of the cervical spine. B: Pathological examination showing numerous giant cells with large vesicular nuclei, which is consistent with giant cell tumor. Hematoxylin–eosin staining; original magnification, 200×. Scale bar = 100 μm. C: Postoperative three dimensional (3D)-CT scan obtained 3 months after surgery showing partial ossification at the level of the C3 vertebral body. D: Postoperative 3D-CT scan obtained 6 months after surgery showing further ossification at the level of the C3 vertebral body. E: Postoperative T2-weighted MRI at 6 months after surgery showed no recurrence of the tumor. Please note the flow void of the vertebral artery on the left side (→).

transverse processes. Rodrigues et al. also recommended embolization of the VA in safe vertebrectomy surgery for total tumor resection to avoid recurrence.[7] However, angiographical evaluation of the brain circulation needs to be carefully done for the safe embolization of the VA before surgery. In the present case, the VA on the left side was completely encased by the tumor. We did not aim to completely resect the tumor, but rather to subtotally intralesional resection, leaving the tumor just around the VA. The priority of surgery for the elderly patient in this case was given to surgical safety and tumor control. Combined posterior and anterior surgical approach was successfully performed with confirmation of the pathological diagnosis of the tumor. Postoperative adjuvant treatment with denosumab followed by bisphosphonate was safely introduced.

Postoperative adjuvant treatment is necessary to decrease the risk of local recurrence after intralesional or subtotal resection of GCT, but the standard treatment regimen has not been fully determined. There is no definitive consensus on the best adjuvant therapy for treating cervical GCT. In general, local radiation, denosumab, or bisphosphonate can be used as adjuvant treatments after partial or subtotal resection of cervical GCT (Table 1).[1,2,8-13] Radiation is administered as an adjuvant treatment to prevent postoperative recurrence in cases in which complete resection is difficult, but its efficacy is still controversial.[14,15] It has also been reported that myelopathy and radiation-induced sarcoma may develop due to radiotherapy.[15,16] Campanacci et al. reported that 27% of patients who received more than 40 Gy of radiation therapy develop malignant transformation.[17] In 2013, the Food and Drug Administration approved denosumab, a monoclonal antibody that binds the receptor of activity nuclear factor kappa-B ligand, which downregulates osteoclast activity. It was approved for unresectable GCT of bone and for cases in which surgery may cause serious complications. Since 2014, denosumab has also become available in Japan. Administration of denosumab is one of the adjuvant therapies for GCT for which curative surgery is difficult. Cases of postoperative treatment with denosumab for 16-24 months for GCT of the cervical spine with no tumor recurrence or complete disappearance of the tumor have been reported.[18,19] However, the efficacy and safety of denosumab treatment after surgery to prevent recurrence have not been fully established.[20] Bisphosphonate is another possible postoperative adjuvant treatment;[21] it inhibits osteoclast activity and has been shown to significantly prolong progression-free survival after subtotal resection for GCT.[22] Although the treatment strategy presented here is by no means the best, it may be helpful for surgeons to make a surgical plan assuming postoperative pharmacological therapy before surgery.

Conclusion

In the case of extensively infiltrating GCT of the cervical spine, subtotal resection of the tumor was achieved by combined posterior and anterior surgical approach, and

Table 1 Postoperative adjuvant treatment in cases of partial or subtotal resection of cervical giant cell tumor

Option	Authors	Year	No. of cases	Surgical resection	Outcome
Local radiation	Junming et al.[2]	2008	18	Total (12), Subtotal (6)	NED (14), AWD (1), DOD (3)
Local radiation	Boriani et al.[1]	2012	6	Partial (6)	NED (5), DOD (1)
Local radiation	Chen et al.[8]	2015	5	Partial (5)	NED (5)
Local radiation	Kim et al.[9]	2015	1	Subtotal (1)	AWD (1)
Local radiation	Jia et al.[10]	2019	4	Partial (3), Subtotal (1)	NED (4)
Denosumab	Tu et al.[11]	2018	1	Total (1)	NED (1)
Denosumab	Law et al.[12]	2018	1	Partial (1)	AWD (1)
Denosumab	Boriani et al.[13]	2020	4	Subtotal (4)	NED (2), AWD (2)
Bisphosphonate	Jia et al.[10]	2019	3	Partial (2), Subtotal (1)	NED (3)

NED, no evidence of disease; AWD, alive with disease; DOD, death of disease

postoperative adjuvant treatment using denosumab followed by bisphosphonate was successfully introduced. Although a longer follow-up was absolutely required, the short-term outcome was satisfactory. This kind of multimodal management may be a good solution for advanced cervical GCT.

Acknowledgments

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Ethical Approval

The current study was performed in accordance with the Declaration of Helsinki. Informed consent regarding the use of medical information was obtained from the patient.

Conflicts of Interest Disclosure

No benefits in any form have been or will be received from any commercial party related, directly or indirectly, to the subject of this manuscript. All authors report no conflicts of interest concerning the materials or methods used in this study or the findings specified in this paper. All authors, except I.B., who are members of The Japan Neurosurgical Society (JNS) have registered to the online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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