Clinical Case Report

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Total spondylectomy of recurrent giant cell tumors in the cervical spine

Two case reports and review of literature

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Abstract

Rationale: Spinal Giant Cell Tumors (SGCTs) are rare, aggressive, and benign tumors. Their presence in the cervical spine is even more exceptional. There are few reports of cervical GCT in the literature, especially recurrent cases. The treatment are challenging to clinically because radical resection is extremely difficult.

Patient concerns: In this study, we present the cases of a 25-year-old man and a 41-year-old woman who suffered from recurrent cervical GCT.

Interventions: They underwent extensive total spondylectomy of C3-5 and C2-4, respectively, by a combined anterior and posterior approach.

Outcomes: Both patients had a satisfactory prognosis after 2 years followe-up, and extensive total spondylectomy provided good disease-free survival rates. Extensive total spondylectomy of cervical recurrent giant cell tumor was successfully achieved combined anterior and posterior approach.

Lessons: This surgical technique can be an effective option for this pathological condition, which is difficult to manage using other conventional treatment options including repeated curettage and radiotherapy. However, there are insufficient data on long-term subjective outcomes in this type of patient, and larger series studies are needed to determine the efficacy of this approach, especially compared with piecemeal resection techniques.

Abbreviations: ABC = aneurysmal bone cyst, GCTs = giant cell tumors, IMRT = intensity-modulated radiotherapy, MRI = magnetic resonance imaging, SGCTs = spinal giant cell tumors, VAs = vertebral arteries.

Keywords: cervical spine, giant cell tumor, total spondylectomy

1. Introduction

Primary spinal tumors are associated with significant morbidity and mortality in spite of low prevalence. Giant cell tumors (GCTs) are one of the common primary bone tumors although they occur infrequently in the spine above the sacrum.[1] The incidence in the mobile spine (above the sacrum) ranges from 1.4% to 9.4%, and GCTs involving the cervical spine are extremely rare.[2] Although it is a benign tumor, it can be locally aggressive and have metastatic potential. The most common surgical option for spinal GCT (SGCT) is curettage; however, incomplete removal of the tumor usually results in local recurrence and metastasis.[3] Some researchers have suggested that en bloc resection should be performed to reduce the amount of blood loss and avoid tumor contamination. However, en bloc resection is hard to achieve, especially in recurrent cases. The optimal surgical procedure for recurrent SGCTs has not yet been established. In this article, we present the cases of two patients with recurrent cervical GCT who were successfully treated using extensive total spondylectomy with a combined anterior and posterior approach.

2. Case reports

2.1. Case 1

A 24-year-old man was admitted to our hospital with a 3-month history of cervicodorsal pain prior to admission. Magnetic resonance imaging (MRI) revealed a mass lesion involving the C4 vertebra. The preoperative biopsy revealed a GCT, and he underwent anterior C4 corpectomy and spinal fusion at an outside institution. The postoperative pathological diagnosis was in accordance with the preoperative diagnosis. He returned to the outside hospital with durative cervicodorsal pain, paresthesias in bilateral extremities, and dizziness approximately 3 months after surgery. Repeat imaging revealed bony destruction of the C3-4

Editor: N/A.

JT, WL, and SS contributed equally to this work

This study complies with ethical standards for human research. The research was approved by the Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology (No: S214). Written informed consent was obtained from all participants included in our study.

This study was supported by a research program from the National Science Foundation of China (Grant nos. 81072187 and 81541056).

The authors have no conflicts of interest to disclose.

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Medicine (2018) 97:20(e10799)

Received: 7 December 2017 / Accepted: 25 April 2018

http://dx.doi.org/10.1097/MD.0000000000010799

Table 1

Summary of patient characteristics.

Case no.	Age, years	Sex	Spinal level	WBB Stage	Margins	EBL, mL/OR Time, hours	Adjuvant therapy	FU, m	SF-36 PCS last FU	Status
1	25	M	C3-5	A-C/7-10	Marginal	3800/15	radiation therapy	24	37	NED
2	41	F	C2-4	B-D/4-9	Marginal	4700/15	Denosumab	24	35	NED

EBL = estimated blood loss, F = female, FU = follow-up, M = male, NED = no evidence of disease, OR = operating room, SF-36 PCS = 36-item Short Form Health Survey, Physical Component Summary score, WBB = Weinstein–Boriani–Biagini scale.

transverse processes and vertebral bend, with a tumor invading the middle and lateral columns of the C3-5 vertebrae. Therefore, he was transferred to our institution where extensive total spondylectomy of C3-5 was planned. Postoperative histopathological investigation revealed that the surgical margins were free and good neurological recovery was obtained after the surgery. He underwent adjuvant radiation therapy after the surgery, and at 1-year follow-up, there was no evidence of local reoccurrence or constitutional symptoms. The short form-36 (SF-36) physical component score was 37 at 24 months (Table 1).

2.2. Case 2

A 41-year-old woman presented to a regional hospital with a two-month history of pain and numbness in the right upper extremity. Initial imaging revealed a C3 vertebral mass (Fig. 1A and B), and biopsy confirmed the diagnosis of cervical GCT associated with aneurysmal bone cyst (ABC). She was admitted to the hospital and underwent curettage of the tumor with cervical stabilization (Fig. 1C and D). Four years after the initial surgery, she presented again with stiffness in the neck and pain in the right upper extremity. Imaging revealed tumor recurrence in the same approximate location (Fig. 1E and F). Therefore, the patient underwent total spondylectomy by combined anterior and posterior approach in our hospital. There was no evidence of tumor recurrence at the latest follow-up examination, 24 months after the surgery. She reports no swallowing dysfunction and has fully returned to work. Her SF-36 physical component score at 10 months was 35 (Table 1).

3. Discussion

Recurrent GCTs in the cervical spine poses a unique challenge. Previous publications on this topic have been limited. Options for managing recurrent GCTs include repeat surgical resection and combined radiotherapy or chemotherapy. Choices of surgeries are usually en bloc vertebrectomy and intralesional resection. The main purpose of an en bloc resection is the prevention of tumor cell contamination of the surrounding tissues during the removal of a solid tumor, so as to prolong disease-free survival.[4] Many

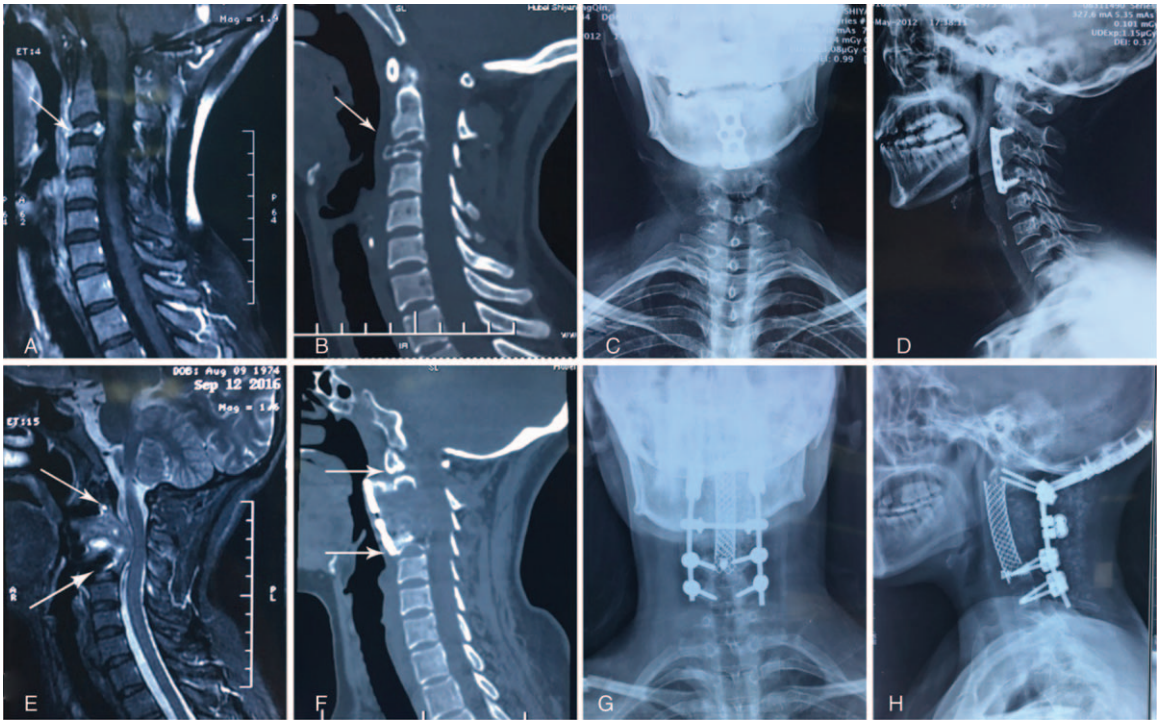

Figure 1. MRI and CT images demonstrating spinal tumor involvement at C3 (white arrow) before the first surgery (A). Frontal (B) and lateral (C) radiographs obtained after the first surgery. MRI and CT images showing the recurrent tumor involving levels C2-4 (white arrow) (E and F, respectively). Frontal (G) and lateral (H) radiographs showing the results of a combined anterior and posterior approach total spondylectomy, performed in a single stage. MRI = magnetic resonance imaging.

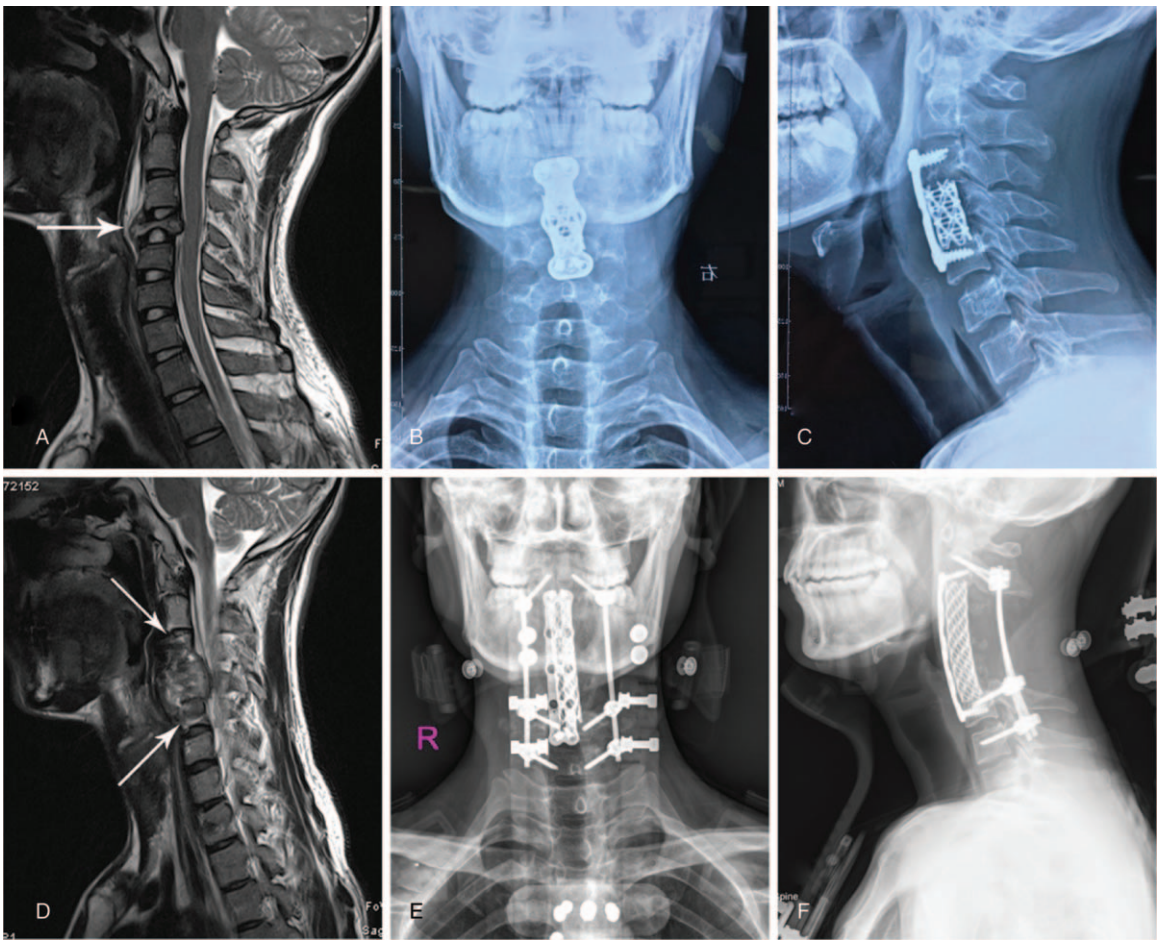

Figure 2. MRI image obtained before the first surgery demonstrating spinal tumor involvement at C4 (white arrow), compressing the spinal cord (A). Frontal (B) and lateral (C) radiographs obtained after the first surgery. MRI images showing the recurrent tumor involving levels C3-5 (white arrow) at 3-month follow-up (D). Frontal (E) and lateral (F) radiographs obtained after combined anterior and posterior approach total spondylectomy was performed in a single stage. MRI = magnetic resonance imaging.

studies have been published validating the role of en bloc resection as the standard of care for primary spinal tumors.[5,6] However, total en bloc resection in the cervical spine, continues to present unique challenges despite the fact that en bloc resection of the thoracolumbar spine is performed routinely now.[4] Cohen et al[6] believe that a strictly en bloc resection is not possible in the cervical spine because of the need to preserve the vertebral arteries (VAs) and the nerve roots supplying the upper extremities. Junming et al[1] analyzed a consecutive series of 22 GCTs of the cervical spine in patients who underwent surgical treatment. Likewise, they claimed that a strictly "en bloc" resection is rarely possible in the cervical spine because of the need to preserve the VAs and the nerve roots. Campanacci et al[7] reported 327 cases of GCT in bone, of which 280 were followed for two to 44 years. Among those followed, the rate of local recurrence was 27% in 151 intralesional procedures, 8% in 122 marginal excisions, and 0% in 58 wide or radical procedures. Chou et al[8] reported 3 cases of en bloc resection of multilevel cervical chordomas using parasagittal osteotomies. As an alternative to multilevel spondylectomy for the treatment of multilevel cervical tumors, the use of this kind of osteotomya-voids intralesional resection and adheres to the oncological principle behind a marginal, en bloc excision. As their study lacks long-term follow-up, they claimed that complete en bloc spondylectomy remains the ideal treatment for malignant spinal tumors.

Compared to en bloc resection, complete spondylectomy for cervical GCT is a more feasible method and technically demanding, especially for recurrent cases. In our two cases, both had operations in other hospitals for a single vertebral lesion. Total spondylectomies were not conducted in either case previously. During follow-up, we unfortunately found that the lesion had not only recurred in the original segment, but also involved the upper or lower adjacent vertebra and the surrounding soft tissue. This is especially notable in the first patient, who relapsed within 3 months. When retrospectively analyzing this case, we have reason to say that limitations in the surgical technique led to tumor recurrence. Some researchers have claimed that the first operative intervention is the best opportunity to treat the disease, and that the treatment of recurrence is always unsuccessful in the long-term regardless of aggressive resection.[9,10] Both of our patients underwent a total spondylectomy by combined anterior and posterior approach, followed by adjuvant therapy (Figs. 2 and 3).

There were several technical difficulties that needed to be overcome. First, the resection of the epidural portion of the tumor

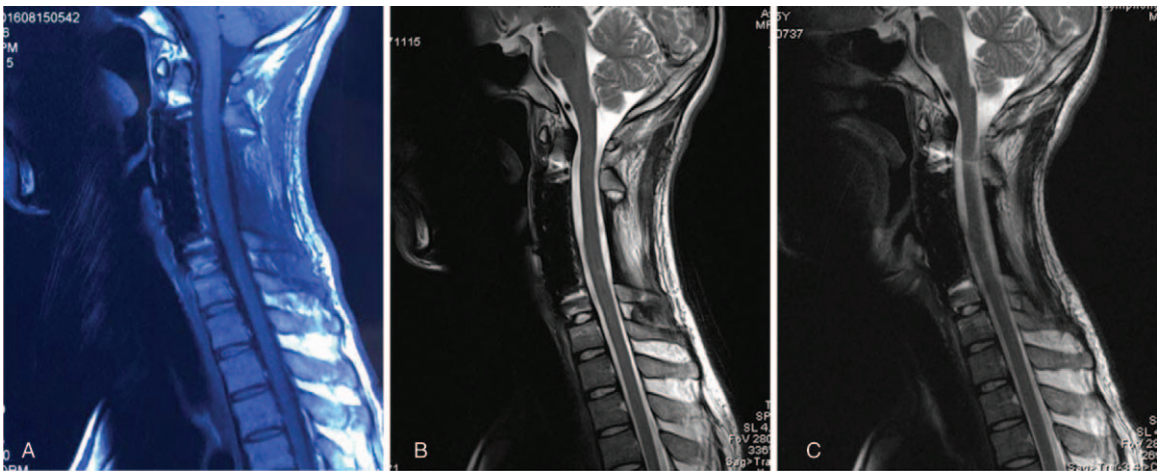

Figure 3. MR study at 6 (A), 12 (B), and 24 (C) months after surgery demonstrating no evidence of recurrence.

was difficult as there were severe adhesions of the tumor to the surrounding neural tissue after the previous surgery. Second, as the tumor usually encases the bilateral or unilateral VAs, exposing the VA is an essential and challenging step, especially for recurrent cases. Removing the transverse foramen to expose the VA is the basis of the tumor resection. Several articles have described VA ligation in the setting of en bloc vertebrectomy to obtain sound oncologic resection. Rhines et al[5] performed a total spondylectomy of C2 and claimed that the sacrifice of a unilateral VA and the nerve roots is necessary when en bloc removal is the goal. Hoshino et al[11] retrospectively analyzed 15 patients with cervical tumors, all of whom were treated with unilateral VA ligation during surgery, and reported no adverse events affecting the brain stem, cerebellum, or spinal cord. Although there are no reports of serious complications by sacrificing VA, the risk is significant because of the importance and variability of the radiculomedullary branches. Therefore, some surgeons perform preoperative embolization in order to reduce intraoperative bleeding and to prevent intraoperative injury of the VA.[12,13] In our two cases, both VAs were encased within the tumor, and there was significant extension of the tumor into the surrounding soft tissues (Fig. 4). Total en bloc spondylectomy was not feasible because both cases were recurrent and there was an need to preserve the VAs and the cervical nerve roots. We felt that a radical resection with planned marginal margins at the preserved VA offered the best chance at long-term survival, and final pathology revealed a marginal margin at the VA. In both cases, both of the VAs were torn and repaired during the surgery (Fig. 4). No related complications occurred during follow-up. As such, we believe that if intralesional total spondylectomy is the goal, the preservation of the VAs and neural structures is feasible and should be attempted in select cases.

Total spondylectomies were performed using combined approaches, the order of which was critical. There is still a controversy about the sequencing of the anterior and posterior operations. It has been shown that conducting the posterior operation first can reduce the risk of failure of column support and VA injury.[14] In the first case, we performed the posterior laminectomy first because this can enlarge the vertebral canal volume and increase the mobility of the cervical cord, thereby reducing the risk of spinal cord injury during the anterior operation. Although conducting the posterior surgery first can reduce the risk of implant migration and VA injury, it can make the anterior operation difficult, especially in the high cervical spine. Posterior occipitocervical fusion limits the range of motion of the cervical spine, limiting surgeons to an anterior transoral approach. In recent years, there have been several modifications to improve the exposure of the transoral approach, such as an extended U-shaped flapincision, the transoral-mandibulotomy-glossotomy approach, or the transmaxillary-transmandibular approach;[15] however, these operations usually involve wide and invasive tissue dissection placing the patient at risk for serious complications. Matsumoto et al[16] reported 3 cases of malignant tumors in the upper cervical spine that were treated surgically by a combination of posterior tumor resection and stabilization, and anterior tumor resection through a mandible-splitting approach after failed ion-beam radiation therapy. However, serious complications developed after surgery. The first patient presented with a deep wound infection, cerebrospinal fluid leakage, and meningitis. The second patient demonstrated prolonged difficulty swallowing, subsidence of the strut graft, and recurrence. The third patient developed a deep wound infection and discitis, causing progressive paralysis. As is shown in our second case, posterior osteotomies could not be performed first, as the site of the surgery was considerably different. Successful resection in this case required wide anterior exposure from the C1 arch down to C5. If a posterior approach had been used to resect the posterior elements of C2-4 first, it would not have been possible to turn the head, and sectioning of the mandible and circumglossal dissection would have become necessary. Therefore, we chose a lateral high retropharyngeal approach in the anterior procedure followed by posterior stabilization. This allowed the head to be tilted to one side, unrestricted by a posterior occipitocervical fusion. The high retropharyngeal approach also provided good access to the upper portion of the tumor, necessitating an extralesional resection, which was beneficial for restoring vertebral height and in bone grafting.

A variety of adjuvant therapies, such as radiation, cryotherapy, and selective arterial embolization have been used in the treatment of SGCTs in order to reduce the rate of recurrence. Khan et al[17] reported 6 patients diagnosed with SGCTs, who were treated with surgery and radiotherapy. At a mean follow-up of 12 years, 5 of 6 patients were alive with no evidence of disease.

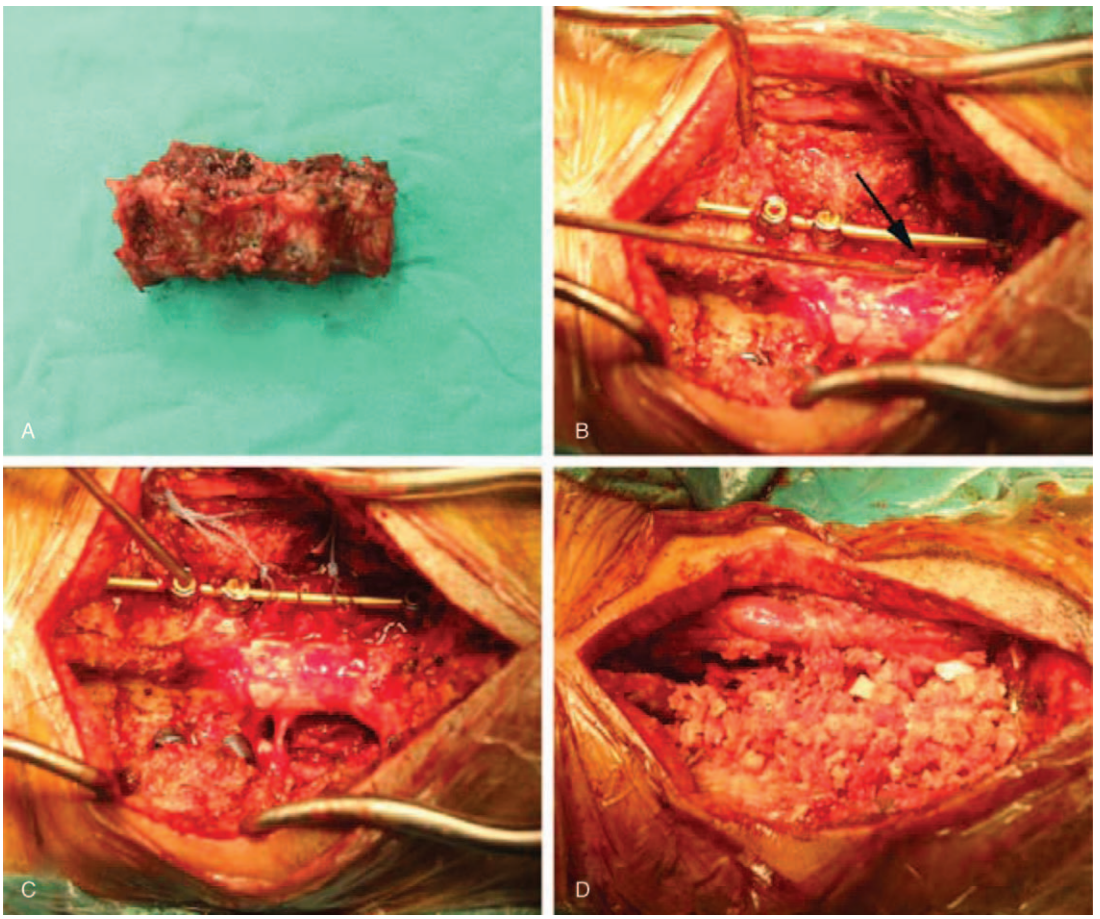

Figure 4. Intraoperative photographs showing the surgical specimen, including the C2-4 spine, the titanium plate placed in the previous surgery (A), the exposed vertebral arteries (B, arrow), the separated outer layer of the dura mater and the total removal of the tumor (C), and ample bone grafting (D).

Sharma et al[18] also analyzed 6 cases of GCTs. Those patients were treated with subtotal resection and postoperative radiation therapy. No patient had a recurrence at a mean follow-up of two years. Although many studies haves shown that radiotherapy is useful for the management of SGCTs, and that conservative surgery with local radiotherapy may be a reasonable alternative for tumors that cannot be completely excised, there are still many researchers who believe that adjuvant radiation therapy has no benefits in the reduction of recurrence rates. Xu et al[19] retrospectively analyzed 102 patients with GCTs and concluded that adjuvant radiation therapy achieved no significant reduction of recurrence rates at either two years or 5 years of follow-up. Ruggieri et al[10] retrospectively studied 31 patients with sacral GCTs treated with intralesional surgery with and without adjuvants, and they concluded that adjuvants had no influence on local recurrence. With the development of radiation therapy, advanced radiation therapy technology may improve the effectiveness for SGCTs. Roeder et al.[20] treated 5 patients with intensity-modulated radiotherapy (IMRT). This kind of radiotherapy uses advanced reconstructive imaging to deliver optional radiation doses to irregularly shaped targets safely, with low dose exposure to the surrounding structures. All patients were treated with IMRT with a median total dose of 64 Gy in conventional fractionation. After a median follow-up period of 46 months, the local control rate was 80% and overall survival was 100%. The majority of patients obtained improvement of their clinical symptoms and there were no severe acute or late side-effects. Medical treatment such as bisphosphonates and denosumabare also used in the treatment of GCTs. Zhang et al[21] presented 3 cases of recurrent SGCTs treated with sodium ibandronate. After 2–6 years of follow-up, two patients recovered both clinically and radiologically without reoperation, and one patient had a recurrent sacral tumor that was well-controlled with sodium ibandronate. Osteoclast differentiation factor receptor activation of nuclear factor kappa-B ligand (RANKL) is heavily involved in GCT pathogenesis. Denosumab belongs to a new class of drugs that inhibit RANKL. In our two cases, both underwent postoperative adjuvant therapies. The first patient underwent adjuvant radiation therapy after surgery because denosumab had not been approved for sale in China. Although denosumab is still being studied for the treatment of GCTs, it has many potential advantages. It does not cause secondary tumors like radiotherapy, which increases the risk of radiation-induced sarcoma, a typically aggressive osteosarcoma.[22] Some studies have shown that it can reduce the relative content of proliferative, densely-cellular tumor stromal cells, replacing them with nonproliferative, differentiated, densely woven new bone.[23] The FDA has approved denosumab for the treatment of unresectable GCTS, or if the surgery is likely to result in severe morbidity.[24] Mattei et al[25] described the case of a 22-year-old female patient with GCT involving the C2 vertebral body and odontoid process. The patient was treated via monotherapy with Denosumab. After 16-

months of follow-up, computed tomography imaging revealed the disappearance of osteolysis, with new bone formation, and no major side-effects occurred during long-term pharmacological treatment with denosumab. Current studies show that denosumab can control GCTs and potentially "harden up the edges" for those with extra-osseous extension to facilitate subsequent surgery. However, no defined end point for the use of denosumab as a stand-alone treatment has been reported.

Ultimately, it is important to remember that the objective of extensive total spondylectomy and other adjuvant therapies is to decrease local recurrence and prolong survival. This study showed that extensive total spondylectomy may result in a relatively low local recurrence rate with favorable overall survival, albeit with a high risk of complications and instrumentation failure. Prospective studies and long-term follow-up are needed to confirm this observation.

Author contributions

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Supervision: Yukun Zhang, Shuahua Yang, Cao Yang.
Visualization: Yukun Zhang, Shuai Li.
Writing – original draft: Ji Tu, Wentian Li.
Writing – review & editing: Yukun Zhang, Cao Yang.

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