Giant cell tumor of the odontoid in an adolescent male:
radiation, chemotherapy, and resection for recurrence with
10-year follow-up

Case report

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Gi ant cell tumors (GCTs) are rare lesions of the cervical spine, with only 14 previously reported pediatric cases in the literature, all occurring in females. The authors present the case of a 15-year-old boy with neck pain who was found to have a lytic GCT of the odontoid process. Following resection, recurrent disease was treated with radiotherapy and chemotherapy and then a final resection. He has remained tumor free for more than 10 years. The rarity of GCTs can make their diagnosis difficult in the cervical spine. Because of their aggressive behavior and relative resistance to adjuvant therapy, GCTs must be monitored diligently and treated aggressively.

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Giant cell tumors are rare neoplasms representing 4%–6% of primary bone tumors.1,2 These benign lytic lesions can be aggressive with high rates of local invasion and recurrence. They most commonly occur at the end of long bones and knees, and yet approximately 2% of these tumors arise in the vertebral column above the sacrum. There are only 14 reported cases involving the cervical spine in children.2,3,8,9,12,13,15,18,20,21

Treatment of GCTs in the cervical spine remains challenging. Management options include resection with possible postoperative radiation and/or chemotherapy.11,15,16 The location of GCTs in the cervical spine presents surgeons with the additional dilemma of subtotal resection and recurrence versus aggressive resection with possible neurological deficits or spinal instability in young patients.15

We present the case of a 15-year-old boy with a GCT arising from the odontoid process of the second cervical vertebrae. This tumor recurred, although biopsy had confirmed GTR. Ultimately, an aggressive surgical approach with GTR following radiation and chemotherapy was curative, and the patient has been neurologically intact and stable for more than 10 years.

This case shows that GCT, although rare, should be considered in the differential diagnosis of lytic cervical spine lesions in children. These tumors can be resistant to chemotherapy and radiation. Surgical removal, despite its inherent risks and challenges, is critical in the care of children with GCTs of the spine.

Case Report

History and Examination. This 15-year-old boy presented with a 1-month history of severe right-sided neck pain and myelopathy, which occurred spontaneously after “heading” a soccer ball. Plain radiographs, CT scans, and MR images/MR angiograms of the cervical spine were obtained at a referring institution. These studies confirmed C1–2 subluxation with a nonenhancing lytic lesion of the C-2 odontoid process, which expanded bilaterally to the vertebral arteries and involved the joint space on the right side (Fig. 1). The vertebral arteries were patent.

First Operation. The patient underwent a transoral approach to the odontoid process and C-2 vertebral body for excisional biopsy and GTR of the tumor.

Abbreviations used in this paper: GCT = giant cell tumor; GTR = gross-total resection.

This article contains some figures that are displayed in color online but in black and white in the print edition.
Histological examination disclosed moderate cellular proliferation of elongated cells with vesicular nuclei and amphophilic to foamy cytoplasm associated with numerous Langerhans-type multinucleated giant cells with up to 40 nuclei/cell (Fig. 2). There were scattered mitoses. Areas of necrosis were seen, but no formation of osteoid or cartilage was detected to suspect a diagnosis of osteosarcoma or chondrosarcoma. A diagnosis of GCT was rendered.

Second Operation. The patient underwent a planned follow-up posterior approach for a C1–2 posterior spinal fusion (Fig. 3). The Sonntag posterior C1–2 technique was used. Specifically, a sublaminar #18 wire cable was passed under the posterior C-1 arch from inferior to superior. Next, the inferior arch of C-1 and the superior aspect of the C-2 spinous process were decorticated before graft placement. A notched iliac crest graft was placed in between the spinous process of C-2 and the posterior arch of C-1. The cable was looped over the iliac crest autograft and placed into the notch created on the inferior aspect of the C-2 spinous process. The cable was then tightened and crimped. Routine biopsies of the vertebral body, paravertebral soft tissue, and C-2 lamina confirmed GTR of the tumor. The postoperative course was unremarkable, and the patient was discharged home with a normal neurological examination.

Third Operation. Approximately 3 months later, the boy presented to the emergency department with a 2-day symptom of bilateral upper-extremity paresthesia and weakness. His neurological examinations showed strength of 3–4/5 in the bilateral proximal and 2–3/5 in the bilateral distal muscle groups. Bilateral lower-extremity strengths were 5/5. He had hyperreflexia of the knee and clonus of the lower extremity. Magnetic resonance imaging of the cervical spine revealed a large recurrent C-2 mass with cord compression (Fig. 4). The patient emergently underwent a transoral approach for debulking of the recurrent tumor. Postoperative MR imaging showed near-total resection and proper alignment of the spine. Pathology once again revealed a GCT.

Radiation and Chemotherapy. The clinical picture of a rapid recurrence initiated a concern for malignancy. Our pathologists believed that giant cells within the bone could be a feature of tumors other than GCT, such as osteosarcoma or malignant fibrous histiocytoma. Additionally, a bona fide GCT can have a dedifferentiated (malignant) component, which might not have been sampled or was poorly preserved for a reliable histological diagnosis. A multidisciplinary team composed of neuro-
surgeons, pediatric oncologists, neuropathologists, and radiation oncologists recommended the start of radiation and proton beam therapy (40 Gy) with the possibility of chemotherapy and a second-look resection. The patient initially had improvement of his strength to 4–5/5 in both the flexor and extensor muscle groups with normal sensation bilaterally. Five months postoperatively, MR imaging studies showed a decrease in cord compression, suggesting good control via radiotherapy. Eight months postoperatively, however, left-sided flexor and extensor muscle weakening developed in the patient, and MR imaging revealed significant enlargement of the mass with lateral extension and cord compression. The tumor was suspicious for sarcoma based on the rapid recurrence, and thus, the patient underwent 10 rounds of chemotherapy (doxorubicin, cisplatin, ifosfamide, and etoposide). However, follow-up MR imaging was without a reduction in the size or appearance of the tumor. Magnetic resonance angiography of the cervical spine was obtained, revealing occlusion of the left vertebral artery at the level of C-2 (Fig. 5A and B).

Fourth Operation. The patient was taken back to the operating room for a second-look surgery via a far lateral transpedicular and translaminal approach with partial excision of the left pedicle and lamina of C-1 and C-2. This procedure allowed exposure of the extraosseous and epidural component of the tumor as well as the intraosseous component. The vertebral artery was dissected out as it traversed through the foramen at C-2 and C-1. Clips were placed on the vertebral artery, and the vessel was cauterized and divided. Further drilling of the vertebral body of C-2 and the anterior aspect of the lateral mass and anterior arch of C-1 was accomplished, allowing resection of the intraosseous component of the tumor, which was both lateral and ventral to the thecal sac. A GTR of the tumor was achieved.

Postoperative Course. Pathological evaluation once again revealed a GCT with no evidence of malignant progression or appreciable radiation changes. The patient tolerated the surgery well without any changes in his neurological examinations, and his postoperative MR imaging studies showed complete resection of the tumor (Fig. 5C and D). Currently, 10 years after his last surgery, the patient has normal reflexes, sensation, and strength of 5/5 in all extremities and remains disease free.

Discussion

Giant cell tumors of the spine are rare pathological lesions in the pediatric population. Giant cell tumors of the cervical spine are even more unusual and occur above the sacrum in only 2% of patients, with the peak incidence in the 3rd decade of life. To our knowledge, only 14 GCTs of the cervical spine have been reported in children. Specifically, there were 8 cases at C-2, 3 at C-4, 1 at C-6, and 2 at C-7. All patients were between the ages of 14 and 17 years except for one 9-year-old patient with a C-4 GCT. All 14 reported cases occurred in females. Our case is the first documented instance of a GCT in an adolescent male.

The standard staging classification systems for GCT outcomes, developed by Campanacci et al. and Enneking, suggest that the higher the radiographic grade the
more radical the required surgery. Eckardt and Grogan specifically recommended intralesional curettage with adjuvant therapy for Stage I and II lesions and en bloc resection for most Stage III lesions. These recommendations are specific for GCTs in the distal extremities (femur, tibia, radius, and so forth) and may not be appropriate for GCTs located in the spine. The anatomy of the spine and the difficulty of surgical removal require specific consideration and classification. Consider, for example, that a Grade III GCT designation can encompass some distinct variations and differentiations, especially for spinal lesions.

Prior reports of GCTs have recommended total excision as the treatment of choice, whereas others have highlighted a partial resection combined with radiation and/ or chemotherapy for tumors in which radical resection may present unacceptable risks of neurological deficit or spinal instability. Our patient underwent a combination of several surgeries, chemotherapy, and radiation treatments to achieve a long-term disease-free survival.

Although GCTs are considered benign, there is a 16%–42% chance of tumor recurrence depending on the initial extent of resection and the biology of the tumor, with disease-free survival of 2 months to 9 years. Adjuvant therapy in previous reports have included embolization, cryosurgery, and radiation for treatment and local control of GCTs. Radiotherapy has been the most controversial therapy for these tumors. Local control rates of 70%–90% (mean 82%) have been reported with doses > 40 Gy. Nevertheless, it should be noted that this success has been mostly seen in nonaxial GCTs (only one-third of the patients in the Feigenberg et al. series had vertebral GCTs). Additionally, with radiotherapy there is a 10% chance of transformation of these tumors to sarcoma, with an average time to radiation-induced malignancy of 12 years.

Physicians face many difficulties in managing these tumors. Complete excision has been proposed as the standard treatment for GCTs, but a 9% subtotal resection rate has been reported, which may be attributable to concerns of possible deficits and poor functional outcome when the tumor presents in a challenging location. With the development of new spinal instrumentation and improved imaging techniques, more radical resections of tumors are more commonly attempted. Additionally, for cases in which the tumor encases the vertebral artery, unilateral artery ligation is well documented in the literature. The contralateral vertebral artery and basilar artery can be evaluated using a preoperative cervical and cerebral angiogram; if the diameter of the vertebral artery that is targeted for ligation is no larger than the patent artery, the mortality and morbidity rates will be low.

Patients with GCTs require close follow-up visits and imaging studies given the aggressive nature of the tumor, their possible transformation to sarcoma, and the potential for metastasis to the lung. Follow-ups should include clinical examinations for neurological changes or symptoms of pain as well as appropriate imaging studies. Pain is the most common symptom in patients with GCTs of the spine, followed by neurological deficit and gradual onset of paraparesis. Because of the location of these tumors, there is a high possibility of nerve root or cord compression. Poor outcomes are more common if a patient presents with neurological deficits. In < 5% of GCT cases, the tumors metastasize to the lung; therefore, a CT of the chest should be obtained as part of the initial workup as well as during the follow-up of patients with these lesions.

Conclusions

A GCT of the cervical spine is a very rare lesion in the pediatric population. Before the present case, all documented GCTs have occurred in females. Both the location and high recurrence rate of these tumors present a great challenge to the treating physician, as neurological deficits from this tumor can be devastating in a young patient. An aggressive surgical approach with the goal of complete resection, adjuvant treatment with chemotherapy and radiation therapy, and long-term frequent follow-ups for recurrence should be considered as the optimal treatment.

Disclosure

The authors report no conflict of interest concerning the mate-
Giant cell tumor at C-2

Materials or methods used in this study or the findings specified in this paper.

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