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Giant Cell Tumor of the Spine

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Giant cell tumor (GCT) of the bone most commonly occurs in the long bones near articulations. It comprises less than 5% of primary bone tumors in the spine and, when involving the axial skeleton, occurs predominately in the sacrum. These uncommon osteolytic lesions occur primarily in females in their twenties and thirties, with likely presenting complaints of corresponding back pain. Metastases may occur, generally to the lungs, which portends a worsened prognosis [1]. Uncommonly, the tumor is multifocal.

Patients with GCTs most commonly present with complaints of back pain. Because tumors can become large, weakness secondary to compression of the spinal cord or nerve roots may occur [2,3]. For tumors of the sacrum, nerve root involvement may result in bowel or bladder symptoms [4,5].

Pathophysiology

GCTs are comprised of multinucleated, osteoclastic giant cells, which are thought to arise from mononuclear cells of macrophage origin. Necrosis and hemorrhage are not uncommon to see both grossly and microscopically. Histologic variability within the tumor includes areas resembling aneurismal bone cyst, areas of spindle, and foam cells. Thus, biopsy specimens should be carefully obtained to avoid tissue sampling error.

Imaging

MRI usually reveals a lesion that is iso- or hypointense to the spinal cord. GCTs contrast enhance heterogenously (Fig. 1) accentuating the extent of paraspinal and epidural disease. The tumor usually involves the vertebral body, but may extend to the posterior elements with an expansile, lytic, nonsclerotic appearance. Hemorrhage may occur, leaving cystic areas and heterogenous signals consistent with hemosiderin. Compression fractures may be observed with tumors at vertebral levels above the sacrum [6].

CT scans are useful in evaluating skeletal involvement and anatomy, particularly if surgery is contemplated, and in assessing for instability (Fig. 2). Following identification of the lesion, a CT-guided core biopsy is indicated. Needle biopsy should be avoided if GCT is suspected because sampling error with small needle samples may lead to erroneous diagnosis. Histopathological analysis reveals osteoclastic giant cells similar to those for Paget's disease of the bone (Fig. 3). A number of mononuclear cells are also seen with spindle cell stroma. GCT is a hypervascular lesion [5,6].

Treatment

The challenge in treating GCTs stems from their propensity for local recurrence. The Enneking system is often used for surgical staging of GCTs. These tumors are usually designated stage 3 aggressive benign lesions (Table 1). Thus, they are optimally treated by *en bloc* excision with wide margins. However, because GCTs can grow to

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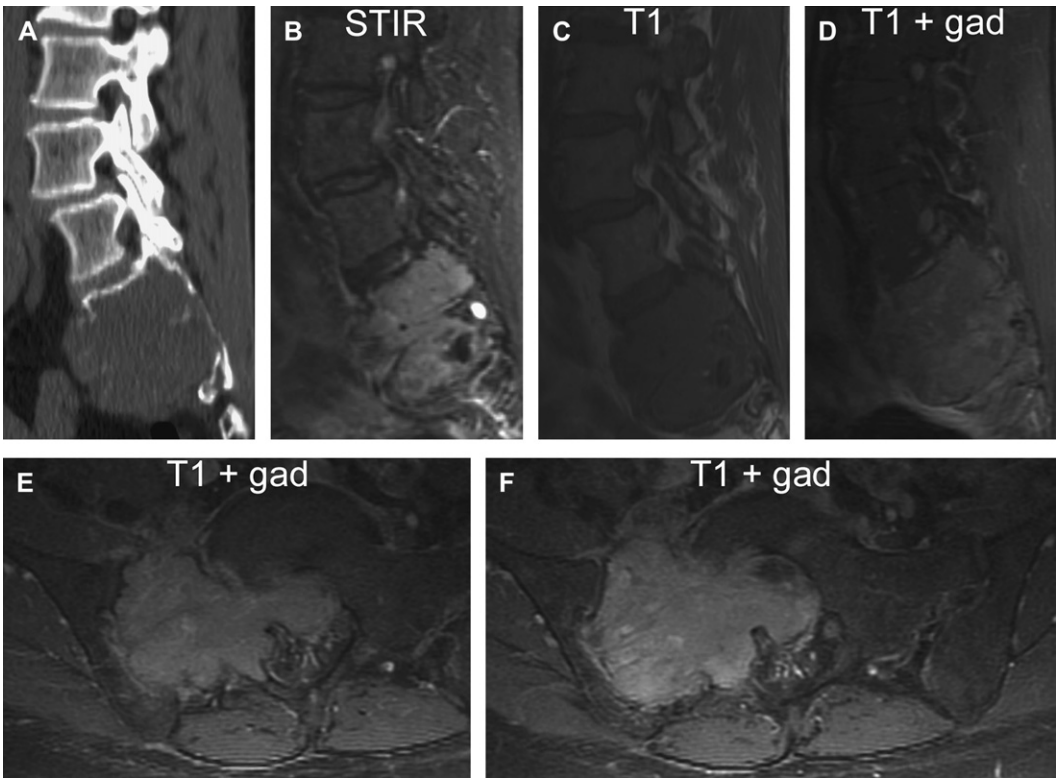

Fig. 1. (*A*) CT sagittal reconstruction and (*B–F*) MRI demonstrating a large, enhancing, slightly hypointense destructive mass of the sacrum. gad, gadolinium; STIR, short TI inversion recovery. (*Courtesy of* J. Chi, MD, MPH, Baltimore, MD.)

a large size before patients experience significant symptoms and because involvement of critical neurovascular structures is likely, *en bloc* or even gross total resection increases the possibility for morbidity compared with intralesional resection.

To this end, tumor embolization and radiation therapy, possibly in concert with subtotal resection, have been advocated as treatment options carrying potentially lower morbidity. A review of the literature with respect to treatment outcomes following tumor embolization and radiation therapy has been conducted, and compared with outcomes following gross total resection. Other alternatives including GCT treatment include cryosurgery, phenol, intra-arterial chemotherapy, laser ablation and polymethyl methacrylate injection are acknowledged but not discussed further [7,8]. Finally, resection of these tumors may create mechanical instability of the spine that requires at times extensive reconstruction with hardware, especially when the tumor involves sacral structures. For these reasons and due to the complex anatomy involved with sacral lesions, the surgical treatment may require a multidisciplinary approach among spinal surgeons and other surgical subspecialists.

Surgery

The extent of tumor resection was classified by Hart and colleagues [9] and can be divided into intralesional curettage and *en bloc* resection. *En bloc* resection can be further divided based on the extent of tumor resection into intralesional, marginal, and wide resection. Classically regarded as the gold standard for prevention of GCT recurrence, *en bloc* surgical removal provides the possibility for surgical cure, but increases the potential morbidity associated with surgery. The hypervascularity and large size of the lesion may lead to problematic intraoperative blood loss. Removal of extensive tumor presence in the vertebral bodies and sacrum is often difficult without a staged procedure, and generally leads to instability requiring instrumentation [2,4,10].

The risk of recurrence following an *en bloc* resection with wide margins of a GCT is small. Leggon and colleagues [4] conducted an extensive review of the literature to determine overall risk

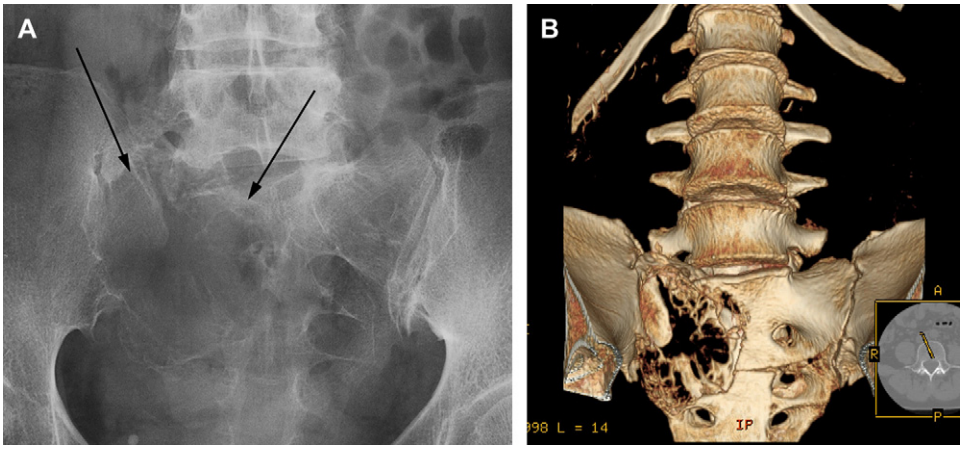

Fig. 2. (*A*) Plain radiograph and (*B*) three-dimensional CT reconstruction of a large sacral GCT. Arrows indicate location of tumor on radiograph. (*Courtesy of* J. Chi, MD, MPH, Baltimore, MD.)

of recurrence following treatment of GCTs of the sacrum and pelvis. In this series, 159 patients with sacral lesions who were treated with surgery, radiation, or surgery with radiation were reviewed at a mean follow-up of 7.8 years (Table 2). Of the 159 patients, 8 had *en bloc* excisions. None of these patients experienced tumor recurrence. There were no perioperative deaths in this subgroup. In 34 patients who underwent incomplete resection, there were 3 perioperative mortalities, highlighting the risk of surgery. This left a total of 31 patients for analysis who underwent incomplete resection without adjuvant treatment. Of those, 15 experienced tumor progression (49%). Specific morbidities and mean follow-up were not reported on all patients. However, a significant risk of neurological morbidity, primarily as a result of sacral instability and/or injury to sacral nerve roots leading to bowel, bladder, or sexual dysfunction, were reported [4,11].

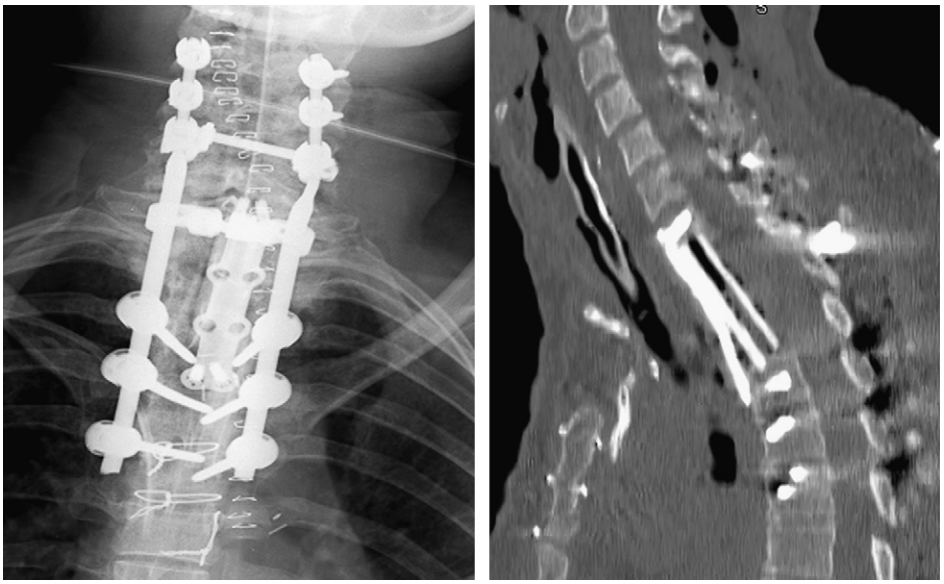

Fig. 3. Postoperative plain film and CT scan of a patient who underwent combined anterior–posterior resection and fusion of a GCT at the cervical–thoracic junction.

Table 1
Enneking surgical classification for benign bone tumors

Stage	Description	Site	Metastasis
1	Latent	T0	M0
2	Active	T0	M0
3	Aggressive	T1 or T2	M0 or M1

Following sacral resection, most investigators recommend stabilization of the pelvis in both an axial (below L5) and transverse (between the iliac bones) direction if the sacroiliac joint is compromised. Both vertical and rotational instability may result from failure to accomplish this union [11–13]. There are multiple methods to stabilize the pelvis. One method, for example, is to functionally replace the sacroiliac joint by iliac bars between the iliac bones. These bars are connected to lumbar rods for axial support. This is a staged reconstruction involving dissection of the rectosigmoid colon, iliac arteries, and potentially a diverting colostomy, and requires a multidisciplinary approach [11].

En bloc resection may also be difficult to achieve for GCTs located more rostrally in the spinal column. This is especially true of tumors involving the cervical spine, where proximity of the vertebral arteries and the important function of nerve roots often preclude complete tumor removal. Total spondylectomy has been advocated as a means to completely remove tumor [10,12,14]. Hart and colleagues [9] report that *en bloc* removal is more difficult and recurrence risk is higher if the tumor extends into the posterior elements or beyond osseous margins (eg, into the paraspinal muscles or canal).

In a series from the Mayo Clinic, Sanjay and colleagues [2] report attempted *en bloc* resection in 10 patients and intralesional resection in 14 patients with GCTs above the sacrum. Of 10 patients who underwent *en bloc* removal, 5 experienced tumor recurrence (50%). Of 14 patients who had documented intralesional margins, 5 experienced recurrence (38%). There were no perioperative deaths, and no neurological complications were reported. The authors recommend intralesional resection as a minimum for therapy for spinal GCTs. There are reports of 3 patients who underwent complete wide excision of cervical GCTs without tumor recurrence [12,15,16], whereas others report the difficulty of achieving *en bloc* resection of cervical GCTs [17,18]. Cases of confirmed *en bloc* resection of GCTs without recurrence are surprisingly uncommon when one considers the numerous treatment reports of GCTs in the literature. The challenge of achieving a wide resection of spinal GCTs underlines the importance of developing effective adjuvant therapy. However, based on the available data from the surgical literature and especially the review by Leggon and colleagues [4], it appears that *en bloc* resection with wide margins, with or without adjuvant treatment, offers the greatest chance of recurrence-free survival.

Radiation therapy

When *en bloc* resection of the tumor is unsafe and not feasible, radiation therapy has been commonly used as an adjunct to treatment. The results demonstrate a significant fall-off from the efficacy of *en bloc* resection. The recommended total radiation dose is typically 25 to 45 Gy using standard fractionated therapy [19]. In their meta-analysis of sacral GCTs, Leggon and colleagues' [4] analysis found 25 of 49 (51%) patients who underwent radiation therapy alone experienced tumor recurrence, and 35 of 71 (49%) patients who had incomplete resections and radiation treatment had recurrence. Sanjay and colleagues' [2] series on GCTs above the sacrum used radiation treatment for 6 patients who experienced recurrence following surgery and in 1 patient at the time of incomplete resection. Of these 7 patients, 2 (29%) experienced a second recurrence following radiation, and both died of disease. In a retrospective review from M.D. Anderson Cancer Institute, Caudell and colleagues [19] observed that 9 of 20 (45%) patients who underwent primary radiotherapy for spinal GCTs experienced local recurrence. An additional 2 patients in this series developed distant recurrence following radiation.

Similarly concerning is the long-term risk for developing malignant sarcomas secondary to radiation therapy for GCTs. Leggon and colleagues [4] found 10 of 95 (11%) patients who underwent radiation for sacral GCTs (and had at least a 5-year follow-up) developed a secondary malignant sarcoma. Nine of these patients died of this secondary disease. In the study from the Mayo Clinic, 1 patient (14%) developed a malignant sarcoma [2]. Two patients in the M.D. Anderson study (10%) developed secondary sarcomas 11 and 12 years following radiation treatment [19]. This risk is far from negligible and must be discussed with the patient in deciding whether to proceed with radiation [2,4,19].

Table 2
Outcomes from select series of spinal GCTs

			Treatment										
			En bloc		Intralesional resection		Radiation		Surgery/radiation		Embolization		
Investigators	Number of tumors	Tumor location	Number of tumors	Recurrences	Number of tumors	Recurrences	Number of tumors	Recurrences	Number of tumors	Recurrences	Number of tumors	Recurrences	Mean follow-up
Leggon, et al [4]	159	Sacrum	8	0	31	15 (49%)	49	25 (51%)	71	35 (49%)	0	Not applicable	7.8 y
Sanjay, et al [2]	24	Above sacrum	10	5 (50%)	13	5 (38%)	0	Not applicable	1	0	0	Not applicable	12.4 y
Caudell, et al [19]	20	Total spine	0	Not applicable	0	Not applicable	20	11 (55%)	0	Not applicable	0	Not applicable	8.8 y (median)
Hosalkar, et al [3]	9	Sacrum	0	Not applicable	0	Not applicable	0	Not applicable	0	Not applicable	9[a]	2 (22%)	9.0 y
Lin, et al [8]	18	Total spine	0	Not applicable	0	Not applicable	0	Not applicable	0	Not applicable	18	3 (17%)	8.8 y (median)

[a] Two patients following therapeutic embolization underwent radiation for recurrence.

Stereotactic radiosurgery (SRS), including image-guided intensity-modulated radiotherapy, has gained increasing importance in the treatment of primary spine tumors and metastases [20–24]. Tumors of the sacrum can also be effectively treated [25]. To our knowledge, there is one report of a patient with GCT who underwent postoperative SRS without complication [21]. This warrants further investigation because SRS has well-documented success in local control for primary and metastatic spine tumors.

Arterial embolization

Preoperative embolization. Spinal GCTs are highly vascularized lesions, and intraoperative blood loss is a well-recognized cause for operative morbidity. Blood loss is even more worrisome for those many patients who become destabilized during surgery and require instrumentation. Preoperative angiogram and embolization is therefore important in minimizing intraoperative hemorrhage and shortening operative time. An angiogram is also important for demonstrating patency of the vertebral arteries for tumors located in the cervical spine and for localizing the major radicular artery of Adamkiewicz for tumors of the low thoracic spine. If sacrifice of a vertebral artery is contemplated, a balloon occlusion test may be warranted to demonstrate a patent circle of Willis or adequate flow from the contralateral vertebral artery. Although no study to date critically evaluates the efficacy of embolization in reducing operative morbidity for GCTs, this technique is well accepted as safe and potentially efficacious in spine tumor management. This is the case for both primary tumors of the spine, including a small subset of reported GCTs, and metastatic lesions [26–28].

Therapeutic embolization. The efficacy of therapeutic embolization has been studied. Recently Hosalkar and colleagues [3] investigated therapeutic embolization as primary therapy in 9 patients with sacral GCTs. A range of three to seven embolizations was performed per patient, and 7 patients required no adjuvant radiation or surgical therapy for their lesions. Of the 2 patients who required additional treatment, 1 underwent radiation and had no tumor recurrence, whereas the other developed pulmonary metastases following radiation and ultimately died of disease. All 7 patients who underwent serial embolization alone remained progression-free at a mean of 8 years follow-up after diagnosis. Additionally, 2 patients showed tumor calcification (ie, reossification) at the periphery and decrease in tumor size. Lin and colleagues [8] previously presented 18 patients who underwent embolization. Kaplan-Meier analysis of their results showed a 31% risk of recurrence 10 years following treatment. Patients also experience symptomatic improvement following embolization [3]. The outcomes in these reviews suggest intra-arterial embolization may have utility in not only lowering perioperative morbidity, but also as a stand-alone front-line therapy for these lesions. Spinal angiography does carry risk: A case has been reported of paraplegia resulting from preoperative embolization of a thoracolumbar GCT [29]. Nonetheless, the benefit outweighs the risk, and we suggest angiography should be performed on newly diagnosed GCTs because these are tumors amenable to embolization.

Summary

As a result of their natural history and presentation, benign GCTs of the spine remain a challenge to treat. It is our recommendation that all suspected and biopsy-proven spinal GCTs undergo angiography for preoperative embolization and definition of vascular anatomy. *En bloc* resection with wide margins remains the goal for every patient diagnosed with a GCT. Patients with neurological deficits or bowel and bladder symptoms require decompression, although embolization and radiation have efficacy in halting neurological progression and treating pain. When complete resection is not possible, adjuvant radiation and potentially therapeutic embolization are effective in maintaining long-term recurrence rates of less than 50%. Finally, radiosurgery warrants further investigation in primary and adjuvant treatment of these locally aggressive benign lesions.

Acknowledgments

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