Primary Extradural Tumors of the Spine – Case Review with Evidence-guided Management

Fred C. Lam, Jeffrey E. Arle, Paul A. Glazer, Ekkehard M. Kasper

Departments of Neurosurgery, Orthopaedics, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

E-mail: Fred C. Lam - fredlam@mit.edu; Jeffrey E. Arle - jarle@bidmc.harvard.edu; Paul A. Glazer - pglazer@bidmc.harvard.edu; Ekkehard M. Kasper - ekasper@bidmc.harvard.edu

*Corresponding Author

Received: 26 April 14   Accepted: 21 June 14   Published: 28 August 14

Abstract

Background: Primary extradural tumors of the spine comprise only a small percentage of all spinal tumors. However, given their relative radioresistance and their typical malignant, invasive nature, surgery may be associated with fairly high morbidity and mortality rates. Furthermore, it may be especially difficult to achieve gross total resections with tumor-free margins.

Case Descriptions: We present two cases and review the literature regarding the presentation, diagnosis, and evidence-based guidance/treatment of primary extradural spinal tumors. The first patient with an L1 chordoma presented with cauda equina syndrome. Following surgery, the second patient, with a giant cell tumor of the cervicothoracic junction, responded well to the novel drug denosumab, a monoclonal antibody to the RANK ligand.

Conclusion: Primary extradural spine tumors pose significant challenges to surgeons as the aim is to achieve satisfactory surgical outcomes with clean tumor margins (e.g., thus avoid recurrence) while minimizing morbidity. Improvements in radiotherapy, chemotherapy, and novel molecular drugs may increase survival rates and improve overall outcomes.

Key Words: Chemotherapy, extradural, malignant, molecular drug treatments, primary, radiotherapy, spine, tumors

INTRODUCTION

Primary extradural tumors of the spine are rare and constitute approximately 4% of all spine tumors. Despite their rarity, these tumors can pose significant surgical challenges as their aggressive nature makes achieving a clean tumor margin difficult; this may be particularly complicated by the critical surrounding anatomy (e.g., nerve roots/spinal cord). Here we reviewed the literature and focus on two cases of primary extradural tumors: An L1 chordoma and a giant cell tumor (GCT) at the cervicothoracic junction.

Case 1 - L1 Chordoma
A 53-year-old male who presented with acute urinary incontinence and right leg numbness, exhibited saddle anesthesia, decreased rectal tone, and numbness in the right L2 distribution on physical examination. Sagittal T2-weighted magnetic resonance imaging (T2W MRI) of the lumbar spine showed a hypointense, nonenhancing intrasosseous lesion at L1 [Figure 1a], while the axial T1WI demonstrated an exophytic component compressing the cauda equina [Figure 1b]. The patient underwent an emergency L1 vertebrectomy with insertion of an expandable carbon fiber cage,
**Table 1: Summary of primary extradural spine tumors**

| Variables               | Benign                                                                 | Malignant                                                                 |
|-------------------------|------------------------------------------------------------------------|---------------------------------------------------------------------------|
| Tumor                   | Aneurysmal bone cyst (*)                                               | Chordoma                                                                  |
| Location                | Mainly posterior elements of the thoracolumbar spine, with extension into the vertebral body in 40% of cases | Over 50% of cases occur in the sacrum followed by the clivus (35%). One-sixth arise in the cervical, thoracic, and lumbar spine 1.4% of primary bony tumors |
| Frequency               | 15% of all primary spine tumors                                        | Cervical (20%); thoracic (20%); lumbar (20%); sacral (20%)                |
| Location                | Sacrum most common, then thoracic, cervical, and lumbar                | 10% of all bone tumors but rarely in the spine                             |
| Frequency               | 2.4% of all primary spine tumors                                       | Most commonly occurs at the sacrum                                         |
| Tumor                   | Hemangioma                                                             | Very rare to have primary spinal disease                                  |
| Location                | Most common in the thoracic and lumbar spine                          | Lymphoma                                                                  |
| Frequency               | Most common tumor of the spine, 12% incidence                          | Mostly involved the thoracic and lumbar spines                            |
| Tumor                   | Osteoblastoma (*)                                                     | Exceedingly rare, 1.7% of all primary bone lymphomas                      |
| Location                | Most common in the cervical spine, then in the sacrum                 | Osteosarcoma                                                              |
| Frequency               | 1.3% of all primary bone tumors                                        | Mostly in the sacrum                                                      |
| Tumor                   | Osteochondroma                                                        |                                                                         |
| Location                | About 60% located in the lumbar spine, cervical (27%), thoracic (12%), sacrum (2%) |                                                                         |
| Frequency               | Most common benign bone tumor (30-40%), 1.4% occur in the spine        | <5% of cases arise in the spine; comprise 3.6-14.5% of primary spinal tumors |
| Tumor                   | Osteoid osteoma                                                       | Plasmacytoma/multiple myeloma                                             |
| Location                | 50% of cases occur in the cervical spine, followed by thoracic region | Lower thoracic and lumbar spine                                           |
| Frequency               | 3% of all primary bone tumors, 10% occur in the spine                  | Most common primary tumor of the spine                                    |

(*): Aggressive benign tumors

followed by T11 to L3 pedicle screw instrumentation [Figure 1c and d]; postoperatively, this was followed by adjuvant radiotherapy. The patient has done well at one-year of follow-up at the time of manuscript preparation with no signs of disease recurrence.

**Case 2: Giant cell tumor of the cervicothoracic junction**

A 38-year-old female presented with several months of neck pain. On physical examination, she only demonstrated midline cervicothoracic tenderness; otherwise she was neurologically intact. Sagittal [Figure 2a] and axial [Figure 2b] T2W MRI of the spine demonstrated a large hyperintense lesion involving the T1 vertebral body with a hypointense rim associated with a large ventral soft tissue component. The patient underwent a staged circumferential surgical procedure first involving an anterior T1 corpectomy with strut graft placement and anterior plating, followed by a posterior instrumented fusion utilizing lateral mass screws from C5 to C7 and pedicle screws from T2 to T4 [Figure 2c]. Intraoperatively, hematoxylin and eosin staining showed a uniform distribution of osteoclast-like giant cells in a background of mononuclear cells consistent with the diagnosis of a GCT. Postoperative imaging confirmed a generous decompression of her spinal canal [Figure 2d]. Nevertheless, her residual disease involving the lateral masses warranted her enrollment in a clinical trial with denosumab, a monoclonal antibody to the RANK ligand. She tolerated the treatment well, and has not shown any signs of recurrence at 40 months follow-up at the time this manuscript was prepared.

**DISCUSSION**

**Chordomas**

Chordomas are slow growing, locally aggressive lesions that can occur anywhere along the axial skeleton, but are most commonly found at the craniovertebral junction and the sacrum. Sacral chordomas are often associated with large, exophytic soft tissue masses that can contribute to a neurogenic bladder and obstipation. En bloc resection of chordomas decreases local recurrence rate to 22% while intralesional surgery leads to 78% recurrence.

Conventional radiation therapy has little effect on chordomas, but may still be offered as palliation for subjective pain control and to delay the time to recurrence. Recent advances in radiation therapy have allowed for higher conformal doses of radiation to be applied to a focal area with sparing of critical adjacent structures: (e.g., combined photon/proton beam therapy - approximately 70-80 Gy may increase response to treatment; inverse modulation protocols using LINAC; hypofractionation protocols; and radiosurgery). The ability to achieve a wide en bloc resection offers the best prognosis and constitutes the only independent factor best avoiding tumor recurrence and tumor-related deaths. Furthermore, patients with primary disease treated with surgery and radiotherapy have better local disease control than those with recurrent disease, regardless of surgical margins achieved.

**Giant cell tumors**

GCTs comprise 5% of all adult primary bone tumors and occur most frequently at the epiphysseal–metaphysseal
junction of long bones. They most commonly involve the sacrum, followed by the cervical and thoracic regions. Although they are aggressive benign tumors, their size and vascularity make resection difficult; therefore, patients may require preoperative embolization to decrease intraoperative blood loss.

Surgical management of spine GCTs involving the thoracic and lumbar spine should include en bloc resection to decrease the rate of local recurrence. Intralesional resection can provide adequate control for Enneking stage II tumors. Cryotherapy, phenolization, and bone cement may be used as adjuvant treatments to wall off the resection cavity. Patients should be monitored for at least 5 years for disease recurrence. There is currently very low quality evidence supporting the role of radiation for treatment of recurrent GCTs. Although radiotherapy may be used as an adjunct to surgery to treat local recurrences, there have been no documented benefits of adjuvant radiation following surgical debulking of sacral GCTs; furthermore, this may increase the risk for radiation-induced sarcomas.

A recent clinical trial using denosumab, a monoclonal antibody to the RANK ligand to modulate osteoclast activation, showed a response rate of 86% and functional improvement with decreased pain in 84% of patients. Our patient was enrolled in this trial following her surgery for treatment of residual disease; she tolerated the therapy well with good response at 40 months follow-up.

Summary

Primary extradural spine tumors are rare, and there is little high quality evidence outlining the optimal treatment for these lesions. Trends in the literature support en bloc spondylectomy for low grade malignant tumors, but this aggressive approach proves technically challenging and may be associated with relatively high morbidity and mortality rates. Improvements in radiotherapy technology, advances in chemotherapy, novel molecular drug targets, and other multimodality protocols may increase survival rates.

REFERENCES

1. Almefty K, Pravdenkova S, Krish At. Skull Base Chordoma. Contemp Neurosurg 2008;30:1-6.
2. Boriani S, Bandiera S, Biagini R, Bacchini P, Boriani L, Cappuccio M, et al. Chordoma of the mobile spine: Fifty years of experience. Spine (Phila Pa 1976) 2006;31:493-503.
3. Boriani S, Bandiera S, Casadei R, Boriani L, Donthiini R, Gasbarrini A, et al. Giant cell tumor of the mobile spine: A review of 49 cases. Spine (Phila Pa 1976) 2012;37:E37-45.
4. Harrop JS, Schmidt MH, Boriani S, Shaffrey CI. Aggressive “benign” primary spine neoplasms: Osteoblastoma, aneurysmal bone cyst, and giant cell tumor. Spine (Phila Pa 1976) 2009;34 (22 Suppl):S39-47.
5. Kelley SP, Ashford RU, Rao AS, Dickson RA. Primary bone tumours of the spine: A 42-year survey from the Leeds Regional Bone Tumour Registry. Eur Spine J 2007;16:405-9.
6. Leggon RE, Zlotecki R, Reith J, Scarborough MT. Giant cell tumor of the pelvis and sacrum: 17 cases and analysis of the literature. Clin Orthop Relat Res 2004;423:196-207.
7. Noel G, Feuvret L, Calugaru V, Dhermain F, Mammar H, Haie-Meder C, et al. Chordomas of the base of the skull and upper cervical spine. One hundred patients irradiated by a 3D conformal technique combining photon and proton beams. Acta Oncol 2005;44:700-8.
8. Park L, Delaney TF, Liebsch NJ, Hornickel FJ, Goldberg S, Mankin H, et al. Sacral chondromas: Impact of high-dose proton/photon-beam radiation therapy combined with or without surgery for primary versus recurrent tumor. Int J Radiat Oncol Biol Phys 2006;65:1514-21.
9. Sundaresan N, Rosen G, Boriani S. Primary malignant tumors of the spine. Orthop Clin North Am 2009;40:21-36, v.
10. Thomas DM, Chawla S, Skubitz K, Staddon A, Henshaw R, Clay J, et al. Denosumab for the treatment of giant cell tumor (GCT) of bone: Final results from a proof-of-concept, phase II study. J Clin Oncol 2009;27:s15.