

VOLUME 10 NUMBER 11 NOVEMBER 2009

Osseous Spinal Tumors: Malignant Neoplasms

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LEARNING OBJECTIVES: After participating in this activity, the surgeon should be better able to:

- Describe the diagnostic work-up of primary malignant tumors of the osseous spine.
- Explain differential diagnosis of malignant osseous spinal lesions.
- 3. Recall the common treatment principles for malignant osseous spinal tumors.

Tumors of the osseous spine occur infrequently but nonetheless represent an important consideration in the patient presenting with back pain. Malignant neoplasms in the osseous spine have a different clinical course and treatment compared with typically benign neoplasms, which were described in the previous review.

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DEFINING DIAGNOSTIC FEATURES

A crucial clinical challenge lies in differentiating primary neoplasms of the spine from competing diagnoses that include metastatic disease, trauma, and infection. Whereas primary neoplasms are overwhelmingly solitary, multiple sites of involvement are typical of metastatic disease. Metastatic lesions are 30 times more common than primary tumors. Metastatic spread is exceedingly common, as it is estimated that 50%-70% of patients with carcinoma develop skeletal metastases before death (up to 85% of women with breast carcinoma).¹ A high index of suspicion is thus necessary in patients with systemic disease and/or a history of malignancy. Furthermore, vertebral collapse is characteristic of a pathologic as well as traumatic fracture. A soft tissue mass or calcification and a periosteal reaction that outdates a recent traumatic event should suggest neoplasm as the likely source. Pyogenic osteomyelitis also can present as a solitary spinal lesion that appears similar on initial x-rays; however, disc height is usually destroyed with infectious causes but preserved with neoplasm.

The following assessment will cover the common clinical features, radiographic findings, treatment, and clinical course of the most commonly encountered primary malignant neoplasms of the osseous spine (Table 1).

OSTEOSARCOMA

Osteosarcoma is the most common malignant tumor of bone after multiple

myeloma, but it is rare in the spineaccounting for just 1%-2% of all osteosarcomas and 4%-14% of all primary malignant tumors of the spine.² Patients with spinal osteosarcoma are older than those with tumor in the appendicular skeleton, with the peak incidence in the fourth decade of life. Women are more commonly affected than men. These tumors affect the vertebral body in 90% of cases, but extension into the posterior elements is also common.³ The cervical spine is rarely affected, as osteosarcoma occurs with proportionally higher frequency in the thoracic spine and sacrum.⁴ Patients often present with pain (either axial or radicular) and long-standing neurologic deficits. The nonspecific nature of symptoms often causes a delay in diagnosis (mean of 5 months, in one study).⁴ Serum alkaline phosphatase levels are frequently elevated.⁵ There is a common association between spinal osteosarcoma and both previous radiation therapy (with a 5-20-year latent period) and Paget's disease, linked with a more advanced age at onset (average, 67 years) and an especially poor prognosis.^{6,7}

On x-rays, osteosarcoma of the spine typically features an osteoblastic lesion with a dense mineralized matrix, although osteolytic or mixed lesions also occur.^{4,8} Other common findings include compression fractures, loss of vertebral height, and intervertebral disc sparing. Malignant invasion of the spinal canal is commonly seen on CT and MRI (Figure 1).

Osteosarcoma of the spine has an especially poor prognosis compared with

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osteosarcoma originating elsewhere, despite chemotherapy and radiation treatment.⁵ Contributing factors to this include the close proximity of the spinal cord from its origin in the vertebral bodies and the inability to achieve adequate surgical margins. En bloc resection with neoadjuvant chemotherapy has been advocated as the most effective current therapy for nonmetastatic lesions.^{9,10} Osteosarcomas are aggressive and relatively radioresistant tumors, which limits the effectiveness of radiation as a solitary agent.¹¹ However, radiation has been noted to provide some local control when used postoperatively after intralesional resection.⁴ Despite advances, death frequently occurs within the first year secondary to metastatic spread, and few patients live beyond 2 years after diagnosis.12,13

EWING'S SARCOMA

Ewing's sarcoma is a small, round, blue-cell tumor of unknown origin. It is especially common in children, in whom it is the most common nonproliferative primary malignant osseous tumor of the spine.^{14,15} The neoplasm is clinically and radiographically indistinguishable from a primitive neuroectodermal tumor. Genetically, Ewing's sarcoma has a characteristic chromosome 11:22 translocation as well as specific immunohistochemical staining for the antigen HBA-71. The sarcoma accounts for 10% of malignant muscu-



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Publisher: Marcia Serepy • Customer Service Manager: Audrey Dyson

Suscription rates: Personal \$298.98 US, \$403.98 Foreign. Institutional: \$432.98 US, \$558.98 Foreign. In-training: \$108.98 resident nonscored, \$114.98 Foreign. Single Copies \$23. GST Registration Number: 895524239.

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loskeletal tumors, and it frequently affects the spine via both primary growth and metastatic spread.³ The most frequent primary location is the sacrum (50%–70%), followed by the lumbar and thoracic spine.¹⁶ Lesions are typically centered on the vertebral bodies, but extension into the posterior elements is frequently seen. Patients typically present between 10 and 30 years of age with nonspecific pain and neurologic symptoms, although systemic symptoms such as fever can lead to an erroneous diagnosis of infection.^{9,17}

Radiographic findings for Ewing's sarcoma are variable. Diffuse sclerosis associated with osteonecrosis and reactive bone formation—is seen in up to 69% of spinal lesions; however, lytic lesions with a permeative or moth-eaten appearance also can be seen.² Bone destruction and extension into adjacent vertebral bodies and soft tissues is common, often with partial or total vertebral collapse.¹⁸ A soft tissue mass is also typically present. CT of the chest is imperative to stage for micrometasasis.⁹

Prognosis for Ewing's sarcoma is highly dependent on lesion location, although it has improved dramatically with aggressive surgical resection, chemotherapy, and radiation treatment. If spinal compression is present, urgent decompressive surgery is warranted. Otherwise, systemic chemotherapy should be the initial treatment for Ewing's sarcoma.¹⁹ Considerable debate exists as to the preferred method for local control (radiation versus surgery). In contrast to osteosarcoma, Ewing's sarcoma is radiosensitive. Radiation after chemotherapy is commonly considered the preferred therapeutic course;⁹ however, improvements in en bloc resection have made surgical resection an alternative option to achieve local control. The 5-year survival rate associated with Ewing's sarcoma has been variously reported from 48%-58%.8

CHORDOMA

Chordomas arise from the embryonic notochord and represent the most common primary nonlymphoproliferative malignant bone tumors of the spine in adults.^{20,21} Although they occur throughout the neural axis, they arise most often in the sacrococcygeal region or in the cervical spine, particularly the C2 region.²² Chordomas occur most often in patients older than 40 years, with a male predominance. These lesions are typically slow-growing, invasive lesions that rarely metastasize, thereby accounting for the gradual onset of symptoms. Nonspecific back pain is the most common presenting feature of sacral lesions, although 40% also describe symptoms of rectal dysfunction such as constipation, tenesmus, or rectal bleeding. A palpable tumor on digital rectal examination is a reliable finding.^{9,23} In patients with lesions elsewhere on the spine, symptoms are recognized sooner. Neck/back pain with a radicular component and shoulder weakness are most commonly found with cervical lesions.22

On plain x-rays, chordomas appear as destructive lesions, frequently with a soft tissue mass (70% of cases). Lesions are typically midline in either the sacrum or the vertebral body.^{21,24} Calcification and areas of sclerosis are common. CT shows both the osseous and soft-tissue components, providing detail on neuroforaminal involvement. Lesion mineralization occurs on the peripherv in an amorphous pattern.² MRI represents the preferred modality for visualization of the tumor along tissue planes, with low-intermediate signal intensity on T1-weighted images and high signal intensity on T2-weighted images.²⁵ Grossly, chordomas are lobular, gray, glistening, cystic masses that resemble mucin-producing carcinoma. Histopathologic analysis is notable for long cords of physaliphorous (soap bubble) cells, which are pathognomonic for chordoma.⁹

Complete en bloc resection is the preferred treatment for a patient with chordoma when achievable. The surgical approach should be staged, involving either a posterior sacrectomy or a combined anterior-posterior approach.9 Prognosis is dependent on complete resection, which may be difficult to achieve given the difficulty of removing lesions with extensive sacral involvement.²⁶ If complete resection is impossible, marginal excision along the pseudocapsule combined with postoperative radiotherapy, brachytherapy, and proton-beam treatment have been used

Tumor	Nature	Location	Level	l Frequency	Peak Age (years)	Sex	Common Presentation	lmaging Findings	Treatment
Osteosarcoma	Malignant		S, T>L, C	4%–14% of primary malignant osseous spine lesions	20–40	F>M	Pain, neurologic deficits (long-standing) palpable mass	Osteoblastic and osteolytic areas	En bloc resection w/neoadjuvant chemotherapy; radiation w/intralesional resection
Ewing's sarcoma	Malignant	Sacrum; vertebral body ± posterior element extension	S>L, T	Most common primary malignant osseous spine tumor in children	10–30	M=F	Pain, neurologic deficits	Sclerosis>lytic appearance; destruction of vertebral body, soft tissue extension on CT/MRI	Systemic chemotherapy + radiation/ surgery for loca control
Chordoma	Malignant	Sacrum, posterior elements with paraspinal soft tissue extension	S>C, L, T	Most common overall primary malignant osseous spine tumor	>40	M>F	Pain, rectal symptoms, soft-tissue mass	Lytic lesion with areas of calcification; paravertebral soft tissue mass; foraminal enlargement	En bloc resection w/postoperative radiotherapy, brachytherapy, proton-beam treatment; imatinib emerging
Chondrosarcoma	Malignant	Posterior elements ± vertebral body extension	T>L>C, S	Rare in spine	30–50	M>F	Pain, neurologic deficits	"Arcs and rings" calcification; osseous destruction; soft tissue expansion ± spinal cord distortion	Resection; chemotherapy, particle beam treatment
Multiple myeloma	Malignant	Vertebral bodies	T, L	Second most common hematologi malignancy		M>F	Bone pain, instability, radiculopathy, anemia, infection	Localized osteolytic lesions w/o marginal sclerosis; pathologic fractures; osteoporosis	Bisphosphonates; kyphoplasty/ vertebroplasty; surgical resection (instability); radiation; chemotherapy



Fig. 1 T2-weighted MRI scan showing telengiactic osteosarcoma in a 45-year-old man who was misdiagnosed initially as having an aneurysmal bone cyst. An axial slice demonstrates a mixed lesion featuring osteoblastic and osteolytic regions, with invasion of the spinal cord. (Image courtesy of Kern Singh, MD.)

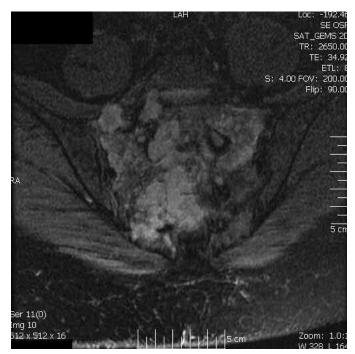


Fig. 2 T2-weighted MRI scan showing chondrosarcoma in a 47year-old woman. Coronal slice demonstrates complete infiltration of the sacrum. (Image courtesy of Kern Singh, MD.)

with varying results. Chordomas are resistant to chemotherapy, and conventional external irradiation is associated with a high recurrence rate. Chordomas have been responsive to molecular targeted agents such as imatinib (Gleevec, Novartis), which represent an emerging therapeutic option for the future. The 5-year disease-free survival rate is approximately 65% (with many late failures), and the only treatment protocol associated with improved survival is complete en bloc resection.^{9,27}

CHONDROSARCOMA

Chondrosarcoma accounts for approximately 10% of bone tumors, although it rarely originates in the spine.⁹ It is a malignant tumor with neoplastic tissue that features developed cartilage in a myxoid matrix with increased cellularity, nuclear atypia, and permeation of bone trabeculae.²⁸ Men are at higher risk than women, and the mean age of presentation is 45 years. Lesions can originate in either the posterior elements or the vertebral body of any spinal level, with the thoracic spine affected most frequently (60%).²⁹ Patients typically present with nonspecific back pain, and as many as 50% are affected by a neurologic deficit at the time of diagnosis.²⁹ Lesions are typically slowgrowing, and size larger than 8–10 cm supports the diagnosis of malignancy.⁹ Chondrosarcomas can arise de novo or undergo sarcomatous transformation from a previous benign neoplasm, often after unsuccessful attempts at surgical removal.

Typical radiographic findings for chondrosarcomas demonstrate a lytic, destructive lesion producing destruction of either the posterior elements (40%) or both the posterior elements and the vertebral body (45%).³⁰ Formation of the characteristic flocculent and "arcs and rings" calcification pattern from mineralization can be seen in 70% of x-rays.² CT can visualize the integrity of the cortex and the configuration of calcification within the tumor. MRI demonstrates the lobulated contour typical of the cartilaginous neoplasm and spinal cord distortion, with a hypointense lesion on T1-weighted images and hyperintense lesion on T2-weighted images (Figures 2 and 3).

The mainstay of treatment for chondrosarcomas is complete surgical excision.^{31,32} Tumor location within the axial skeleton, however, often precludes complete removal. Chondrosarcomas are largely resistant to chemotherapy, although recent use of particle beam therapy and high-dose radiotherapy may slow tumor progression.⁹ With incomplete excision, recurrence is frequent.³² One series noted a cure rate of only 26% after complete en bloc resection³⁰ (Figures 4 and 5).

MULTIPLE MYELOMA-PLASMACYTOMA

Multiple myeloma and plasmacytoma are malignancies of plasma cells that represent two manifestations along a continuum of B-cell lymphoproliferative diseases. Although they are often considered systemic diseases, the presence of bone marrow lesions in the spine merits their inclusion in this review. Multiple myeloma is the second most common hematologic cancer after non-Hodgkin's lymphoma, representing 10% of all hematologic malignancies.³³ Diagnosis is based on meeting several major and minor criteria, which include lytic lesions on x-ray, M protein in the urine/blood, low antibody levels, and greater than 10% plasma cells on bone marrow biopsy (from multiple sites).³⁴ In contrast, diagnosis of plasmacytoma involves only plasma cell dvscrasia at



Fig. 3 T2-weighted MRI scan of the patient shown in Figure 2. Sagittal slice shows a lobulated mass of mixed intensity in the sacrum, with spinal cord invasion. (Image courtesy of Kern Singh, MD.)



Fig. 4 Sacrectomy for chondrosarcoma of the patient shown in Figures 2 and 3. Complete excision can include a total sacrectomy, as seen in a pathologic sample. (Image courtesy of Kern Singh, MD.)

a single site.³³ Musculoskeletal symptoms are the most common presenting symptoms: 70% of patients report bone pain, and 50% are found to have compression fractures.³⁵ Radiculopathy from nerve root invasion is another common symptom. Spine is the most commonly affected skeletal organ, with vertebral bodies affected in 66% of cases.³⁶ The lower-thoracic and upper-lumbar vertebral levels are the most frequent targets.

Solitary plasmacytoma represents the solitary form of multiple myeloma, comprising 3%–7% of all plasma-cell neo-

plasms.³⁷ Some debate exists regarding whether plasmacytoma might represent an early stage of multiple myeloma as opposed to a distinct clinical entity. It is known that patients with plasmacytoma frequently develop multiple myeloma, although the time frame is variable, with some cases developing more than 20 years after the initial manifestations. Owing to the rarity of the disease, its clinical course is largely uncertain.³⁸ Compared with multiple myeloma, plasmacytoma more commonly affects younger patients with a male predominance, and only two-thirds of patients demonstrate paraprotein production.³⁷

Classic radiographic features include compression fractures, localized osteolytic lesions without reactive marginal sclerosis, and a reduction in bone density. A complete skeletal survey should be issued if the diagnosis of multiple myeloma or plasmacytoma is considered, although up to 20% of patients with multiple myeloma will have no lesions.³⁹ CT and MRI offer improved visualization of the extent of bony involvement, spinal deformity, and spinal cord or nerve root compromise. MRI findings initially are nonspecific, with hypointense to normal marrow on T1-weighted images and hyperintense signal on T2-weighted images. With disease advancement, multiple foci of cortical destruction with soft tissue invasion become evident.³⁶

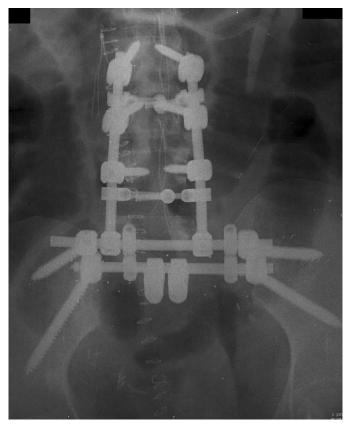


Fig. 5 Postoperative anteroposterior x-ray of the patient shown in Figures 2–4, showing instrumentation placement in the ilium with double-bolt fixation and proximal fixation into the lumbar spine. The sacrum is reconstituted with a carbon fiber cage spanning from ilium to ilium. (Image courtesy of Kern Singh, MD.)

Management of patients with multiple myeloma or plasmacytoma is multifaceted and tailored to the patient's initial presentation. Conservative treatment includes the use of bisphosphonates, which have been shown to reduce skeletal-related events.⁴⁰ In younger patients, the ultimate goal in most cases is definitive therapy with high-dose chemotherapy and hematopoietic stem cell transplantation, if possible.⁴¹ Radiation therapy is frequently used as adjuvant therapy postresection or palliative therapy due to the disease's radiosensitivity. If spinal cord or nerve root compression exists, surgical decompression with stabilization may be indicated. A substantial portion of patients with myeloma develops pain from segmental instability and compression fractures, for which recent advances in kyphoplasty/vertebroplasty have succeeded in reducing pain and providing stability.⁹ Prognosis is poor for both malignancies but improved for plasmacytoma; in some cases, local radiotherapy can result in long-term cure.42 The median survival period for patients harboring a solitary plasmacytoma exceeds 60 months, but in patients with multiple myeloma, the survival period is just 28 months.³⁴ Serum and urine protein electrophoresis should be performed to follow tumor burden. Treatment methods are evolving, including the role of spinal radiosurgery and the use of innovative agents such thalidomide/dexamethasone, proteasome inhibitors, and RANK ligand inhibitors.³

CONCLUSION

Familiarity with the basic characteristics of primary malignant tumors of the spine is critical, given the large number of patients that experience back pain and the necessity for timely clinical action in the event of malignancy. We reviewed the basic findings in this broad spectrum of disease to provide a basis for appropriate management. Treatment methods are evolving, and they should be individualized to the patient.

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- **1.** The most common nonproliferative malignant tumor of the osseous spine in children is
 - A. chordoma
 - B. osteosarcoma
 - C. Ewing's sarcoma
 - D. multiple myeloma
- 2. A 30-year-old man with a history of hemangiomas and multiple bony lesions presents with gradual onset of neck pain and palpable mass. Treatment should consist of
 - A. en bloc resection
 - B. chemotherapy
 - C. radiation
 - D. bisphosphate
- 3. Among spinal tumors, all of the following occur commonly in the sacrum, *except*
 - A. chordoma
 - B. chondrosarcoma
 - C. osteosarcoma
 - D. Ewing's sarcoma
- **4.** In which one of the following tumors does radiation play the most integral role?
 - A. Osteosarcoma
 - B. Chondrosarcoma
 - C. Chordoma
 - D. Ewing's sarcoma

- 5. A 50-year-old man presents with a 4-month history of progressive back pain without radiculopathy. X-rays reveal a lytic lesion with a calcification pattern consisting of "arcs and rings" in the posterior elements of the thoracic spine, at the T10 level. The most likely diagnosis is
 - A. chordoma
 - B. chondrosarcoma
 - C. osteosarcoma
 - D. Ewing's sarcoma
- 6. Typical radiographic findings for osteosarcoma include
 - A. loss of vertebral height
 - B. intervertebral disc sparing
 - C. an osteoblastic or osteolytic lesion
 - D. all of the above
- 7. A 70-year-old man presents with neurogenic claudication and a history of vague joint pain. Laboratory studies demonstrate extremely high levels of alkaline phosphatase. X-rays demonstrate a mixed lytic/ blastic mass in the lumbar spine and thickness of trabeculae and cortices in the hips. The spinal lesion is likely
 - A. multiple myeloma
 - B. osteosarcoma
 - C. chondrosarcoma
 - D. hemangioma

- 8. Imatinib (Gleevec) has emerged as a promising therapy in the treatment of
 - A. chordoma
 - B. chondrosarcoma
 - C. Ewing's sarcoma
 - D. multiple myeloma
- **9.** A patient presents with renal failure and lytic lesions in the bone. A bone scan is cold. Initial treatment should consist of A. nonsteroidal anti-inflammatory drugs
 - B. bisphosphonates
 - C. chemotherapy
 - D. local radiation
- **10.** A CT scan is helpful in the management of Ewing's sarcoma to assess for
 - A. metastatic spread to the chest
 - B. a soft tissue mass
 - C. primary skeletal lesions
 - D. all of the above