Diagnosis and Treatment of Vertebral Column Metastases

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The vertebral column is recognized as the most common site for bony metastases in patients with systemic malignancy. Patients with metastatic spinal tumors may present with pain, neurologic deficit, or both. Some tumors are asymptomatic and are detected during screening examinations. Treatment options include medical therapy, surgery, and radiation. However, diversity of patient condition, tumor pathology, and anatomical extent of disease complicate broad generalizations for treatment. Historically, surgery was considered the most appropriate initial therapy in patients with spinal metastasis with the goal of eradication of gross disease. However, such an aggressive approach has not been practical for many patients. Now, operative intervention is often palliative, with pain control and maintenance of function and stability the major goals. Surgery is reserved for neurologic compromise, radiation failure, spinal instability, or uncertain diagnosis. Recent literature has revealed that surgical outcomes have improved with advances in surgical technique, including refinement of anterior, lateral, posterolateral, and various approaches to the anterior spine, where most metastatic disease is located. We review these surgical approaches for which a team of surgeons often is needed, including neurosurgeons and orthopedic, general, vascular, and thoracic surgeons. Overall, a multimodality approach is useful in caring for these patients. It is important that clinicians are aware of the various therapeutic options and their indications. The optimal treatment of individual patients with spinal metastases should include consideration of their neurologic status, anatomical extent of disease, general health, age, and quality of life.


ANATOMICAL LOCALIZATION AND PATHOPHYSIOLOGY

Spinal metastases can occur in 3 locations: extradural, intradural extramedullary (IDEM), and intramedullary (IM). More than 98% of spinal metastases are extradural because the dura mater provides a relative barrier for metastatic disease; IDEM and IM disease account for less than 1% of spinal metastatic disease.6-10 Both IDEM and IM disease most commonly originate from drop metastases in the setting of patients with either primary or metastatic brain disease. This review focuses on extradural metastases.

Paralleling vertebral body size, metastases occur most frequently in the lumbar spine followed by the thoracic and then the cervical spine.31 However, thoracic lesions (70%) are most often symptomatic due to the smaller space available for the spinal cord in this region, followed by lumbar (20%) and cervical (10%) lesions.3,12 Eighty percent of spinal metastases involve vertebral bodies rather than posterior vertebral elements.13 Extradural metastases are believed to occur through 3 mechanisms: (1) direct local extension into the extradural space, (2) retrograde spread through the valveless extradural venous channels of the spine (Batson plexus), and (3) arterial emboli with subsequent spread through cortical veins.14,15

PRESENTATION

The presentation of bony metastases includes bony pain, pathologic fracture, radiculopathy, myelopathy, and progressive deformity. Spinal cord compression can occur from fracture, tumor invasion, or progressive osteoblastic remodeling.16 Among patients with spinal cord compression, 90% present with pain and 47% present with neurologic symptoms.17-19 Symptomatic spinal cord compression occurs in 8.5% to 20% of patients with vertebral column metastases.20,21 Radiculopathy secondary to posterior element involvement and subsequent nerve root impingement also can occur. Only 11% to 34% of patients presenting with spinal cord compression are ambulatory at diagnosis.22 Sensory loss occurs in 70% to 80%, paraparesis or
paraplegia in more than 60%, and bowel and/or bladder difficulty in 14% to 77%. Simple neurologic grading scales similar to that of Brice and McKissock or the Karnofsky scale allow clinicians to communicate clearly and to assess clinical outcome (Table 1).

### DIAGNOSIS

Initial evaluation should begin with a detailed medical history, clinical examination, and directed laboratory tests. Preoperative assessment and documentation of bowel/bladder function, motor weakness, and sensory deficits are critical to postoperative outcome assessment. Determination of general health and nutritional status is essential in the preoperative assessment of the patient with cancer because both affect healing and infection risk. Laboratory studies should include the following: complete blood cell count, creatinine, electrolytes, liver function, albumin, prealbumin, amylase, lipase, and coagulation. Electrolyte imbalance, coagulopathy, and neutropenia should be corrected. Nutritional optimization should be pursued in patients with malnutrition. Ultrasonography and computed tomography (CT) of both the abdomen and chest may be helpful for localizing primary neoplasms.

The imaging armamentarium available to the clinician includes plain radiography, CT, magnetic resonance imaging (MRI), myelography, radionuclide bone scan (BS), single-photon emission CT (SPECT), and positron emission tomography (PET). In the setting of complete subarachnoid block, myelography may increase the risk of neurologic deterioration. Therefore, it is used most often in patients who cannot undergo MRI because of implanted devices or foreign bodies. More than 85% of patients have multiple-level involvement if results from MRI, CT, plain radiography, and surgery are pooled. Plain radiography, CT, and MRI comprise the core imaging modalities for patients with vertebral metastases.

Plain radiography is useful and should be obtained for most patients. Common findings on plain radiography include vertebral body collapse, pedicle erosion, osteoblastic and osteolytic lesions, and pathologic fracture-dislocation. The disk margins usually are spared in contrast to marked disk destruction seen in infectious processes. Bone destruction and substantial sclerosis are reliable indicators of metastases. However, vertebral body collapse can be associated with nonneoplastic lesions in up to 22% of cases. To be visible on plain radiography, 30% to 40% of the bone must be eroded; therefore, lesions can be missed on plain radiography alone. However, about 90% of patients with symptomatic disease have abnormal findings on plain radiography.

Contrast-enhanced MRI of the entire spinal axis is the current standard for the diagnosis and evaluation of spinal column metastases. Misleading sensory levels in up to 26% of patients, multiple levels of asymptomatic disease, and the large amount of bone destruction necessary to visualize metastases on plain radiography necessitate liberal use of MRI, often of the complete spinal axis. With its superior delineation of soft tissue, MRI provides unparalleled imaging of paraspinal and epidural masses, multi-level distortion of cerebrospinal fluid (CSF) spaces, and occult metastases. However, MRI is second to CT in imaging of the bony anatomy of the spine.

Tailored CT with sagittal, coronal, and 3-dimensional reconstruction provides excellent detail of the bony anatomy of the spine, essential to both preoperative and intraoperative surgical planning and postoperative evaluations. Also, CT angiography can visualize the vertebral arteries in the foramen transversarium and as they enter the cranium, which assists surgical decision making and patient safety. The patient avoids the risk of conventional angiography. The angulation, rotation, and overall instability of a fracture; the extent of erosion of the vertebral body, pedicles, and posterior elements; and the degree of osteoblastic canal compromise are well visualized on CT.

Other imaging modalities include radionuclide BS, SPECT, and PET, which are available at multiple institutions. Although BS is the oldest technique, almost 50% of its results are false-negative for bone metastases. Also, BS does not accurately distinguish between pathologic and nonpathologic fractures. A recent comparison of BS, SPECT, and PET with fluorodeoxyglucose F 18 found that PET with fluorodeoxyglucose F 18 was as accurate as MRI. However, because of limited availability and resources, SPECT and PET are not part of the standard evaluation.

Either needle or open biopsy can be used to obtain tissue for diagnosis. With serial lumbar taps, CSF cytology results are positive in up to 90% of patients with leptomeningeal carcinomatosis. In patients with an unknown primary neoplasm, CT-guided needle biopsy is a safe and easily performed procedure with a 70% to 95% chance of yielding a pathologic diagnosis. In patients with compressive and/or unstable lesions, progressive neurologic deficit, and nondiagnostic needle biopsies, open biopsy or surgical excision usually is needed. Preoperative angiography...
TREATMENT OF SPINAL METASTASES

Treatment options available for metastatic disease of the spine include medical therapy, surgery, and radiation. Operative intervention is most often palliative with pain control, maintenance of neurologic function, and spinal stability as primary goals. For years, many considered surgery the best initial therapy, with the goal of gross total resection. Realistically, such an aggressive approach requires en bloc resection, which is not feasible in most patients. This is because spinal cord or vital neural elements commonly locate within the margin of the tumor. Laminectomy, the most common procedure, has a poor track record in recent studies, in large part due to the usual location of spinal metastatic disease in the anterior components of the spine, which is inaccessible via laminectomy. Subsequently, radiation therapy has become the most common treatment, with surgery reserved for salvage or adjuvant therapy. With advances in surgical technique and surgical thinking including refinement of anterior and lateral approaches to the anterior spine, the location of most spine metastases, surgical outcomes have improved. Patchell et al showed that patients with spinal cord compressions treated with radical direct decompressive surgery plus postoperative radiotherapy survived longer and regained the ability to walk more often than patients treated with radiation alone. With these refinements, a team of surgeons including neurosurgeons and orthopedic, general, vascular, and thoracic surgeons is often needed to access, decompress, and reconstruct the spine. In summary, treatment of individual patients with spinal metastases should include consideration of neurologic status, general health, age, anatomical extent of disease, and the relative sensitivity of the tumor to radiotherapy and chemotherapy.

The mean postoperative survival of patients with symptomatic spinal metastases ranges from 10 to 16.5 months, according to previous studies. The patient’s life expectancy needs to be considered before such extensive surgery is performed.

CORTICOSTEROIDS AND BISPHOSPHONATES

Although the mechanism for improvement is not understood fully, intravenous or oral corticosteroid use often leads to improvement or resolution of neurologic symptoms and pain in patients with epidural spinal metastases. Decrease in reactive vasogenic edema in the spinal cord and nerve roots has been shown experimentally. There is no standard dosage regimen. It has been our practice either to start with 10 mg of dexamethasone and then taper to 4 mg 4 times daily, or to use the spinal cord injury protocol of a 30 mg/kg bolus followed by 5.4 mg/kg of methylprednisolone for 23 hours before surgery.

Bisphosphonates are assuming a greater role in the treatment of bony metastatic disease in the spine and axial limbs. By preventing osteoclastic resorption of bone, these pharmaceuticals help with both cancer pain and prevention of fracture. Their potential to delay bony metastatic disease is intriguing. Patients with breast cancer, prostate cancer, and multiple myeloma all have shown benefit.

VERTEBRAL AUGMENTATION

In patients with painful metastases without epidural compression, minimally invasive surgical techniques are now available to help alleviate their pain. Vertebroplasty, the injection of methylmethacrylate into the compression fracture, and kyphoplasty, the injection of methylmethacrylate into a balloon inflated in the vertebral body, are performed increasingly in patients with epidural metastatic lesions with good pain relief. Most of these procedures are performed under biplane fluoroscopy; however, they can be used as intraoperative adjuvants to bolster fusions or to treat painful levels without epidural compression. Kyphoplasty in selected patients can lead to restoration of vertebral body height. More than 80% of patients experience significant pain relief, leading to greater mobilization. Major complications include extravasation of contrast into the canal with nerve root or spinal cord compression and leakage of cement into large venous fistulas, leading to pulmonary embolus. The latter can be minimized with preinjection venography and potentially plugging of the fistula with absorbable gelatin sponge. The overall complication rate for both vertebroplasty and kyphoplasty is less than 10%. Vertebra plana fractures and extensive epidural compression are the main contraindications.

RADIATION

External beam radiation is an effective treatment for many patients with radiation-sensitive tumors including hematopoietic, prostate, and germ cell malignancies. In radiosensitive lesions, radiation therapy alone can be successful in more than 80% of patients. Overall, with radiation, more than 30% of patients experience neurologic improvement from epidural compression, and more than 60% gain significant pain relief. A typical dose is 30 Gy in 10 fractions. Nausea, vomiting, and radiation-induced esophagitis are common. Delayed radiation myelopathy can occur but is rare with modern treatment paradigms. Radiation therapy usually is recommended postoperatively in patients with radiosensitive tumors in whom gross or microscopic disease remains after surgery.
VERTEBRAL COLUMN METASTASES

Stereotactic radiosurgery has substantially enhanced treatment of patients with intracranial metastases. New stereotactic systems have been designed that can target lesions in the body and spine. Pain relief and actual shrinkage of epidural tumors with improved neurologic function have been documented in some series. Dosing plans and appropriate patient selection are still not defined.

SURGICAL TREATMENT
The need to access the spine to obtain a diagnosis, to decompress neural elements, or to stabilize and/or reconstruct the spine are indications for surgery. The goals of surgery are to decrease pain, to preserve or to improve neurologic function, and to mobilize the patient without lifelong external orthosis. Many surgical strategies are used...
approximately 10% to 20% through the posterior joints. Although most tumors involve the middle and anterior columns, anterior reconstruction alone may be insufficient for restoring torsional stability or tensile strength because the pedicles and joint may be involved. After radical resection of a metastatic spinal tumor, anterior constructs may be supplemented by posterior fixation.

Because most metastatic disease involves the vertebral bodies and pedicles, it seems that all patients would require anteroposterior fixation. However, clinical experience has found that such extensive surgery is often unnecessary. The rationale for surgery should be based not only on biomechanical considerations but also on the expected goals of therapy and the longevity of the patient. Extensive surgery is rarely justified in patients with limited survival. Elderly, debilitated patients with impaired immune function, poor nutritional status, and low bone marrow reserve are at a much higher risk of mortality and morbidity, regardless of surgical approach.

Emergency surgery is mandated in the setting of rapidly progressive or advanced paraplegia or tetraplegia. Severe and irreversible spinal cord injury will result without prompt decompression of the thecal sac and nerve roots. Surgical decompression is not likely to reverse complete paralysis with a duration greater than 24 hours.

Several attempts have been made to identify clinical prognosticators in cases of spinal metastatic disease. Yamashita et al reported longer survival in patients with spinal or pelvic lesions compared with those with appendicular lesions or both. Tokuhashi et al proposed a scoring system using 6 parameters to determine survival after surgery for metastatic spinal tumors: general condition, number of vertebral metastases, number of metastases to internal organs, number of metastases to extraspinal bone, primary site, and severity of spinal cord injury. Each parameter was given a score of 0 to 2. Although no individual parameter was predictive, summed scores correlated with survival periods. Scores of 9 or higher were predictive of
survival of at least 12 months; scores of 5 or less were predictive of survival of less than 3 months. The authors suggested that patients with scores of 9 or higher undergo surgery with the primary goal of excision, whereas for those with scores of 5 or less, palliation is the goal. Other studies have corroborated the work of Yamashita et al but also have found that ambulatory status, age less than 60 years, and single vertebral segment involvement were independent predictors of good outcome.48,49,67,68 Weigel et al49 showed statistically significant correlation between the postoperative Karnofsky scale and duration of survival. Ambulatory status is influenced by multiple factors including neural compression, pain, and general systemic condition; thus, the initial consideration of a patient for operative management of spinal epidural disease should be multifactorial.

**Posterior Approaches.** Traditionally, decompressive laminectomy has been used to relieve compression of the spinal cord, cauda equina and nerve roots and is performed easily in the cervical, thoracic, and lumbar spine. The approach has undergone review and was revealed to be beneficial in only 40% of patients.69,70 In studies comparing combined radiotherapy and laminectomy with laminectomy alone, authors found no significant difference in outcome.71,72 In a large series, Bach et al73 reported improvement rates of 46% in patients who underwent laminectomy, 35% in patients who underwent radiation, and 59% in patients who underwent combined laminectomy and radiation. Other large series have corroborated these data with improved outcomes from laminectomy alone ranging from 38% to 50%.69,74 Schoeggl et al75 especially analyzed bladder/bowel dysfunction in patients who underwent decompressive laminectomy with partial or total tumor removal. Among their patients, 56% experienced bladder or bowel dysfunction preoperatively. In total, 18% of patients reported improvement postoperatively, although none who required preoperative catheterization showed improvement.

The mediocre outcomes of laminectomy are not surprising because pure posterior lesions are uncommon and the procedure does not adequately decompress the ventral spinal cord. The failure to individualize surgical approach based on tumor location has contributed to the failure of this traditional procedure.76 Major limitations of laminectomy are inadequate access to the anterior aspect of the

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**FIGURE 5.** Positioning of the patient, skin incision line, and exposure of the thoracic vertebral bodies for the anterior transthoracic approach.

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**FIGURE 6.** A 67-year-old man with a history of hyperthyroidism and coronary artery disease presented with sudden onset of interscapular back pain and gait disturbance. The patient had upper motor neuron type weakness in bilateral lower limbs. A preoperative sagittal T2-weighted magnetic resonance image (A) shows a T7 burst fracture associated with marked narrowing of the spinal canal (arrow); T7 corpectomy through left thoracotomy was performed. Postoperative computed tomogram with sagittal reconstruction (B) shows a titanium implant (Synex cage, Synthes, Inc, West Chester, Pa) in place. Postoperative plain radiographs (C and D) show the posterior fusion from T2 through T12 performed in a second staged operation. The pathology was metastatic renal cell carcinoma.
spinal cord and loss of stability, which may play a role in patients who are rapidly deteriorating neurologically and have medical comorbidity or when there is strong suspicion of a radiation-sensitive tumor. Through the same posterior incision, a more lateral pediculectomy can be performed to further decompress the spine and nerve roots with minimal retraction on the spinal cord and nerve roots. This allows better decompression of the anterior spinal elements than laminectomy alone. Notable postlaminectomy kyphosis is a potential complication in long-term survivors.

After decompression of the spinal cord and/or nerve roots, resultant spinal instability requires instrumentation and fusion for reconstruction of the spine. Hooks that attach to the lamina, facet joints, or transverse processes and pedicle screw systems are used for posterior instrumentation. As a general principle, posterior spinal instrumentation is attached to normal spinal elements above and below the decompressed area to restore stability. The number of levels and construct depend on the strength of the bone, the quality of fixation, and the presence of additional metastases within the fusion segment. Although the addition of posterior stabilization may improve pain relief and maintain neurologic function compared with laminectomy alone, overall results are not ideal.

**Posterolateral Approaches.** Posterolateral approaches combine the simplicity of laminectomy with the ability to decompress the ventral aspect of the dural tube. These approaches are useful in patients with ventral disease and comorbidity that prevent transthoracic, transabdominal, or retroperitoneal approaches. Costotransversectomy with removal of 1 or more ribs is the only commonly performed posterolateral approach. This approach involves removal of the proximal rib and the transverse process to expose the posterolateral aspects of the spine (Figure 1). It provides adequate access to the posterolateral spine while allowing concurrent posterior access. The anatomy of the upper and lower thoracic spine presents unique problems.

In the upper thoracic spine, the scapula needs to be mobilized, and the reversal of thoracic kyphosis can make resection of tumor and vertebral bodies difficult. At T11-12, the diaphragm progressively limits the working space. Also, with posterolateral approaches, the working distance can be extensive, making surgery difficult.

**Anterior Approaches. Craniocervical Junction.** The craniocervical junction encompasses the foramen magnum, the C1 and C2 vertebrae, and the structures contained within these bony landmarks including the vertebral arteries, spinal cord, lower cranial nerves, and CSF spaces. Surgical decompression should be achieved from the same vector as the compressive mass. If the tumor is compressing the spinal cord anteriorly, an anterior or anterolateral approach should be used.

The transoral-transpalatopharyngeal approach to the craniocervical junction provides exposure to the ventromedial spine from the midclivus to the C2-3 interspace. The tongue or palate may be split in combination with this approach to gain more exposure (Figure 2). Another route to the upper cervical spine and clivus is the lateral extrapharyngeal approach. This provides exposure limited by the ramus of the mandible, parotid gland, hyoid bone, hypoglossal nerve, and carotid sheath.

A posterior approach provides access to the posterior foramen magnum and extends laterally to the jugular bulb. It combines the standard dorsal midline incision with the lateral cerebellar approach and may include removal of the mastoid process and occipital condyle.

These 3 approaches, described in detail by Menezes, provide circumferential exposure of the upper cervical spine and can be combined with the subtemporal, infratemporal fossa, preauricular, and postauricular exposures to access the cranial base.

**Cervical Spine.** The subaxial cervical spine may be approached anteriorly via a lateral retropharyngeal approach. This corridor is commonly used in degenerative and traumatic spinal disease. Usually, during an anterior approach, corpectomy of the involved bone is performed. Autologous or allogeneic bone graft and other materials such as titanium mesh cages, carbon fiber cages, polyetheretherketone implants, and polymethylmethacrylate are used to replace the excised bone. An anterior plate is used to complete the reconstruction. Exposure usually can be gained from C2 to approximately the T3 level (Figures 3
and 4). The great vessels can be retracted for improved inferior exposure and the brachiocephalic vein ligated as necessary. Posterior instrumentation should be considered at the cervicothoracic junction because there is a high risk of junctional kyphosis. This is due to the transition from the mobile cervical spine to the stiff thoracic spine.

**Thoracic Spine.** The use of anterior transthoracic exposures has paralleled improvements in anesthesia/critical care and surgical techniques. These advances have substantially reduced the morbidity and mortality from thoracic surgery. The midthoracic vertebral bodies are best exposed (Figures 5 and 6). High lesions including T3-4 are usually approached from the right as the aortic arch can limit left-sided visualization. However, T5-10 is generally approached from the left because the liver is difficult to mobilize. In an excellent case series of transthoracic vertebrectomy for metastatic spinal tumors, Gokaslan et al4 reported that postoperatively, 17 of 33 ambulating but weak patients (52%) regained normal strength, 10 of 13 nonambulatory patients (77%) could walk, and 60 of 65 patients (92%) experienced significant improvement in pain. The 30-day mortality rate was 3% with a 1-year survival of 62%.

After tumor exposure and resection, usually a structural allograft or a vertebral bony replacement device and a plate are used to replace the vertebrectomy-removed defect. The aorta, subclavian artery, esophagus, inferior vena cava, thoracic duct, andazygous vein are all at risk of injury in this exposure. Chest tube drainage is routine after such surgery.

**Thoracolumbar Junction.** The thoracolumbar junction provides a challenge to anterior spinal exposure. Opening of the thorax and abdomen adds considerably to patient morbidity. Similar to the anterior thoracic approach, the patient is placed in the lateral decubitus position, and a thoracotomy incision is made over the lower thoracic ribs. The intrathoracic exposure is identical to that of the anterior thoracic approach, but now the diaphragm is divided to expose the upper 2 lumbar levels. This additional exposure places the kidneys, ureters, spleen, sympathetic trunk, and intra-abdominal contents at potential risk. All patients should be expected to have an ileus postoperatively (Figure 7).

**Lumbar Spine.** Anterolateral retroperitoneal approaches through variations of oblique incisions from the 12th rib to the lower abdomen can be used to approach the upper lumbar spine. However, these approaches, although less morbid for higher-risk patients, provide limited exposure for tumor resection and reconstruction compared with paramedian incisions around the rectus muscle. By using a paramedian incision, both transperitoneal and retroperitoneal exposures can be undertaken. Generally, we prefer the retroperitoneal approach because it provides greater protection for the intra-abdominal contents. With a retroperitoneal approach, the intra-abdominal contents and the hypogastric plexus can be mobilized as a unit. After exposure of the appropriate vertebral level, tumor resection and reconstruction can begin (Figures 8 and 9).

Complications of surgery include damage to the great vessels, ureters and intra-abdominal contents. Also, urogenital complications, such as retrograde ejaculation, due to sympathetic injury are well described.89 As with thoracoabdominal exposure, damage to the anterior spinal artery can occur with anterior approaches. There are areas of limited blood supply to the anterior spinal cord at the upper and lower cervical and throughout the thoracic spine. The artery of Adamkiewicz, the largest radiculomedullary artery supplying the inferior thoracic cord, generally branches from the left side between T8 and L2. However, this complication has been described only in scoliosis surgery.90

**CONCLUSIONS**

No prospective studies guide the modern treatment of spinal epidural metastases. It is difficult to generalize regarding outcome with the diversity of surgical approaches, decompressive and reconstructive techniques, patient variables, and tumor pathology. However, it is clear from large modern series that more than 90% of well-selected patients receive pain relief and that more than 50% experience...
significant neurologic recovery.\textsuperscript{91-93} Patient selection is critical to good surgical outcome. Rapid neurologic decline is a poor prognostic indicator. Patients who experience progressive neurologic deficits over a 24-hour period have a 28% to 35% chance of permanent paraplegia, whereas approximately 60% to 76% of those with slowly evolving deficits regain ambulatory function. Overall, prognosis is directly related to neoplastic type, spinal location, and extent of systemic involvement. The patient’s preoperative functional status and level of activity correlate directly with postoperative outcome.\textsuperscript{45} Multimodality therapy with vertebroplasty/kyphoplasty, stereotactic radiosurgery, bisphosphonates, and other pharmacological therapies and a team approach to the operative and nonoperative care of patients with spinal metastases will lead to better outcomes.

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