Metastatic spinal tumors

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Metastatic spinal tumors are the most common type of malignant lesions of the spine. Prompt diagnosis and identification of the primary malignancy is crucial to overall treatment. Numerous factors affect outcome including the nature of the primary cancer, the number of lesions, the presence of distant nonskeletal metastases, and the presence and/or severity of spinal cord compression. Initial management consists of chemotherapy, external beam radiotherapy, and external orthoses. Surgical intervention must be carefully considered in each case. Patients expected to live longer than 12 weeks should be considered as candidates for surgery. Indications for surgery include intractable pain, spinal cord compression, and the need for stabilization of impending pathological fractures. Whereas various surgical approaches have been advocated, anterior-approach surgery is the most accepted procedure for spinal cord decompression. Posterior approaches also have been used with success, but they require longer-length fusion. To obtain a stable fixation, the placement of instrumentation, in conjunction with judicious use of polymethylmethacrylate augmentation, is crucial. Preoperative embolization should be considered in patients with extremely vascular tumors such as renal cell carcinoma. Vertebroplasty, a newly described procedure in which the metastatic spinal lesions are treated via a percutaneous approach, may be indicated in selected cases of intractable pain caused by non- or minimally fractured vertebrae.

KEY WORDS • metastasis • spine • tumor • tumor excision
nique are discussed. Effective treatment decision making involves the cooperation of patient and family, medical and radiological oncologists, and the surgical team.

PATHOPHYSIOLOGY OF METASTATIC DISEASE

A primary carcinoma must undergo several steps before producing a metastases at a distant site. Common primary cancers that spread to bone are lung, breast, renal, prostate, and thyroid. Lung is the most common neoplasm in males, whereas breast is the most frequent in females. Despite the anatomical location, the tumor must grow beyond the bounds of the basement membrane of the cells at the primary site. The process is facilitated by enzymes known as matrix metalloproteinases causing degradation of this layer. Acting most specifically to break down the Type IV collagen in the basement membrane, the cancerous growth is then given access to surrounding blood vessels and lymph vessels. Tumor cells can then travel to distant tissues. For the cell to successfully metastasize, it must adhere to the second site and obligatorily stimulate the growth of new blood vessels. This is known as tumor angiogenesis. Unfortunately, a well-vascularized metastasis will survive at the expense of normal healthy tissue.

In the spinal column, metastatic carcinoma has a predilection for the well-vascularized cancellous bone of the VB. Less frequently, a lesion will develop only in the posterior elements (that is, the neural arch). In some situations, the tumor extends from the the anterior to posterior columns, making it more difficult to plan a surgical debulking or resection of the tumor.

IMPORTANCE OF SURVIVAL PROGNOSIS

Patients with metastatic cancer have limited life expectancies. After primary lung cancer has spread to distant organs, the mean survival time is 6 months. The mean survival after metastasis of breast, renal, or prostate carcinoma is less dismal, averaging approximately 1.5 to 2 years. Fewer than 10% of patients with metastatic renal cancer survive more than 2 years. Because of recent advances in the medical management of certain types of tumors, such as breast and prostate carcinoma, longer survival periods are being achieved, compared with those published in the medical literature from prior decades. Surgical treatment of skeletal disease must be considered in light of a patient’s projected survival. Within the surgical oncological community, it is well accepted that a patient should be expected to live for at least a 6-week to 3-month period. Typically it is the medical oncologist who makes this life expectancy estimation, basing it on natural history of the disease itself. The surgeon, however, must consider the attendant morbidity and negative effects that the surgery itself will have on the patient’s survival. In the surgeon’s best interest to be thoroughly familiar with all factors involved.

Although a number of authors have attempted to identify clinical predictors of survival in cases of metastatic disease, few have studied lesions of the spine specifically. In a retrospective series of patients with metastatic prostate cancer, Yamashita, et al. reported longer survival in patients with spinal or pelvic lesions (Group I) compared with those in whom appendicular spread had occurred (Group II). The mean survival time after initiation of treatment (of primary cancer) in Group I was 5.7 years compared with 2.4 years in Group II. The authors hypothesized that axial metastasis was more likely in general because of the proximity of the primary tumor to the Batson venous plexus (vertebral venous system). The Batson plexus is a valveless venous system that has been frequently implicated as a conduit for the metastatic spread of prostate tumors. Thus, they found that patients who presented with vertebral lesions initially harbored the least aggressive tumor, whereas in those with appendicular lesions the metastasis had bypassed the Batson plexus. Interestingly, patients with both appendicular and axial metastases (Group III) an intermediate life expectancy (3.4 years) was demonstrated, which was better than Group II but worse than Group I.

Some investigators have addressed the question of survival after surgery for spinal metastatic tumors. Tokuhashi and coworkers have studied the results obtained in 64 patients who underwent surgery for spinal metastases. They included all primary diagnoses and operations performed for a variety of indications including pain and paralysis. They formulated a score based on a number of parameters including general systemic condition, number of extraspinal bone metastases, number of spinal metastases, presence of lesions in other internal organs, location of the primary lesion, and the severity of spinal cord injury. Although no single parameter was predictive, scores correlated with survival periods. Scores of 9 or higher were predictive of at least 12 months of survival; scores of 8 and lower indicated survival less than 12 months; and scores of 5 or lower predicted survival of 3 months or less. Based on these data, it appears that the Tokuhashi system would be a valuable tool in preoperative discussions and decision making. Its value has been confirmed by other authors. Enkaoua, et al. found it predictive of survival after surgery in patients with most metastatic tumors to the spine. One exception was in cases of tumors of unknown primary origin. The investigators suggested ascribing a lower score to patients in this group, because their outcomes were generally poorer than predicted. It has been our experience that adenocarcinoma of unknown origin has been particularly lethal and with survival periods frequently less than 3 months.

Some authors have found preoperative neurological status to be highly predictive of survival, whereas those using the Tokuhashi system have not found it to be independently predictive. Perhaps this is related to the simplistic grading of the Tokuhashi system in which spinal cord deficits are divided into motor complete (Frankel Grade A or B), motor incomplete (Frankel Grade C or D), or intact (Frankel Grade E) groups. In subsequent studies, however, other authors have supported the findings reported by Tokuhashi, et al.

Other preoperative parameters have been analyzed. Sioutos and coworkers found that patients who were ambulatory preoperatively and those in whom the disease involved only one vertebral survived statistically longer than patients who were nonambulatory and those with multilevel disease. Overall extent of disease, age, and tu-
Spinal cord or cauda equina injury is most effectively treated by means of decompressive surgery.\textsuperscript{5,9,30,38} Radiotherapy, although a useful adjuvant, does not produce long-lasting results by itself.\textsuperscript{35} In a series of 43 patients, Sundaresan, et al.,\textsuperscript{35} reported neurological improvement in 45% of patients in whom radiotherapy alone was performed, whereas surgery before or after radiotherapy resulted in 100 and 60% improvement, respectively. In the short term, radiotherapy may be more effective in patients in whom no evidence of bone compression is present.\textsuperscript{27} In contrast, the use of high-dose corticosteroid therapy has demonstrated beneficial effects on outcome in patients with metastatic spinal cord compression. In a prospective randomized study of 57 patients, high-dose dexamethasone therapy resulted in 18% more patients becoming ambulatory than those who had undergone radiotherapy.\textsuperscript{54} Side effects, such as GI or infectious complications, must be considered, because they occur in approximately 11% of cases. Although some may advocate moderate- or low-dose steroid treatment to minimize these side effects, there is little evidence that they have an impact on metastatic spinal cord compression.\textsuperscript{15} To our knowledge, the use of steroids for cauda equina injury is not beneficial, because this is a lower motor neuron lesion.

Nonoperative Management

This group of treatment modalities can be termed palliative care. Tokuhashi, et al.,\textsuperscript{37} reported that palliative treatment should be reserved for patients who are poor candidates for surgery. There are limited conservative options for the treatment of metastatic spinal tumors. Practitioners must keep in mind the goals of nonsurgical treatment. Pain relief is probably the most common indication. Radiation therapy localized to the area of the lesion can successfully relieve pain and is probably a useful first-line modality in cases of most tumors. Some tumors are inherently radioresistant, such as renal cell and GI tumors, with fewer than half of cases responding. The benefit of radiotherapy must be balanced against the potential harmful side effects to the local tissue and skin. This can be an issue if surgery is planned in the near future. A minimum of 3 weeks should be allowed between the completion of external-beam radiotherapy and surgery in the zone of treatment.

Spinal instability is not cured by radiotherapy, and in some cases, it can cause further bone weakening. Although there is little evidence in the literature to support their benefit in the long term, braces are commonly prescribed for patients with pathological spinal fractures. Usually, extension-type braces are most useful in the thoracolumbar spine, because impeding kyphotic deformities secondary to anterior column destruction are the frequent presentation. Patients harboring cervical lesions may receive some degree of comfort from wearing a hard or soft cervical collar. The collar’s effectiveness in preventing an impending pathological fracture is unknown. Lesions at the cervicothoracic junction may require a custom-made orthosis that includes both a cervical and upper thoracic/pectoral component. In cases of lesions in the upper cervical spine, a halo fixator can be a better option. In all situations, the patient’s comfort should be the primary goal.

Metastatic spinal tumors

Spinal cord compression, or more accurately, neurological deficit is an unfortunately common sequela of spinal metastatic tumors. Because of its perceived influence on prognosis and its high incidence, this topic deserves particular discussion. The basic pathological feature causing spinal cord compression is encroachment of tumor or bone into the spinal canal. In the cervical and thoracic regions, this causes spinal cord compression, whereas lesions in the lumbar spine can cause stenosis and cauda equina syndrome. The exact mechanism of disruption of nerve function remains unclear. Commonly accepted theories include pressure-induced impedance of neural firing and cord ischemia secondary to compromise of the blood supply.\textsuperscript{29} The actual mechanism is likely a combination of these two factors.

Spinal metastases–induced canal compromise can be caused by a number of factors. Most commonly, lytic lesions weaken the supporting bone of the VB, creating an impending fracture. With little undue force, a pathological fracture can ensue. The posterior VB can be retropulsed in a burstlike pattern, compressing the neural structures. Another mechanism occurs via direct extension of the lesion beyond the confines of the posterior VB, which can, by itself, compromise the spinal canal without a frank pathological fracture. The third mechanism is the rarest but an important one of which to be aware. Blastic tumors can cause pathological bone overgrowth in the region of the spinal canal. Hirschfeld, et al.,\textsuperscript{16} have reported two such cases: one in a woman with metastatic breast cancer and another in a man with prostate carcinoma. In contrast to renal cell or lung carcinomas, both breast and prostate cancers are well-known causes of blastic lesions.

Neurological injury occurs in 5 to 10% of patients with cancer.\textsuperscript{1,3,28} The mean survival after spinal cord compression–induced paraplegia is 3.4 months.\textsuperscript{38} Compression can occur at one or more sites. More than one site of compression is present in 23% of patients with spinal cord compression secondary to prostate metastasis. Although one site might be obvious, systemic clinical and radiological examination of the entire spine is essential to detect additional lesions. The most sensitive neurodiagnostic imaging studies for detecting additional lesions are MR imaging, with and without intravenous contrast, or bone scanning.

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SURGERY-RELATED GOALS AND INDICATIONS

Prior to the 1970s, surgery was considered an overly aggressive treatment for malignant spinal tumors.12 With improvements in technique and the routine use of prophylactic antibiotics, indications broadened. In 1970, Martin and Williamson summarized their indications for surgery: a documented progressive neurological deficit, an impending pathological fracture, or obtaining a biopsy sample of a lesion of unknown primary origin. More recently, the concept of surgical stabilization to provide pain relief and to treat progressive deformity has been introduced, and the clinical results have been good.17,25

TREATMENT-RELATED OUTCOMES

Pain relief is accomplished by partial or total excision of the lesion from the vertebra. This lesion may be in the anterior or posterior elements. The rate of pain relief after surgery for metastatic tumors is generally high. Weigel, et al.38 have reported at least moderate pain relief in 89% of patients after performing anterior decompressive surgery and stabilization. Similarly, Rompe, et al.,30 and Hussein, et al.,13 have documented pain relief in approximately 90% of their cases. Both Shimizu, et al.,32 and Cahill and Kumar have reported 100% pain relief after undertaking surgery via posterior approaches. The mechanism of pain relief is not clearly understood but is most likely effected after removal of the offending lesion in addition to the increase in mechanical stability.

Neurological deficits are common sequelae of metastatic spinal tumors. They can occur at the level of the spinal cord or cauda equina. Progressive deficits are an indication for surgical decompression, which can be effected by anterior or posterior methods.5,17,18,38 Corpectomy at the site of the lesion is performed to decompress the anterior canal, whereas a posterior decompression is achieved via laminectomy. The details of these procedures including reconstruction will be discussed in greater detail below. Although both methods have been used with success, most authors currently believe that in patients with better prognoses restoration of the anterior weight-bearing portion of the spine may help prevent collapse of the involved vertebral segment. This can be achieved using an anterior corpectomy or posteriorly using a lateral extracavitary approach.

Laminectomy for decompression of spinal metastatic tumors has fallen out of favor. Because the anterior column destruction was not treated, progressive kyphotic deformity was frequent. Removal of the posterior elements can further destabilize an already compromised spine. In some relatively rare cases in which a metastatic carcinoma predominantly invades the posterior elements of the spine, a laminectomy may be appropriate (Fig. 1). Although the anterior resection and reconstruction more directly address the typical site of spinal cord compression and vertebral column destruction, some surgeons believe these procedures are associated with a high rate of morbidity, which may not be justified in this patient population.23,30 The failures of earlier series involving simple posterior decompression, without stabilization, were probably secondary to inadequate fixation above and below the site at which laminectomy was performed in patients with significant loss of the anterior weight-bearing portion of the spine. In more recent reports the authors have placed elongated rigid posterior constructs after decompressive laminectomy (Fig. 2). Despite these differences and trends, the rates of neurological improvement after surgery are comparable.

Rompe, et al.,30 undertook surgery via the posterior approach in 50 patients with metastatic tumors of multiple origins, they used long segmental hook stabilization alone. Twenty-six patients suffered a neurological deficit, of whom 14 (53%) improved at least one Frankel grade postoperatively. One patient (4%) became worse and 11 (42%) remained unchanged. The authors recommended the posterior approach in cases of multi-level metastatic disease that would be difficult to manage via an anterior approach. Interestingly, the only two cases of hardware-related failure occurred in patients with single-level disease. Similar rates of neurological improvement were documented by Shimizu, et al.32 Of 11 patients with multilevel metastatic disease, nine patients (82%) experienced neural improvement after undergoing posterior decompression and stabilization.

Fig. 1. A 54-year-old woman with known metastatic renal cell carcinoma who was neurologically intact with back pain. Upper Left: Sagittal T2-weighted MR image demonstrating involvement of the posterior elements of L-3 (arrow). Lower Left: Axial T2-weighted MR image revealing the L-3 spinous process and lamina infiltrated by tumor, with anterior structures intact (arrow). Right: Bone scan demonstrating numerous additional sites of metastatic disease (ribs, skull, and scapula) in addition to L-3 (arrow). The patient underwent simple posterior decompression.
Weigel, et al.\textsuperscript{38} used a variety of approaches in 45 cases of metastatic disease with a neural deficit. Sixty-two percent of patients improved after anterior surgery whereas 50\% improved after laminectomy. The investigation was retrospective and there was no attempt to randomize patients. King, et al.\textsuperscript{18} reported a 50\% rate of neurological improvement of at least one Frankel grade in 20 patients after anterior decompression combined with posterior stabilization without laminectomy. Based on these data, it is difficult to conclude that anterior surgery leads to a better rate of neurological improvement. There are no randomized prospective studies currently available, however, in which the authors compare anterior and posterior approaches, and thus, nonuniform selection criteria likely create a bias.

**PREOPERATIVE EVALUATION**

Obtaining a complete history and performing a physical examination are the initial steps in preoperative evalua-
tion. A review of systems must include pulmonary, cardiac, and urinary issues. It is essential to document bowel and bladder status before surgery because these results may indicate neurological involvement. Obstructive sleep apnea can occur in patients with GI tumors and should be evaluated before spinal surgery. The general overall health of the patient must be assessed, as should nutritional status. The likelihood of malnutrition in terminally ill cancer patients is high, which can influence wound healing and the rate of infection. Optimization by tube feedings, hyperalimentation, or parenteral supplementation should be considered.

Standard laboratory workup includes complete blood count with differential, serum electrolytes, amylase levels, and liver function tests, as well as albumin levels. Serum transferrin levels are useful to assess the patient’s nutritional status. Furthermore, hypercalcemia can be present in patients with metastatic spinal lesions, and this can be a risk factor for cardiac irregularities in the perioperative period. Whenever possible, electrolyte imbalances should be corrected prior to surgery. Collaboration with the medical oncology team is paramount.

Patients often have multiple areas of metastatic disease. Lesions around large weight-bearing joints such as the hip and knee can affect postoperative ambulatory status and recovery. In most situations, an impending hip fracture should be treated first, provided the neurological status is static (Fig. 2). Whole-body bone scanning is a useful modality for a global survey to detect these lesions, as well as additional spinal metastases.

Plain radiography is the first-line imaging modality. Lesions can be missed, however, because approximately 30 to 40% of the bone must be eroded before it is detectable on plain x-ray films. At obvious sites of fracture, angulation should be measured, and the pattern of the pathological fracture, if present, is characterized. Middle-column disruption is difficult to appreciate on plain radiographs. Computerized tomography scanning is a more effective method of evaluating spinal canal compromise secondary to bone or lesional retropulsion.

The level of decompression should be evaluated preoperatively using CT myelography or, preferably, MR imaging. The latter provides true sagittal and coronal images of long segments of the spine. The entire spine should be evaluated to detect any missed lesions. In planning reconstruction of the spine, instrumentation should not end at the level of an involved segment; rather, it should be spanned so as not to create a stress riser that may potentiate pathological fracture. Additionally, constructs should be placed to avoid terminating the stabilization at the apex of a kyphosis or at a junctional region (either the cervicothoracic or thoracolumbar junctions).

Specifically in cases of renal cell metastasis, a preoperative arteriogram is recommended (Fig. 2). Because these tumors are highly vascular, intraoperative bleeding can be life threatening. The benefit of preoperative embolization of renal cell spinal tumors has documented numerous studies.11,18,26 In cooperation with the interventional radiologist, exhaustive attempts should be made to avoid embolizing major spinal feeding arteries, which are present in the lower thoracic spine (that is, the artery of Adamkiewicz). With special attention to this detail, Olerud, et al.,26 documented no neurological complications related to embolization in 21 patients.

SURGICAL PROCEDURES

Posterior Approach

Standard techniques of laminectomy are well known to spine surgeons. The principles of spinal canal decompression in cases of metastatic tumors are identical. The dura mater should be protected throughout the procedure. Foraminal encroachment should be assessed following central canal decompression and treated accordingly.

After decompression, reconstruction of the spine can be performed using a number of different constructs. Hook or pedicle screw systems can be used for segmental fixation along the segments to be fused. When posterior fixation alone is required after laminectomy, the construct must span a number of levels above and below (Fig. 2). This is influenced by the strength of the bone, the quality of fixation, and the presence of additional metastases within the fusion segment.30 A sound biomechanical plan is mandatory to provide sufficient fixation for the remainder of the patient’s life.

Noting the limitations of laminectomy and posterior surgery, some surgeons have devised methods to treat the anterior and posterior columns via a single posterior approach. Cahill and Kumar1 have reported the use of such a procedure in nine patients with metastatic spinal disease. After performing a wide laminectomy, the neural elements were protected using a rigid retractor resting on the posterior aspect of the VB. This allowed aggressive removal of the anterior and middle columns through the interval between the retractor and the lateral elements (remaining pars or facet joints). With the body excavated bilaterally, the anterior column was reconstructed by pouring MMA cement around two metal pins longitudinally interposed between the cranial and caudal VBs. The authors warned that extreme caution is necessary to avoid contact between the MMA and the dura mater. In addition, a shell of anterior bone should be maintained to avoid extravasation of cement into the retroperitoneum where it could cause vascular injury. Once the MMA hardened, it provided an effective anterior column reconstruction. Supplemental posterior stabilization was provided by a segmental hook construct. The authors reported no technique-related deaths or neurological injury. One case of hardware-related failure occurred because of construct ended at an apex of kyphotic deformity.

Anterior Surgery

Various options are available for exposure of the anterior column of the spine. Standard retroperitoneal approaches in the lumbar spine or thoracotomy in the thoracic spine are useful. The upper thoracic vertebral region is more challenging to access anteriorly. It lies outside the zone of the standard anterior cervical exposure and is usually too rostral to expose using a thoracotomy. Kurz, et al.,19 Comey, et al.,6 and Sundaresan, et al.,36 have described a similar approach to pathological lesions in the upper thoracic spine. An L- or T-shaped incision is centered over the sternum and clavicle. After developing the plane between the sternocleidomastoid muscles and the midline strap muscles, they are reflected superiorly from the borders of the sternum and the medial clavicle. The superior part of the manubrium and the medial third of the clavicle
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are carefully resected. This allows deeper exposure of the interval between the carotid artery sheath and esophagus. The arch of the aorta can be palpated at the inferior extent of the field and is protected with a renal vein retractor. Retraction of the carotid artery sheath and the esophagus exposes the anterior longitudinal ligament along the VBs. Resection, corpectomy, and reconstruction with MMA cement can then be performed. Exposure down to the T-3 or T-4 level can be achieved. Because of difficulties associated with healing of these complex upper anterior thoracic exposures, we have favored use of a median sternotomy approach to the upper thoracic spine. In our experience, this has provided quicker access with exposure to T-4 and possibly T-5, as well as a lower rate of postoperative morbidity (Fig. 3).

Corpectomy is an effective means of decompressing the anterior spinal canal. In cases of metastatic lesions, care must be taken when burring down to the posterior longitudinal ligament. The diseased tissue often adheres to the dura or has already broken through the ligament, making decompression a daunting task. Although complete excision of the tumor is not necessary, sufficient bone and lesion must be removed to relieve the pressure on the neural elements. One should observe the standard principle of a pedicle-to-pedicle decompression of the involved vertebra (Fig. 4).

Resection of the VBs leaves an anterior column deficiency. This must be reconstructed using a stable strut. Most authors have agreed that PMMA bone cement is preferable to allograft struts because it has less of a chance to subside. King et al. have reported construct-related failure when using an iliac crest strut graft. Because of the limited life expectancy of these patients incorporation of a bone graft seems unlikely. The prime objective is immediate stability that is durable enough to last approximately 1 year. Some authors warn that PMMA is durable for only 6 months.

Reconstruction using PMMA can be achieved in conjunction with the use of various metallic devices. Metal pins can be placed longitudinally to span the defect and PMMA molded around them in a doughy state. Alternatively, various types of cages have recently become available. These cages may be made of titanium mesh or carbon fiber, which can be filled with cement or bone and interposed between the vertebrae. Supplemental rod or plate fixation can also be added (Fig. 4). Screw purchase can be augmented using additional PMMA injected into the drilled holes in the intact VBs.

Vertebroplasty for Pathological Lesions

Vertebroplasty is a relatively new technique of stabilization in the treatment of pathological lesions of the spine, requiring minimally invasive surgery. The procedure involves cannulation of the pedicle by using a hollow bore needle and injection of PMMA into the cancellous bone of the VB. Initially developed for the treatment of osteoporotic compression fractures, numerous authors have documented successful pain relief in patients with metastatic spinal tumors. The technique requires the presence of an intact posterior VB wall to prevent cement extravasation into the spinal canal. The main goal of a vertebroplasty in patients with tumors is to enhance the anterior column of the spine (Fig. 5). Pain relief has been dramatic, with reports of success between 50 and 80% in carefully selected patients.

CONCLUSIONS

Indications for surgery in patients with metastatic spi-
nal tumors are intractable pain, progressive neurological deficit, or an unknown histological diagnosis. Treatment can effectively relieve pain and improve neurological function in patients with canal compromise. Candidates for surgery should have a life expectancy of at least 3 months. Operative choices include anterior, posterior, and combined approaches, each with its advantages and disadvantages. Newer percutaneous procedures such as vertebroplasty can be efficacious in a selected group of patients in whom pain presents without neurologic deficit.

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