Management of Metastatic Cervical Spine Tumors

Abstract
The skeletal system is the third most common site of metastases after the lung and liver. Within the skeletal system, the vertebral column is the most common site of metastases, and 8% to 15% of vertebral metastases are in the cervical spine, consisting, anatomically and biomechanically, of the occipitocervical junction, subaxial spine, and cervicothoracic junction. The vertebral body is more commonly affected than the posterior elements. Nonsurgical management techniques include radiation therapy (stereotactic and conventional), bracing, and chemotherapy. Surgical techniques include percutaneous methods, such as vertebroplasty, and palliative methods, such as decompression and stabilization. Surgical approach depends on the location of the tumor and the goals of the surgery. Appropriate patient selection can lead to successful surgical outcomes by restoring spinal stability and improving quality of life.

Anatomy of the Cervical Spine
Biomechanically and anatomically, the cervical spine can be divided into three regions: the occipitocervical region, the subaxial region, and the cervicothoracic junction. The occipitocervical spine encompasses the occiput down to C2. Metastatic lesions localize to the thoracic spine in 68% to 80% of cases, the lumbar spine in 16% to 22% of cases, and the cervical spine in 8% to 15% of cases. Metastasis is commonly spread via a hematogenous route. The arterial supply to the vertebral body and the Batson plexus, a valveless vertebral venous complex, is a route for hematogenous spread of metastatic lesions. The vertebral body is most commonly affected compared with the posterior elements. Common histologies associated with metastatic lesions to the spine include lung, breast, renal cell, lymphoma, thyroid, and prostate cancers.

There were 1.2 million cases of cancer and 557,000 deaths due to cancer in the United States in 2012. Following the lung and liver, the skeletal system is the third most common site of metastases; within the skeletal system, the spine is the most common site of metastases. Metastatic lesions localize to the thoracic spine in 68% to 80% of cases, the lumbar spine in 16% to 22% of cases, and the cervical spine in 8% to 15% of cases.

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approach, the location of the manubrium and clavicle in relation to C7-T1 needs to be closely monitored by radiography or CT. If a low anterior (Smith-Robinson) approach is not feasible, then plans for a manubrium- or clavicle-splitting approach are required. However, because of the morbidity associated with a manubrium- or clavicle-splitting approach, alternative posterior-based surgical approaches may be considered.

**Clinical Presentation**

Pain is the most common presentation of primary and metastatic lesions of the cervical spine.\(^{11,12}\) Axial pain is mechanical in nature; it can be relieved by lying down and worsens with ambulation and axial load.\(^{13}\) Localized pain is attributed to stretching of the vertebral body periosteum and is not responsive to changes in position.\(^{13}\) Localized pain is the common night time pain seen in cancer patients. If cervical spine metastases are the first manifestation of a malignancy, in the initial phases it may present with axial pain and radicular symptoms. Prior to the malignancy’s being discovered clinically or on imaging, it is common for such a patient to undergo physical therapy and oral analgesics on the assumption that he or she has cervical spondylosis or a disk herniation.

Upper cervical radiculopathy, C2 to C4, manifests with pain in the sub-occipital region and headaches in the retro-auricular and/or retro-orbital regions.\(^{14,15}\) Radiculopathy from C5 to C8 manifests in the anatomic distribution that the respective nerve innervates. It is common to have overlap of the sensory distribution of the nerves roots. In addition to burning or aching pain, the patient will have paresthesias and sensory deficits. Usually the symptoms are ipsilateral in nature. Weakness of the affected extremity on physical examination may also be present.

Metastatic epidural spinal cord compression (MESCC) can manifest with symptoms of myelopathy or radiculopathy. The initial presentation of myelopathy is dependent on the location of the compression. Some findings include changes in fine motor skills, such as handwriting and buttoning buttons.\(^{16}\) Depending on how the myelopathy progresses, problems with balance and gait abnormalities ensue. Pathologic reflexes such as the Hoffmann reflex, extensor hallucis longus reflex (ie, up-going toes on the Babinski test), and the inverted radial reflex may be present. Eventually, progressive upper and lower extremity weakness may ensue, and the patient can become wheelchair dependent. Changes in bowel and bladder function, including urinary retention and incontinence, can also be present.

With pathologic fractures of the cervical spine, it is common to have symptoms of radiculopathy and myelopathy. Loss of height associated with the fracture will cause foraminal collapse and symptoms of radiculopathy.

Although rare, fracture fragment retro-propulsion into the spinal canal can cause compression of the spinal cord and symptoms of myelopathy.

**Imaging**

Radiographs are the first step in imaging the cervical spine and are helpful in identifying tumor-related deformity. Odontoid and swimmer's views should be obtained, depending on the levels involved. Upright radiographs are preferred to assess spinal alignment, kyphosis, and instability as a result of the metastases. In cases of lytic lesions, >50% of the vertebral body needs to be involved before the lesion can be identified in the vertebral body.\(^{17}\) MRI with and without contrast is the gold standard for the imaging evaluation of cervical spine tumors. CT can be used for surgical planning and to assess the extent of bony destruction. If the primary cause is unknown, or for a presumed primary malignant lesion, then CT of the chest and abdomen can be performed for staging. Total body scans (eg, positron-emission tomography, bone scan) can be used to study the presence of metastases. Positron-emission tomography can be used to evaluate response to chemotherapy.

**Diagnosis**

CT-guided biopsy is the modality most commonly used for diagnosis.
Biopsy is especially critical in patients with a new lesion and no metastases elsewhere.18,19 Benign lesions and infections can be missed without proper biopsy; inadvertent surgeries for malignant tumors that are chemosensitive and radiosensitive can also be avoided. In addition, vascular lesions such as renal cell cancer, hepatocellular carcinoma, and thyroid cancer that can benefit from preoperative embolization can be identified in advance. There are conflicting reports on the accuracy of image-guided biopsies of the spine compared with those of other skeletal locations.20,21 In a series of 703 percutaneous CT-guided spine biopsies, 22 were in the cervical spine.20 The authors noted difficulty in the accuracy rate of the biopsies because of the small size of the vertebrae. In another series of 410 spine biopsies in which 9 were in the cervical spine, 100% accuracy was reported. Thus, in cases in which percutaneous biopsy is not diagnostic, open biopsies can be useful and sufficient tissue can be obtained.21

The clinical scenario of a solitary metastasis to the cervical spine is uncommon. When a biopsy is needed, staging studies will typically identify other sites of metastasis—usually extraspinal—that are safer to biopsy than the cervical spine. If no other lesions are identified and a biopsy of the cervical lesion is needed, careful planning should be done to ensure that the tract can be appropriately resected if a primary malignant tumor is identified.

### Management
Once a diagnosis is made, management is decided based on the histology of the lesion and the clinical presentation. A multidisciplinary team involving the medical oncologist, radiation oncologist, and spine surgeon, along with the patient and family, is necessary. Consideration of referral to a spine tumor specialty center may be indicated for appropriate cases, such as patients with neurologic changes resulting from metastatic epidural spinal cord compression. When postoperative radiation therapy is indicated, it can also be completed at these centers. For metastatic lesions, the histology helps determine whether surgical management is indicated. Radiosensitive tumors such small cell lung cancer, multiple myeloma, and lymphoma can be treated without surgery as long as no signs of neurologic deterioration or gross instability are present.

Factors to consider in a multidisciplinary approach include the patient’s prognosis and the stability of the spine. The modified Tokuhashi score helps to correlate the extent of surgical intervention with a patient’s prognosis.22 The score has six components that take into account the Karnofsky Performance Status, presence of extraspinal bone metastases, number of metastases in the vertebral body, metastases to major internal organs, the primary sites of cancer, and the patient’s neurologic status (Table 1). A score ranging from 0 to 15 is generated, with a higher score indicating better prognosis. More aggressive surgeries can be planned with a higher score; palliative surgery or nonsurgical options may be considered for patients with a low score.

The Tomita score is another validated scoring system for prognosis in spine tumors.23 It has three components that evaluate the type of tumor, presence of visceral metastases, and presence of bone metastases. Scores of 2 to 10 can be generated, with a higher score indicating worse prognosis and a lower score indicating consideration for excisional surgeries.

To determine spinal instability, the Denis three-column system and the Kostuik classification have been used in the past. With the Denis classification, surgeons have used tumor involvement of two columns as indicating instability. In the Kostuik
classification, the vertebra is divided into six components; involvement of more than three components of the spine is used to define instability.\textsuperscript{24} Recently, a multidisciplinary group has validated the Spinal Instability Neoplastic Score (SINS) as a prognostic score to determine spinal instability.\textsuperscript{25} The SINS has six components (Table 2); scoring ranges from 0 to 18. A score of 0 to 6 is a stable spine, 7 to 12 indicates impending instability, and 13 to 18 indicates an unstable spine. This multidisciplinary group scored 30 spine tumor cases (10 in the cervical spine) using SINS and had high interobserver and intraobserver reliability scores when the cases were scored into stable, impending instability, and unstable categories. The sensitivity rate for SINS was 96\%, and the specificity was 80\%.\textsuperscript{25}

Once the SINS and the Tokuhashi/Tomita scores are tabulated, a thoughtful discussion should be had with the patient regarding whether there will be benefits to surgical management. When considering surgical intervention for spinal instability, it is useful to remember that metastatic disease to the spines does not affect ligamentous structures. Thus, the occipito-cervical junction, which relies significantly on ligamentous stability, is less likely to sustain gross instability with osseous metastases compared with the cervicothoracic region.

**Nonsurgical**

With radiosensitive and chemosensitive tumors and neurologically intact patients, nonsurgical management is indicated unless the patient presents with spinal instability or a significant neurologic deficit requiring urgent decompression of the neural elements. Traditional radiotherapy is given over fractions—for example, 3 Gy × 10 fractions. Radiation has been successful in treating metastases of the upper cervical spine.\textsuperscript{3} Stereotactic radiosurgery (SRS) or stereotactic body radiotherapy is an alternative to conventional radiation therapy; it can deliver focused, high-energy radiation to isolated lesions in the vertebral body (Figure 1). Typically, one or two fractions may be sufficient; the dosage can range from 12.5 to 25 Gy. SRS has been shown to be effective in pain relief.\textsuperscript{26} Recent evidence-based guidelines recommend SRS for patients expected to survive >3 months, with limited metastatic burden, and with previously radiated spinal segments.\textsuperscript{27} Relative contraindications to this technique are epidural extension of the tumor and mechanical instability. There is a risk of spinal cord damage if radiosurgery is attempted for the treatment of epidural disease extension.\textsuperscript{26} Laufer et al\textsuperscript{28} have reported on “separation surgery,” which involves posterior-based decompression of MESSC, followed by SRS 2 to 4 weeks later. In their series of 186 patients with spine metastases (15 in the cervical spine), these authors found that high-dose hypofractioned SRS (ie, 24 to 30 Gy in three fractions) results in low local tumor progression (<5\%).\textsuperscript{28}

Compression fracture of the treated vertebra is a complication of SRS, with a prevalence of 13\% to 39\%.\textsuperscript{29-31} Risk factors for vertebral compression fractures following SRS include osteolytic tumors, liver and lung metastases, and dose >20 Gy in one fraction.\textsuperscript{29-31} In regard to SRS for the cervical spine, Cunha et al\textsuperscript{31} reported a 7\% rate of compression fractures (2/30), and Boehling et al\textsuperscript{30} noted one fracture in five cervical SRS cases. Rose et al\textsuperscript{29} had 6 cervical lesions out of 71 spine lesions that underwent SRS (ie, 24 to 30 Gy in three fractions) results in low local tumor progression (<5\%).\textsuperscript{28}

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Score</th>
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<tbody>
<tr>
<td>Location</td>
<td>3</td>
</tr>
<tr>
<td>Mobile spine (C3-C6, L2-L4)</td>
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<tr>
<td>Semi-rigid (T3-T10)</td>
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</tr>
<tr>
<td>Rigid (S2-S5)</td>
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<tr>
<td>Pain</td>
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<tr>
<td>Occasional pain but not mechanical</td>
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</tr>
<tr>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Bone lesion</td>
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</tr>
<tr>
<td>Lytic</td>
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</tr>
<tr>
<td>Mixed (lytic/blastic)</td>
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<tr>
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<tr>
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</tr>
<tr>
<td>No collapse with &gt;50% body involved</td>
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</tr>
<tr>
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<tr>
<td>Posterior involvement of spinal elements</td>
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<tr>
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</tr>
<tr>
<td>Unilateral</td>
<td>0</td>
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<tr>
<td>None of the above</td>
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*Score: 0-6 = stable; 7-12 = impending instability; 13-18 = unstable.*

Surgical intervention is indicated for metastatic lesions causing neurologic compromise, instability, and rapid deterioration of function.
Vertebroplasty is a percutaneous technique that is not widely used for the management of cervical spine tumors; however, studies have reported successful pain relief with vertebroplasty for pathologic cervical compression fractures of the upper and subaxial cervical spine. Larger series are needed before widespread adoption of the technique in the cervical spine but may be a promising alternative.

In the randomized study of patients with MESCC by Patchell et al., the superiority of surgical decompression followed by radiation therapy 30 Gy (ie, 3 Gy × 10 fractions) over radiation therapy alone was clearly demonstrated. Fifty-one patients were in the surgery-plus-radiation group, and 51 were in the radiation-only group. Thirteen cervical cases (five in the radiation-alone group and eight in the surgery-plus-radiation group) were included in the study; a subgroup analysis on the cervical cases was not performed. Exclusion criteria for the study by Patchell et al. were multi-level compression, very radiosensitive tumors, and paraplegia for 48 hours; thus, the findings of the study cannot be extrapolated to such patients. However, the study is important in demonstrating the beneficial effects on neurologic recovery of direct surgical decompression and radiation compared with radiation alone. Limitations of the study by Patchell et al. include the definition of ambulation, that is, taking a minimum of two steps assisted or unassisted. The clinical relevance and importance of taking two steps in not clearly defined in their study. Others have questioned the utility of surgery before radiation therapy in cases in which the patient’s spine is stable and neurologic function is intact. Finally, although there was a statistically significant difference in survival noted (100 days versus 126 days, \( P < 0.03 \)), the clinical significance of this difference of 26 days is unclear.

Instability and impending instability are important factors in the surgical decision making of cervical spine malignancies. The SINS score can help determine whether an impending instability or an unstable spine is present. The Tokuhashi and Tomita scores serve as useful guides to objectively evaluate prognostic factors and help formulate an appropriate plan. A comprehensive multimodal approach designed to individualize care will prove to be the best strategy for surgical management of cervical spine malignancies.

Management of metastatic lesions to the cervical spine is predominantly palliative. Corticosteroids can be given to diminish the tumor burden in radiosensitive tumors such as multiple myeloma and lymphoma. High rates of complications have been noted with use of high-dose corticosteroids. In the past, palliative procedures included posterior-based laminectomy without fusion. However, in the cervical and thoracic spine, the high rates of post-laminectomy kyphosis preclude the use of this modality. Intralesional resection followed by stabilization is typically performed for metastases to the cervical spine (Figure 2). Conventional radiotherapy is usually performed 3 to 4 weeks following surgery.

Prior to surgery, it is critical to know the histology of the lesion so that appropriate preoperative embolization can be performed to minimize intraoperative bleeding. Preoperative embolization should be a consideration for metastatic lesions arising from renal cell
cancer, hepatocellular cancer, and thyroid cancer. Angiography can also be useful in assessing the vascular supply to the cervical spinal cord and dominance of the vertebral arteries.

In the cervical spine, the location of the lesion is important in determining the surgical approach to undertake. Anterior, posterior, or circumferential surgical approaches can be pursued, depending on the pathology and the goals of the procedure. In the upper cervical spine, having an otolaryngologist perform the anterior exposure is an option.

With metastatic lesions causing significant destruction of C1 or C2, posterior-based reconstruction that extends up to the occiput and caudally into the subaxial spine is preferred. Occipital plate systems with rod connectors to the upper cervical spine screws are routinely used. Lateral mass screws can be placed at C1; pars, pedicle, or translaminar screws can be placed at C2. Posterior-based transpedicular corpectomy of upper cervical spine tumors has also been reported. In a series of eight cervical spine tumor cases (five involving C2), posterior transpedicular decompression of the anterior lesions was performed. Anterior stabilization was performed, followed by posterior stabilization. The upper cervical spine may be suitable for this approach because the C2 and C3 nerve roots can be sacrificed without concern for motor deficits.

The subaxial spine is the most common site of metastases. Because the vertebral body is commonly destroyed, an anterior-based corpectomy and debulking, followed by anterior and posterior stabilization, is usually performed (Figure 3). The standard Smith-Robinson approach can be used for single-level or multiple-level corpectomies. Anterior instrumentation options include a titanium mesh cage, expandable cage, fibula strut allograft/autograft, polymethyl methacrylate, and an anterior plate. When further stabilization is needed, posterior cervical instrumentation and fusion can also be performed. If corpectomies of two or more levels are performed, it is advisable to supplement with posterior instrumentation. Posterior fixation in the subaxial spine consists of lateral mass screw-rod systems from C3 to C6. Spinal process cables can also be used to strengthen the construct. Poor bone quality is frequently encountered in patients with metastatic lesions; depending on the bone quality, one should consider posterior augmentation of an anterior fusion.

Metastatic lesions in the cervicothoracic junction can be challenging to address. Anterior approaches via low Smith-Robinson or clavicle- or manubrium-splitting approaches can be performed, depending on the location of the patient’s C7 and T1 vertebral bodies. During surgical planning, one must take into account the comorbidities associated with the manubrium- and clavicle-splitting approaches. A posterior-based approach is also used to stabilize the affected levels because of the biomechanical stresses of the cervicothoracic junction. Pedicle screws are placed at C7 and the thoracic spine. Various posterior instrumentation options to bridge the cervicothoracic junction; these include dominoes (side-to-side or end-to-end) to connect a cervical rod to a thoracic rod; extending a cervical rod into the thoracic spine; and using a tapered rod from the thoracic to the cervical spine. At the cervicothoracic junction, transpedicular corpectomies are becoming more popular; the main benefit is avoiding the morbidity of the anterior approach.

Following palliative surgical procedures, radiation treatment can be administered, usually 3 to 4 weeks postoperatively. It is critical to ensure
that the patient’s nutritional status is monitored with pre-albumin testing (normal, 15 to 36 mg/dL) to minimize the risk of wound breakdowns. Bracing with a hard collar postoperatively is an option in the setting of multilevel anterior and posterior surgery.

Outcome of Surgery for Cervical Spine Tumors

Only one prospective study exists on outcomes (i.e., a validated questionnaire evaluating quality of life and pain relief) following surgery for cervical spine metastases. In this study of 26 patients, median survival was 6 months, and two postoperative complications occurred. Using the European Organization for Research and Treatment of Cancer QLQ-C30 questionnaire, significant improvement in health outcomes was observed from preoperative values. Significant improvement in pain and relief of radicular symptoms was also observed.

In a recent series, 46 patients with subaxial cervical spinal metastases were evaluated retrospectively; a mean survival of 17 months, with a recurrence rate of 39%, was noted. Patients with higher preoperative Japanese Orthopaedic Society scores were noted to have better neurologic outcomes.

Complications of Surgical Management

The most common perioperative complication in spine tumor surgery is surgical site infection (SSI), with a rate of 9.5%. Preoperative radiation therapy has been associated with wound complications and infections. Other risk factors for infections include a comorbidity of diabetes mellitus, prior surgery in the surgical area, complex plastic surgery assisted wound closure, involvement of more than one surgical team, and blood transfusions. Intra-wound vancomycin powder is being increasingly used during closure of spine surgical wounds. Vancomycin powder has resulted in a significant decrease in SSI for spine surgery in posterior-based cervical spine surgeries, although no large study to date has evaluated the rate of SSI in

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spinal tumor surgery after administration of vancomycin.

Healthcare disparities in the treatment of spinal metastases have been noted to contribute to higher complication rates. In an evaluation of 2,157 patients undergoing surgery for spinal metastases, complication rates and mortality rates were higher for uninsured and Medicaid patients compared with privately insured patients.46

Instrumentation failure and pseudarthrosis are complications that can also be encountered, especially at junctional regions such as the cervicothoracic and occipitocervical junctions. Postoperative radiation can contribute to pseudarthrosis by inhibiting the development of a fusion mass.

At the occipitocervical junction, Bilsky et al9 used iliac crest autograft in nine patients with an estimated >6-month of life expectancy and noted no pseudarthrosis. Similarly, in 23 patients with metastatic and primary lesions who underwent instrumented occipitocervical fusion with iliac crest autograft, a 95.6% fusion rate (22/23) was noted on imaging.47 Neither of these studies reported instrument failure, which correlates with their high fusion rate. However, the risk of spreading tumor cells during iliac crest harvesting should be noted. The iliac crest may also have metastatic spread, and imaging of the pelvis should be studied carefully when planning to harvest autograft.

Finally, symptomatic tumor recurrence is another complication that can occur and may be expected with palliative procedures. In the upper cervical spine, no recurrences were noted in 13 patients who underwent surgical stabilization for metastases.9 In a series of 18 patients with occipitocervical metastases, Zimmermann et al19 noted 1 tumor recurrence (5.6%) causing construct instability. In a series of 46 patients undergoing surgery for subaxial cervical spine metastases, a local recurrence rate of 39.1% (18/46) was noted.11 The most common tumors were lung cancer (12), thyroid cancer (6), and hepatocellular cancer (6). Postoperative adjuvant treatment was the only factor found to reduce recurrence.11 In a smaller prospective series of 26 patients with cervical spine metastases, a recurrence rate of 7.7% (2/26) was noted.12

**Conclusion**

Management of malignant cervical spine tumors is approached in a multidisciplinary manner. When possible, surgical planning should incorporate the Tokuhashi/Tomita scoring systems and the SINS system. The unique anatomy and junctional regions of the cervical spine allow for the possibility of various approaches, depending on the location of the pathology. Innovations in radiation oncology techniques such as SRS are useful adjuncts to surgical management. Most lesions in the cervical spine are metastatic and are treated with palliative surgical principles.

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