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Epidemiology of spinal cord and column tumors

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Abstract

The spine is a frequent location for metastatic disease. As local control of primary tumor pathology continues to improve, survival rates improve and, by extension, the opportunity for metastasis increases. Breast, lung, and prostate cancer are the leading contributors to spinal metastases. Spinal metastases can manifest as bone pain, pathologic fractures, spinal instability, nerve root compression, and, in its most severe form, spinal cord compression. The global extent of disease, the spinal burden, neurologic status, and life expectancy help to categorize patients as to their candidacy for treatment options. Efficient identification and workup of those with spinal metastases will expedite the treatment cascade and improve quality of life.

Keywords

bone metastasis | metastasis | spinal cord compression | spine

As survival rates for primary malignancies increase, metastatic bone disease is a frequently encountered scenario. Metastatic bone disease as it relates to spinal metastasis can cause significant morbidity. Spinal metastases can manifest as pain, weakness, epidural extension causing spinal cord or nerve root compression, and pathologic fracture possibly resulting in spinal instability. All of the aforementioned sequelae of spinal metastasis result in a reduction of quality of life.[1–4]

Broadly speaking, the mechanism of metastasis begins with a loss of cellular cohesion and release of a small number of cells from the primary site followed by cell migration, evasion of the native immune response, and subsequent growth and angiogenesis at the secondary site.[3,5,6] Bone metastasis ranks as the third most common site of metastasis behind the lung and liver, while the exact incidence of bone metastasis remains unknown.[3,7–10] Multiple myeloma, prostate, breast, thyroid, lung, colon, bladder, and renal cell rank among the top metastatic tumors that metastasize to bone.[3,7,10–13]

The management of patients with spinal metastases requires multidisciplinary input from the requisite specialties including oncology, radiation oncology, and spine surgeons. The complexity of these patients is significant. Decision-making algorithms depend on the primary tumor, the patient's functional status on presentation, visceral metastasis, the extent of spinal metastasis, and the presence of spinal cord compression and/or instability. The goal is to efficiently and appropriately identify patients as it relates to their candidacy for optimal treatment (medical and/or surgical) to enhance outcomes while limiting treatment-related morbidity. This text will provide an update on the presentation, diagnosis, and incidence of spinal metastases.

Identifying Patients With Metastatic Spinal Disease

The hallmark symptom for spinal metastases is back pain, with 80% to 95% of patients having this symptom.[10,14] Pain can be further characterized as local pain, mechanical pain, or radicular pain.[14,15] When back pain exists in the setting of a known prostate or breast cancer patient, a spinal lesion is present 15% and 20% to 30% of the time, respectively.[3,16] Motor dysfunction is the second most common complaint on presentation, present in 35% to 75% of patients.[14] When there is significant neural compression, sensory disturbances can be present

and usually accompany pain and/or motor complaints.[14,15] A detailed history and neurologic exam is necessary, and the provider is obligated to obtain radiographs.

In its most severe form, metastatic disease can cause spinal cord compression. Although relatively rare, in 10 per 100 000 patients spinal cord compression necessitates emergent evaluation.[10] The symptoms are often advanced and include weakness (60%-85%), sensory disturbances including saddle anesthesia, and bowel/bladder disturbances.[15] Untreated spinal cord compression can progress to paralysis, sensory loss, and bowel/bladder dysfunction.[17]

Imaging

The full gamut of imaging is available to the provider as it relates to bone metastases in general. Plain radiographs are the most economical and are specific, but have a relatively low sensitivity rate of 44% to 50%.[10] As expected, plain radiographs are dependent on the size of the lesion and its osteolytic vs osteoblastic nature.[3,18]The sensitivity increases with CT, ranging from 71% to 100%.[19] MRI is the most sensitive (82% to 100%) and specific (73% to 100%) imaging modality for bone metastasis.[10] MRI is the preferred imaging modality for identifying spinal metastases, particularly epidural extension and spinal cord compression. In the setting of an appendicular neurologic change, MRI is the imaging modality of choice.[3,20] Bone scintography and more so PET are useful for evaluating skeletal, specifically vertebral, metastases.[21,22] When a new or progressive neurologic deficit is discovered, an urgent MRI with and without gadolinium contrast of the index area is warranted.

Location of Metastases

Of all potential osseous sites of secondary metastasis, the spine is the most common, accounting for 70% of all osseous metastases.[9,10,23] The most common location for spinal metastasis is the thoracic spine (60%-80%), followed by the lumbar spine (15%-30%) and lastly the cervical spine (< 10%).[13,14] In a retrospective review of spinal cord metastases in China, the most common level of metastases was multilevel metastasis (≥ 2 levels) followed in descending order by thoracic, lumbar, and cervical vertebral segments.[13]

The location of a metastasis can be further classified based on its anatomic origin. The 3 spaces are extradural, intradural extramedullary, and intradural intramedullary (within the parenchyma of the spinal cord). Upward of 95% of spinal metastases are extradural in nature.[10] In a retrospective review of 1196 patients with spinal metastases, Wang et al found that 54% sustained a spinal cord injury from extradural compression.[13]

Intradural metastasis are very rare.[24–26] In a retrospective study of more than 600 cancer patients, the frequency of intramedullary spinal metastasis was 8.5% of all cases that had CNS metastasis and 2.1% of all cancer patients.[25] In a separate study by Ryyken and colleagues, it was estimated that 20% of patients with intramedullary metastasis had multiple metastases, 8% being asymptomatic.[26] Additionally, the finding of intramedullary metastasis preceded the diagnosis of the primary tumor in 20% (10/49) of patients with intramedullary metastasis.[27]

Leptomeningeal carcinomatosis can be observed in late stages of cancer patients. At the time of diagnosis of leptomeningeal disease, the average survival is 2 to 4 months regardless of treatment.[28] Leptomeningeal carcinomatosis is seen in 5% to 8% of solid tumors, with a larger frequency of 15% in hematologic malignancies.[28,29] The incidence of leptomeningeal disease, of course, varies based on the primary tumor. Breast cancer leptomeningeal carcinomatosis ranges from 5% to 8%.[30] Melanoma progresses to leptomeningeal disease 6% to 18% of the time.[31] The burden of leptomeningeal carcinomatosis is higher yet at 9% to 25% in lung cancer, with small-cell pathology being the most significant culprit.[32]

A less-common but well-recognized pathology is the so-called drop metastasis from distant CNS tumors. The dissemination of CNS tumors most commonly occurs at the levels of the lower thoracic spine, conus, cauda equina, and lumbosacral nerves.[33–35] Drop metastases can spread to the leptomeninges, parenchyma, or both. Expectedly, the symptoms can include back pain, sensory disturbances, paresis, or bowel/bladder symptoms.[34,36] The overall incidence of drop metastases is less than 2%.[34] By comparison, malignant spinal cord compression due to glioblastoma multiforme drop metastases has been reported to be approximately 1%.[36]

Sequelae of Spinal Metastases

Bone metastases can cause a variety of complications, including hypercalcemia, epidural extension with spinal cord compression, nerve root compression, and bone pain.[11,37] Pathologic fractures can result in pain, spinal instability, and/or neurologic injury. Hypercalcemia is the most common metabolic complication from malignant disease. In addition to increased bone resorption, metabolic sequelae include constipation, fatigue, polydipsia, polyuria, and cardiac arrhythmias.[3,38]

The presence of bone metastasis can significantly reduce the quality of life and bring about limited or loss of mobility and loss of functional independence.[4,39–41] Treatment of spinal metastases may require surgery, chemotherapy, and/or radiation, all of which carry their own risk profiles. Patients who have skeletal metastasis are more likely to experience additional bone metastasis, impaired health-related quality of life, and worse prognosis, and use more health care resources compared to patients without bone metastasis.[7,42,43] By the time bone metastasis occurs, the aim of treatment is for palliation of pain and maintenance of quality of life with a strong emphasis on prevention of future spinal and skeletal complications.[8,16]

Solid-Tumor Metastasis

The pathogenesis of bone metastasis was described by Paget in 1889, broadly describing microenvironments

favorable to secondary site seeding of a primary tumor.[11,44] The affinity of a primary tumor for bone is not by chance. Rather, it is an incompletely understood sequence of cytokine and growth factor secretion by the primary tumor that promotes a niche for seeding. The continuous turnover of bone via the balanced dance between osteoblast and osteoclast activity can be easily manipulated to provide fertile grounds for metastasis with the aid of local stromal and mesenchymal cells.[3,11,45]

Roughly 70% of all bone metastases occur in the spine, with 10% of all spinal metastases being symptomatic. Although liver and lung precede bone as the most common sites for metastasis, 60% to 70% of patients with metastatic cancer acquire spinal metastasis.[9,10,46] It is estimated that less than 10% of patients with spinal metastasis are symptomatic, and almost half of those with spinal metastasis have more than one site of metastasis.[10,46,47] The most common age group for developing spinal metastasis is 40 to 70 years, with men at a higher prevalence, which is believed to be because of the propensity of prostate cancer to metastasize to bone.[10,13,14]

The increasing identification of cancer patients with spinal metastasis as a result of increasing survival rates for primary tumor is a testament to the effectiveness of modern systemic treatments. The time interval between primary cancer site diagnosis and spinal metastases is 32 months and just 27 months when epidural extension and spinal cord compression are present.[10,48] Identifying cancer patients with spinal metastases is critical because survival rates are lower for those with the advancing disease process of spinal metastases, and furthermore, those with epidural spinal cord compression. Historically, those with spinal column metastasis have a median survival of 7 months, and when epidural extension occurs the median survival rate drops to 3 to 6 months.[9,10] Longer-term estimates of survival of all cancer patients with spinal metastases show 10% to 20% survival at 2 years.[9,10] As it relates to breast and prostate cancer specifically, median survival rates after the diagnosis of bone metastasis are 19 to 25 and 12 to 53 months, respectively.[3]

Numerous retrospective studies have found an average age of 58.6 to 64.8 years at the time of diagnosis of spinal metastasis.[13,49–51] Wang et al observed that at the time of diagnosis, women are diagnosed 2 years earlier than men, at age 59.4 vs 57.4 years, respectively.[13]

Although nearly all tumors can metastasize to bone, the top 3 primary sites are breast, lung, and prostate cancers.[8,38] There are varying reports (breast vs lung) as to which primary tumor pathology has a higher incidence of spinal metastasis.[10,13] Additional primary tumors with an affinity for bone metastasis include malignant melanoma, renal, gastrointestinal, gynecological, bladder, thyroid, and colorectal tumors.[7,10]

Breast cancer is the most common cancer in women, and bone is the most common site of metastasis.[10,52] Walkington and Coleman estimated that 70% of women with advanced breast cancer will develop bone metastasis.[53] Metastases to the spine account for two-thirds of all bone metastasis in breast cancer.[54,55] Intuitively, the extent of metastasis influences survival rates. Plunkett et al described a significant difference in median survival between those with osseous metastases vs those with osseous and liver metastasis, 34 vs 5.5 months, respectively.[56] Furthermore, Coleman and colleagues reinforced the impact of extraosseous metastases on driving down the survival rate compared to those with only osseous metastases, 1.6 vs 2.1 years respectively.[57]

Lung cancer is routinely recognized as one of the most commonly diagnosed cancers worldwide. Non–small cell lung cancer (adenocarcinoma, large cell carcinoma, squamous cell carcinoma) accounts for 80% and small cell lung cancer accounts for the remaining 20% of lung cancers.[10] Lung cancer is the most common primary tumor, accounting for 36% of all spinal metastases.[10,13] Because lung cancer is often diagnosed at a late stage, up to 40% of patients may have bone metastases.[58]

Prostate cancer is the most common cancer in men older than 50 years and the most common cancer cause of death in this cohort. Expectedly, survival decreases with metastatic disease. When prostate cancer advances to metastatic disease, the 5-year survival rate is 30%.[10] Additionally, a Gleason score of greater than 6 has a significant association with spinal cord compression.[10] A review by Sutcliffe et al[10] found that the risk of spinal cord compression was 24% in patients with castration-resistant metastatic prostate cancer. In a retrospective review by Drzymalski and colleagues, of 9010 patients identified with prostate cancer, 333 (3.7%) had spinal metastasis and 23% of these patients suffered from spinal cord compression.[59] Wang et al estimated a higher incidence of spinal metastasis at 7.9%.[13]

Primary Spinal Osseous Tumors

When an osseous spinal tumor is the offending pathology on initial presentation, the workup must differentiate between a primary spinal pathology vs metastatic disease. Primary spinal osseous tumors are relatively rare compared to metastases from a primary tumor. Primary spinal osseous tumors account for 10% or less of all spinal osseous tumors.[23,60] There are regional differences in the reporting of benign and malignant primary osseous tumors of the spine.[60–62] In no specific order, plasma cell myeloma, chordoma, and osteosarcoma are the leading malignant tumors.[60–62] The differential for benign tumors includes osteoblastoma, osteoclastoma, giant cell tumor, aneurysmal bone cyst, osteoid osteoma, eosinophilic granuloma, and hemangioma.[60–62] Primary spinal osseous tumors can certainly mimic metastatic disease, emphasizing the importance of a thorough workup including biopsy to differentiate between these pathologies.

Conclusion

With improved local treatment and increasing survival rates, the prevalence of metastatic disease to the spine is on the rise. The palliative phase of treatment is therefore prolonged, offering providers an opportunity to efficiently

identify and treat metastatic spinal disease.[49] Mitigating the morbidity and mortality of the disease while optimizing treatment regimens must be driven toward enhancing the quality of life for those suffering from spinal metastases.

Conflict of interest statement. None declared.

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