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Intramedullary Spinal Cord Metastasis: Clinical Management and Surgical Considerations

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Although spinal column metastases can be found in up to 85% of patients with cancer at autopsy, the spinal cord itself is an extremely rare location for systemic spread of malignancy. Although historically considered untreatable lesions with rapid decline and death after diagnosis, current techniques and therapies have demonstrated good functional outcome and extended survival after aggressive treatment of intramedullary spinal cord metastasis (ISCM). Because of its overall rarity, most of the current knowledge on ISCM derives from autopsy series and small case series. Nevertheless, as diagnostic capabilities and treatment options for cancer improve, more patients with ISCM are likely to present earlier, live longer, and increase in number.

Demographics

The incidence of ISCM in patients with cancer ranges from 0.1% to 2.0% [1,2]. The true incidence may be higher but clinically silent, because 2% to 4% of patients with cancer show findings of metastasis to the spinal cord at autopsy [3,4]. Primary intramedullary spinal cord tumors are the most common spinal cord neoplasm but are still relatively infrequent lesions in the central nervous system (CNS). Metastatic cancer to the spinal cord comprises only 1% to 3% of all intramedullary spinal cord tumors [5]. By far, most common metastases to the spinal axis are extramedullary (eg, vertebral body, epidural or paraspinal) and account for most malignant epidural spinal cord compression. Only 0.8% to 3.5% of symptomatic metastases to the spine are intramedullary [6,7]. Regarding CNS metastasis as a whole, most cases are intracranial, with only 8.5% located in the spinal cord parenchyma [2]. The overall incidence of ISCM seems to be slowly rising as patients with cancer survive longer with current hormonal, chemotherapeutic, and radiation therapy protocols [8,9].

Any malignant cancer can theoretically spread to the spinal cord (Table 1). Bronchogenic cancer types are the most common primary source of ISCM, comprising 54% to 85% of cases [2,10,11]. Small cell lung cancer (SCLC) accounts for 47% of these metastases and far outnumbers the other bronchogenic cancer types. Five percent of all patients with SCLC have ISCM, whereas less than 1% of patients with non-SCLC have ISCM [2]. Breast cancer is the second most common primary site, and makes up 11% to 13% of ISCM cases [1,11]. Melanoma has relatively high rates of CNS metastasis, with 27% to 92% of patients with melanoma reported to have some form of CNS involvement, but only 8% to 9% of ICSM comes from a melanoma primary [12]. Lymphoma (4%), renal cell carcinoma (9%), colorectal cancer, and several other cancers represent the remainder of ICSM cases [7,10].

The presence of ISCM also seems to correlate with brain metastasis and leptomeningeal disease

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Table 1
Intramedullary spinal cord metastases by primary tumor site (%)

Primary type	Percentage
Bronchogenic	41%–85%
Breast	11%–13%
Melanoma	8%–9%
Lymphoma	4%–5%
Renal	4%–9%
Colorectal	3%
Thyroid	2%
Ovarian	1%–2%
Unknown	3%–6%

Data from Refs. [1,3,4,6,8,10,12].

(LMD). Fifty-seven percent of patients with ISCM have brain metastases, whereas 27.5% have evidence of LMD after a complete workup [4]. ISCM is seemingly an indicator of advanced systemic involvement of malignancy. This may account for the historically short life expectancy reported after the diagnosis of ISCM (80% mortality rate within 3–4 months).

The average age at presentation with ICSM is approximately 58 years (range: 38–78 years), and ICSM is more common in men (64%) than in women (46%) [10]. There is no ethnic or racial preponderance reported.

Tumor location

ISCM can occur anywhere along the spinal cord itself. A recent review of the literature reported the location of tumor to be the cervical cord in 24% of patients, the thoracic cord in 22%, and the lumbar cord or conus in 28% [10]. Fifteen percent had multiple cord level involvement. Individual case series, however, have reported conflicting evidence, with some stating that cervical cord metastasis is most common and others purporting that the thoracolumbar cord is most susceptible [4,6,11].

Three possible mechanisms of metastatic spread to the spinal cord have been suggested. Hematogenous dissemination probably accounts for most cases and is the most frequently suggested mechanism. Spinal necroscopy shows that ISCM primarily involves the posterior horns. These areas represent spinal gray matter that not only receives five times the arterial output compared with neighboring white matter but has the densest capillary bed in the spinal cord, along with the anterior horns [13]. Metastatic tumor cells bound in blood would naturally reside in areas of high blood perfusion. The higher incidence of bronchogenic cancer may be explained by its proximity to pulmonary veins that provide a direct conduit for tumor cells to enter the bloodstream and circulation. Venous plexus networks throughout the vertebral column frequently contribute to vertebral body metastasis but probably contribute less to ICSM. In the presence of LMD, tumor cells ''floating'' in cerebrospinal fluid (CSF) may infiltrate the Virchow-Robin spaces of vessels, penetrating the pial layer of the spinal cord and invading spinal cord parenchyma directly. Finally, direct extension through dura or perineural spread through nerve roots may provide access for tumor bulk contiguous with neural elements into the spinal parenchyma.

Histopathologic characteristics of ISCM include (1) distinct demarcation between tumor and parenchyma, (2) hemorrhagic foci within tumor, and (3) involvement of posterior roots [8]. The histology of metastases mirrors the histology of the primary malignancy; however, in 3% of ICSM cases, no known histopathologic tissue pattern can be discerned [10], and in an equally small percentage of patients, ICSM is the first manifestation of systemic cancer [7,14].

Clinical presentation

ISCM usually presents in the setting of known malignancy and involves a rapid progressive myelopathy occurring over several days or weeks (Table 2). Initial presenting complaints commonly include sensory changes and/or loss in 42.5% of patients, pain in 30%, weakness in 30%, gait changes and/or abnormalities in 5%, and incontinence in 2.5% [4,10]. Actual clinical examination findings include weakness in 93% of patients, sensory changes and/or loss in 78% to 87%, pain in 52% to 72%, bowel and/or bladder dysfunction in 62%, and systemic symptoms in 37% [4,10]. Weakness and pain tend to occur earlier in a patient's clinical course, whereas sensory changes and bowel and/or bladder involvement seem to be later manifestations. Weakness is frequently lateralized to one side and to a particular spinal level, whereas sensory loss is frequently referable to a specific dermatome. Paraplegia is present in 15% of cases [10]. The medullary pain of ICSM follows a pattern of a burning, dysesthetic, nonradicular bilateral pain [15]. Weakness and sensory changes manifest as Brown-Sequard syndrome in

Table 2
Symptoms at presentation and signs on physical examination in patients diagnosed with intramedullary spinal cord metastases

Presenting complaint	
Sensory loss	42.5%–79%
Pain	30%–38%
Weakness	30%–90%
Gait abnormality	5%
Incontinence	2.5%
Physical examination	
Weakness	93%
Sensory loss	78%–87%
Pain	52%–72%
Brown-Sequard syndrome	23%
Bowel/bladder dysfunction	60%–62%
Systemic symptoms	37%

Data from Refs. [1,4,6,8,10].

22.5% of patients and with pseudo– or partial Brown-Sequard syndrome in another 22.5% [4,14]. Asymmetric physical examination findings are noted in approximately 45% of cases. The average duration of symptoms before the diagnosis of ISCM is from 28 days to 6 months, with a range from 3 days to 18 months [4,10,15].

The mechanism for the relatively sudden development of symptoms relates to the limited reserve capacity of the spinal canal for rapid tumor growth. Direct compression of neural elements and vascular channels by tumor bulk contributes to the onset of myelopathic signs. Tethering of the spinal cord by dentate ligaments and the filum terminale may become symptomatic when enough stretch is produced by an expanding mass. Naturally, any mass lesion in the spinal column can cause these effects in the spinal cord, and distinguishing ICSM from epidural or paraspinal metastasis and compression from vertebral body metastasis becomes nearly impossible based on clinical grounds alone. The presence of Brown-Sequard syndrome suggests ICSM but is not pathognomic, because extramedullary tumors also produce identical clinical findings. Radicular pain is less common in ICSM and more frequent in the setting of nerve root compression by extramedullary lesions or schwannomas.

In addition to ICSM and spinal column metastasis, nonneoplastic myelopathies related to malignancy or treatment of cancer may also present with progressive deterioration in function localizable to the spinal cord and are included in the differential diagnosis of ICSM. Paraneoplastic necrotizing myelopathy occurs in patients with evidence of systemic cancer and can be indistinguishable from ISCM based on clinical symptoms alone. Radiographic findings include a rostrocaudal pencil-shaped necrosis in the thoracic cord. The presence of nonneoplastic cerebellar symptoms relates to paraneoplastic autoimmune effects, and these symptoms are not present in ISCM. ISCM is also more often associated with advanced metastatic disease than is paraneoplastic myelopathy. Patients receiving radiation therapy with exposure of the spinal cord are also at risk for delayed dose–related radiation-induced myelopathy. Symptoms usually present at least 4 months after the last dose of radiation and rarely occur in patients with less than 6000 rads if given in daily fractions less than 200 rads/d or weekly fractions less than 900 rads/wk [10]. Obviously, the pathologic lesion of radiation-induced myelopathy must lie within the boundaries of radiation-exposed spinal cord. In comparison to ISCM, both of these nonneoplastic myelopathies rarely have pain as an early or predominant symptom.

Diagnostic imaging and tests

Historically, spinal and CT myelography and myelography have been the mainstays of diagnostic imaging in evaluation of spinal cord tumors. Today, MRI with gadolinium enhancement has superseded myelography in diagnostic accuracy and precision. Multiplanar T1-weighted MRI sequences with contrast and T2-weighted MRI sequences can demonstrate ICSM and distinguish it from an extramedullary lesion (Fig. 1) [16,17]. Multiple and small lesions can also be detected on MRI, and the degree of cord edema can be quantified. Unfortunately, current acquisition techniques still cannot differentiate ICSM from nonneoplastic myelopathies or primary cord neoplasm, although future developments in diffusion-weighted, single-photon emission computed tomography (SPECT), and metabolic or perfusion imaging may allow for this degree of precision.

CSF analysis does not have a defined role in the diagnosis of ICSM. Studies have demonstrated elevated protein levels in cases of ICSM. Cytology is usually unremarkable, although in the setting of leptomeningeal dissemination, white blood cell (WBC) counts may be elevated. Overall, CSF analysis is uninformative, and abnormalities are grossly nonspecific.

Recently, staging of patients with cancer has included full-body nuclear radioisotope scans to

Fig. 1. MRI T1-weighted image with intense contrast enhancement of a C7-to-T1 lung adenocarcinoma.

detect potential sites of metastatic disease. These screening diagnostic scans may be helpful in detecting ISCM long before symptoms present, but treatment strategies for asymptomatic small ISCM are poorly defined [16].

Treatment

Traditionally, treatment for ICSM has consisted of dexamethasone dosing and external radiation therapy. Steroid dosing can reduce pain and provide some neurologic improvement in up to 85% of patients and is used in the acute setting as a bridge to more specific treatment [15]. Fractionated external radiation therapy is the primary treatment modality for ICSM, and general protocols use 16.3 to 45.2 Gy in 5 to 25 fractions over 2 to 4 weeks [4]. Radiation therapy is obviously indicated for radiosensitive (eg, SCLC, lymphoma, germ cell tumors) and partially radiosensitive (eg, breast, prostate) metastases. In the event of an unknown primary, a biopsy and pathologic diagnosis are mandatory. Whole-spine irradiation has been considered in the past, but the marrow toxicity involved has precluded its widespread use. Stereotactic radiosurgery has developed rapidly in the past decade and is a major treatment modality for intracranial metastatic disease. Its application in the treatment of spinal tumors and ICSM is currently under study [18,19]. Stereotactic radiosurgery alone or as boost therapy may be ideal for radioresistant metastasis (eg, melanoma, renal cell).

Recently, several reports have advocated surgery of ICSM as an adjunct to standard therapy [10,15]. Good neurologic outcome and extended survival are purported, but the actual outcome benefit of surgical removal is still unknown. If an open biopsy is required, safe excision of an intramedullary metastasis can be achieved. The surgical technique is similar to that used for removal of a primary spinal cord neoplasm, such as ependymoma, given a well-demarcated border between the metastasis and spinal cord affording relatively easy removal. If surgery is planned, radiation treatment should wait until after surgery, because radiation exposure can initiate scarring and obscuration of tissue planes, making surgery dangerous and difficult. Some authors have recommended undertaking surgery for ICSM for medium to large-sized tumors only, because too small a lesion may be difficult to localize and technically more complicated [20,21]. Currently, generous cytoreductive surgery for ICSM is a reasonably safe and beneficial adjunct to standard treatment [14,20,22].

Chemotherapy protocols exist for most metastatic malignancies and are applied as indicated by staging and prior responses. No single or combined drug strategy is unique for ICSM. Intrathecal administration of chemotherapeutic agents is possible, but the current literature supporting this adjunct is limited to case reports.

The most important factor correlating with good outcome after treatment of ICSM is early intervention. Patients with a shorter duration of symptoms and smaller lesions at the time of therapy tend to have better functional and survival outcomes based on several small case series [4,10,12,15].

Outcome

In general, the presence of ICSM serves as an indicator of extensive and advanced systemic involvement of malignancy and carries a poor prognosis. The average time to death after the diagnosis of ICSM is approximately 3 to 4 months (range: 3 weeks to 27 months) [10]. Death is usually

secondary to systemic metastatic involvement, but the disability caused by ICSM may predispose patients to complications like aspiration, pulmonary embolism from immobility, and accidents. Prolonged survival correlates with the aggressiveness of treatment in several small studies [4,10,15,20]. Patients receiving only steroids had an average survival of 5 weeks, whereas those with radiation and combined radiation and chemotherapy had average survivals of 15 weeks and 29 weeks, respectively [10]. Prolonged functional outcomes have been reported as small case series after aggressive surgery and radiation treatment with survival up to 103 weeks. Interestingly, melanoma demonstrates exceptionally good rates of functional survival after treatment compared with lung and breast cancer for metastatic lesions in intracranial and spinal disease [5,23]. Accordingly, patients with metastatic melanoma more likely deserve aggressive treatment options, including surgery, radiation, or stereotactic radiosurgery, in the setting of ICSM. Additionally, patients with breast cancer have demonstrated improved survival after treatment for metastatic disease in the brain and spine, which is likely attributable to improved hormonal, chemotherapeutic, and radiation strategies that have extended the average length of survival with breast cancer [24–26].

Summary

As patients survive longer from metastatic cancer with advancing treatment modalities, the incidence of intramedullary spinal cord metastases is likely to rise steadily. Although ICSM currently heralds a poor prognosis and short survival, even with maximal therapy, attempts at delineating optimal treatment strategies incorporating radiation, chemotherapeutics, and surgery are still necessary. Earlier detection and newer treatment modalities with aggressive but safe cytoreductive surgery may afford extended survival with good functional status.

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