

Malignant Spinal Cord Compression: An Overview

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Citation

A Dubey, R Koul. *Malignant Spinal Cord Compression: An Overview*. The Internet Journal of Oncology. 2009 Volume 7 Number 2.

Abstract

Malignant spinal cord compression (MSCC) occurs when malignant cells grow in, or near to the spinal cord, and compresses the thecal sac and nerve roots. These results in swelling and decrease in the blood flow to spinal cord and causes increase in the venous permeability and eventually interstitial edema. Interstitial edema compresses blood in small arterioles and arrest of capillary flow, resulting in ischemia. Ischemia impairs cord functions resulting in weakness and sensory impairment Any type of cancer can spread to the bones of the spine, which may lead to spinal cord compression. However, it is more commonly seen in hematological malignancies and in solid neoplasms such as breast, lung and prostate cancer. Consistent anatomical definitions of MSCC, clinical follow-up of definitive imaging studies and the addition of information on the natural history of cancer to traditional neurological and radiographic evaluation may all improve clinical assessment of suspected SCC in cancer patients. However, early detection and urgent treatment of malignant spinal cord compression is the only way to prevent paraplegia and severe neurological deficit.

INTRODUCTION

Malignant spinal cord compression (MSCC) in majority of cases results from hematogenous dissemination of malignant cells that often express tropism for vertebral column bone marrow. More frequently tumor cells grow in well vascularised marrow spaces of posterior vertebral body and lead to spinal metastasis which can produce cord or adjacent nerve roots compression. Sometimes destruction of cortical bone by malignancy can cause vertebral body collapse and displacement of bony fragments into the epidural space against the thecal sac and epidural venous plexus.

Compression of cord or blood vessels can also result from posterolateral direction thru neural foramina. Paraspinal masses or huge retroperitoneum nodal metastasis can also cause direct compression. Finally intramedullary metastases due to hematogenous dissemination can also cause internal cord compression¹.

PATHOPHYSIOLOGY

The pathophysiology of spinal cord compression is vascular in nature. This has been demonstrated in animal models. Initially there is venous compression which causes increase in venous permeability and interstitial edema. Interstitial edema compresses blood in small arterioles and arrest of capillary flow, resulting in ischemia. Ischemia triggers more swelling and reduction in the blood supply to the spinal cord and nerve roots resulting in impaired cord functions and

eventually weakness and sensory impairment.²

Experiments have demonstrated that during this phenomenon there is release of Prostaglandin E2 (PGE2). Further research have shown that vascular endothelial growth factor VEGF also play some role in cord compression. VEGF increases vascular permeability and vasogenic edema in response to ischemia³. During the process of ischemia, many excitotoxins are released which cause direct neuronal death.

ETIOLOGY

The clinically evident symptoms of spinal cord compression are caused by this cycle of increasing pressure (compression) on the spinal cord and nerves. Any type of cancer can spread to the bones of the spine, which may lead to spinal cord compression. However, it is more commonly seen in people with cancers of the breast, lung, prostate and myeloma. Slowly developing compression may be due to a tumor in the spinal cord or spine, an infection, arteriovenous malformation, or an abnormal bone growth⁴. Spinal stenosis can gradually compress the cord, causing back pain. An injury, cancer, or osteoporosis may cause vertebrae to collapse, compressing the spinal cord. Collapse of a vertebra is called a compression fracture.⁵

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SYMPTOMS

Compression of the spinal cord is minimal, if only some nerve signals going up and down the spinal cord may be disrupted. Symptoms may include discomfort only in the back, minor weakness, tingling, other changes in sensation, erectile dysfunction, easy fatigue and gait disturbance. The cervical spine disease produces quadriplegia while as thoracic spine disease produces paraplegia. Disease involving lumbar spine disease produce sensory loss and paraesthesia. Light touch, proprioception and joint position may be also reduced. Tendon reflexes are often either increased below the level of compression or absent at level of compression. Sphincter disturbances are late features of cervical and thoracic cord compression. If cauda equina is compressed then there is spectrum of neurological dysfunction including loss of perianal sensation, root pain in both legs and painless urinary retention. If patient has pain on movement, it suggests vertebral fracture or collapse. If degree of compression increases, symptoms may worsen. If compression is complete, most nerve signals may be blocked, causing severe weakness, numbness, incontinence or retention of urine, and loss of bowel control. If all nerve signals are blocked, paralysis and complete loss of sensation result. A belt like band of discomfort may be felt at the level of spinal cord compression. Once spinal cord compression begins to cause symptoms, the damage usually worsens from minimal to substantial unpredictably but rapidly in a few hours to a few days⁶.

INVESTIGATIONS

Early diagnosis, usually by magnetic resonance imaging or myelography, is essential but the diagnosis is often delayed. Plain x-rays may show bony or paravertebral soft tissue disease but often is not helpful. CT scan of spine is more sensitive than plain films and can locate cord compression at multiple levels and associated bony fractures. However, Magnetic resonance imaging is the best tool for diagnosing

metastatic spinal cord compression and is able to identify spinal cord compression in 32-35% patients with back pain, bone metastases and normal neurological examination. Moreover, magnetic resonance imaging gives the extension of the lesion, can diagnose other unsuspected clinical metastatic spinal cord compression sites, and is useful for the radiation oncologist in defining the target volume. Bone scan sometimes is helpful to indicate disease pattern and extent of bone pathology.

SPINAL CORD COMPRESSION AND ONCOLOGY

Many early autopsy studies have approximated the incidence of SCC in cancer patients to be 4-6 % but it is arguably an underestimate of the true incidence. Prostate, breast, and lung cancers constitute 60-70% and renal cell cancer, non-hodgkin's and plasmacytoma comprise 15-20% of MSCC. Generally, metastatic seeding appears in the thoracic spine (accounting for about 70% of cases), with the lumbar spine being the next most involved site (20% of cases). The cervical spine is affected in approximately 10% of cases. Multiple spinal levels are affected in about 30% of patients. Gastrointestinal and pelvic malignancies tend to affect the lumbosacral spine; lung and breast cancers are more likely to affect the thoracic spine⁷. Sometimes primary spinal tumors can also cause compression. Most primary spinal cord tumors are astrocytomas or ependymomas. Primary tumors that affect the paravertebral area may spread and compress the cord through expansion, particularly in an intervertebral foramen. Metastases to the substance of the cord (intramedullary) are relatively rare. Leptomeningeal metastases spread by means of diffuse or multifocal seeding of the meninges from systemic cancer (e.g., lung or breast cancer, melanoma, lymphoma). Hemangiomas are usually discovered incidentally and usually do not produce symptoms. However, symptoms emerge if pathologic vertebral fractures or epidural extension occurs. Nerve tracts most vulnerable to mechanical pressure include the corticospinal and spinocerebellar tracts and the posterior spinal columns⁷.

ASSESSMENT

Urgent detailed history and physical examination is mandatory to evaluate motor deficits and the pre-treatment ambulatory status. In literature there is a scoring system to estimate the survival of patients with metastasis spinal cord compression (MSCC). The system includes the 6 prognostic factors such as tumor type, interval between tumor diagnosis and MSCC, other bone or visceral metastases at the time of

radiation, ambulatory status, and duration of motor deficits. The score for each prognostic factor is determined and dividing the 6-month survival rate (given as the percentage) by 10. The total score represents the sum of the scores for each prognostic factor. Total scores ranges between 20 and 45 points. In study the patients were divided into 5 groups. For each group, the survival was compared for short-course or long-course RT. The 6-month survival rates were 4% for patients with a score of 20 to 25 points, 11% for patients with a score of 26 to 30 points, 48% for patients with a score of 31 to 35 points, 87% for patients with a score of 36 to 40 points, and 99% for patients with a score of 41 to 45 points ($P < .001$). Patients with scores ≥ 36 were found to have a significantly longer survival when comparing long-course versus short-course RT, and those with scores < 36 were found to have similar survival regardless of whether short-course or long-course RT was used. Using this scoring system, patients with MSCC can be grouped to estimate survival. Patients with scores ≥ 36 were found to survive longer with long-course RT, whereas patients with lower scores had a similar survival regardless of whether long-course or short-course RT was used⁸.

TREATMENT

The goals of therapy for MSCC include pain control, avoidance of complications, and a rational attempt to preserve or improve neurological functioning utilizing techniques appropriate to the patient's burden of disease, life expectancy, and values. Patients may present in a variety of health care settings to any health care professional. Majority of patients will have a pre-existing known malignancy however some may not have a definite diagnosis. All patients irrespective of known malignancy require urgent admission and assessment. Where a patient has no history of primary malignancy they should be referred to the nearest spinal surgery or neurology service.

The standard treatment for spinal cord compression caused by metastatic cancer is corticosteroids and radiotherapy. Patients with pain but minimal neurological dysfunction receive a bolus of 10 mg followed by 16 mg daily initially in divided doses. The dose is gradually tapered once definitive treatment is well underway. Patients with small epidural lesions and a normal neurological examination and those with relative contraindications to therapy may forgo the use of steroids. Corticosteroids are amongst the most effective treatments of neurological dysfunction resulting from compression. It reduces edema, inhibits PGE₂ synthesis and decrease specific gravity of the compressed tissue. It has

been shown that it delays the onset of neurological symptoms. It down regulates VEGF expression in smooth muscle cells and helps to prevent changes in muscles induced by increased impermeability. However the optimal dose and scheduling is controversial⁹. Patients with cancer usually have hyper coagulable state. Although the value of prophylaxis against venous thromboembolism has not been studied in patients with MSCC, it would seem reasonable to give prophylactic subcutaneous heparin or sequential compression devices to non ambulatory patients who are risk. Autonomic dysfunction from the cord lesion, limited mobility, and narcotics contribute to the development of constipation occasionally perforation of an abdominal organs, so aggressive bowel preparation is recommended.

The radiation has been the integral part of MSCC management since time immemorial. Radiation reduces pain in 70% of the patients and improves motor functions in 45% to 60% and reverses paraplegia in 10% to 20% of the patients¹⁰. The dose and scheduling of radiation has been area of interest for researchers and radiation oncologists. The optimum radio therapeutic regimen is still debated; studies comparing different radiation schedules on therapeutic outcome are scarce. In one of the analysis the effect of two radiation schedules 30 Gray/10 fractions vs. 37.5 Gray/15 were compared for post-treatment functional outcome and ambulatory status. Response and ambulatory status were evaluated directly, 3, 6 and 12 months after radiotherapy. Between the two radiation schedules no significant difference was observed for post-treatment ambulatory rates (p values: 0.450-0.888) and for functional outcome (p values: 0.940-0.999). According to the multivariate analysis, the strongest predictors for functional outcome were the time of developing motor deficits before radiotherapy ($p < 0.001$) and the pre-treatment ambulatory status ($p < 0.001$), followed by the type of primary tumor ($p = 0.058$). For the radiation schedule a significant impact on functional outcome was not observed ($p = 0.822$)¹¹.

In another trial, 1304 patients (irradiated 1/92-12/03) were studied. The schedules 1x8Gy in 1 day ($n=261$), 5x4Gy in 1 week ($n=279$), 10x3Gy in 2 weeks ($n=274$), 15x2.5Gy in 3 weeks ($n=233$), and 20x2Gy in 4 weeks ($n=257$) were compared for post-treatment motor function, ambulatory status, and in-field recurrences. The 5 treatment groups were balanced for the potential prognostic factors. Motor function improved in 26% (1x8Gy), 28% (5x4Gy), 27% (10x3Gy), 31% (15x2.5Gy) and 28% (20x2Gy) ($P=0.90$). Post-treatment ambulatory rates were 69%, 68%, 63%, 66%, and

74% ($P=0.58$), respectively. On multivariate analysis, better performance status ($P<0.001$), favorable histology ($P<0.001$), involvement of only 1-2 vertebrae ($P<0.001$), and a slower progression of motor deficits before RT (>14 days, $P<0.001$) were associated with a better functional outcome. Pre-treatment ambulatory status achieved borderline significance ($P=0.06$). The radiation schedule had no significant impact ($P=0.96$)¹².

A prospective study of 301 new patients diagnosed with cord compression were examined to evaluate interval from onset of symptoms to presentation and treatment, delay at each stage of referral, and functional deterioration. The author found that the median (range) delay from onset of symptoms of spinal cord compression to treatment was 14 (0-840) days. Of the total delay, 3 (0-300) days were accounted for by patients, 3 (0-330) days by general practitioners, 4 (0-794) days by the district general hospital, and 0 (0-114) days by the treatment unit. Initial presentation to the regional cancer centre with symptoms of malignant spinal cord compression led to a significant reduction in delay to treatment and improved functional status at the time of treatment. Deterioration of motor or bladder function 1 grade occurred at the general practice stage in 28% (57) and 18% (36) of patients, the general hospital stage in 36% (83) and 29% (66), and the treatment unit stage in 6% (19) and 5% (15), respectively. Unacceptable delay in diagnosis, investigation, and referral occurred in most patients with malignant spinal cord compression and resulted in preventable loss of function before treatment.¹³

The role of surgery has evolved recently. In this one of the famous randomized, multi-institutional, non-blinded trial, patients with spinal cord compression caused by metastatic cancer were randomly assigned to either surgery followed by radiotherapy ($n=50$) or radiotherapy alone ($n=51$). Radiotherapy for both treatment groups was given in ten 3 Gray fractions. The primary endpoint was the ability to walk. Secondary endpoints were urinary continence, muscle strength and functional status, the need for corticosteroids and opioid analgesics, and survival time. After an interim analysis the study was stopped because the criterion of a predetermined early stopping rule was met. Significantly more patients in the surgery group (42/50, 84%) than in the radiotherapy group (29/51, 57%) were able to walk after treatment (odds ratio 6.2 [95% CI 2.0-19.8] $p=0.001$). Patients treated with surgery also retained the ability to walk significantly longer than did those with radiotherapy alone (median 122 days vs. 13 days, $p=0.003$). 32 patients entered

the study unable to walk; significantly more patients in the surgery group regained the ability to walk than patients in the radiation group (10/16 [62%] vs. 3/16 [19%], $p=0.01$). The need for corticosteroids and opioid analgesics was significantly reduced in the surgical group. Direct decompressive surgery plus postoperative radiotherapy is superior to treatment with radiotherapy alone for patients with spinal cord compression caused by metastatic cancer¹⁴. Although surgical treatment of spinal metastases has become safer, less invasive, and more efficacious in recent years, there remains a subset of patients for whom other treatment modalities are needed.

Stereotactic radiosurgery, which has long been used in the treatment of intracranial lesions, has recently been applied to the spine and enables the effective treatment of metastatic lesions. Future challenges involve the refinement of noninvasive fiducial tracking systems and the discernment of optimal doses needed to treat various lesions. Additionally, dose-tolerance limits of normal structures need to be further developed. Increased experience will likely make stereotactic radiosurgery of the spine an important treatment modality for a variety of metastatic lesions¹⁵.

To improve the quality of care for metastatic spinal cord compression over 6 months by ensuring that $>90\%$ of patients should receive definitive treatment within 24 h of radiological diagnosis. Using clinical practice improvement project methodology, the clinical pathway of 17 patients treated with radiotherapy for metastatic spinal cord compression within the last 6 months was reviewed in this article to identify gaps and delays in the system. Post-intervention of 22 subsequent patients was monitored for time to start of steroids and radiation therapy, length of stay and hospitalization bill. With the interventions implemented, the mean response time to start steroidal therapy was reduced from 8.4 to 2.6 days and radiotherapy from 9.9 to 3.9 days. These translated into shorter mean length of stay from 23.8 to 14.7 days and smaller hospitalization bill. A clinical practice improvement project, to improve the quality of care for patients with metastasis spinal cord compression, can shorten response time to start steroidal therapy and definitive radiotherapy resulting in shorter length of stay and smaller hospitalization bill.¹⁶

Chemotherapy and hormonal therapy has been tried such as in prostate, breast cancer, lymphoma and myeloma. The use of chemotherapy and radiation has been shown to prolong survival in patients with epidural compression due to non Hodgkin lymphoma¹⁷. Palliative care is a treatment option

for patients that have failed to respond to either chemotherapy or radiation therapy and are not suitable for any surgical intervention. These patients are treated with analgesia, nerve blocks and corticosteroids. Overall the patient's prognosis for recovery depends largely on the degree of ambulation at the time of diagnosis. Around 80% of ambulatory patients will remain so if treated immediately, approximately 30% of non ambulatory patients may regain the ability to walk after treatment. In situations where SCC has already caused complete paralysis the chances of regaining the ability to ambulate are 0 to 10%.¹⁸

CONCLUSION

In summary, results of a randomized trial indicates that surgical resection followed by post operative external radiation increases the likelihood of regaining the function and ability to walk and of maintaining ambulation following treatment, while those undergoing radiation alone will have a lower functional status. However, careful selection is required to identify patients with an adequate life expectancy and good medical status who are candidates for this aggressive approach. Paraplegia from malignant spinal cord compression is preventable if diagnosed early and treatment started before severe neurological deficits develop. It is very important that physicians at the community level are educated so that referral to a Cancer center is made in time.

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