Epidural spinal cord compression in cancer patients: Diagnosis and management

**ABSTRACT**

In most patients with spinal cord compression due to epidural metastasis, the initial symptom is progressive back pain with an axial or radicular distribution, but early symptoms are often nonspecific. Since the key prognostic factor is the neurologic status at the time of presentation, and since early complaints are often nonspecific, a high index of suspicion is needed to diagnose this complication early.

**KEY POINTS**

With prompt management, ambulatory status can be maintained in about 80% of patients, but delays result in a rapid loss of function.

Back pain tends to be localized initially and may increase with lying supine, coughing, sneezing, flexing of the neck, and moving.

Differentiating back pain of epidural spinal cord compression from that of degenerative joint disease is critical. Pain of degenerative joint disease almost always affects the low cervical or low lumbar spine, whereas pain of metastatic compression occurs at any level. Lying down improves the pain of degenerative disease but typically worsens pain due to metastatic compression.

Magnetic resonance imaging is the diagnostic test of choice for epidural spinal cord compression.

Steroids should be given to all patients suspected of having spinal cord compression.

**PATHOPHYSIOLOGY**

Epidural metastasis needs to be recognized early and treated promptly, since any delay may doom the patient to a very uncomfortable demise, with pain, immobility, and incontinence. With prompt treatment, 80% of patients maintain their ability to walk. In most patients, the initial symptom is progressive back pain with an axial or radicular distribution, but early symptoms are often nonspecific. Therefore, a high index of suspicion is needed to diagnose this complication early.

In cancer patients, epidural spinal cord compression is usually the result of hematogenous spread of primary tumor cells to the bone marrow of the vertebral column, where metastatic tumors grow. In time these tumors can cause cord compression, either by extending into the epidural space or by causing vertebral body collapse. In addition, animal studies have demonstrated that blood flow abnormalities such as vascular congestion, edema, and hemorrhage of the spinal cord at the level of the compression also play a role. These findings could be caused either by occlusion of venous outflow from the cord, or by occlusion of the central perforating vessels of the spinal cord. Animal studies have also demonstrated that neurologic deficits are more likely to reverse when compression is gradual rather than acute.

Vasogenic cord edema has been correlated with increased synthesis of prostaglandin E2, which can be inhibited by steroidal and non-
steroidal anti-inflammatory drugs, as well as by serotonin antagonists (eg, cyproheptadine). These findings may lead to new types of therapy for this condition.

### CLINICAL PRESENTATION

**Back pain**

Back pain is the most common presenting symptom, occurring in 95% of patients with epidural spinal cord compression. It may precede neurologic symptoms by weeks or months.

Caused by expanding metastases stretching the periosteum, the pain:
- Can be either localized or referred, although it is usually localized initially
- May increase with lying supine, coughing, sneezing, flexing the neck, moving
- May be described as a deep, dull ache
- May awaken the patient from sleep
- May not respond to analgesics
- May include tenderness on percussion over the involved area
- May be radicular, occurring near the area of compression in a dermatomal pattern—unilaterally when the cervical or lumbar spine is involved, and bilaterally when the thoracic spine is involved.

**Spinal cord compression vs degenerative joint disease**

Differentiating the pain of metastatic epidural spinal cord compression from the pain of degenerative joint disease is critical. Clinical clues include:
- **Location** of the pain: pain of degenerative joint disease almost always affects the low cervical or low lumbar spine, whereas pain of metastatic compression occurs at any level
- **Positional relief**: lying down improves the pain of degenerative disease but typically worsens pain due to metastatic compression.

**Neurologic signs**

Neurologic signs or symptoms in patients with metastatic epidural spinal cord compression usually indicate disease progression.

**Motor weakness** usually follows the development of pain by weeks or months. It affects proximal muscles, creating difficulty when climbing stairs or rising from a chair.

When weakness is present, hyperreflexia and an extensor plantar response confirm involvement of the corticospinal tracts.

**Sensory loss** may occur below the level of cord compression and corresponds to a skin dermatome. Loss of proprioception is common when the posterior spine is involved.

**Signs and symptoms of autonomic dysfunction** such as hesitancy, urinary retention, and urinary and fecal incontinence occur late and are particularly ominous. Although narcotic analgesics can cause urinary retention, spinal cord compression should be ruled out first in any patient at risk.

### PROGNOSIS

The prognosis depends very much on the patient’s neurologic status at the time of diagnosis. Indicators of poor prognosis include:

- **Impaired ambulation** is the most reliable indicator. If ambulatory at the initiation of therapy, 80% of patients remain able to walk after treatment. Only 30% to 40% of patients with motor dysfunction before treatment are able to walk after treatment.

- **Rapid symptom onset**. Animal studies show that neurologic deficits are more likely to reverse when compression is gradual rather than acute.

- Duration of motor dysfunction greater than 48 hours indicates that the underlying injury has become irreversible.

- **Poor sphincter control at presentation** indicates that epidural spinal cord compression is in the later stages, when treatment has little or no effect.

### IMAGING STUDIES

Cancer patients in whom metastatic epidural spinal cord compression is suspected should undergo an immediate, careful, detailed neurologic examination, including imaging studies. The following imaging studies help to confirm the diagnosis.

**Plain radiography**

Plain radiography detects bony abnormalities (eg, absence of a pedicle, luencies in the vertebral body) in 70% of patients with epidural spinal cord compression. However, more
TABLE 1

Current management of metastatic epidural spinal cord compression

<table>
<thead>
<tr>
<th>Radiotherapy</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radiotherapy</strong> is the treatment of choice for most patients: 30 Gy delivered in 10 fractions over a period of 2.5 weeks</td>
<td><strong>Surgery</strong> is appropriate if the patient has:</td>
</tr>
<tr>
<td>Spinal instability</td>
<td>Spinal instability</td>
</tr>
<tr>
<td>Unknown diagnosis</td>
<td>Unknown diagnosis</td>
</tr>
<tr>
<td>No response to radiotherapy</td>
<td>No response to radiotherapy</td>
</tr>
<tr>
<td>Already received the maximum tolerable dose of radiation therapy to the area</td>
<td>Already received the maximum tolerable dose of radiation therapy to the area</td>
</tr>
<tr>
<td>Intractable pain despite radiotherapy and large doses of corticosteroids</td>
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</tr>
</tbody>
</table>

Autonomic dysfunction has a poor prognosis

Magnetic resonance imaging

Magnetic resonance imaging (MRI) is the imaging study of choice for diagnosing epidural spinal cord compression. It is noninvasive, easily detects paraspinal soft-tissue masses, detects additional sites of vertebral involvement (multiple sites of compression can be detected in 9% to 30% of patients), and is as accurate as myelography or computed tomography. The addition of gadolinium contrast offers better detection of epidural, intradural extramedullary, intramedullary, and leptomeningeal lesions.

Computed tomographic myelography

Before the advent of MRI, computed tomography—performed after injecting metrizamide—was the tool of choice for diagnosing metastatic epidural spinal cord compression. This procedure is currently indicated in the following specific clinical situations:

- If MRI is not available
- If the patient has a pacemaker
- If the patient is too large to fit in the MRI machine
- If the patient has severe claustrophobia, is unable to lie flat for the duration of the test, or has uncontrolled pain.

In a patient with complete myelographic block, contrast can be administered from above through a C1-2 puncture to demarcate the upper border of the block and to look for other epidural lesions.

Adverse effects associated with this procedure include infection, bleeding, and a 10% to 20% risk of iatrogenic neurologic deterioration attributed to the lumbar puncture in patients with complete subarachnoid block.

MANAGEMENT: RELIEVING PAIN AND PRESERVING FUNCTION

Treatment of metastatic epidural spinal cord compression (TABLE 1) should focus on relieving pain and preserving neurologic function. Achieving these two goals will not only preserve the patient's quality of life, but also reduce the burden on the caregiver, since patients who progress to paraplegia require extensive and costly care.

Corticosteroids

Corticosteroid therapy is generally started as soon as the diagnosis of spinal cord compression is entertained. The goals of corticosteroid therapy are to reduce the vasogenic edema caused by the expanding cancer, to control pain, and to maintain neurologic function.

Exact dosages, schedules, and duration of therapy have not been established. A loading dose of dexamethasone 10 to 100 mg intravenously followed by 4 to 24 mg orally or intravenously every 6 hours has been suggested. The addition of gadolinium contrast offers better detection of epidural, intradural extramedullary, intramedullary, and leptomeningeal lesions.

Corticosteroid therapy is usually continued throughout radiation therapy and is tapered slowly toward the end of treatment. During the tapering period, patients should be carefully followed, and any neurologic deterioration should prompt an increase in the steroid dosage.

High-dose dexamethasone. Some experts have hoped that high-dose corticosteroid therapy would be more efficacious than conventional regimens. But three prospective,
randomized trials\textsuperscript{11-13} of high-dose dexamethasone therapy showed varying results:

- Greenberg et al\textsuperscript{11} found that high-dose dexamethasone (a 100-mg intravenous bolus, followed by 96 mg/day orally for the first 3 days, then tapered) brought substantial pain relief in patients undergoing radiation therapy, but had no effect on motor ability.
- Sorenson et al\textsuperscript{12} found that patients who received high-dose dexamethasone (a 96-mg intravenous bolus, followed by 96 mg orally for 3 days, then tapered) in conjunction with radiation therapy maintained gait function longer than patients who received no dexamethasone with radiation therapy.
- Vecht et al\textsuperscript{13} found no advantage of high-dose dexamethasone therapy vs conventional doses in terms of either pain relief or neurologic function.

High-dose regimens carry a risk of serious toxicity; the incidence of serious toxic effects was 14\% in one study.\textsuperscript{14} This risk must be weighed against the anticipated benefits.

Radiation therapy

Radiation therapy is the treatment of choice for most patients with epidural spinal cord compression. A common schedule is a dose of 30 Gy delivered in 10 fractions over 2.5 weeks. The treatment field includes the area of spinal cord compression, with a margin of two vertebral bodies above and below the area involved with disease. Patients with prostate or breast cancer often present with multiple areas of involvement.

Response to radiation therapy is evaluated in terms of pain relief and stabilization or reversal of neurologic deficit. Tumors classified as "radiosensitive" (eg, lymphoma, seminoma) respond better than "radioresistant" tumors (eg, sarcoma, melanoma), with a complete response rate of 77\% vs 30\%.\textsuperscript{15} Predictors of more favorable response include favorable histology (prostate or breast cancer, myeloma), earlier diagnosis, and less neurologic deficit at presentation.\textsuperscript{16}

Surgery

Although radiation therapy is the treatment of choice for most patients with epidural spinal cord compression, surgery is also useful in selected patients. Indications include the need to establish a diagnosis in patients with no known cancer, to treat spinal instability, to treat pathological fractures caused by symptomatic spinal metastases, and failure to respond to radiation therapy. On the other hand, recovery from spinal surgery is not devoid of complications, and this potential morbidity should be taken into account when surgery is considered for patients with poor life expectancy and several sites of metastatic disease.

Anterior decompression with mechanical stabilization is the surgical technique of choice for epidural metastases arising from the vertebral body. Several retrospective studies\textsuperscript{17} and a small prospective study\textsuperscript{18} failed to show any advantage of laminectomy when compared with radiotherapy alone.

Chemotherapy

Chemotherapy has only a limited role in the management of epidural spinal cord compression. It may be used in adults who have a chemosensitive tumor (eg, germ cell tumor, Hodgkin disease) and who cannot undergo surgery or radiation therapy, or as adjuvant therapy after surgery or radiotherapy.

In children with chemosensitive tumors (eg, neuroblastoma, Ewing tumor), chemotherapy should be considered because of the risk of radiation-induced growth abnormalities or secondary tumors. Chemotherapy should also be considered in cases of recurrent spinal cord compression by a chemosensitive tumor in a site of previous radiation or surgery.

\textbf{REFERENCES}

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