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Metastatic spinal cord compression

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Abstract

Metastatic spinal cord compression is compression of the spinal cord or cauda equina as a result of metastatic deposits in the spinal column. It affects approximately 4000 cases per year in England and Wales. Prompt identification and treatment of metastatic spinal cord compression is necessary to prevent irreversible neurological injury, treat pain and maintain patients' mobility, function and independence. Survival of patients with common malignancies has improved significantly with the ongoing development of radiotherapy and chemotherapy, as well as improved surgical treatment of resectable primary tumours. This article outlines the clinical approach to presentation, pathophysiology, diagnosis and management.

Key words: Cancer; Compression; Metastatic; Spine; Spinal cord

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Introduction

Metastatic spinal cord compression is compression of the spinal cord or cauda equina as a result of metastatic deposits in the spinal column (Figures 1 and 2). Metastatic spinal cord compression occurs in 2.5–5% of patients with cancer (Al-Qurainy and Collis, 2016; Wänman et al, 2017; Lawton et al, 2019). This may translate to around 80 cases per million people per year (Al-Qurainy and Collis, 2016), or approximately 4000 cases per year in England and Wales (National Institute for Health and Care Excellence, 2008). Metastatic spinal cord compression is most common in patients with a known primary cancer diagnosis, but it can be the initial manifestation of malignancy in undiagnosed cancer (Wänman et al, 2017).

Prompt identification and treatment of metastatic spinal cord compression is necessary to prevent irreversible neurological injury, treat pain and maintain patients' mobility, function and independence. Survival of patients with common malignancies has improved significantly with the ongoing development of radiotherapy and chemotherapy, as well as improved surgical treatment of resectable primary tumours. This increased survival may increase the prevalence of metastatic spinal cord compression, as it is often a feature of advanced disease (Al-Qurainy and Collis, 2016).

Clinical presentation

Malignant disease frequently advances in severity despite treatment. The history of a patient with metastatic spinal cord compression is characterised by an insidious onset and progression of symptoms, but deterioration can be rapid. The clinical presentation of metastatic spinal cord compression is dependent on the structures in the spine that have been compromised and the associated neural compression.

Examination of patients with possible metastatic spinal cord compression should include a 'look, feel, move' examination of affected areas of the locomotor system. A complete neurological assessment should then be performed, including autonomous sensory areas, and function in dermatomal/myotomal distribution should be fully mapped and recorded (Figure 3). Classically patients will display upper motor neurone signs below the level of cord compression and a dermatomal sensory level may be elicited with altered or reduced sensation. Compression below the level of the termination of the spinal cord (the conus, usually at the level of the L1 vertebra) tends to present with symptoms of cauda equina syndrome. Upper motor neuron deficits are often symmetrical while lower motor neurone deficits tend to be asymmetric (Lawton et al, 2019). These findings should be documented on a 'ASIA Impairment Scale Scoring Chart' (Roberts et al, 2017).

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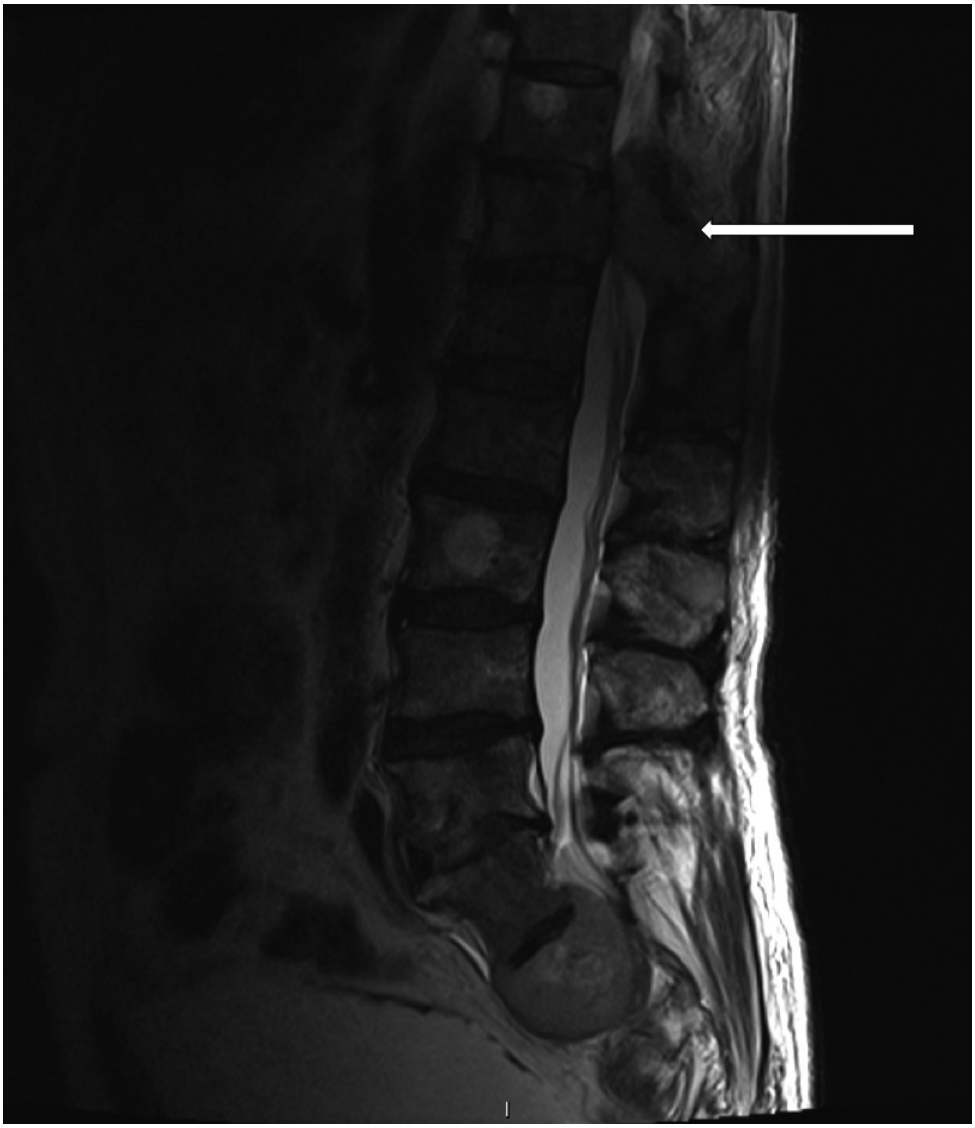

Figure 1. Sagittal T2-weighted images of metastatic spinal cord compression at T12, further lesions in the sacrum and throughout the axial skeleton (arrow).

Back pain is present in up to 95% of patients for up to 2 months before specific signs of metastatic spinal cord compression occur (Al-Qurainy and Collis, 2016). The pain is typically constant and worse at night or early morning. It may be exacerbated by coughing and straining or on lying flat (Macdonald et al, 2019). Pain in metastatic spinal cord compression has the typical distribution and nature of radicular pain in 79% of patients (Lawton et al, 2019). This is a common symptom and can therefore be overlooked or its significance misjudged. About 70% of spinal metastases occur in thoracic and 10% in cervical regions (Klimo and Schmidt, 2004). Midthoracic and upper cervical pain and tenderness are uncommon in other medical conditions, so should be viewed as a 'red flag' symptom requiring urgent specialist review. Other red flag symptoms are identified in the National Institute for Health and Care Excellence (2008) guidelines, which suggest an urgent referral (for review within 24 hours) to a metastatic spinal cord compression coordinator if a patient with cancer reports any of the following:

- Pain in the thoracic or cervical spine
- Progressive lumbar spinal pain
- Severe unremitting lower spinal pain
- Spinal pain aggravated by straining (eg at stool, or when coughing or sneezing)
- Localised spinal tenderness
- Nocturnal spinal pain preventing sleep.

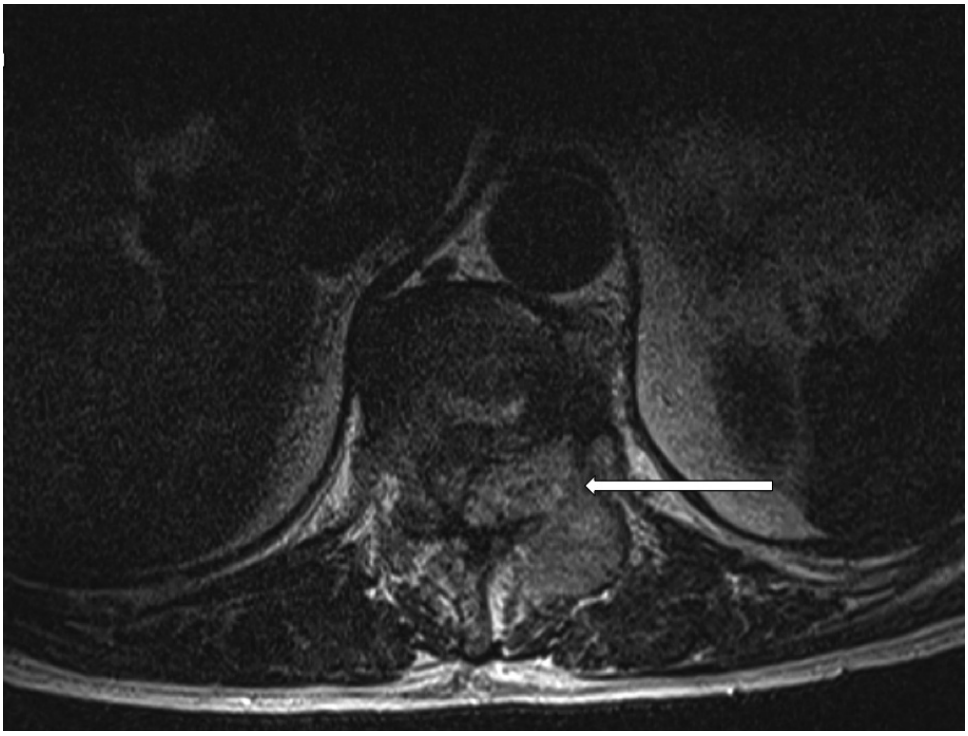

Figure 2. Axial cut through the level of T12 showing obliteration of CSF and compression of the cord as a result of a left posterolateral tumour mass (arrow).

And an immediate referral with any of the following, representing an oncological emergency:

- Neurological symptoms, including radicular pain, any limb weakness, difficulty in walking, sensory loss or bladder or bowel dysfunction
- Neurological signs of spinal cord or cauda equina compression.

The second most common feature of metastatic spinal cord compression at presentation is limb weakness – 85% of patients experienced weakness at the time of diagnosis (Levack et al, 2001). This is reported by patients and carers as a sudden increase in difficulty in standing, walking or transferring from bed to chair over days or a few weeks (Al-Qurainy and Collis, 2016).

Sensory symptoms, such as paraesthesia, reduced sensation and numbness of the fingers and toes, may extend 1–5 dermatomes below the level of the actual cord compression. Sensory loss in a radicular pattern and absence of tendon reflexes may correlate more closely to the compressive site that reported symptoms (Al-Qurainy and Collis, 2016).

Autonomic dysfunction secondary to metastatic spinal cord compression is a late manifestation and is rarely present without signs and symptoms. This may present as bladder and bowel dysfunction in the form of urinary retention, incontinence and constipation, or impotence (Bucholtz, 1999).

Pathophysiology

Bone is the third most frequent site of metastasis, behind lung and liver. Approximately 5–10% of patients with cancer develop metastatic spinal cord compression (Levack et al, 2001). The most common primary tumours resulting in metastatic spinal cord compression are cancers of the prostate, breast and lung, which account for approximately 50% of cases. The majority of patients diagnosed with metastatic spinal cord compression have a known cancer diagnosis, but in 10–20% of cases, metastatic spinal cord compression is the presenting feature (Wänman et al, 2017).

Spinal metastases can be classed as intradural (intramedullary or extramedullary) or extradural. Approximately 95% of extradural lesions are either pure epidural lesions, which are rare, or those arising initially from the vertebra but migrating to and causing compression of the thecal sac and its contents (Bartels et al, 2007).

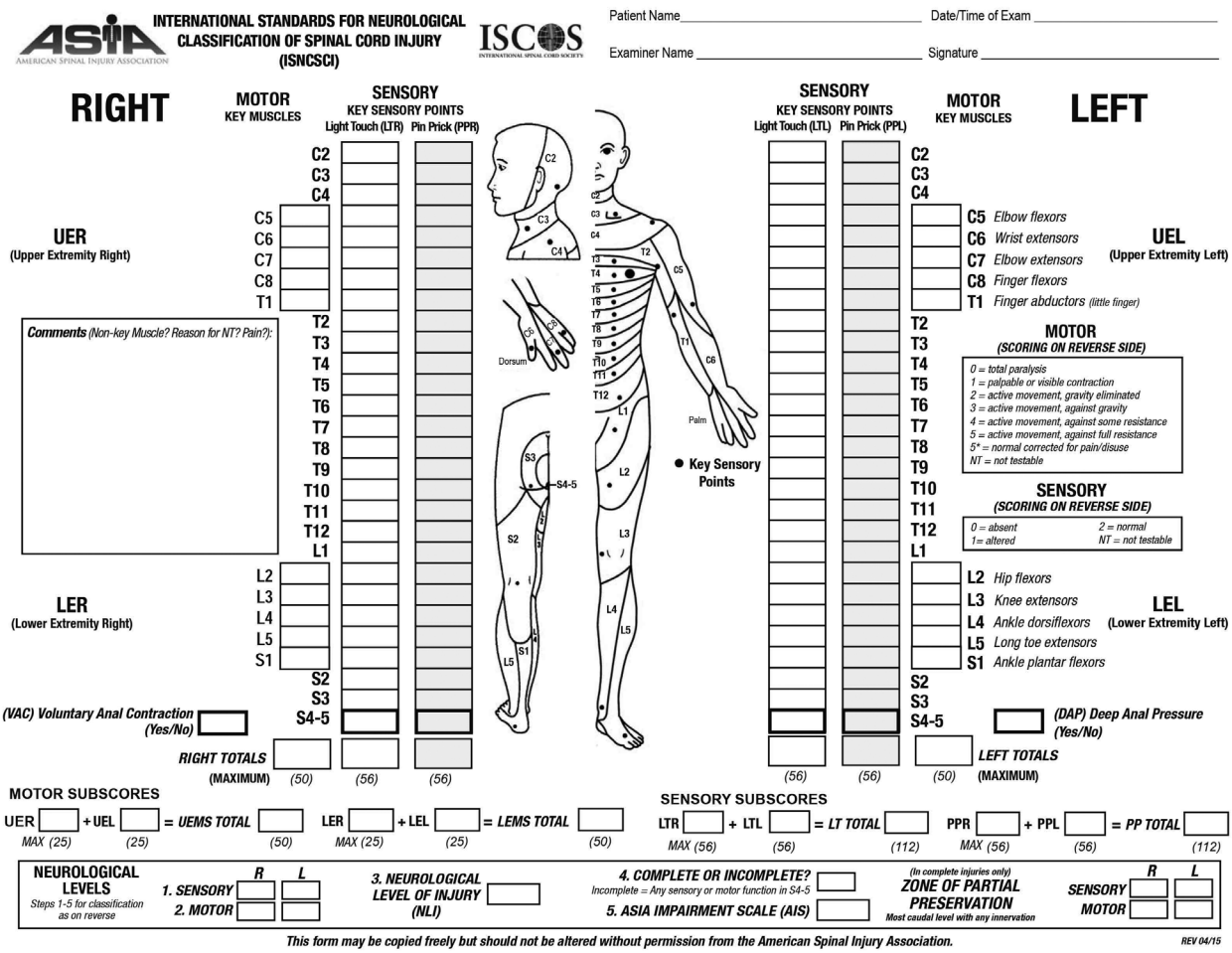

Figure 3. ASIA International standards for neurological classification of spinal cord injury.

Three mechanisms are mainly responsible for metastatic spinal cord compression. The most common method of spread of cancer to the spine is haematogenous, accounting for over 85% of cases (Al-Qurainy and Collis, 2016). Direct pressure caused by growth of cancerous deposits can threaten neural vascularity and compromise bony integrity, leading to collapse of the vertebra(e). Spinal instability can develop causing neurological signs and symptoms. It can also occur secondary to direct extension of tumour into the vertebral column or less commonly by direct tumour deposition (Bucholtz, 1999). The compressive effects resulting in oedema and venous congestion are similar to those seen in other tissues, but the resulting cell damage is characterised by neural demyelination. Prolonged and untreated compression causes vascular injury resulting in spinal cord infarction (Patchell et al, 2005), which is often unsalvageable.

Investigations

Diagnosing the presence of a metastatic lesion causing spinal cord or cauda equina compression and predicting the spinal level using clinical signs and symptoms alone is difficult and can be misleading (Lawton et al, 2019). Magnetic resonance imaging of the whole spine is the preferred imaging modality to confirm metastatic spinal cord compression, with a sensitivity of 93% and a specificity of 97% (Al-Qurainy and Collis, 2016). Whole spine imaging is necessary as 20–35% of patients have multiple, non-contiguous levels of compression (Lawton et al, 2019).

Computed tomography scanning may have a role in surgical and radiotherapy treatment planning, but magnetic resonance imaging is better for confirming the diagnosis. Sagittal T1 and/or short-T1 inversion recovery (STIR) sequences have a high sensitivity for identifying metastatic disease within the bone. Sagittal T2 imaging, supplemented with

axial T1- or T2-weighted scans, shows the soft tissue components of any mass and the degree of spinal cord compression that is being caused. For patients in whom magnetic resonance imaging scanning is contraindicated, such as those with a cardiac pacemaker, computed tomography myelography or positron emission tomography scanning may be required. Plain film radiography is not sensitive for detecting metastatic deposits or spinal cord compression (Shah and Salzman, 2011).

Overall, a high index of suspicion and vigilance for concerning symptoms is required, especially in patients with a history of malignancy or red flag symptoms.

Regional pathways

Patients who develop aberrant neurology secondary to metastatic deposits are at risk of irreversible loss of neurological function. To promptly confirm diagnosis and treat metastatic spinal cord compression to prevent neurological deterioration, a national framework of services must be established. In the UK, the National Institute for Health and Care Excellence has produced recommendations for the structure of the metastatic spinal cord compression network, including:

- Availability of urgent magnetic resonance imaging scanning (within 24 hours) for suspected metastatic spinal cord compression incorporating out of hours service
- The appointment of a network metastatic spinal cord compression lead and local coordinators in each institution with specific roles in managing the investigation, treatment and collecting data
- A joint approach with local social services
- The provision of adequate information for patients
- Consistent nursing procedures (National Institute for Health and Care Excellence, 2008).

Management

Treatments for metastatic spinal cord compression include pain control, prevention of spinal collapse and/or paralysis, prolongation of survival, and palliation of residual symptoms.

Glucocorticoids

Initial management with high-dose steroids is commenced in a patient with high clinical suspicion of metastatic spinal cord compression to reduce spinal cord oedema and preserve neurological function (Cole and Patchell, 2008). The optimum dosing of steroids is unknown and a 2015 Cochrane review concluded that there are higher levels of serious complications, such as perforated gastric ulcer, psychoses or even death from infection after high-dose dexamethasone (96–100 mg bolus), and whether high dosing provides any benefit over moderate dosing (10–16 mg bolus) is unclear (George et al, 2015). Dexamethasone 16 mg orally or intravenously as a starting dose and then 16 mg once daily before noon is advised along with gastric protection. It is then gradually tapered as tolerated, and steroid-related side effects like elevated glucose levels and fungal infections are monitored (National Institute for Health and Care Excellence, 2008).

If radiotherapy is given, then steroid treatment is continued for 5 days from the start of radiotherapy to reduce radiation-induced inflammation and peri-tumour swelling.

Pain management

Most patients with metastatic spinal cord compression require opioids, which are often combined with adjuvant analgesics. Corticosteroids (eg dexamethasone) help with both neuropathic pain and inflammatory pain from vertebral metastasis. Other neuropathic adjuvants include anticonvulsants (eg gabapentin, pregabalin) and tricyclic antidepressants (eg amitriptyline). Although they have not been evaluated for pain directly resulting from metastatic spinal cord compression, they alleviate pain in patients with spinal cord injury and neuropathic cancer pain (Dworkin et al, 2007). Bisphosphonates, non-steroidal anti-inflammatory drugs and acetaminophen help with relief of pain from bony metastasis, although they have not been evaluated for use in patients with metastatic spinal cord compression (Wong and Wiffen, 2002).

Surgery

Following imaging of the spinal cord that reveals compression, several scoring tools can help to determine which patients will benefit from early surgical intervention. Of the many methods available, the two scoring systems that are commonly used and have shown strong inter-user reliability are the spinal instability neoplastic score (SINS) for stability (Table 1) and the prognostic revised Tokuhashi score (Table 2). The SINS assessment considers the site of compression, presence and nature of pain, the type of the metastasis (sclerotic, mixed or lytic), the extent of posterior element involvement, degree of vertebral collapse and radiological spinal malalignment. A score over 7 suggests spinal instability (Fisher et al, 2010) (Table 1).

The revised Tokuhashi score (Tokuhashi et al, 2005), a prognostic score, incorporates the Karnofsky performance status, the number of vertebral body and extra-spinal metastases, site of the primary cancer and metastasis to major internal organs, along with the degree of palsy. The resultant score provides estimated survival of >6 months, 6–12 months and >12 months.

Once the magnetic resonance imaging scan and the SINS and Tokushashi scores are available, an urgent decision about definitive management is taken. Surgery is indicated in patients with:

- Limited levels of cord compression
- Minimal neurological impairment
- Spinal instability (leading to mechanical and functional pain)
- Previous radiotherapy which has been administered at the level of metastatic spinal cord compression (Lawrie, 2010).

Table 1. Elements of the spinal instability neoplastic score (SINS)

Location	Junctional (occiput–C2, C7–T2, T11–L1, L5–S1)	3
	Mobile spine (C3–C6, L2–L4)	2
	Semi-rigid (T3–T10)	1
	Rigid (S2–S5)	0
Pain relief with recumbency and/or pain with movement/loading of the spine	Yes	3
	No (occasional pain but not mechanical)	1
	Pain-free lesion	0
Bone lesion	Lytic	2
	Mixed (lytic/blastic)	1
	Blastic	0
Radiographic spinal alignment	Subluxation/translation present	4
	De novo deformity (kyphosis/scoliosis)	2
	Normal alignment	0
Vertebral body collapse	>50% collapse	3
	<50% collapse	2
	No collapse with >50% of body involved	1
	None of the above	0
Posterolateral involvement of the spinal elements (facet, pedicle or costovetebral joint fracture or replacement with tumour)	Bilateral	3
	Unilateral	1
	None of the above	0

From Fisher et al (2010)

Table 2. Tokuhashi scoring system		
General condition (performance status; PS)	Poor (PS 10–40%)	0
	Moderate (PS 50–70%)	1
	Good (PS 80–100%)	2
Number of extraspinal bone metastases foci	≥3	0
	1–2	1
	0	2
Number of metastases in the vertebral body	≥3	0
	2	1
	1	2
Metastases to major internal organs	Unremovable	0
	Removable	1
	No metastases	2
Primary cancer site	Lung, osteosarcoma, stomach, bladder, oesophagus, pancreas	0
	Liver, gallbladder, unidentified	1
	Others	2
	Kidney, uterus	3
	Rectum	4
	Thyroid, breast, prostate, carcinoid tumour	5
Palsy	Complete (Frankel A, B)	0
	Incomplete (Frankel C, D)	1
	None (Frankel E)	2

Criteria of predicted prognosis: total score 0–8 <6 months, total score 9–11 ≥6 months, total score 12–15 ≥1 year. From Tokuhashi et al (2005)

Surgery involves stabilisation procedures (percutaneous or open pedicular screw fixation, with or without excision of tumour via a vertebral body resection or laminectomy). In special circumstances, eg metastasis from renal cell carcinoma, which can be angiogenic and/or hypervascular, embolisation of the tumour mass is needed within 24 hours of surgery to minimise the risk of catastrophic bleeding.

Radiotherapy

Radiotherapy is administered to reduce pressure on the spinal cord by shrinking the tumour and also to achieve some local control. It can also be given as a palliative pain control measure and helps control loss of remaining sphincter control. Many patients with metastatic spinal cord compression will receive radiotherapy as part of their treatment. Radiotherapy alone is indicated when:

- The patient is unfit for surgery
- Multiple vertebral levels are involved
- There is extensive vertebral involvement
- The tumour is radiosensitive, eg small cell carcinoma and myeloma (Lawrie, 2010).

In patients where surgery is contraindicated, radiotherapy to the site of metastasis is usually delivered to try and achieve symptomatic control. Primary chemotherapy may be the preferred definitive treatment in the minority of patients with metastatic spinal cord compression who have relatively chemo-sensitive disease resulting from germ-cell tumours or lymphoma (Macdonald et al, 2019).

In a randomised control trial, Patchell et al (2005) showed that surgery followed by radiotherapy resulted in improved patient outcomes and better independent mobility than radiotherapy alone. A meta-analysis of studies comparing radiotherapy vs surgery followed by radiotherapy, undertaken by Lee et al (2014), not only confirmed improved ambulatory outcomes, but also improved survival at 6- and 12-month time periods for patients undergoing combined modality treatment.

Key factors in delivering radiotherapy include the dose and fractionation and consideration of whether to re-irradiate sites of prior radiotherapy. Short-course radiotherapy in patients with poorer prognosis is supported by randomised control trials (Hoskin et al, 2017).

There is no standardised radiotherapy treatment regimen for metastatic spinal cord compression. Many schedules and fractionation doses are used worldwide and there is currently a lack of comparative studies demonstrating superiority. A shorter treatment time is desirable for patient comfort and convenience, especially in patients with worse life expectancy. The practicalities of travel and patient positioning for treatment can be associated with significant discomfort. Rades et al (2005) retrospectively evaluated five radiation schedules and prognostic factors in a multicentre study, and demonstrated that the five tested schedules were comparatively effective. They therefore recommend that the shortest treatment time (1×8 Gy) be offered to patients with a poor estimated survival. This is associated with good initial functional results (Rades et al, 2005).

In patients in whom the prognosis for the cancer and mobility is better, oncologists prefer a higher dose in a fractionated regimen (Pease et al, 2004). Longer schedules (eg 10×3 Gy) can be offered to patients with estimated survival greater than 4–6 months. Data suggest that more protracted treatment schedules can be associated with fewer relapses and better recalcification (Rades et al, 2005). Even if the risk of radiation-induced myelopathy is low, there are limited data to support re-irradiation to the spine for recurrent metastatic spinal cord compression (Nieder et al, 2005).

Rehabilitation

The independence and quality of life of patients with cancer can be impacted by the sequelae of the disease. Ischaemia to the spinal cord resulting from metastatic spinal cord compression can lead to permanent neurological deficit with reduction in ability to perform activities of daily living. In this case, attempting major surgical intervention is unlikely to improve symptoms or increase function. Decrease in mobility is a common feature in patients with advanced metastatic spinal cord compression. Bedbound patients are at a higher risk of development of thromboembolic disease, urinary and respiratory tract infections, and pressure ulcers. Therefore, pharmacological and nursing strategies must be considered to minimise these risks.

Patients with metastatic spinal cord compression may develop life-threatening vascular and cardiorespiratory changes. Rehabilitation should therefore include appropriate medical management and preventative strategies. Alteration of bladder and bowel function can have a profound effect on these patients. This is ideally provided in the form of specialist inpatient neurological functional rehabilitation or, where appropriate, care in the patient's own home. The social, physical and psychological needs of the patient must be considered together with a combined approach from social services, occupational health and psychological support.

Prognosis

The physiological effects on ambulation for patients with metastatic spinal cord compression put them at risk of significant morbidity and mortality, as with all non-ambulatory patients. The prognosis of their primary tumour also plays an important role in both decision making with regards to surgery and general prognosis following metastatic spinal cord compression.

Conclusions

Metastatic spinal cord compression is an emergency complication of neoplastic disease and must be managed urgently. The approach should be pragmatic, aiming to reduce

Key points

- Metastatic spinal cord compression is a serious complication that occurs in 2.5–5% of patients with cancer and can lead to irreversible neurological injury if left untreated.
- Prompt identification and treatment of metastatic spinal cord compression is necessary to prevent significant deterioration in function and quality of life.
- This is delivered in the UK through use of a national network of regional pathways and multidisciplinary team working.
- Treatment is focused on pain control, prevention of spinal collapse and/or paralysis, prolongation of survival, and palliation of residual symptoms.

Curriculum checklist

This article addresses the following requirements from the general internal medicine training curriculum

- Able to successfully function within NHS organisational and management systems
- Managing a multidisciplinary team including effective discharge planning
- Managing end of life and applying palliative care skills

advancement and re-establish and preserve function where possible. Each case should be assessed by a multidisciplinary team, with due consideration to the patient's needs at the time of presentation and rehabilitation needs after treatment.

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Conflicts of interest

The authors declare no conflicts of interest.

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Figure 3 is reprinted with permission from the American Spinal Injury Association.

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