Spinal metastasis

Introduction

The spine is the third most common site of cancer metastasis after the liver and lung (Sciubba et al, 2010). In the UK approximately 300 000 people are diagnosed with cancer per year, of which 60–70% will have spinal metastasis. Early diagnosis and management can have a significant impact on the morbidity and prognosis of these patients. It is therefore vital for doctors to be able to recognize, investigate and be aware of the management of spinal metastasis.

Epidemiology and pathology

Approximately 9% of symptomatic spinal metastases arise from prostate cancer, 15% from lung cancer and 16% from breast cancer (Brihaye et al, 1988). Spinal metastases are more common between the ages of 40–65 years, with a predominance in men (Perrin, 1992). This may be because men have the added risk of prostate cancer and a higher rate of lung cancer. Spinal metastases are mostly extradural, i.e. involving the vertebral column and its associated external structures.

The frequency of specific spinal segment involvement is thoracic (70%), lumbar (20%) and cervical (10%). Spinal metastasis can also occur at multiple levels (50%) and usually presents in the anterior portion of the vertebra (60%). Half of spinal metastases will need some intervention, but only 10% will need some form of surgical intervention (Bell, 1997).

Mr Zafar Ahmad *is Clinical Research Associate in the Orthopaedic Research Unit and* **Mr Sheraz Malik** *is Orthopaedic Registrar in the Department of Orthopaedics, Addenbrookes Hospital, Cambridge CB2 0QQ,* **Dr Faisal Mehmood** *is Medical House Officer, Mayo Hospital, Lahore, Pakistan,* **Dr Asif Saifuddin** *is Consultant in Radiology in the Department of Radiology,* **Professor Tim Briggs** *is Consultant in Orthopaedics in the Department of Bone Tumours and* **Mr Adrian Casey** *is Consultant in Neurosurgery in the Department of Spinal Injuries, Royal National Orthopaedic Hospital, Stanmore, Middlesex*

Correspondence to: Mr Z Ahmad (zafar.ahmad@doctors.org.uk)

The mechanisms through which cancer metastasizes to the spine include haematogenous spread, direct invasion and seeding through the CSF. As the vertebral column has a rich blood supply, haematogenous spread is the most common method by which cancer reaches the vertebral column (Arguello et al, 1990). The Batson plexus – valveless veins that connect the vertebral veins with other bodies of venous drainage including the caval, portal and renal veins – is one common source. Prostate cancer is thought to spread through this plexus to the spine. Cancer can spread to multiple levels through the venous and arterial systems.

Locally aggressive cancers can extend directly into the spine. Tumours of the lung can enter the thoracic spine, whereas prostate or colorectal tumours can enter the lumbar or sacral spine by direct invasion. Spread via the CSF is less likely because the related cancers, which are usually within the dura, or cerebral or cerebellar cancers, have a low incidence (Perrin et al, 1982). Surgeons need to be aware of cancer metastasizing as a result of manipulation during surgery.

Clinical features

Pain

The most common symptom of spinal metastasis is pain, which usually precedes neurological symptoms by weeks or months (Bach et al, 1990). The pain from spinal metastasis can be divided into three types. The first is local pain which is believed to be caused by the periosteum of the bone stretching as the tumour expands. It is described as an aching pain, worst at night, and is relieved by anti-inflammatories or corticosteroids. The second type is mechanical pain, ascribed to instability caused by spinal metastasis in the vertebrae (e.g. pathological fracture) that results in strain of the surrounding structures, e.g. ligaments or muscles. Supportive devices such as a brace will help to relieve the pain, but anti-inflammatories have little effect. Third, radicular pain occurs when the tumour compresses the nerve roots. It is described as a sharp or shooting pain along the related area supplied by the nerve root.

Neurological symptoms

Motor weakness is the most common neurological symptom, and can be related to radiculopathy or myelopathy (Greenberg et al, 1980). It is caused by direct compression of the nerve by the tumour or by an indirect method, e.g. as a result of a pathological fracture fragment compressing a nerve. Autonomic symptoms include bladder, bowel and sexual dysfunction. Sensory symptoms include numbness, paraesthesiae and hypesthesia. Patients with myelopathy may report a band-like sensory abnormality over the chest.

The survival rate drops dramatically when a patient has neurological symptoms. Therefore the clinician should maintain a high index of suspicion when assessing a patient with back pain and a known history of cancer. As non-neoplastic spinal conditions less commonly present in the thoracic spine (Sciubba and Gokaslan, 2006), pain in this area should raise suspicion for cancer as the cause.

Red flags

There are a number of red flags that should be considered when reviewing a patient (*Table 1*).

Investigations

To delineate the nature and extent of the disease, a thorough work up is essential. In the history, local symptoms such as noc-

Table 1. Red flags for cord compression: symptoms and signs

Radicular pain
Sensory loss
Saddle anaesthesia
Recent onset of bladder dysfunction
Recent onset of faecal incontinence
Perianal or perineal sensory loss
Laxity of anal sphincter
Severe or progressive neurological deficit in limbs
Difficulty walking

turnal spinal pain, neurological disturbance and gait disturbance should be elicited, as well as systemic ones such as weight loss or organ dysfunction (e.g. sexual organ dysfunction). The risk factors for malignancy should be considered, including smoking history, environmental and occupational exposure, and travel history. Past medical history should check for previous cancer, inflammatory conditions and immunosuppression. Examination should include a thorough neurological examination, as well as examination of related systems if the primary cancer is not known. Routine blood tests should include blood counts and biochemistry including bone and liver profile. Specific blood tests for the suspected primary include protein electrophoresis (urine or serum) and tumour markers such as prostate-specific antigen.

Imaging

As it is cheap and easy to obtain, the first image study requested is plain radiographs. Prostate or breast cancer may present as sclerotic or blastic lesions, but most cases of spinal metastasis present as lytic lesions (*Figure 1*). However, radiographs have a low sensitivity, as the lesions are only visible if 30–50% of the vertebra has been eroded (O'Mara, 1974).

Computed tomography can produce highly detailed images of the bone anatomy (*Figure 2*). This can be enhanced by performing myelography, giving a highly accurate representation of the spaces involved by the tumour. Computed tomography can also be used to identify the primary tumour, and in combination with angiography can be used to identify the blood supply of the tumour.

Magnetic resonance imaging is currently the gold standard imaging study for spinal metastasis. Its superior resolution of the vertebral column and associated soft tissue makes it the most sensitive method of identifying metastasis. Magnetic resonance imaging provides detailed images of the tumour invasion, compression of the bone, neural or other soft tissue structures (*Figure 3*).

Nuclear imaging such as bone scans has a much higher sensitivity (62–89%) than radiographs in detecting lesions as small as 2 mm (Peterson et al, 2003). However, as nuclear imaging works on the basis of detecting metabolic activity, it is not specific for metastatic lesions. It also has poor resolution, so more specific imaging is needed to exclude benign processes (Moore, 2004).

Other more advanced imaging modalities include single-photon emission computed tomography, positron emission tomography and angiography. Single-photon emission computed tomography scanning is a form of nuclear imaging involving computed tomography that gives a three-dimensional, higher detailed image which can distinguish between benign and neoplastic lesions. Positron emission tomography scans allow earlier detection of lesions, as they measure metabolic activity and not bone turnover like other nuclear scans. Currently positron emission tomography scanning is expensive and the resolution is limited. Angiography can be useful for identifying and sometimes for embolizing the vascular supply to spinal metastases.

Biopsy

Although advances in technology have improved the detection of cancer, the primary origin of up to 10–20% of spinal

Figure 1. Anteroposterior radiograph of the lumbar spine showing a lytic lesion in the right side of the L3 vertebra with absence of the pedicle (arrow).

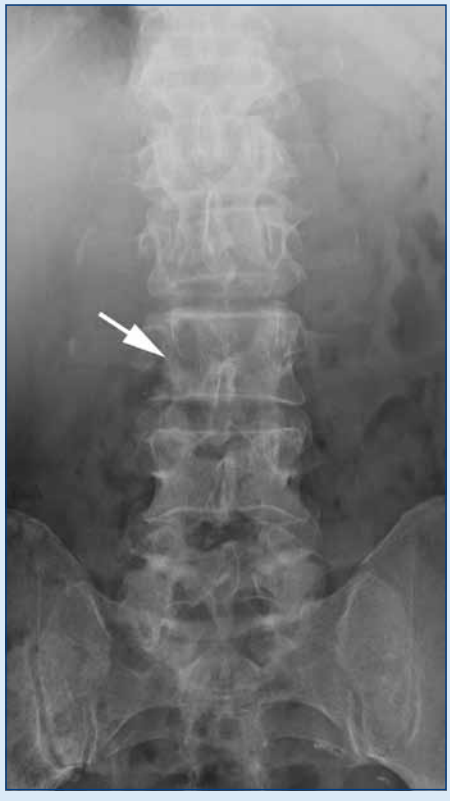


Figure 2. Sagittal computed tomography multiplanar reconstruction of the lumbar spine in a patient with prostatic cancer showing a combination of sclerotic (arrows) and lytic (arrowhead) spinal metastases.

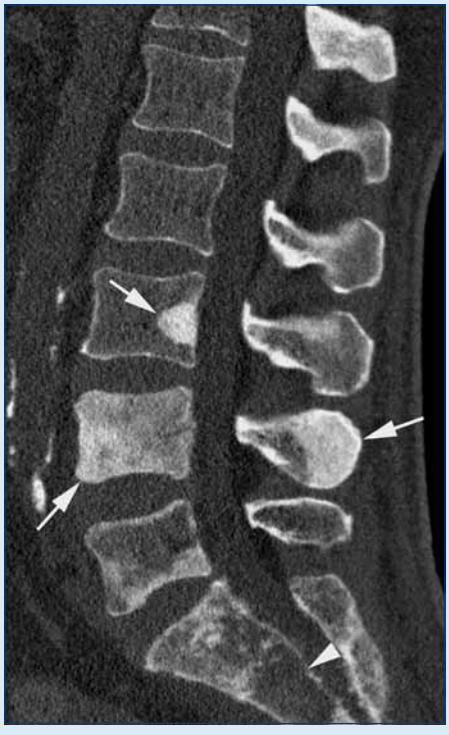
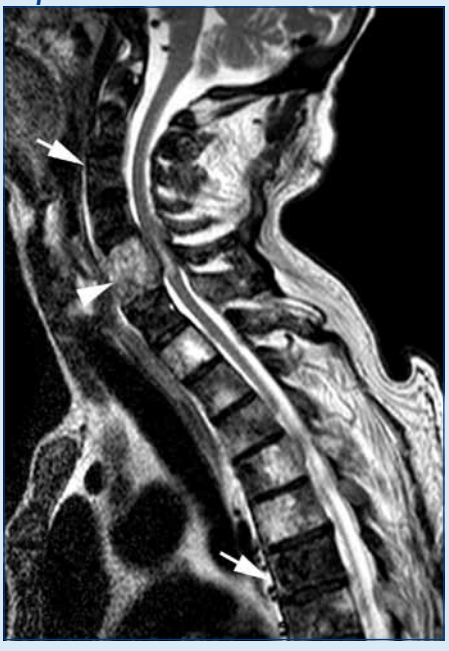


Figure 3. Sagittal T2 weighted full spin echo magnetic resonance image of the cervical and upper thoracic spine in a patient with prostatic cancer showing a combination of sclerotic (arrows) and lytic (arrowhead) spinal metastases, and cord compression at the C5-C6 level.



metastases can remain unknown (Cahill, 1996), and therefore it may be necessary to carry out a biopsy. Biopsy has an accuracy rate of up to 90% (Kattapuram et al, 1992). It is important that the surgeon is careful to prevent further seeding of the cancer when taking the biopsy.

Management

Treatment of spinal metastasis has evolved considerably in the past few years, and with that comes improved survival rates. There are many options in the treatment of spinal metastasis, including surgery, radiotherapy, chemotherapy and other adjuvant treatment (Sciubba et al, 2010). Selecting the best form of treatment is a complex decision and depends on the best evidence, clinical expertise, experience of the clinician, and patient preference. Management will normally involve a combination of different treatments. The goals of treatment are to provide stability, minimize symptoms such as pain, and prevent neurological deterioration.

Surgical options include stabilization, decompression or resection. Several scoring methods such as the Tomita (Tomita et al, 1994) and Tokuhashi (Tokuhashi et al, 1990) methods have been established to help clinicians decide which treatment would benefit a specific patient the most. These are not binding, but provide a useful guide for selecting patients for the most suitable treatment.

Radiotherapy

The mainstay of treatment for spinal metastasis is radiotherapy. It provides many benefits, such as shrinkage of the tumour, prevention of pathological fractures and reversal of neurological deterioration. As a result radiotherapy for spinal metastasis can provide symptomatic relief, especially if there are multiple metastases on a background of widespread metastatic disease.

Options in radiotherapy include conventional radiotherapy, stereotactic radiosurgery and proton beam therapy. Whereas conventional radiotherapy is wide field, spinal stereotactic radiosurgery involves focusing numerous cross-fired beams of radiation to a targeted area, while minimizing exposure to surrounding tissues. This allows treatment of previously solitary metastases that are 'radioresistant tumours'. Radiosurgery for spinal metastasis is not widely available in the UK currently.

Proton beam therapy delivers protons to a targeted area with minimal adverse effects on surrounding tissue. This technology is still limited, but is undergoing rapid development that may produce promising results for treatment in the future. Proton beam therapy is not currently available in the UK, and spinal metastasis is not on the UK list for referral abroad for protons on the NHS. Although radiotherapy provides much benefit, it is unable to stabilize or correct deformities as a result of spinal metastasis. The decision about whether to have surgery or radiotherapy first depends on the patient. However, a gap of 4 weeks is recommended between having surgery and starting or finishing a course of radiotherapy, as radiotherapy impairs healing.

Spinal instability

The vertebrae of the spine support approximately 80% of the axial load of the spine (Magerl et al, 1994), and therefore spinal metastatic lesions which are destructive can significant weaken the spine. It should also be noted that radiotherapy can reduce spinal stability or cause vertebral collapse, by the shrinkage or disappearance of tumour. These lesions can lead to compression or burst fractures, the bony fragments from which may cause compression of neurological components such as nerve roots or the spinal cord. Therefore deciding when and what to stabilize is a critical issue. Cybulski (1989) proposed imaging criteria to assess spinal instability which include:

1. Anterior and middle column destruction (>50% collapse of the vertebrae height)
2. Collapse of two or more adjacent vertebra
3. Tumour involvement of the middle and posterior column
4. Previous surgical laminectomy, with failure to recognize anterior and middle column disease.

Cybulski recommended surgical decompression and fixation if one of these criteria is met, or the patient has neural compression and a life expectancy of more than 5–6 months, a competent immune and nutritional status, incomplete neurological deficit, or a radioresistant tumour.

Surgical decompression and resection

Selecting the optimal approach for surgery depends on the location of the lesion, spinal segment involved, tumour histology and spinal reconstruction required. Surgical experience and familiarity also influences the approach used. As the anterior portion of the vertebrae is the most common area for spinal metastasis to present, the anterior approach is most commonly used. A multidisciplinary approach may be required, with the involvement of a general or cardiothoracic surgeon. This may not be possible at some sections of the spine, e.g. segments of the thoracic spine which are obstructed by the great vessels. In these cases, a right-sided thoracotomy or posterior approach would be appropriate.

Adjuvant therapies

The aim of these therapies is to offer symptomatic relief, reduce the size of the tumour and minimize its consequences. The effectiveness of these therapies will depend on the origin of the tumour.

The treatment of pain involves the analgesic ladder, including anti-inflammatory medications. Anti-inflammatory tablets offer pain relief by reducing inflammation, spinal oedema, and hence reducing tumour-associated pain. Other medications such as corticosteroids can be osteolytic in some tumours. Adjuvant chemotherapy and pharmacotherapy has limited benefits in the spine, except for a few cancers such as osteosarcoma or Ewing's sarcoma. Hormone therapy on the other hand is more effective in tumours of breast or prostate origin. Bisphosphonates can reduce osteoclastic activity and help reduce the risk of pathological fractures.

A new technique, vertebroplasty, involves injection of polymethyl methacrylate cement into a vertebral defect, whereas kyphoplasty is the injection of a balloon into the defect to create a space for the cement to be injected. These provide useful pain relief and stability to pathological fractures. Kyphoplasty and vertebroplasty may also be used instead of radiotherapy for treatment of spinal metastasis and prevention of vertebral collapse (rather than as an adjuvant).

Combination therapies

Patchell et al (2005) conducted a clinical trial involving 101 patients who required treatment for spinal metastasis. The patients were randomized to having surgery with radiotherapy or having radio-

therapy alone. The primary end point was the patient's ability to walk, and secondary end points included urinary continence, muscle strength and functional status. Patients treated with surgery and radiotherapy were able to walk significantly longer than those with radiotherapy alone (122 days *vs* 13 days). The need for corticosteroids and opioid analgesics was significantly reduced in the surgical group. This trial found that decompressive surgery plus postoperative radiotherapy produced better outcomes than radiotherapy alone for patients with spinal cord compression caused by metastatic cancer.

Spinal cord compression

This is an oncological emergency and all patients with spinal metastasis should be aware of its symptoms. Compression of the spine can occur directly by the tumour, or indirectly via pathological fracture fragments compressing the spine. If compressed below L1, then there is a risk of cauda equina. *Table 1* lists spinal cord compression symptoms. Magnetic resonance imaging should be ordered if there is any suspicion of spinal metastasis (National Institute for Health and Clinical Excellence, 2008). The first line of treatment for cord compression as a result of spinal metastasis can be corticosteroids, radiotherapy or surgery, and varies case by case. Surgical decompression and stabilization is indicated in radioresistant tumours, an unstable spine or bony compression of the spinal cord. These lesions will require aggressive resection, and this is only possible if the vertebral column has enough good quality bone to allow fixation and stabilization.

Conclusions

Spinal metastasis can be a late stage sign of a cancer. Patients with this condition have a 10-month survival rate (Grant et al, 1991), whereas patients with cord compressions only have a 3-month survival rate. Early detection and aggressive treatment are key to minimizing patient morbidity and mortality. Although prognosis is still poor, rapid development in detection and treatment are occurring in this area. As advances come about, treatments will improve, increasing patient survival. **BJHM**

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KEY POINTS

- Patients with a past medical history of cancer who present with back pain should always be investigated for spinal metastasis.
- About 60% of people with cancer will have metastatic spread.
- Red flags to look out for in terms of cancer include: age over 50 years, past medical history of cancer, night pain, thoracic pain and immune suppression.
- The optimal investigation at the moment for spinal metastasis is magnetic resonance imaging.
- Treatment involves multiple options, including radiotherapy, surgery and other adjuvant treatment.