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Neurosurgical emergencies in spinal tumors: pathophysiology and clinical management

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Abstract

Whether they are spinal metastases or primary spinal neoplasms, spinal tumors cause a myriad of complications given their critical location. Spinal tumors can be extradural, intradural extramedullary, or intramedullary, with extradural metastatic tumors the most commonly encountered. Spinal cord and/or cauda equina compression is one of the most devastating complications of cancer and represents a true oncologic emergency. Patients present with progressive paralysis, paresthesiae, and/or autonomic dysfunction. In addition to spinal cord compression (SCC), extradural spinal tumors can cause mechanical spinal instability and axial loading pain which often warrant surgical consultation. The diagnosis of SCC begins with clinical suspicion even before neurological deficits ensue. Patients presenting with back or neck pain who have a history of cancer should be evaluated carefully for SCC. MRI is the imaging modality of choice. Management of SCC generally requires a multidisciplinary approach, with goals of symptom control and prevention of irreversible functional loss. Patients with metastatic epidural SCC who undergo surgical decompression and reconstruction followed by radiotherapy exhibit better outcomes in preservation of function and symptom control than do those undergoing radiotherapy alone. Recent advances in the surgical management of SCC include minimally invasive spinal surgery (MISS), spinal laser interstitial thermotherapy (SLITT), and vertebral augmentation of pathologic vertebral compression fractures. Generally, SCC in patients with cancer serves as evidence of uncontrolled and aggressive disease. Although it is associated with poor outcome in most patients, effective palliation is possible with early diagnosis and careful application of modern surgical techniques for the elimination of cord compression, prevention or reversal of neurological deficits, and restoration of mechanical spinal stability. In addition to SCC from spinal tumors, other spinal complications can be seen in cancer patients who develop spine infections such as surgical site infection (SSI), spinal epidural abscesses (SEA), subdural empyema (SDE), or vertebral osteomyelitis. These complications can be due to inoculation from the spinal surgery itself or as a result of the patients' immunocompromised state. This article provides a scoping review of the clinical presentation, pathophysiology, and diagnosis of major spinal oncologic emergencies and summarizes current modes of surgical and nonsurgical management.

Keywords Spine surgery, Spine tumors, Surgical site infection, Spinal cord compression, Spinal instability, Neurosurgical oncology

Introduction

Whether they are spinal metastases or primary spinal neoplasms, spinal tumors cause a myriad of complications given their critical location. Not only can they compress the spinal cord, they can also trigger mechanical instability of the vertebral column in some patients. Surgery for tumor resection is also associated with such complications as hematoma formation leading to spinal

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cord compression (SCC), surgical site infection, vascular injury, and other neurological complications as a result of direct injury to the neural tissue or surrounding vascular structures.

Compression of the spinal cord and/or cauda equina represents a true oncologic emergency. In fact, it is one of the most debilitating complications in patients with advanced systemic cancer. Patients present with progressive neurological deficits, paresthesiae in the extremities, and/or autonomic derangements. Spinal tumor location can be extradural, intradural extramedullary, or intramedullary (Fig. 1). *Extradural* tumors, occupying the vertebral body, pedicle, or other structures outside the dura, are the most common spinal tumors. They are usually metastatic in origin. *Intradural extramedullary* tumors, located inside the dura but extrinsic to the spinal cord, are the second most common and arise from the dura, leptomeninges, or nerve roots. Such tumors include meningiomas, nerve sheath tumors, and metastases. *Intramedullary* tumors, arising from, eroding, and compressing the spinal cord's gray and white matter, are the least common (2–5%). Examples of the latter include primary spinal tumors such as ependymomas, astrocytomas, and hemangioblastomas. Metastatic intramedullary tumors are rare and most frequently originate from tumors of lung or breast [1, 2].

Intradural tumors represent a minority of the cases presenting with SCC. Most patients with SCC have extradural metastases capable of compressing the dural sac and causing myelopathy (Fig. 2). SCC caused by spinal metastasis is usually provoked either by pathological vertebral collapse, in which worsening bone involvement destroys the cortical and cancellous portions of the vertebral body and causes extrusion of bone into the spinal canal, or by direct tumor extrusion through the vertebra which compresses the spinal dura and the spinal cord within. On average, it takes 32 months to develop spinal metastases after a primary tumor diagnosis, and 27 months to develop SCC after detecting spinal metastases [2, 3]. The frequency of SCC following spinal metastasis is only 5–20%, and this depends on the incidence of the primary tumor and how often that tumor metastasizes to the spine. Lung, breast, and prostate cancers account for most SCC cases [2]. Patients with spinal metastases and subsequent SCC still have a poor prognosis; life expectancy

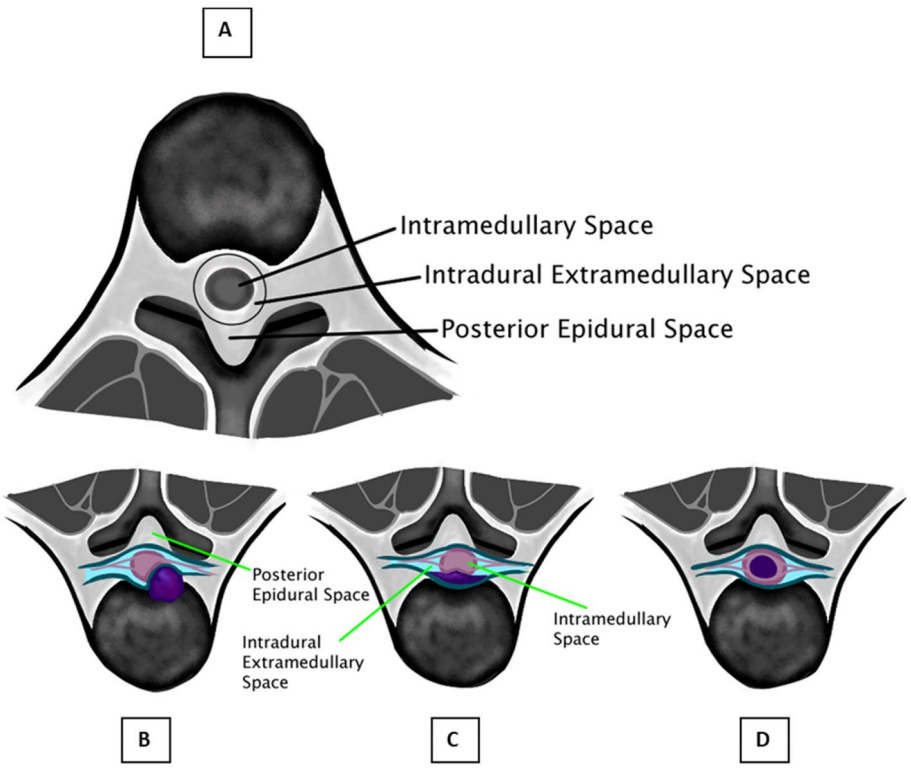


Fig. 1 Axial appearance of the spinal cord showing the different spinal cord compartments (**A**), and a tumor occupying the extradural space (**B**), intradural-extramedullary space (**C**), and intramedullary space (**D**). The tumor in B indents the dura but does not fully occlude the subarachnoid space. In C, the tumor indents the spinal cord and displaces it posteriorly. In D, the tumor is contained completely within the spinal cord, and expands its cross-sectional area

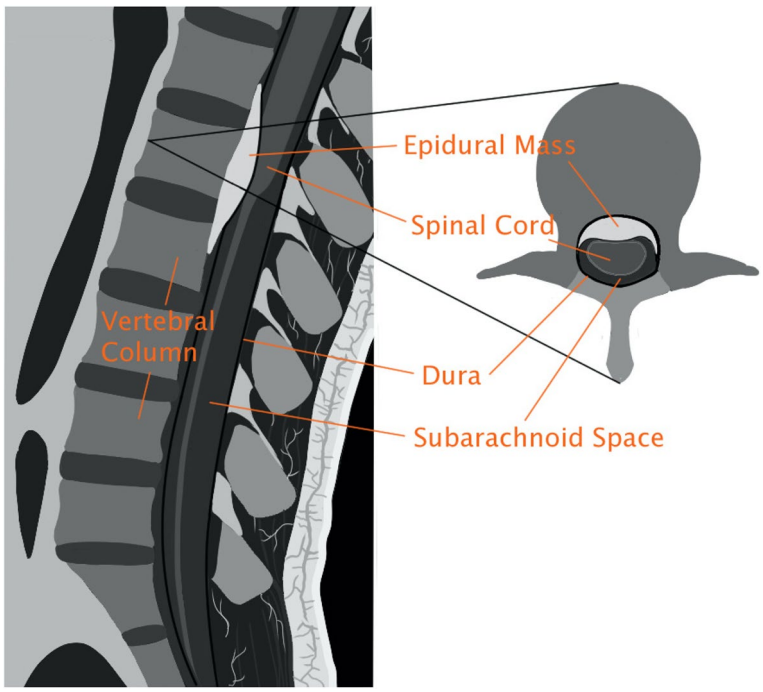


Fig. 2 Sagittal (left) and axial (right) appearances of an epidural mass causing spinal cord compression on T1-weighted post-contrast MRI

is somewhat impaired by an ongoing permanent paraparesis or quadriparesis, but more so by the association of vertebral metastasis with multiple metastases in vital organs. It is estimated that the overall survival once spinal metastases develop ranges between 3 and 16 months, with a median of 7 months. Overall survival is primarily determined by the primary tumor type. For instance, the 2-year survival rate is the lowest for lung cancer (9%) but much higher for breast and prostate cancer (44%). The survival rate for patients with spinal metastases is estimated to be 10–20% 2 years after diagnosis [2, 4]. Spinal metastases most commonly afflict individuals between 40 and 70 years of age [2, 5].

Over the past decade, significant advances have occurred in the diagnosis and management of SCC. Even in the absence of neurological deficits, patients with systemic cancer and back pain should be evaluated for SCC. Treating it generally requires a multidisciplinary approach, with goals of symptom control and prevention of irreversible functional loss. Extradural spinal tumors can also cause mechanical spinal instability and axial loading pain which warrant surgical consultation. Generally, SCC predicts a poor outcome if effective treatment was not administered. These infectious complications may result from bacterial inoculation at the surgical site or from the immunocompromise often seen in cancer patients. This article provides a scoping review of the clinical presentation, pathophysiology, and diagnosis of major spinal oncologic emergencies and summarizes current modes of surgical and nonsurgical management.

Pathophysiology

As mentioned above, spinal tumors can be extradural, intradural extramedullary, or intramedullary. Only a minority of patients present with SCC by an intradural tumor. Extradural metastatic tumors are encountered much more frequently [2, 6]. Metastatic disease of the spine remains a common problem, the incidence of which is increasing given the increase in patients' life expectancies associated with new diagnostic methods and treatment modalities for primary cancers. It is estimated that 5–20% of patients with spinal metastases eventually develop SCC when metastases to the spinal column extend into the epidural space [2]. Metastatic SCC most commonly affects the thoracic spine, followed by the lumbosacral and cervical spinal segments [7, 8]. Metastases can reach the epidural space and there cause SCC in either of two ways: (1) the less common path is the growth of paravertebral tumors, such as lymphomas and neuroblastomas, directly into the spinal canal; (2) more commonly, hematogenous spread of malignant cells into the vertebral body causes it to weaken and expand, spill tumor and/or bone fragments into the epidural space, and compress the epidural venous plexus, anterior spinal artery, thecal sac, and spinal cord [7, 9]. Hematogenous spread can occur

via the valveless Batson venous plexus or via the more common route of arterial embolization [10]. The clinical onset of SCC can be gradual or acute. Acute SCC occurs when the tumor causes destruction of the vertebral cortical bone and collapse of the vertebral body with bony fragments protruding sufficiently into the epidural space to displace and distort the spinal cord [9].

SCC injures the spinal cord either directly through demyelination and axonal damage, or by vascular compression. If direct cord compression is of short duration, the effects are reversible and recovery is possible. However, a longer period of compression paves the way for secondary vascular injury. Vascular compromise causes breakdown in the blood-spinal cord barrier leading to vasogenic edema and spinal cord infarction. Obtaining meaningful recovery becomes more difficult after vascular injury [9, 11].

About 2.5–5% of patients with terminal cancer have SCC within the last 2 years of their illness [12–14]. Incidence of SCC varies with age and primary disease histology. Any systemic cancer can metastasize to the spinal column, but prostate, breast, and lung cancers are those most commonly associated with SCC (Table 1). Other cancers associated less frequently with SCC include multiple myeloma, renal cell carcinoma, non-Hodgkin lymphoma, colorectal carcinoma, sarcomas, and tumors of unknown primary origin [13]. Primary tumor type correlates with gait function at the time of SCC diagnosis and with the latency period between diagnosis of the primary cancer and SCC onset. Indeed, post-treatment ambulatory function depends on the baseline ambulatory function at the time of SCC diagnosis, and most particularly, on prompt treatment of SCC. Furthermore, survival time after SCC diagnosis correlates with the length of the latency period between primary tumor diagnosis and SCC, ambulatory function at the time of SCC diagnosis, and final post-treatment ambulatory function [15].

Table 1 Frequency of primary tumors causing epidural spinal cord compression

Primary tumor type	Percentage
Lung	15–20
Prostate	15–20
Breast	15–20
Non-Hodgkin's lymphoma	5–10
Renal cell carcinoma	5–10
Multiple myeloma	5–10
Other malignancies (colorectal carcinoma, sarcoma, melanoma, etc.)	15–20
Unknown primary	7

Diagnosis

The diagnosis of SCC caused by vertebral metastasis begins with clinical suspicion even before neurological deficits ensue. Patients presenting with back or neck pain who have a history of cancer should be evaluated carefully for SCC. The initial steps are taking a detailed medical history and performing a thorough physical examination.

Although pain is a non-specific sign, it can be categorized into various types. These include referred, radicular, and localized pain. *Localized* pain is confined to the location of metastasis and increases in intensity over time. It is caused by the tumor's extending to stretch the periosteum or invade neighboring tissues. *Radicular* pain is caused by compression or invasion of spinal nerve roots. It can be unilateral if lumbosacral or cervical spine is involved, or, less commonly, bilateral if thoracic spine is involved. Radicular pain is worse at night or in the recumbent position and is exacerbated by Valsalva maneuver and by movement. *Referred* pain is pain felt in a region distant from its true site of origin (a prime example is the pain of cholecystitis producing shoulder pain). A more ominous form of pain is the mechanical back pain caused by vertebral body collapse. It is indicative of spinal instability and is exacerbated by movement and spinal axial loading and relieved by lying still in a supine position [9].

Neurological deficits may become apparent at the time of presentation and include motor weakness or paraplegia, dermatomal sensory loss, saddle anesthesia, neuropathic pain, and urinary/fecal incontinence. Sphincter disturbances are particularly concerning as they often indicate a poor prognosis. Notably, neurological deficits are often identified after the patient has reported pain for a considerable period. Patients may exhibit bilateral upper motor neuron symptoms below the spinal level of compression. Additionally, a sensory level below which sensation is reduced or altered may be observed, typically starting distally in the feet and ascending gradually until a stable sensory level is established at the level of the cord injury. Symptoms vary based on the tumor's location but do not reliably indicate the level of involvement [12, 16].

A detailed physical examination is necessary in the diagnosis of SCC. Thorough scrutiny of sensation, motor strength, muscle tone, and reflexes is mandatory. Often, spinal tenderness is present overlying the vertebra involved by tumor and can be elicited by percussion of its spinous process. Any spinal deformity should be noted. If cervical or thoracic spinal instability is suspected, the patient's spine may need external immobilization with a

collar or brace. Upper motor neuron findings like hyperreflexia, clonus, and a positive Babinski sign (extensor plantar response) are common.

Patients with previously stable back pain who present with new pain escalation should trigger both suspicion of SCC and prompt acquisition of imaging within 24 h of presentation to show whether it is present [17]. If spinal metastasis but not SCC is suspected, the 2023 National Institute of Health and Care Excellence (NICE) guidelines recommend imaging be performed within 1 week at the local hospital [17]. An overnight MRI can be performed if an urgent diagnosis is warranted for immediate medical intervention. Imaging in patients with a known history of spinal metastases does not need to be performed if no symptoms of SCC are present. MRI is the imaging method of choice for the diagnosis of SCC with a sensitivity of 93% and specificity of 97% [18, 19]. Sagittal T1-weighted and/or short tau inversion recovery (STIR) sequences of the whole spine are enough to make the diagnosis. To detect intradural spinal tumors with full clarity, however, gadolinium-enhanced images are usually needed (Fig. 3). Additionally, sagittal T2-weighted sequences can elucidate intradural lesions as well as the level and degree of cord compression [17]. Conventional myelography techniques, with or without CT, were used prior to the advent of MRI. These latter techniques are still helpful when MRI is contraindicated or when magnetic susceptibility artefact from metal implants prevents full visualization of the contents of the spinal canal (Fig. 4) [8, 9]. With the advent of stereotactic radiosurgery (SRS) for the treatment of spinal metastases, characterizing the degree of epidural SCC became crucial because tumors that abut or compress the spinal cord may be excluded from SRS consideration. As such, Bilsky and colleagues developed a 6-point grading system to determine the degree of epidural SCC (Table 2) [20]. Grade 0 in this system signifies that the disease is limited to the bone and there is no epidural disease. Grade 1 signifies that there is epidural impingement and is further sub-classified according to thecal sac deformation and spinal cord abutment. There is no SCC in grade 1. Grades 2 and 3 both include SCC, but the CSF is visible in grade 2, whereas it is not visible in grade 3.

Delays in diagnosis and treatment are common; back pain is present for a median interval of 62 days before treatment is initiated [12, 21]. Sadly, many patients are diagnosed too late for an intervention to confer major benefit [12]. van Tol and colleagues investigated the causes of delay in administering surgical treatment for spinal metastases [22]. They categorized the delays into patient delay (time from symptom onset to medical attention), diagnostic delay (time from seeking medical consultation to diagnosis), referral delay (time from diagnosis to referral to a spine surgeon), and treatment delay (time from referral to a spine surgeon until surgical treatment). The delays in their study amounted to a total of

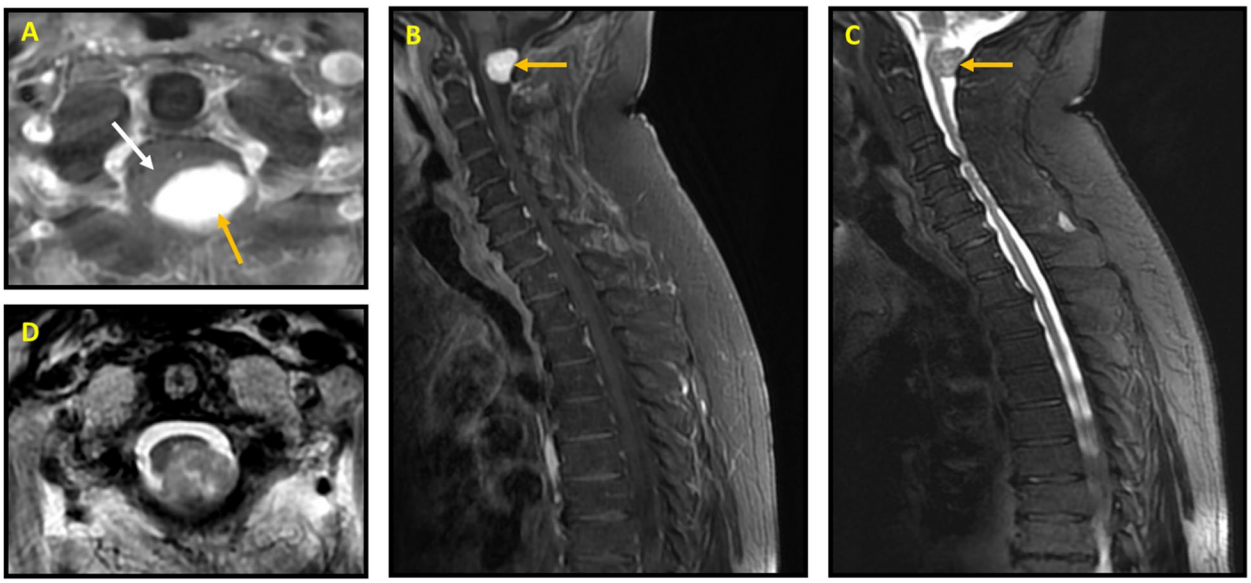


Fig. 3 Intradural-extramedullary metastatic tumor causing Bilsky grade 2 cervical spinal cord compression. This patient with a history of *BRAF* wildtype melanoma presented with a large C1 metastasis (*yellow arrow*) and subsequent clinical signs of subtle myelopathy and radiographic compression of the upper cervical spinal cord with cord edema (*white arrow*). Axial (**A**) and sagittal (**B**) MRI (T1-weighted, post-contrast) showing an enhancing irregular intradural extramedullary mass in the left side of the posterior spinal canal at C1 measuring 2.3 (CC) × 1.6 (transverse) × 2.5 cm (AP). The lesion appears hyperintense compared to the spinal cord on T2-weighted sagittal MRI (**C**, **D**)

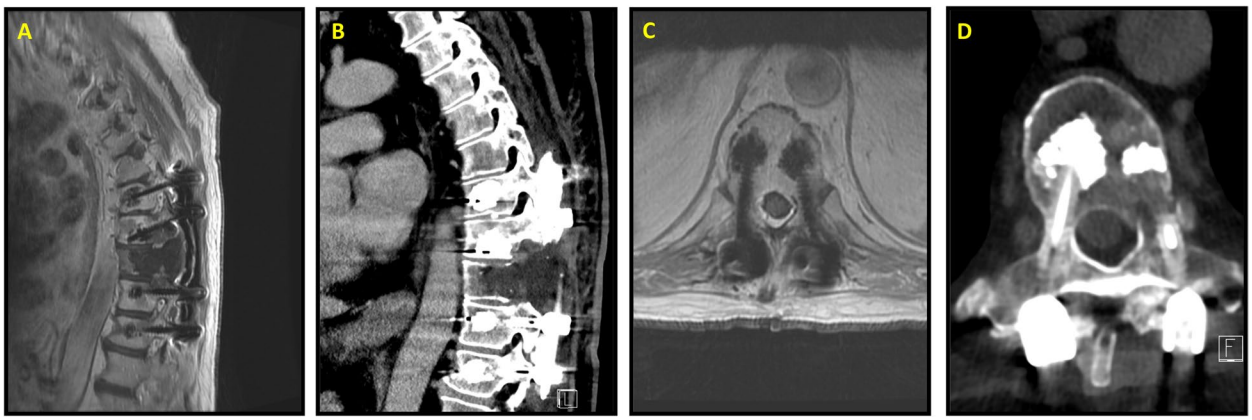


Fig. 4 Thoracic laminectomy and transpedicular vertebrectomy at T9 with spinal cord decompression and instrumentation causing an artefact on T1-weighted MRI (**A**, **C**) and on CT (**B**, **D**), sagittal and axial views. This 59-year-old male patient has esophageal adenocarcinoma metastatic to the T9 vertebra, involving the left side of the vertebral body, left pedicle, transverse process, and facets, and causing significant SCC with Bilsky grade 3 disease. He underwent T9 laminectomy and partial vertebrectomy for spinal cord decompression as well as posterior segmental stabilization from T7–T11 (**A**, **B**), with cement augmentation and bilateral pedicle screws placed at T7, T8, T10, and T11 (**C**, **D**)

Table 2 Bilsky's epidural spinal cord compression grading system

Grade		Description
Low grade	**0**	Bone involvement only
	1a	Epidural impingement, without deformation of thecal sac
	1b	Epidural impingement, deformation of thecal sac but no spinal cord abutment
	1c	Epidural impingement, deformation of thecal sac, spinal cord abutment, no SCC
High grade	**2**	SCC, CSF visible around spinal cord
	3	SCC, CSF not visible around spinal cord

Abbreviations: *SCC* Spinal cord compression, *CSF* Cerebrospinal fluid

99 days from the first symptom onset to definitive treatment. Although there was a delay in patient presentation, considerable delays also occurred after the patient has already presented to medical attention. Having a previous history of malignancy did shorten patient and diagnostic delay, but the total delay time remained comparable to that in patients without a prior history of malignancy, mainly due to delays in referral and treatment. Other studies have reported similar delays from symptom onset to treatment (75–90 days) [16, 21].

Management

Medical therapy

Corticosteroids Steroid therapy is a mainstay of treatment for SCC. It is recommended in all patients with SCC, particularly those with neurological deficits, as it reduces edema and improves symptoms and functional level [8, 9, 23, 24]. The main concern with corticosteroid use, particularly at higher doses, is its systemic side effects such as hyperglycemia, peripheral edema, infections, proximal myopathy, insomnia, and gastritis [25]. For this reason, the optimal dosage has been controversial. Multiple studies have tried to tease out the most effective dosing of corticosteroids while keeping in mind the side effect profile. One early study found that high-dose corticosteroid therapy gave encouraging results, but because it was immediately followed by radiotherapy, a solid assessment of its independent benefits was difficult to establish [26]. Vecht and colleagues in 1989 sought to compare high-dose (100 mg followed by 16 mg P.O./day) and low-dose (10 mg followed by 16 mg P.O./day) dexamethasone in patients with SCC. While both dosages provided significant short-term pain relief, there was no significant difference between the two cohorts in survival, pain control, or ambulation [27]. In 1992, Heimdal et al. found that higher doses of dexamethasone (6 mg I.V. loading dose, which was then tapered to 0 over 15 days), as compared to lower dose (4 mg I.V. 4×/day initially, then tapered to 0 over 15 days) did in fact cause serious side effects while not meeting the expectation of better rates of ambulation [28].

In a 1994 study by Sørensen et al., adjunct high-dose dexamethasone given concomitantly with radiotherapy did offer benefits in treating SCC, in terms of restoration or preservation of gait function; however, the side effect profile hindered optimal delineation of the dosing regimen [29]. In that study, patients were divided into a control group (given only radiation monotherapy) and a treatment group (given both radiotherapy and adjunct dexamethasone of 96 mg delivered intravenously, and followed initially by 24 mg P.O. 4×/day for 3 days after which the dose was tapered over a 10-day period). Of the patients in the dexamethasone treatment group, 81% (vs. only 63% in the control group) showed preservation of gait if they were already ambulatory, or restoration of gait within 3 months of treatment if they were non-ambulatory. Hypomania, psychosis, and perforated gastric ulcer were the adverse effects seen in the treatment group.

As a result of the aforementioned studies, the benefits of high-dose corticosteroid therapy for SCC can be summarized as follows: pain control, gait preservation in baseline ambulatory patients, restoration of gait in baseline non-ambulatory patients, and slowing or halting the progression of neurological symptoms. However, due to the possibility of serious adverse effects, a more cautious dosage (i.e., an initial 10 mg intravenous loading dose, followed by 6 mg every 6 h) has been proposed [30].

Pain and symptom management Opioids (morphine, oxycodone, hydromorphone, fentanyl) are the mainstay of pain control for patients with SCC. It can be challenging when patients become tolerant to opioids and start requiring higher doses. Thus, continuous intravenous opioid administration is reserved for patients with moderate to severe pain. For breakthrough pain, boluses or patient-controlled analgesia (PCA) are recommended. Dexamethasone, anticonvulsants (gabapentin, pregabalin), and tricyclic antidepressants can also be administered for neuropathic pain. Furthermore, bisphosphonates, non-steroidal anti-inflammatory drugs, and acetaminophen (which is especially effective when given intravenously) can help relieve pain from bone metastases. Stimulant and osmotic laxatives (senna, polyethylene glycol) are used prophylactically to mitigate the risk of constipation associated with opioid administration, limited mobility, and autonomic injury. More severe constipation may require an escalation to suppositories, enema, lactulose, or methylnaltrexone [7].

Radiotherapy

Management of SCC requires a true multidisciplinary approach. The Neurologic, Oncologic, Mechanical instability, and Systemic disease (NOMS) criteria for decision-making have been used to guide surgeons in choosing between up-front radiotherapy and surgery [31]. This framework does not consider radiographic parameters of spinal instability and focuses only on mechanical pain as a measure of instability. Radiotherapy is often indicated to improve neurological deficits, help with pain relief, or as an adjunctive procedure after decompressive surgery if residual tumor is present. Radiotherapy can be in the form of standard external beam radiation or SRS. Standard external beam radiation therapy is given in 10 fractions to a total dose of 30 to 40 Gy, whereas SRS requires five or fewer sessions. SRS provides higher doses of radiation while minimizing the exposure of nearby healthy tissue. If the patient is not a surgical candidate but the need arises to improve or protect his or her neurological status, radiotherapy is often performed [32]. If patients fail radiotherapy, they can be referred for surgery. If surgery is not possible then, re-irradiation is sometimes warranted; however, the dose tolerance of the spinal cord must be considered to prevent treatment-related neurotoxicity [32, 33].

Metastatic breast, small cell lung, and prostate cancer are typically radiosensitive, while non-small cell lung cancer and renal cell carcinoma are more radioresistant. Because of their good response to non-surgical therapy, many metastases from breast and small cell lung cancers do not need surgical intervention. In prostate cancer, the spinal involvement is usually blastic and multifocal. Thus, the role of surgery is to correct spinal instability, control pain, or prevent neurological decline. In patients with metastatic non-small cell lung cancer whose general condition precludes surgery, SRS is preferred over standard radiation therapy given in small fractions since it yields better control due to a more concentrated dosing [34]. Renal cell carcinoma usually requires surgical resection in a piecemeal fashion. It is, however, a highly vascular tumor and bleeds easily during resection. Therefore, preoperative embolization is used to minimize intraoperative hemorrhage. Careful and comprehensive isolation of the tumor and devascularization are needed prior to removal of such hypervascular metastases.

Radiotherapy can cause the tumor to shrink which ultimately helps in pain control. However, neurological outcomes after radiotherapy often depend on the patient's initial neurological status, particularly the ambulatory status prior to treatment and the rate at which motor deficits developed [32]. Loblaw et al. found that 94% of those ambulating unassisted and 63% of those with assisted ambulation retained their gait ability after radiotherapy. On the other hand, those who were already paraplegic or paraparetic showed poorer outcomes [35]. Other factors that help predict functional outcomes after radiotherapy

include the histology of the primary tumor, the Eastern Cooperative Oncology Group (ECOG) performance status, the number of involved vertebrae, and the interval from primary tumor diagnosis to the development of metastatic epidural SCC [15, 36, 37]. Similarly, ECOG performance status, number of involved vertebrae, time interval between primary tumor diagnosis and the development of SCC, ambulatory status prior to radiotherapy, primary tumor type, rate of motor deficit development, and response to irradiation were each significantly associated with survival [37].

The total dosage and number of fractions used both vary widely in the literature. Given that such patients may have a limited lifespan, attempts have been made to decrease the total time a patient receives radiotherapy. In a study by Maranzano and colleagues in 2009, a single dose of 8 Gy was as effective as 16 Gy delivered in two separate fractions 1 week apart [38]. In a prospective non-randomized study conducted in Holland and Germany on patients with motor deficits from SCC, patients in Holland received short-course radiotherapy (1×8 Gy or 5×4 Gy over 1 day to 1 week), while patients in Germany received a longer course (10×3 Gy, 15×2.5 Gy, or 20×2 Gy over 2 to 4 weeks). Motor function and 1-year survival were similar in both groups, but local tumor control was significantly better with the longer course of treatment. Hence, it was concluded that patients with a poorer prognosis may benefit from shorter courses, while those who will live longer and have a greater possibility of local recurrence should receive a longer course of treatment [39]. A 2019 randomized clinical trial, SCORAD III, randomized 686 patients to 8 Gy in a single dose or 20 Gy in five fractions of radiotherapy. Single-dose treatment did not meet the criterion for non-inferiority for the primary outcome of being ambulatory at 8 weeks. However, secondary endpoints such as ambulatory status at 1, 4, and 12 weeks as well as overall survival were not significantly different between the two dose schedules [40].

Surgery

Prospective data show that surgical decompression and reconstruction followed by radiotherapy produce better outcomes in preservation of function and symptom control than does radiotherapy alone for patients with epidural SCC [11]. Hence, it is crucial to identify those patients with SCC who are candidates for surgery, as well as to delineate the optimal timing of surgery. In fact, establishing a patient with spinal metastasis as a surgical candidate depends on a myriad of factors, namely spinal stability, patient health (malnourishment, cachexia, steroid effects, pain, osteopenia, neurological compromise), prognosis, tumor histology, and iatrogenic issues (chemotherapy or radiotherapy effects). Because surgical intervention carries short-term morbidity, the patient's expected survival must be long enough to make enduring this procedure worthwhile, hence, prognostication and risk assessment factor into the decision-making process. The most cited scoring system for metastatic spinal tumors is the Tokuhashi system which includes the primary tumor location, presence of extraspinal metastases, number of spinal metastases, neurological functional status, and general condition of patients (Table 3) [41].

The concept of spinal stability rests on the anatomical and functional complexity of the spinal structure. As such, the clinical presentation of spinal instability is nuanced when caused by a neoplasm, each of which proceeds with its own array of bony and ligamentous involvement, neurological symptoms, bone quality, and prospect for effective repair. The Spine Oncology Study Group (SOSG) defines spinal instability as "the loss of spinal integrity as a result of a neoplastic process that is

Table 3 Revised Tokuhashi scoring system[a]

Characteristics	Score[b]
1. Preoperative KPS	
Poor (10–40)	0
Moderate (50–70)	1
Good (80–100)	2
2. Extent of extraspinal disease	
≥ 3 lesions	0
1–2 lesions	1
No lesions	2
3. Vertebral body metastases	
≥ 3 lesions	0
2 lesions	1
1 lesion	2
4. Status of major internal organ metastases	
Non-removable lesions	0
Removable lesions	1
No lesions	2
5. Primary cancer location	
Lung, osteosarcoma, stomach, bladder, esophagus, pancreas	0
Liver, gallbladder, unidentified	1
Others	2
Kidney, uterus	3
Rectum	4
Thyroid, breast, carcinoid tumor	5
6. Palsy or myelopathy	
Complete	0
Incomplete	1
None	2

KPS Karnofsky Performance Status

[a] This table is based on the scoring system by Tokuhashi and colleagues[41]

[b] Predicted prognosis based on total score: (0–8), < 6 months; (9–11), 6–12 months; (12–15), ≥ 1 year

associated with movement-related pain, symptomatic or progressive deformity, and/or neural compromise under physiologic loads" [42]. Furthermore, impending spinal instability is also a critical topic in spine tumors. In patients with spinal tumor but without neurological deficit, it is crucial to identify which cases are unstable or pending instability to allow timely intervention. SOSG developed an evidence-based scoring system for spinal instability in neoplastic disease called the Spine Instability Neoplastic Score (SINS) (Table 4). SINS is made up of six components: vertebral level, mechanical pain, bone lesion quality, spinal alignment, vertebral body collapse, and posterolateral involvement of spinal elements. In SINS, the minimum score is 0 and the maximum is 18. Scores of 0 to 6 are considered stable, 7 to 12 are indeterminate or may indicate impending instability, and 13 to 18 denote instability. Generally, scores of 7 to 18 warrant a surgical consultation [42]. Tumor size and location can be predictive of instability, especially when the tumor involves more than 50% of the vertebral body [43, 44]. The risk of burst fracture also increases with tumor size [43, 45, 46].

Table 4 Spine instability neoplastic score (SINS)[a]

Component	Score[b]
1. Location	
Junctional (O-C2; C7-T2; T11-L1; L5-S1)	3
Mobile spine (C3-6; L2-4)	2
Semirigid (T3-10)	1
Rigid (S2-5)	0
2. Pain level	
Mechanical pain: improves with rest, exacerbated with movement	3
Occasional pain but not mechanical	2
Pain-free lesion	1
3. Bone lesion	
Lytic	2
Mixed	1
Blastic	0
4. Radiographic spinal alignment	
Subluxation/translation present	4
Deformity (kyphosis/scoliosis)	2
Normal	0
5. Vertebral body collapse	
> 50% collapse	3
< 50% collapse	2
No collapse with > 50% body involved	1
None of the above	0
6. Posterolateral involvement	
Bilateral	3
Unilateral	1
None of the above	0

[a] This table is based on the SINS scoring system by Fisher and colleagues [42]

[b] Spine instability based on total score: (0–6) = stable; (7–12) = impending instability; (13–18) = instability. Total scores of 7 to 18 warrant surgical consultation

Historically, surgery in the form of a simple posterior laminectomy (removal of the dorsal elements of the vertebral column) without instrumentation was performed to decompress the spinal cord. However, several studies showed that laminectomy alone or in combination with radiotherapy did not add any advantage [26, 47–49]. In fact, laminectomy is not the best option in many patients with metastatic SCC whose spinal metastases infiltrate the vertebral body anteriorly. Laminectomy further destabilizes the spine by removing the posterior osseous and ligamentous elements that contribute some of its stability [11]. Another surgical technique was thus developed consisting of an anterior approach for tumor removal with immediate posterior decompression by laminectomy, followed by spinal instrumentation for renewed stability. Evidence supporting direct decompressive surgery for metastatic SCC over radiotherapy alone followed [49–61]. Procedures such as vertebral body resection and its replacement with a bone substitute made from any of several materials, transthoracic vertebrectomy, pedicle screw fixation, and single-stage posterolateral transpedicular approach have been employed for malignant spinal tumor resection and spinal stabilization. These procedures provide considerable pain relief and can restore or preserve neurological function and ambulation, all while having an acceptable rate of morbidity and mortality [55–61].

Today, the role of surgery is well established in patients with spinal metastatic disease with a neurological deficit or a high-grade SCC without deficits. In such cases, surgery is indicated regardless of the SINS score. Surgery is also indicated if there is impending SCC, spinal instability, bony retropulsion, pain resistant to other conventional therapies, or a need for tissue diagnosis (Fig. 5) [62]. Surgical approaches are chosen based on a variety of factors including whether there is a need for cord decompression, tumor location, a need for spinal stabilization, how much surgical morbidity is considered acceptable for the patient, and what other treatment options can be offered afterwards [32]. In a landmark prospective randomized trial published by Patchell and colleagues in 2005, patients with SCC who were treated with decompressive surgery and adjuvant radiotherapy regained their ability to walk more often, and retained this ability for a longer duration, than did patients treated with radiotherapy alone. Surgery was also shown to increase survival, possibly because the patients stayed ambulatory for longer and were thus protected from venous thrombosis and infections that can result in the death of patients

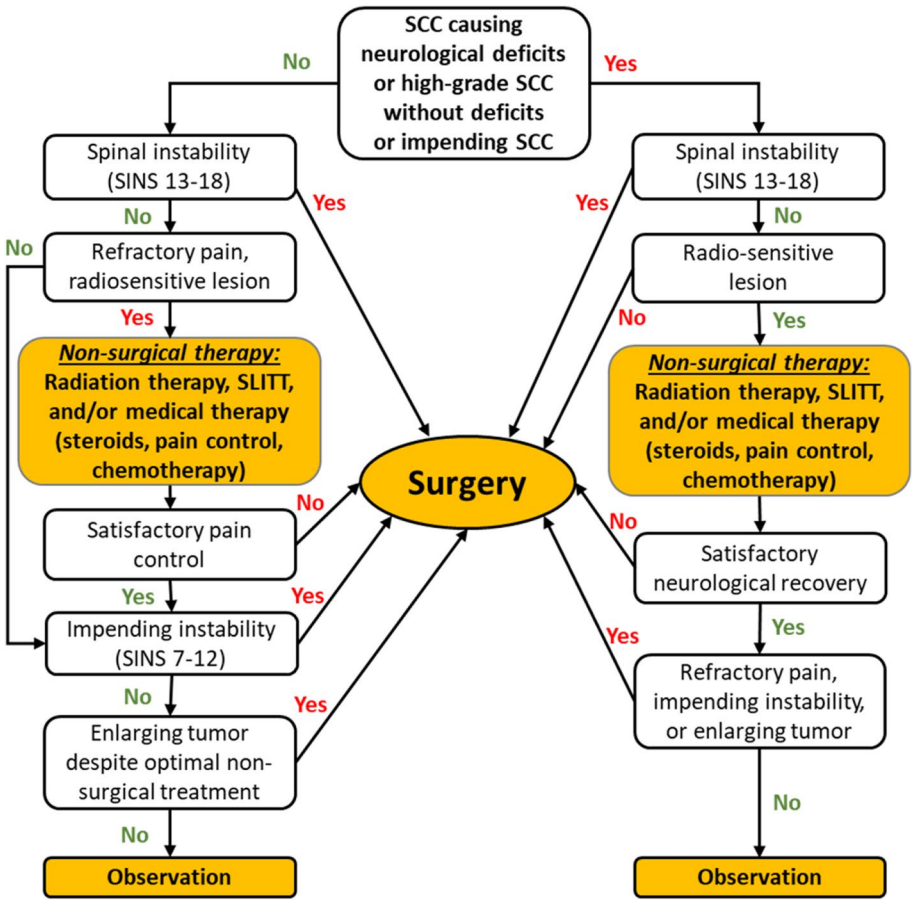


Fig. 5 Treatment algorithm for metastatic tumors of the spine. Strategy adapted and modified from Walker et al. [64]. SCC, spinal cord compression; SINS, spine instability neoplastic score; SLITT, spinal laser interstitial thermal therapy

immobilized by paraplegia. Surgery also reduces the need for corticosteroids and pain control. The limitation of this randomized trial was its selective recruitment of patients with less radiosensitive tumors and with only one area of SCC [11]. Despite such limitations, two subsequent meta-analyses found that decompressive surgery followed by radiotherapy is superior to radiotherapy alone in preserving or restoring ambulation [50, 63]. Moreover, the urgency of surgical management of SCC cannot be disputed. Surgery should be performed as soon as possible after the discovery of symptomatic metastatic SCC, as early surgery leads to significantly better neurological outcomes. However, the timing of surgery has been shown not to influence the length of hospital stay, complication rate, or survival [64].

The risk factors predicting loss of ambulation following surgical decompression were preoperative ambulation loss, recurrent or persistent tumor after radiotherapy to the surgical site, a procedure other than vertebral corpectomy (removal of the damaged vertebrae and intervertebral discs that are compressing the spinal cord and spinal nerves), and a primary tumor other than breast cancer [60]. In addition, surgery within 48 h of the onset of motor deficits was shown to provide better ambulatory outcomes [64, 65]. Reduced survival was encountered whenever an operation addressed tumor in two or more spinal segments, recurrent or persistent tumor after irradiation of the surgical site, a primary tumor other than breast cancer, and a resection involving the cervical region [60].

Table 5 Indications for surgical treatment of metastatic epidural SCC

Indications
1) SCC with neurological deficits, or high-grade SCC without neurological deficits, or impending SCC
2) Spinal instability
3) Unknown primary tumor
4) Refractory pain
5) Radioresistant primary tumor

Furthermore, a better ambulatory profile prior to surgery correlates with greater survival [15].

The indications for surgical decompression in metastatic epidural SCC are summarized in Table 5. However, one should still employ clinical judgment and follow a multi-disciplinary decision-making approach in selecting patients for surgery.

Complications of spine tumor surgery

Surgical site infections (SSI) are the most common complication seen following spinal tumor surgery [66–71]. Patients with primary or secondary vertebral tumors are in many cases immunocompromised owing to nutritional depletion as well as prior exposure to radiotherapy or chemotherapy. Such immunodeficiency predisposes them to less efficient wound healing. Preoperative radiotherapy is a risk factor for SSI. Preventative measures, such as glycemic control, antibiotic prophylaxis, and the direct sterilization of the surgical wound with vancomycin powder and/or dilute betadine solution, help in reducing the risk of SSI [66]. Moreover, neurological impairment (including paraplegia) was reported in a recent systematic review as the second most common complication encountered after surgery for spinal metastasis. Such deficits are the result of direct intra-operative injury to the spinal cord or its associated vascular structures [66]. Another complication is development of a hematoma within the surgical wound, which should be suspected in patients with coagulopathy (thrombocytopenia, anticoagulant use) who present with sudden-onset back pain and neurological deficits. Finally, spinal instrumentation failure is a common complication, and an especially important one, since instrumentation is needed to maintain spinal stability following tumor resection and decompression. Screw pullout or cage subsidence can be seen early on, before the typical time for bony fusion (3–6 months). Such events can stem from low mineral bone density caused by prior use of steroids or radiotherapy, and their incidence can also be correlated with the initial construct length (those spanning more than six spinal levels are more likely to exhibit symptomatic instrumentation failure) [66, 72]. SSI are the most common reason for re-operation after surgery for spinal metastasis, followed by instrumentation failure and tumor recurrence [66].

New paradigms in the surgical management of SCC

Minimally invasive spinal surgery (MISS) (Fig. 6) has been on the rise because in selected patients it can provide safe resection of symptomatic spinal metastases and effective stabilization of the spinal column with shorter hospital stays and a lower incidence of surgical morbidity [73–76]. MISS typically uses microsurgical approaches, image guidance, and percutaneous pedicle screw fixation methods [75, 76]. MISS using percutaneous pedicle screw fixation has been shown to maintain or improve functional outcomes in patients with spinal metastases [74]. These approaches can best be used in medically frail patients with spinal instability or in cases in which separation surgery (removal of only the portion of the tumor in close proximity to the spinal cord) is followed by addressing the residual tumor with other treatment modalities like radiotherapy. This approach can be employed for high-grade SCC followed by stereotactic body radiosurgery or laser interstitial thermal therapy [76].

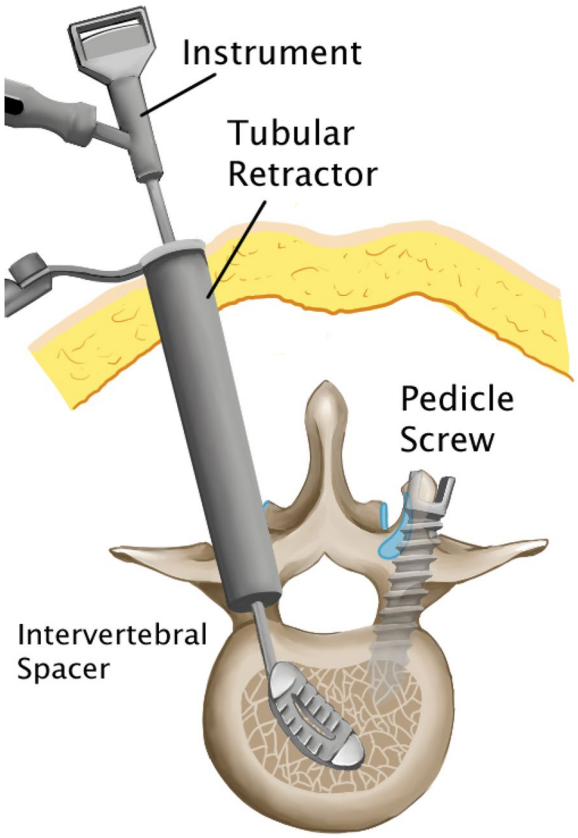


Fig. 6 Minimally invasive spine surgery. The instruments shown are used to perform an interbody fusion (between two adjacent vertebral bodies) supplemented by pedicle screw placement, which enables posterior fusion/fixation by a screw-and-rod construct

Spinal laser interstitial thermal therapy (SLITT) is another minimally invasive approach that allows for prompt and durable decompression of the spinal cord (Fig. 7). The process involves insertion of a laser probe into a spinal epidural tumor under real-time image guidance, so that the probe tip is placed ≥ 6 mm from the dura. MRI thermometry is used to monitor the heating process. When the tumor reaches a critical temperature

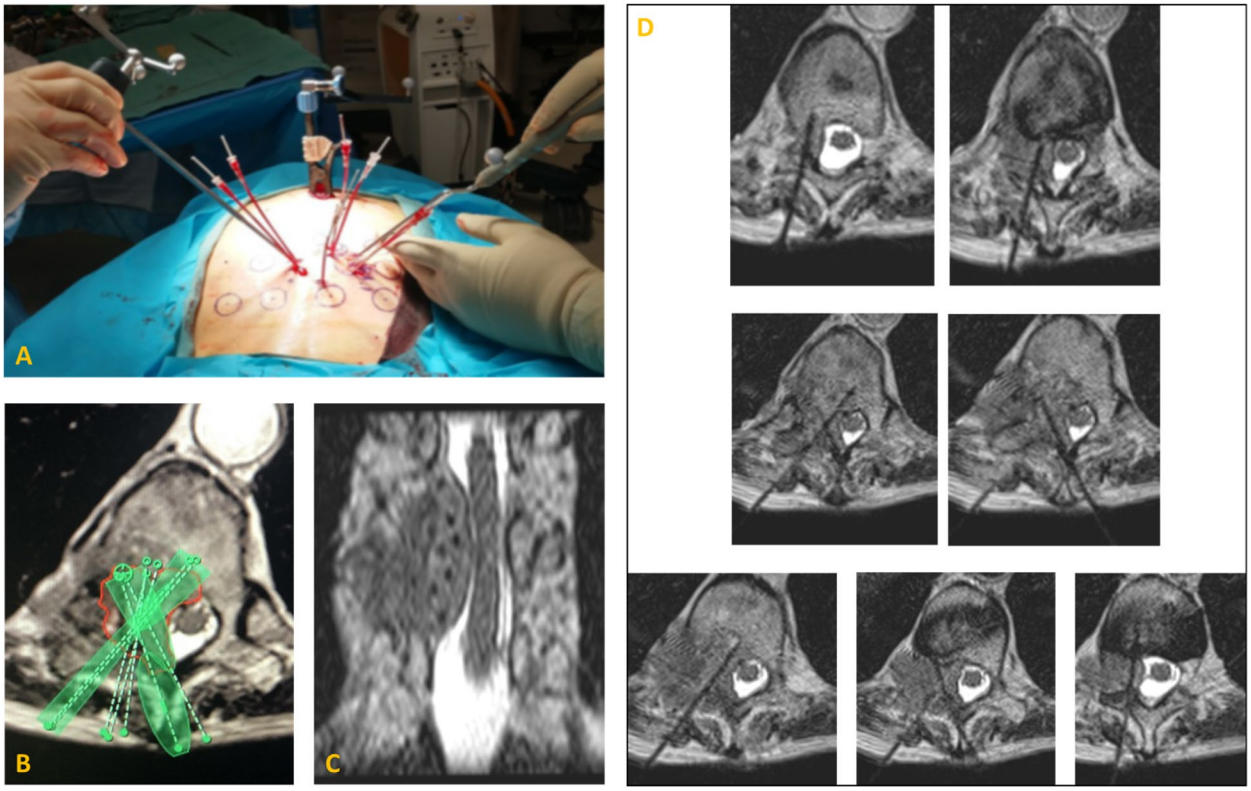
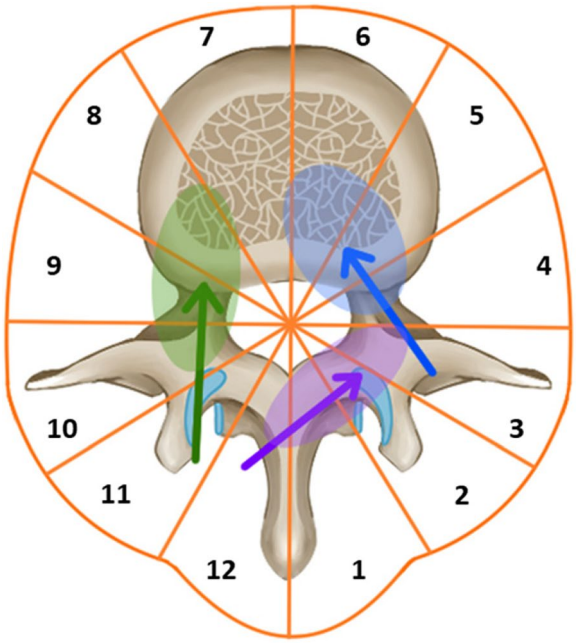


Fig. 7 Spinal laser interstitial thermal therapy (SLITT) for a metastatic spinal epidural tumor causing SCC. Real-time image guidance by a fiducial array attached percutaneously to a spinous process is used for accurate percutaneous laser probe placement (**A**). The process of SLITT starts with placement of Jamshidi needles that are registered to the intraoperative spinal navigation system, placed into plastic cannulas, and then imaged by intraoperative MRI to confirm the localization of each needle (**B**, **C**). The laser probe trajectory, which can be transpedicular or translaminar (**D**). Axial T2-weighted MRI showing a titanium needle artefact in the tumor. The coordinates are then maintained, and the titanium insert is replaced by a laser fiber (**D**)

at the dural edge, the system deactivates to prevent any thermal damage to nearby healthy tissue. SLITT is then followed by stereotactic radiosurgery with standard isodoses covering the entire tumor volume. In a study by Tatsui et al. of their experience with SLITT as an alternative to separation surgery, SLITT provided excellent local control with low morbidity, reduction of pain and improvement in the patients' quality of life, and short hospital stays. Their cohort included 11 patients with high-grade SCC caused by radioresistant tumors, and they excluded patients with acute neurological deficits and with epidural tumors spanning more than one vertebral level [77].

The same authors later published an updated series establishing the same conclusion about the safety and feasibility of MRI-guided SLITT in patients with no neurological deficits but with progressive systemic disease. Such patients are candidates for open surgical decompression, but their comorbidities portend a high operative risk. In this later study, Tatsui et al. highlighted the sequential procedural workflow during SLITT [78]. A modified Weinstein-Boriani-Biagini classification scheme can be used to establish a safe trajectory for the laser probe depending on tumor location. Vertical transpedicular, posterolateral transpedicular, and contralateral translaminar approaches are generally used (Fig. 8). Mechanical ventilation is halted during thermal ablation to prevent motion from altering heat distribution within the tumor target. It is resumed (and the procedure is stopped) if O_2 saturation falls below 94%, or at onset of any spontaneous breathing by the patient [78].

Vertebral augmentation of pathologic vertebral compression fractures has also been intently investigated and reported in the literature. Vertebroplasty, kyphoplasty, and stent-assisted vertebroplasty are examples of this technique. In vertebroplasty, viscous bone cement is injected percutaneously into a fractured vertebral body, thereby promoting structural integrity of the vertebra and improving pain control (Fig. 9). Kyphoplasty is a modification of vertebroplasty that involves inflating a balloon within the fractured body, thereby creating a space into which the cement can be injected at lower



Targeting Zone	Trajectory
4-6 or 7-9	Posterolateral Transpedicular
3-5 or 8-10	Vertical Transpedicular
10-3	Translaminal

Fig. 8 Modified Weinstein-Boriani-Biagini classification scheme

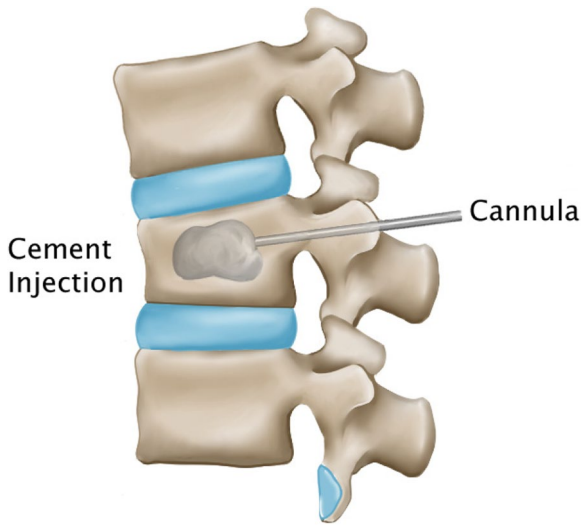


Fig. 9 Vertebroplasty. Viscous bone cement is injected percutaneously into a fractured vertebral body

pressures (Fig. 10) [32, 76]. Although these techniques are considered relatively safe [79], on rare occasions, the cement escapes from the vertebral body and extrudes into the spinal canal where it can cause SCC. In addition, new fractures sometimes occur in adjacent levels, or tumor cells might escape to cause unusually rapid spread of the tumor in adjacent areas [76, 80].

Despite these advancements, open invasive surgery remains to date the treatment of choice for patients who develop spinal tumors with mechanical instability and high-grade SCC.

Spinal infection in cancer patients

Post-operative SSI in spine surgery are challenging events that complicate patients' existing disease. They cause prolonged hospital stays, exacerbation of neurological deficits if the infection spreads to the CNS, and substantial surgical morbidity as they often induce wound dehiscence [67, 81]. Deep incisional SSI usually show purulent wound discharge and spontaneous dehiscence. Identification of the causative microorganism(s) in culture is imperative to drive effective antibiotic therapy. Most patients with SSI have at least one sign of infection (fever, erythema, localized tenderness, and pain) manifesting as an abscess identified by imaging or direct inspection. Generally, patients with such infections need surgical revision to optimize subsequent wound healing [82]. Spine tumor surgery is associated with a higher incidence of SSI than is non-tumor spine surgery. This association is explained by patients' multiple comorbidities, the complexity of their antecedent surgical procedures, use of spinal instrumentation, exposure to radiotherapy, steroid usage, and their immunocompromised status induced by anti-cancer therapies and often by the cancer itself [83, 84].

In an effort to determine the risk factors for SSI in spine tumor surgery, McPhee et al. showed that pre-operative protein depletion and perioperative corticosteroid use are associated with poor wound healing in spinal surgery for metastatic tumors [84]. Omeis et al. found that complex plastic surgical closure, more comorbidities, hospital-acquired infection during primary surgery, and a longer hospital stay are associated with a higher risk of SSI in multivariate analysis. In univariate analysis, preoperative radiotherapy had a higher risk of SSI as it leads to impaired wound healing. Repeat surgery for spine tumor recurrence was also associated with a higher incidence of infection that was the initial surgery. This difference is explained by the distorted local anatomy and soft tissue damage induced by prior surgery [67]. Another study showed that in patients with metastatic spine disease and spinal instability who underwent surgical stabilization, radiotherapy within 21 days of surgery led to higher rates

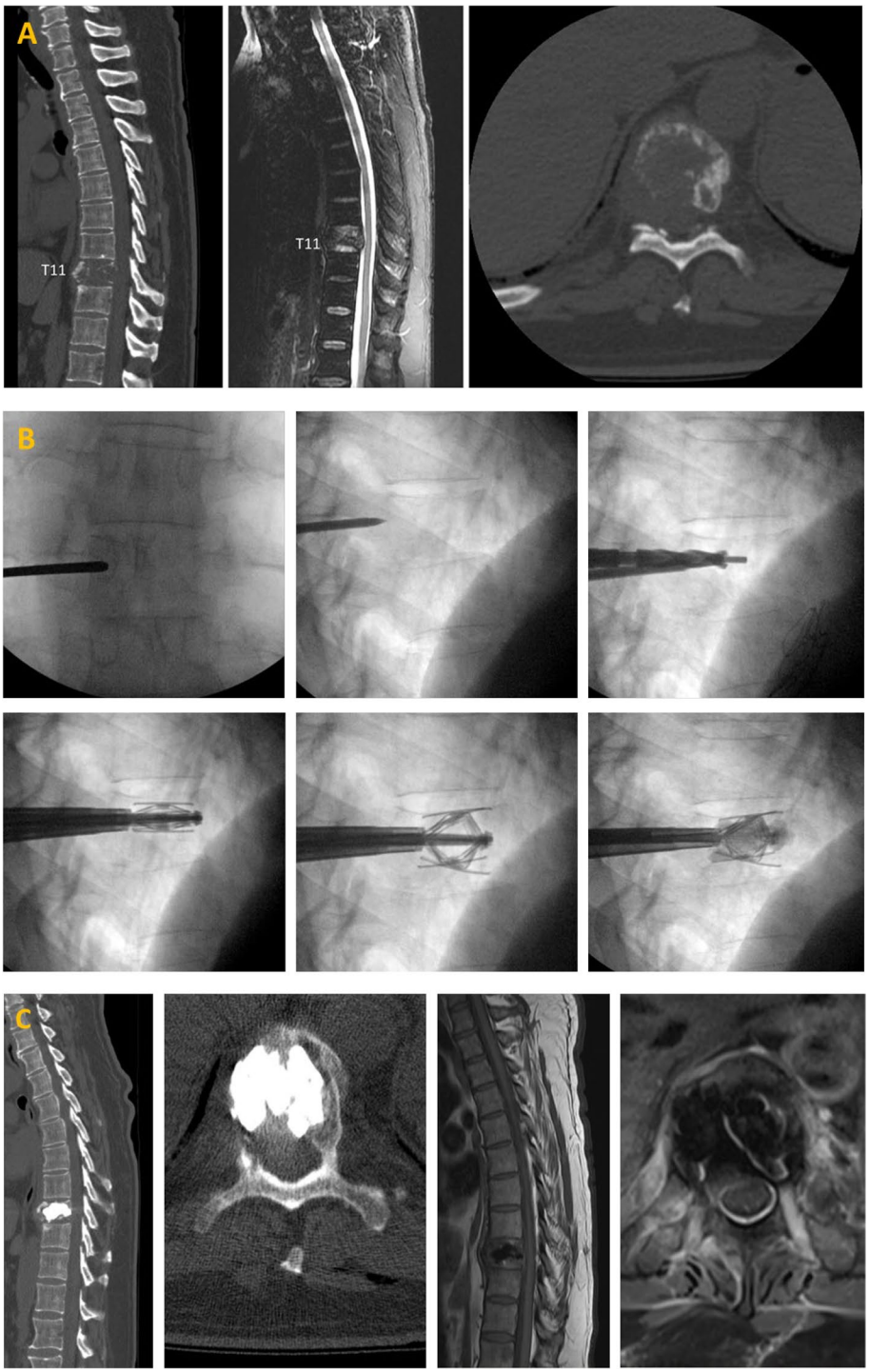


Fig. 10 Device-assisted kyphoplasty. **A** Sagittal section on a CT (left) and T2-weighted MRI (center) and axial CT (right) showing a compression fracture of the T11 vertebra. **B** Intraoperative fluoroscopic images in the anteroposterior projection showing balloon inflation inside the vertebral body to create space for cement augmentation. **C** Postoperative sagittal and axial CT (left two panels) and T1-weighted MRI (right two panels) showing the distribution of bone cement within the T11 vertebral body without significant leakage

of wound-related complications (SSI or delay in wound healing longer than 3 weeks) [85].

Finally, in a systematic review and meta-analysis of primary and metastatic spine tumor surgery, primary spine tumors had a different set of risk factors for SSI than those seen with metastatic tumors. In primary tumors, the spinal level (mainly sacral) and use of instrumentation (which can provide a niche for infection by creating dead space in which bacteria may grow) were identified as risk factors. In contrast, metastatic spinal tumors were associated with risk factors pertaining to preoperative conditions and treatments. These included female gender, a history of smoking, and prior exposure to non-surgical therapies (chemotherapy, radiotherapy, and/or corticosteroids) as well as to prior spine surgery [86].

Cancer patients in general are at risk for developing spontaneous spinal epidural abscess (SEA), subdural empyema (SDE), and vertebral osteomyelitis due to their immunocompromised state. These conditions are serious and sometimes life-threatening, and carry high rates of morbidity and mortality, so prompt diagnosis and treatment are crucial. Microorganisms can reach the epidural space via a hematogenous route (50%), from direct extension of a contiguous infection (35%), by introduction through spinal apertures (15%), or through other unidentified mechanisms [87]. *Staphylococcus aureus* is the root bacterium for the majority of spinal abscesses. Patients can present with signs and symptoms of infection as well as acute neurological deficits secondary to direct SCC by the abscess. MRI is the method of choice for diagnosis of SEA (Fig. 11). However, a delay in diagnosis is very common (75–89%) as only a few patients present with the classic findings of fever, back pain, and localized neurological deficits [87, 88]. Additionally, the presentation of patients with SEA is highly variable, as some have merely back pain for months while others can go from mild symptoms to complete paralysis within hours. Since fever and progressive neurological deficits are not always present, experts sought to implement new decision guidelines to avoid diagnostic delays in SEA. Clinical suspicion for SEA should be elevated in patients with back pain and risk factors for infection including diabetes, trauma, intravenous drug use, chronic liver or kidney disease, infection elsewhere in the body, recent spinal intervention or indwelling hardware, or immunocompromise [87, 88]. In such patients, elevated erythrocyte sedimentation rate (ESR) was also shown to be highly sensitive and moderately specific screening test for SEA. In fact, the rate of diagnostic delay dropped from 84 to 10% following the incorporation of ESR and C-reactive protein (CRP) in the decision-making algorithm for identifying SEAs [88]. Treatment can be conservative or surgical. Conservative management, i.e., antibiotics only and close monitoring, can be used in a specific group of patients

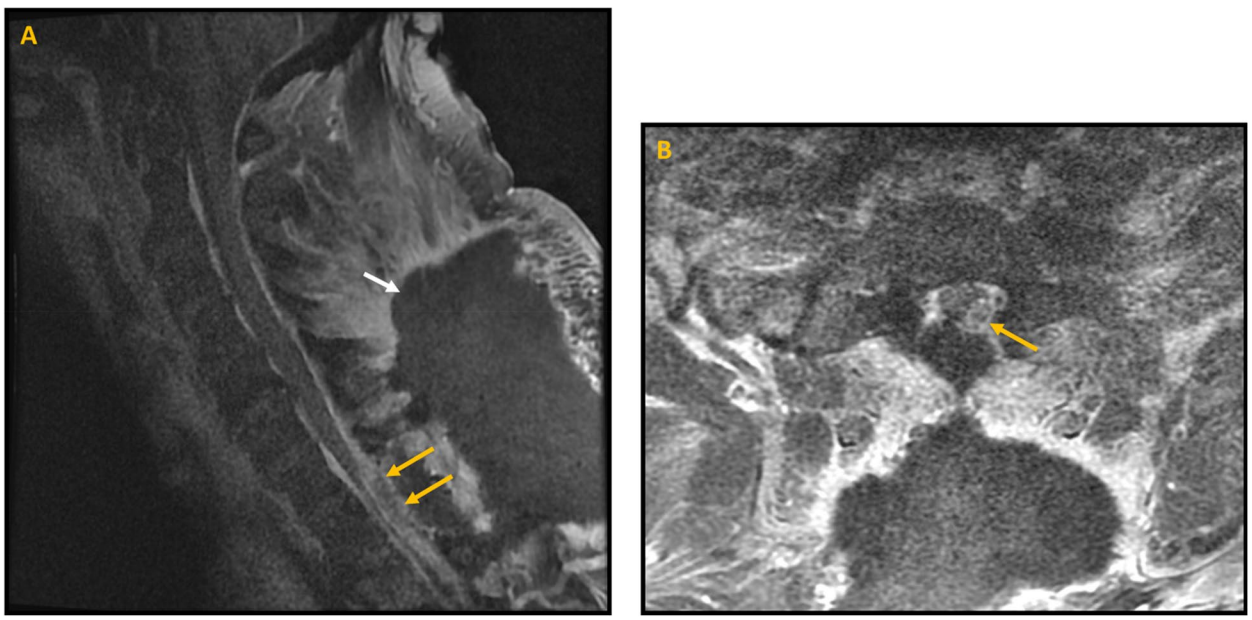


Fig. 11 Spinal epidural abscess at the cervicothoracic junction. This patient has a history of multiple prior laminectomies at C7-T2 for recurrent intradural-extramedullary meningioma resection causing SCC. He presented with drainage from the surgical incision 2 weeks after the most recent surgery. Sagittal (**A**) and axial (**B**) sections of MRI (T1-weighted, post-contrast) reveal an early epidural abscess along the left dorsal aspect of the spinal canal at T1–T2 *(yellow arrows)* and a large seroma *(white arrow)* bounded by inflamed paraspinal muscle. This is consistent with postoperative wound infection

who fit the following criteria: cannot undergo surgery, have a complete spinal cord injury of > 48 h duration with low clinical or radiographic concern for an ascending lesion, or are neurologically stable and lack risk factors for failure of medical treatment. However, if the patient is deemed a good surgical candidate, then emergency surgery is advisable as the onset and rapidity of clinical deterioration are unpredictable in patients with SEA [87]. Clinical outcomes and quality of life were shown to be significantly better when surgery is done within 12 h of admission in patients with SEA [89].

SDE is an infection located between the dura and the arachnoid. It is rare and occurs mostly through hematogenous spread or by extension of infection from a focus of osteomyelitis in an adjacent vertebra. As is true for SEA, early surgical drainage of SDE followed by appropriate antibiotic therapy is crucial. In the worst-case scenario, SDE can cause thrombosis of blood vessels on the surface of the spinal cord and lead to infarction of the cord, from which the chances of neurological recovery are very low. SDE is thus a medical and neurosurgical emergency, and morbidity and mortality are directly related to treatment delay [90]. In vertebral osteomyelitis (Fig. 12), hematogenous spread of infection is the primary route, as opposed to osteomyelitis of an extremity in which contiguous spread from skin infection is the more common cause. It can also occur following spinal procedures. *S. aureus* is the most common pathogen [91]. Antibiotic therapy given intravenously for 6 weeks is the mainstay of treatment. Surgery is not indicated unless there is neurological compromise, vertebral destruction with spinal instability, epidural or subdural abscess formation, intractable back pain, or failure of medical therapy [92].

Summary

Spinal tumors can compress the spinal cord and cause spinal instability. Spinal cord compression is a devastating complication and represents a true oncologic emergency. Its clinical presentation ranges from the patient who is neurologically intact with little or no back pain to one with total paraplegia and intractable pain. Management can be non-surgical or surgical, with a goal of pain control, prevention of irreversible neurological deficits, and improvement of reversible deficits. Non-surgical management is recommended when the tumor has not yet caused spinal instability, neurological deficits, or intractable pain. Non-operative methods include steroid therapy, chemotherapy, and/or radiotherapy. Advances in surgical techniques have paved the way for their greater use in patients with spinal instability, neurological deficits, or SCC with intractable pain that does not respond to conventional solutions. Given the variety of treatment options, management ought to rely on a multidisciplinary approach that accounts for the patient's clinical and neurological presentation as well as the histopathological diagnosis and overall prognosis.

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Authors' contributions
All authors contributed to the conception, development, writing, and revisions of the manuscript. Each author read and approved the final manuscript.

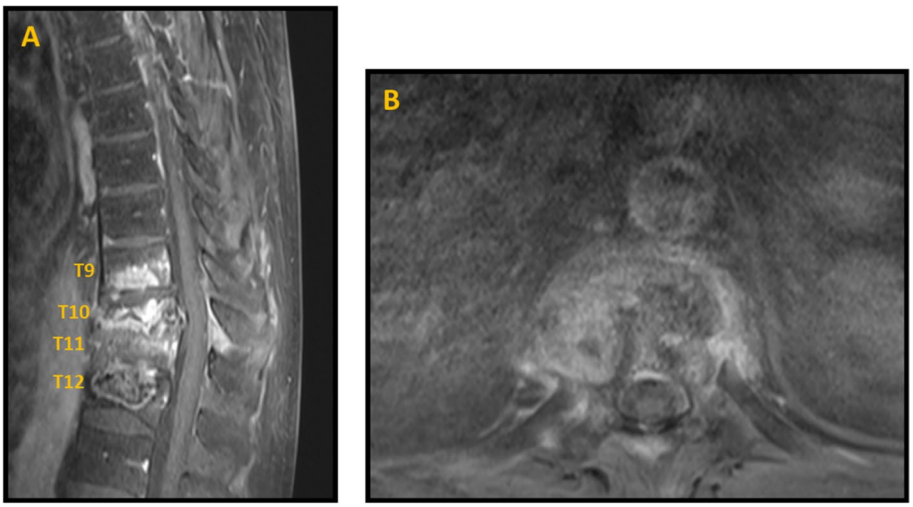

Fig. 12 Vertebral osteomyelitis and spondylodiscitis. This patient with a previous history of T12 vertebroplasty presents with worsening mechanical back pain and SCC. Sagittal MRI (T1-weighted, post-contrast) shows (**A**) signal abnormality and enhancement at the T9-12 levels suggesting vertebral osteomyelitis and spondylodiscitis. There are pathological fractures at T10 and T11 with retropulsion and narrowing of the spinal canal. **B** Axial MRI (T1-weighted, post-contrast) shows total collapse of the T10–T11 disc space and phlegmon adjacent to its anterior and lateral edges

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