Intradural-Extramedullary and Intramedullary Spinal Metastases

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19.1 Introduction

Intradural metastatic disease to the spinal cord is an uncommon phenomenon, and accounts for up to 6% of all spinal metastases [1]. Intramedullary spinal cord tumors are even more uncommon, affecting approximately 2% of all cancer patients [2]. The more common location for intradural spinal metastases is to the vertebral body, causing extradural compression, which is beyond the scope of this chapter. Regardless, the management of spinal metastases can be complex and must take into account the patient's complaints, overall clinical status (i.e., tumor burden and Karnofsky status), radiographic findings, and life expectancy. The acuity and intensity of the interventions are largely determined by the severity of the neurologic deficit.

Current management strategies employ a multi-disciplinary approach, which promotes a more rigorous treatment protocol to optimize patient outcomes. A multitude of rigorous clinical studies have been published to address metastatic spinal disease in general, from which treatment models have been generated [3–6]. This chapter provides a comprehensive review of management strategies and offers recommendations in the treatment of intradural spinal metastases.

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19.2   Epidemiology

Improved survival from cancer has increased the prevalence of spinal metastases, and is estimated to be present in up to 40% in patients with cancer [7]. About 300,000 patients have bony metastases with upwards of 60% having a spinal lesion [7–9]. In this regard, the spine is the most common site for bony metastases [7]. The incidence of spinal metastases is estimated to be 10% [10], and an additional 10% will eventually develop spinal cord compression [7].

Over 95% of all spinal metastases are extradural within the vertebral body, and more than 50% of cases have more than 1 level of involvement [1]. Less common are the metastases to the intradural-extramedullary and intramedullary areas, accounting for only 5–6% and 0.5–2%, respectively [1, 2]. The most common primary source of spinal metastases is lung (31%), followed by breast (24%), other (13%), gastrointestinal tract (9%), prostate (8%), lymphoma (6%), melanoma (4%), and kidney (1%). The infrequency of intradural and intramedullary lesions have resulted in difficulties with delineating the true epidemiology—a few studies have identified the most common source as lung, but they can also originate from the breast, prostate, or renal cells, or from lymphoma and melanoma [8, 11]. Depending on the primary lesion, either osteoblast or osteoclast activity can be promoted. This increased activity can result in a varied phenotype of osteoblastic, osteolytic, or mixed lesions [12].

The most common mode of metastasis to the spine is arterial, and accounts for the increased frequency of bone marrow involvement. Venous spreading through Batson's plexus has also been proposed as a source of spread. Contiguous spreading can occur as well. The most common area of involvement is the thoracic region (70%), followed by the lumbar (20%) and cervical regions (10%) [1]. Within the vertebral body, about 60% of metastases are localized to the anterior portion, with the remaining 30% affecting the pedicle or lamina.

The presence of an intramedullary spinal cord lesion is a poor prognosticator with an estimated survival of less than a month [13]. The increased prevalence of the spinal metastases necessitates a heightened sensitivity to the patient's signs and symptoms, as undetected spinal cord compression can result in devastating consequences.

19.3   Presentation and Clinical Evaluation

Intradural metastatic spinal cord lesions commonly cause radicular and myelopathic symptoms secondary to spinal cord compression or vascular incompetence. Unlike bony metastases, in which pain is secondary to bony instability, the pain is usually radicular in nature. Intramedullary tumors can also cause unilateral motor and sensory symptoms, such as with Brown-Sequard syndrome [14, 15]. A subset of patients will present with a rapidly progressive neurologic deterioration,

necessitating an urgent diagnosis and treatment [16, 17]. The preoperative performance status is critical to the determination of the treatment protocol; thus, the initial clinical evaluation must be performed with great detail. A thorough history—which includes the duration of systems, systemic cancer history and treatments, and overall quality of life—must be taken into consideration. Next, a detailed neurologic examination with a focus on the motor and sensory function, deep tendon and pathologic reflexes, and rectal tone must also be performed.

Overall performance status is critical in the determination of the treatment plan as patients with metastatic disease may have a shorter life expectancy, making more invasive and time-consuming interventions less ideal since they may harm the patient and decrease quality of life. The typical mode of assessment of performance status is the Karnofsky performance status (KPS) [18, 19], which has been shown to be a good prognosticator of treatment [20–22]. In general, a KPS of less than 40 portends a poor prognosis, as evidenced by a multitude of scoring systems [4–6, 23]. The basic tenant of all these scoring systems is that the overall burden of disease must be considered [5]. While the majority of surgical interventions for metastatic disease are aimed at local control, preservation of neurologic function, maintenance of spinal stability, and life expectancy, KPS must be considered in the overall treatment. Less invasive efforts, such as kyphoplasty, vertebroplasty, or medical management, should be offered in cases with poor prognoses.

19.4 Imaging Studies

In situations in which there is a concern for spinal cord involvement, such as new radiculopathy or myelopathy, the next step in the work-up is to obtain imaging studies. The goal of imaging is to determine the presence and location of a pathological lesion, and to ascertain the degree of compromise to the overall stability based on neural compression and bony destruction. In this regard, computed tomography (CT) and magnetic resonance imaging (MRI) studies are the most informative imaging modalities. These 2 studies will provide the greatest breadth and depth regarding the presence of spinal cord compression and pathologic fractures. Additional information can be obtained with ancillary studies, such as bone scans and positron emission tomography (PET), which provide details on the overall tumor burden. Static X-rays are of limited utility due to its low resolution and poor soft tissue detail. In contrast, dynamic X-rays with flexion and extension could provide some insights to identify additional areas of instability for surgical planning purposes.

Metastases most commonly involve the vertebral body and posterior elements with its affinity for bone marrow. Most tumors are lytic in nature; however, osteoblastic lesions can also occur. Thus, a combination of imaging modalities yields the greatest insights. A recent meta-analysis reviewed the advantages of multi-modality imaging to assist in the diagnosis and treatment of bony metastases [24].

19.4.1 Nuclear Imaging and Positron Emission Tomography

A PET scan is the traditional screening study for metastatic disease involving the spine. This imaging study carries a high sensitivity of 95%. PET scans detect metabolic activity, which can be helpful when bony involvement is minimal, as is the case with isolated bone marrow involvement. Additionally, whole-body imaging is possible to further delineate overall disease burden. However, in contrast to MRI, the spatial resolution is more limited. Various tracers can be used, such as 18F-FDG, 11C-choline, 18F-choline, and MIBG. The optimal tracer can vary depending on the primary tumor, and is currently an area of intense research [25, 26]. Tumor-specific tracers are also in development, and currently in preliminary investigations [27].

19.4.2 Computed Tomography

CT scans are most useful to characterize bony involvement with cortical destruction, demarcation of lesion margins, and tumor calcification. The tumor can also be delineated as a lytic or blastic lesion. These features combined can be utilized to narrow the differential diagnosis, as certain features are pathognomonic for specific lesions. This modality carries a greater degree of spatial and temporal resolution compared with conventional radiography, and has thus supplanted it as primary modality for bony anatomy.

The extent of vertebral involvement is important in assessing the risk for instability. A CT scan is helpful in determining the presence of a compression fractures, trabecular bone thinning, sclerotic pedicles, cortical destruction, and multiple column involvement that increases the risk of pathologic instability [10, 28–30].

19.4.3 Magnetic Resonance Imaging

The most informative imaging modality is a contrasted MRI study, which provides the greatest detail on the location and involvement of the surrounding soft tissues (i.e., paraspinal region). This modality is highly sensitive and specific at greater than 90% for detecting spinal malignancies [31]. The pathologic lesion can be further defined as extradural, intradural, or intramedullary. The degree of spinal cord and nerve root impingement can be characterized. MRI is also the most sensitive in detecting isolated bone marrow infiltration, which permits an earlier diagnosis, in contrast to other modalities that would not be able to detect abnormalities until after at least 50% of the bone is destroyed [10, 30, 31]. As such, it is important to image the entire spine when a metastatic lesion is suspected since concurrent lesions are common. Metastatic lesions are commonly hypointense on T1 and hyperintense on T2 sequences, and will enhance to a varying degree [32, 33]. Restricted diffusion-weighted imaging (DWI) can also be used to differentiate a pathologic from an osteoporotic fracture [34, 35]. The gradient echo sequence provides some insights into the effect of the tumor on bone.

19.5 Treatment Planning

The treatment plan is predicated on the philosophy of "first, do no harm." The initial assessment of the patient must take into consideration the patient's current functional status, systemic tumor burden, overall health/co-morbidities, and patient preference. The complexity of this situation necessitates a multi-disciplinary approach to develop the ideal management strategy. Several studies have highlighted key considerations and developed some algorithms for treatment stratification [36]. One caveat is that these scoring systems apply to the whole population with spinal metastases, of which almost 95% of the patients have vertebral body involvement. In this regard, the applicability to isolated intradural and intramedullary metastases may be limited. However, some insights can be obtained from these scoring systems.

The most common prognostic score is "LMNOP," which represents Location of disease, Mechanical stability, Neurological risk, Oncological parameters, and Preferred treatment [37]. The mechanical stability of the spine is crucial for maintaining neurologic function with instability also resulting in increased pain and disability. Several scoring systems have been devised with the most common system being the Spine Instability Neoplastic Score (SINS) [38–40]. SINS describes 6 categories that can contribute to spinal instability: location, pain, bone lesion, radiographic spinal alignment, vertebral body collapse, and posterior spinal element involvement. A SINS greater than 13 signifies instability, while a score of 7–12 is potentially unstable. The advantage with SINS is a high inter- and intra-observer reliability within and across various specialties [38, 41]. The neurological risk is determined from the current neurologic examination and potential for further neurologic compromise, but also radiographic findings of spinal compression. Unfortunately, no grading system currently exists for intradural lesions. Bilsky et al. developed a scoring system to grade the level of spinal cord compression epidurally [42]. Oncological parameters take into account the tumor type and its responsiveness to radiation therapies. Radio-responsiveness can push treatment recommendations for less-invasive therapies, such as stereotactic radiosurgery. Lastly, the preferred treatment is the compilation of the multiple specialties based on the clinical and radiographic findings previously discussed.

Other scoring schemes for survival estimates from spinal metastases have also been described [4–6, 23], and differ on the weight placed for various factors. A recent meta-analysis aimed at identifying prognostic factors in metastatic spinal disease found 17 poor prognostic factors separated into cancer-specific and nonspecific factors, from which a tumor-specific scoring system was developed [43].

19.6 Treatment/Intervention

Surgery and radiation therapy are the mainstay treatments for spinal cord metastases, and are frequently combined as a multimodal therapy to improve outcome [44, 45]. This was described in the seminal randomized clinical trial by Patchell et al.,

which identified a definitive role for direct decompression surgery with radiation as a superior treatment for spinal cord compression from metastatic lesions [45].

19.6.1 Surgery

The goals of surgery in metastatic spinal disease are diagnosis and decompression of the neural elements to prevent further neurological decline. In the case of intradural lesions, preoperative MRI is critical in the determination of the surgical goals. As previously described, MRI can aid in the determination of the location of the lesion relative to the dura, and if intramedullary infiltration is present. The extent of neural involvement from a clinical and radiographic standpoint will define the degree of resectability, but also the tumor characteristics (i.e., tumor consistency and presence of a tumor margin) found intraoperatively. The ideal situation is for an en bloc resection with clear surgical margins, but this can cause substantial neurologic morbidity. In the setting of intramedullary metastases, a clear margin can be appreciated to facilitate en bloc resection [11, 46]. In cases where en bloc resection is not feasible, subtotal decompression can be pursued and followed with adjunctive radiation therapy.

In the setting of an intradural or intramedullary lesion without osseous involvement, spinal stabilization is not likely necessary. The priority is maximal resection as safely as possible. This is facilitated by intraoperative neurophysiological monitoring. Gross total resection is a priority for intradural and intramedullary lesions. As previously stated, complete resection is often not possible, thus necessitating adjunctive radiation therapy for further tumor control. Cases of intradural-extramedullary and intramedullary metastases are few, but suggest that surgery may be effective to maintain neurologic function [47, 48].

19.6.2 Radiation

Radiation therapy offers a less invasive means of tumor control, and can be utilized as the initial treatment or as an adjunct in the postoperative setting. The decision to use radiation therapy largely depends on factors described in the previous section, namely neurologic compromise, overall performance, and systemic tumor burden. Unfortunately, there is a paucity of rigorous data regarding radiation treatment for intradural and intramedullary spinal metastases. However, many case studies have advocated the use of radiation for patients with intramedullary spinal cord tumors due to their overall poor prognosis [16, 49, 50]. Conventional external-beam radiotherapy (EBRT) is the most common mode of radiation for bony spinal metastases, and consists of daily low-dose radiation in single or daily fractions ranging from 8 to 30 Gy [21]. There are data to suggest that hypofractionation decreases the likelihood of retreatment with improved rates of local control [51, 52]. However, the biggest disadvantage to dose escalation with this modality is the toxicity to the spinal cord at 45–50 Gy.

Stereotactic spinal radiosurgery (SSRS) and spinal radiotherapy (SRT) have emerged as viable alternatives in the treatment of metastatic spinal lesions with the

ability to deliver a very high dose of radiation with improved accuracy, thus decreasing toxicity to local tissues. SSRS is delivered in a single fraction whereas SRT is delivered in 2–5 treatments. Studies for osseous metastatic lesions yield control rates of up to 90% at 2 years for bony metastatic disease [53–55]. Some studies have shown promise of SRS for the treatment of intradural lesions [56–58]. Although no studies for intramedullary lesions exist, the theoretical advantage compared to EBRT is a 3-times higher biologically effective dose. SSRS can also induce a higher rate of deoxyribonucleic acid (DNA) damage, which improves the control rate for traditionally radioresistant tumors [59–63]. The increased accuracy is a function of improved planning with the contouring of the tumor to minimize radiation to the adjacent tissues, namely the spinal cord. This necessitates a thorough understanding of the neuroanatomy, and may require a decompression or separation surgery to delineate the lesion. For this reason, SSRS and SRT require a multidisciplinary team consisting of medical oncologists, radiation oncologists, physicists, and neurosurgeons. Shin et al. previously described the safety of SRS for intradural and intramedullary metastases in a small case series [64]. SSRS and SRT comparisons to EBRT warrants further investigations.

19.7   Multimodal Treatment Algorithm

There is currently a paucity of clinical data to recommend a definitive framework for the treatment of intradural and intramedullary lesions. However, several insights can be obtained from the clinical data and algorithms derived for bony spinal metastases. The degree of neurologic compromise coupled with the acuity of the decline, the systemic tumor burden, and overall performance are important considerations as to the aggressiveness of the interventions. The location and degree of involvement of the neural elements will determine the role of surgery and the timing of radiation therapy as either a primary or secondary treatment. Tumor histology also plays an important role as certain metastases are more radiosensitive, and newer immunotherapies may be utilized to improve outcomes [65, 66].

The combination of surgery followed by radiation therapy has been shown to improve outcomes for spinal metastases [45]. For intradural lesions, gross total resection is favored with adjuvant radiation for any residual tumor. This can also be applied to intramedullary lesions; however, surgical intervention should be pursued with caution in patients with a poor performance status.

19.8   Follow–Up and Further Interventions

Patients with intradural and intramedullary lesions will likely need rehabilitation, which can substantially improve the patient's functional outcomes [67]. Bracing is not necessary, but may provide some relief if there is concurrent osseous involvement. Radiculopathic complaints can improve with pregabalin or gabapentin, and muscle relaxants can help with pain control. Follow-up radiography should be pursued at 3 weeks and thereafter at least every 6 months, but is as the discretion of the multidisciplinary treatment team.

19.9 Conclusions

The treatment of intradural and intramedullary spinal metastases is complex and necessitates a multidisciplinary team for multimodal therapies. Important considerations, such as the patient's performance status, systemic tumor burden, location of the tumor, tumor type and patient preference, are critical to define when developing a treatment plan. Surgery and radiation are the mainstays of treatment, which the few clinical studies available have supported. More rigorous studies are necessary to determine outcomes from these treatments.

19.10 Case Illustrations

19.10.1 Case 1

WY is a 54-year-old woman with a history of metastatic breast carcinoma who had previously undergone a successful resection of a large right cerebellar metastasis. She presented emergently 3 months later with acute onset left-sided hemiplegia. An MRI of her cervical spine (Figs. 19.1 and 19.2) was significant for multi-focal intradural metastases: an intradural extramedullary lesion at C2–3. The patient underwent a multi-level laminectomy and resection of the extramedullary lesion. Postoperatively, her strength improved with rehabilitation. A follow-up MRI of her lumbar spine revealed additional metastases, and the decision was made to place an Ommaya reservoir placement for intraventricular/intrathecal chemotherapy. She underwent adjuvant whole brain radiation therapy with 3000 cGy in 10 fractions, and reduced field boost to the posterior fossa and upper cervical spine of 3900 cGy in 13 fractions. As her systemic disease progressed, she passed about 9 months from her diagnosis of spinal cord metastases.

19.10.2 Case 2

BW is 69-year-old man with non-small cell lung cancer treated previously with resection, irradiation, and chemotherapy presented with left-sided hemiplegia and intramedullary spinal metastasis at the C4–C5 level. The lesion was resected and postoperative irradiation planned after surgery (Fig. 19.3) [68].

19.10.3 Case 3

KS is a 55-year-old woman with a history of renal cell carcinoma and known metastases to the lung. She underwent immunotherapy and was found to be in remission with regards to her systemic disease. She recently developed right-sided leg
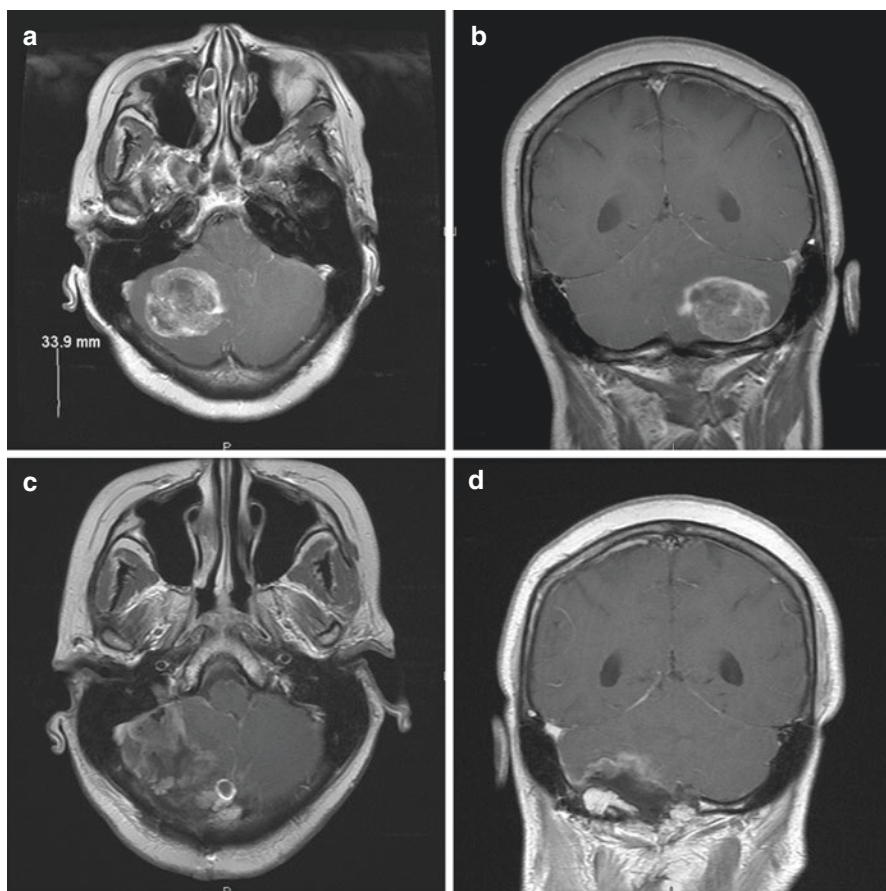
Fig. 19.1 Breast carcinoma metastasis. MRI brain T1-weighted post contrast axial (**a**) and coronal (**b**) images showing a large right cerebellar metastasis. Postoperative post-contrast T1-weighted axial (**c**) and coronal (**d**) MRI of brain showing resection of tumor

weakness for the past couple of weeks that progressed to bowel and bladder dysfunction. An MRI was performed, which was significant for an intramedullary lesion at the conus medullaris (Fig. 19.4). The remainder of her neural axis was without disease.

The patient underwent a multi-level laminectomy with electrophysiological monitoring to resect this lesion, with pathology consistent with renal cell carcinoma. Post-operatively, she experienced some improvement with regards to her lower extremity function, and is currently undergoing rehabilitation. Her future treatment plan is to undergo adjuvant stereotactic radiation.
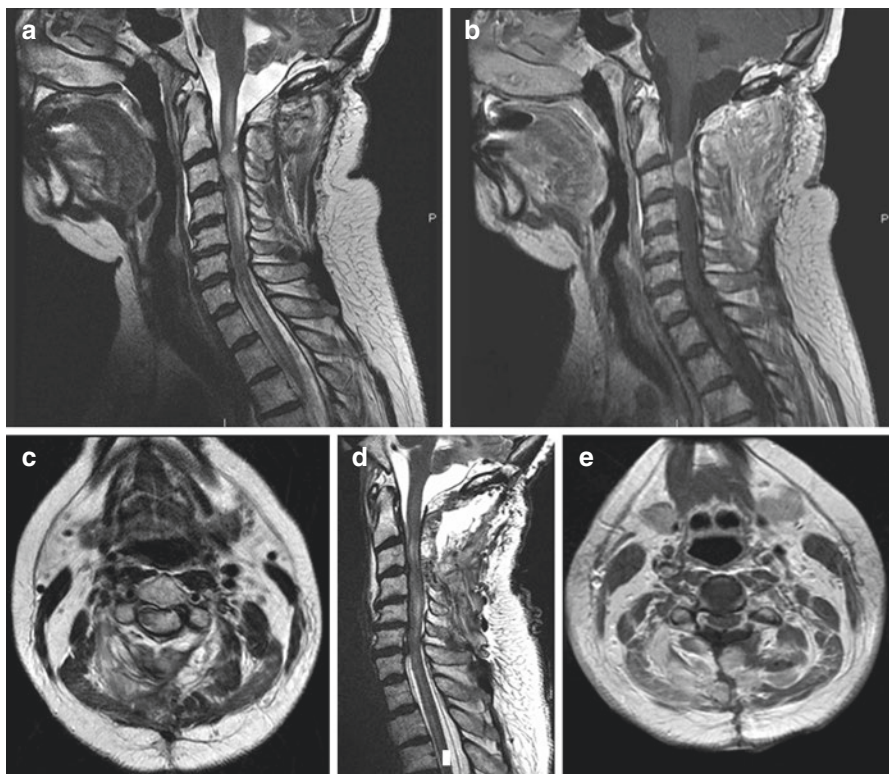
Fig. 19.2 An MRI of cervical spine 2.5 month after initial cerebellar metastasis resection. (**a**) Sagittal T2-weighted MRI. (**b**) Sagittal T1-weighted postcontrast MRI. (**c**) Axial postcontrast T-weighted MRI showing intradural extramedullary tumor at C3. (**d**) Sagittal T2-weighted MRI. (**e**) T2-weighted MRI showing tumor resection
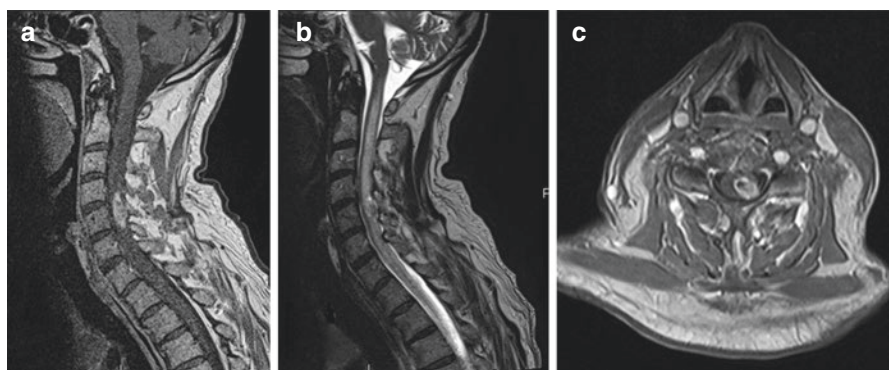

Fig. 19.3 Non-small lung cancer intramedullary metastasis. (**a**) Preoperative T1-weighted post-contrast sagittal MRI of the cervical spine showing tumor at C4–C5. (**b**) Sagittal T2-weighted preoperative MRI showing same tumor and adjacent spinal cord edema. (**c**) Post-contrast, T1-weighted axial MRI showing left-sided intramedullary tumor. (**d**) Post-contrast, sagittal, T1-weighted MRI showing tumor resection. (Note the fat graft dorsal to the dura to avoid cerebrospinal fluid leak or pseudomeningocele.) (**e**) T2-weighted postoperative MRI showing tumor resection and fat graft dorsal to the dura. (**f**) Postoperative, post-contrast T1-weighted MRI showing tumor resection and fat graft
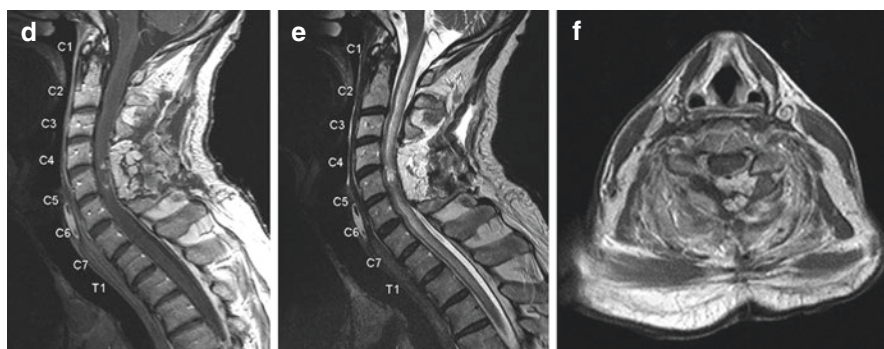
Fig. 19.3 (continued)

Fig. 19.4 Renal cell carcinoma metastasis. An MRI of the lumbar spine that is significant for an enhancing conus medullaris lesion seen on T1 post-contrast sagittal (**a**) and axial (**b**) cuts

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