Neoplastic Myelopathies

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REVIEW ARTICLE

CONTINUUM AUDIO INTERVIEW AVAILABLE ONLINE

ABSTRACT

PURPOSE OF REVIEW: **This article reviews the current classification system of primary spinal cord tumors and explores evolving diagnostic and therapeutic strategies for both primary tumors and metastatic tumors to various compartments of the spinal cord.**

RECENT FINDINGS: **The 2016 World Health Organization classification system allows for more precise prognostication of and therapy for spinal cord tumors and has identified new entities, such as the diffuse midline glioma, H3 K27M mutant. Whole-exome sequencing reveals that the genetic background of primary glial spinal cord neoplasms differs from that of their intracranial histologic counterparts in ways that can potentially influence therapy. Targeted and immune checkpoint therapies have improved survival for patients with melanoma and lung cancer and have simultaneously produced novel complications by enhancing radiation toxicity in some cases and by facilitating the emergence of novel autoimmune and paraneoplastic syndromes involving the spinal cord, such as neuromyelitis optica spectrum disorder and syndromes associated with anti-Hu and collapsin response mediator protein-5 (CRMP-5) antibodies. These conditions must be distinguished from tumor or infection. Epidural spinal cord compression treatment paradigms have changed with the advent of robotic surgery and advances in radiation therapy.**

SUMMARY: **Neoplastic myelopathies subsume a wide spectrum of pathologies. Neoplastic cord involvement may be primary or secondary and may be approached diagnostically by the particular spinal cord compartment localization. Primary spinal cord tumors account for only 2% to 4% of primary central nervous system tumors, ranging from low-grade glial neoplasms to malignant tumors. Metastatic malignancy to the epidural or leptomeningeal spaces is more common than primary cord tumors. Differential diagnoses arising in the course of evaluation for cord tumors include myelopathies related to radiation or chemotherapy and paraneoplastic syndromes, all of which are sources of significant morbidity. Knowledge of genetic syndromes and the biologic behavior of diverse histologies together with selective application of surgery, radiation, and targeted therapies can facilitate diagnosis, minimize surgical morbidity, and prolong quality of life.**

CITE AS:
CONTINUUM (MINNEAP MINN) 2021;27(1, SPINAL CORD DISORDERS): 121–142.

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UNLABELED USE OF PRODUCTS/INVESTIGATIONAL USE DISCLOSURE:
Dr Pruitt reports no disclosure.

INTRODUCTION

Although spinal cord tumors represent only 2% to 4% of all primary central nervous system (CNS) tumors, they cause significant morbidity and are often confused clinically and radiographically with non-neoplastic processes.[1] Early identification of these neoplasms guides appropriate management and can minimize

symptoms. Difficult decisions regarding when and if to consider biopsy or to perform major surgery accompany a diagnosis of spinal cord neoplasm, and neurologists can provide a guided workup that can lead to a diagnosis of neoplastic or other disease process without hazardous invasive procedures.

Neoplastic myelopathies are classified by the compartment affected as intramedullary, intradural-extramedullary, and extradural tumors. Differential diagnostic considerations and workup are dictated by the particular neuroanatomic compartment involved (FIGURE 5-1).[1]

Overall, metastatic tumors, which are usually in the epidural space, account for many more cases of adult spinal cord tumors than do primary spinal tumors, whereas in children (in whom primary tumors are more common), the intramedullary compartment is the most common tumor site. Absolute numbers of tumors show that 1322 children and adolescents were diagnosed with spinal cord tumors between 2012 and 2016, whereas adults aged 20 and older accounted for 18,184 cases.[2] Among children, the most common primary tumors are ependymomas (20.6%) followed by nerve sheath tumors, neuroepithelial tumors, astrocytoma, oligodendroglioma, glioblastoma, meningeal tumors, and pilocytic astrocytomas. Other aggressive high-grade glial spinal neoplasms include the H3 K27M-mutant diffuse midline gliomas of pediatric and younger adult populations. Ependymomas are the most common primary intramedullary spinal tumors in adults (17.6%), but the most common primary spinal tumor overall in adults is meningioma (38.8%) followed by nerve sheath tumors (20.5%).[2] Metastatic tumors most frequently are extradural, but systemic cancer can involve the leptomeningeal and, less commonly, intramedullary

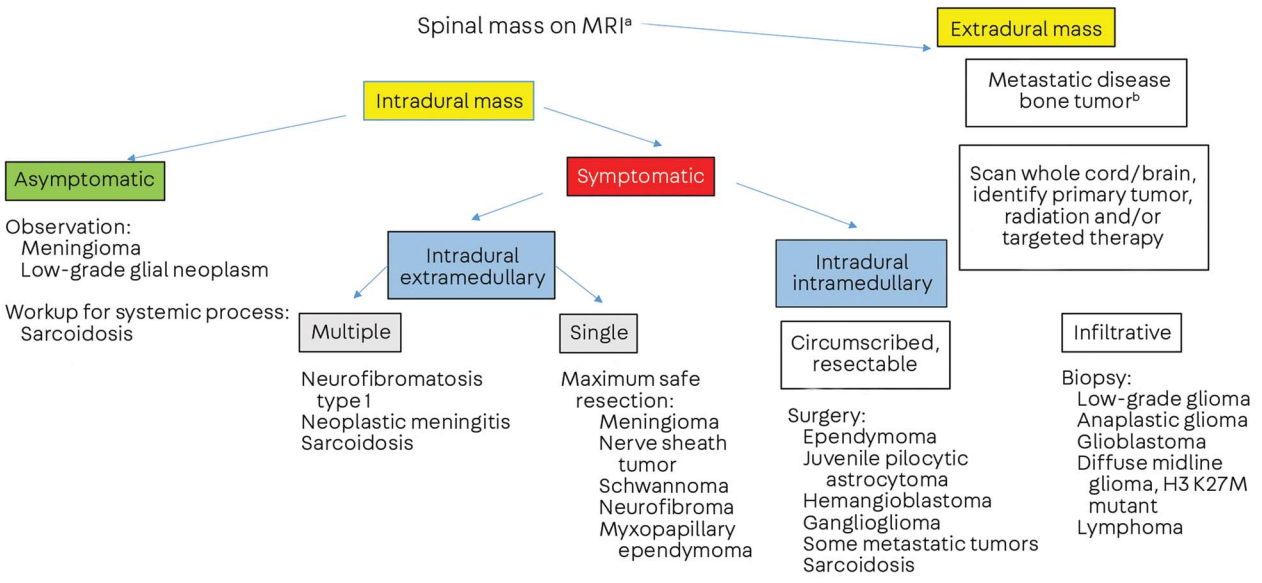

FIGURE 5-1

Algorithm for diagnosis and management of spinal mass on MRI.

[a] Whole-neuraxis imaging usually indicated to delineate other levels of pathology.

[b] Benign: bone cyst, angiolipoma, hemangioma, Langerhans cell histiocytosis, osteochondroma, osteoma. Malignant: angiosarcoma, chondrosarcoma, chordoma, Ewing sarcoma, lymphoma, myeloma, plasmacytoma.

compartments. Lung, breast, prostate, thyroid, and renal cell cancers represent the majority of spinal metastatic tumors, the vast majority of which are extradural. Leptomeningeal dissemination is seen most frequently with adenocarcinoma of the breast, lung carcinoma, non-Hodgkin lymphoma, melanoma, and gastrointestinal tumors. Several paraneoplastic syndromes involve the spinal cord and can occur before a cancer diagnosis or emerge in the setting of immune checkpoint inhibitor therapy.

PRIMARY SPINAL CORD TUMORS

Primary spinal cord tumors arise in the cord, spinal nerve roots, or dura. Between 900 and 1800 new adult cases of primary spinal cord tumors are diagnosed annually in the United States.[2] Intramedullary spinal tumors represent about 10% of all primary spinal cord tumors.[2] In adults, meningeal and nerve sheath tumors are the most common diagnoses, whereas in children and adolescents, ependymomas and astrocytomas are the most common histologies. Ependymomas are the most common intramedullary primary spinal cord tumor in all age groups. Other histologies include astrocytoma, oligodendroglioma, hemangioblastoma, ganglioglioma, germinoma, and primary CNS lymphoma. Histiocytic tumors, such as in Erdheim-Chester disease, occasionally involve the spinal cord and can be mistaken for meningiomas. The major histologies by compartment are listed in TABLE 5-1.[3-6] Spinal cord tumors differ clinically, histologically, and genetically from their primary intracranial counterparts in several ways:

- Back, radicular, or central pain, often asymmetric and without motor involvement, is the most common symptom preceding the diagnosis of an intramedullary neoplasm (CASE 5-1 and CASE 5-2).
- Neuroimaging cannot precisely pinpoint histology, but some general patterns are evident. Astrocytomas are commonly found in an eccentric location within the cord. Ependymomas, usually more central, can have an associated cyst or syrinx (CASE 5-1). Ependymomas and hemangioblastomas are often hypointense on susceptibility-weighted images (SWI), suggesting prior hemorrhage. CNS lymphomas are hyperintense on diffusion-weighted images, consistent with their marked cellularity.
- Spinal glial tumors show no association between increasing grade of malignancy and patient age at diagnosis.
- The majority of intracranial low-grade astrocytomas harbor *IDH1*/*IDH2* mutations; however, in one series, 0 of 13 spinal cord cases had this mutation.[7] Aggressive high-grade astrocytic tumors may harbor H3 K27M mutations.[8-10] *BRAF* V600E mutations found in pediatric and adult pilocytic astrocytomas occur much less frequently in spinal astrocytomas.[11-13]

Ependymoma

The World Health Organization (WHO) 2016 classification system reclassified ependymomas to better reflect their biological behavior.[14] Nine molecular subgroups are now recognized, three each arising in the supratentorial region, posterior fossa, and spine. Cellular ependymomas may be WHO grade II or grade III and arise from the intraspinal canal, usually in the cervical and thoracic regions; myxopapillary ependymoma, a WHO grade I tumor, is most frequently seen in the conus medullaris arising from the filum terminale, where they comprise 90% of tumors.[14] Subependymomas are rarely found in the spine; if present, they are usually cervical, eccentric, and T2-hyperintense and T1-hypointense lesions that infrequently enhance with gadolinium.[15] In children,

KEY POINTS

- Although spinal cord tumors represent only 2% to 4% of all primary central nervous system tumors, they cause significant morbidity and are often confused clinically and radiographically with non-neoplastic processes.
- Neoplastic myelopathies are classified by the compartment affected as intramedullary, intradural-extramedullary, and extradural tumors. Differential diagnostic considerations and workup are dictated by the particular neuroanatomic compartment involved.
- Overall, metastatic tumors, which are usually in the epidural space, account for many more cases of adult spinal cord tumors than do primary spinal tumors, whereas in children (in whom primary tumors are more common), the intramedullary compartment is the most common tumor site.
- Ependymomas are the most common primary intramedullary spinal tumors in adults, but the most common primary spinal tumors overall in adults are meningiomas.
- Lung, breast, prostate, thyroid, and renal cell cancers represent the majority of spinal metastatic tumors, the vast majority of which are extradural. Leptomeningeal dissemination is seen most frequently with adenocarcinoma of the breast and lung, non-Hodgkin lymphoma, melanoma, and gastrointestinal tumors.

ependymomas are frequently in the posterior fossa; however, in adults, ependymomas are most common in the spine. Neurofibromatosis type 2 (NF2) mutations are found in some ependymomas.[7]

Several radiographic features distinguish ependymomas from astrocytomas. Ependymomas are often well-demarcated isointense lesions that enhance with gadolinium. They may have a cyst and syrinx, and hemorrhage may be seen on SWI sequences. Some have a rim of extreme hypointensity called the hemosiderin cap sign, visible on T2 and SWI sequences. Patients present with low back pain, leg weakness, and bladder dysfunction and are more likely to have a central cord syndrome than a Brown-Séquard syndrome pattern.

Distinguishing ependymomas from astrocytomas radiographically is important in preoperative planning as gross total resection of astrocytomas is unlikely, but ependymomas, which are often encapsulated, are more amenable to

TABLE 5-1

Primary Spinal Cord Tumors

Intramedullary

- **Ependymoma**
  - Ependymoma (World Health Organization [WHO] grade II)
  - Anaplastic ependymoma (WHO grade III)
  - Myxopapillary ependymoma (WHO grade I)
  - Subependymoma (WHO grade I)
- **Astrocytoma**
  - Pilocytic astrocytoma (WHO Grade I)
  - Diffuse astrocytoma (WHO grade II)
  - Anaplastic astrocytoma (WHO Grade III)
  - Glioblastoma (WHO Grade IV)
    - → Midline glioma (H3 K27M mutation)
- **Oligodendroglioma**
  - Oligodendroglioma (WHO grade II)
  - Anaplastic oligodendroglioma (WHO grade III)
- **Atypical teratoid/rhabdoid tumors**
- **Mixed neuronal/glial tumors**
  - Ganglioglioma (WHO grade I)
- **Mesenchymal tumors**
  - Hemangioblastoma (WHO grade I)
  - Lipoma
  - Melanocytoma
- **Hematopoietic tumors**
  - Primary central nervous system lymphoma
  - Leukemia (myelocytic sarcoma)

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total resection. Intraoperative monitoring can be used to assist with complete resection. However, if on surgical resection the ependymoma capsule is entered, these tumors can seed the neuraxis and frequently recur. Adjuvant radiation therapy is suggested for incompletely resected tumors, and long-term surveillance of the neuraxis is important (CASE 5-1). No chemotherapy regimen has been established for incompletely resected ependymomas, but intracranial ependymoma may respond to bevacizumab or lapatinib.[16,17]

Astrocytoma

Intramedullary astrocytomas represent about 7% of all primary spinal cord tumors.[2] Most are low grade, but their location and infiltrative behavior preclude effective resection. They are often lateralized to one side of the cord, and patients may present with local pain or a Brown-Séquard syndrome. Many patients will

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Intradural-extramedullary

- **Meningioma**
- **Schwannoma**
- **Neurofibroma**
- **Hemangioblastoma**
- **Myxopapillary ependymoma**
- **Paraganglioma**
- **Lipoma**
- **Sarcoma**

Extradural

- **Meningioma**
- **En plaque meningioma**
- **Schwannoma**
- **Myxopapillary ependymoma**
- **Histiocytic tumors**
  - ◇ Erdheim-Chester disease

Primary brain tumors that disseminate to spinal canal[a]

- **Medulloblastoma**
- **Central nervous system neuroblastoma**
- **Ependymoma**
- **Primary central nervous system lymphoma**
- **High-grade glioma[b]**
- **Primary dural lymphoma (low-grade B-cell marginal zone lymphoma)**

[a] Drop metastases or leptomeningeal metastases.
[b] These complications usually occur late in the disease course, after multiple surgical interventions.

CASE 5-1

A 53-year-old man with type 2 diabetes developed right arm pain. A cervical MRI with contrast was obtained, and he was found to have a cervical spinal cord neoplasm (FIGURE 5-2). After being followed for 4 years, during which there was slow tumor growth with concomitant increase in arm paresthesia, he underwent surgery with partial excision of a World Health Organization grade II cellular ependymoma. He remained numb from the cervical level down, with whole-body hyperalgesia "like a tight wetsuit." Proprioceptive problems produced balance difficulties that were a limiting factor in his functional abilities such as driving. Three years after the original surgery, he underwent radiation for a new tumor 2 cm caudal to the original side (3600 cGy in 20 fractions with an additional radiation boost of 50.4 Gy to the area of greatest contrast enhancement). Five years after radiation, he developed urinary retention, left calf pain, and left footdrop and was found to have a conus medullaris/cauda equina lesion.

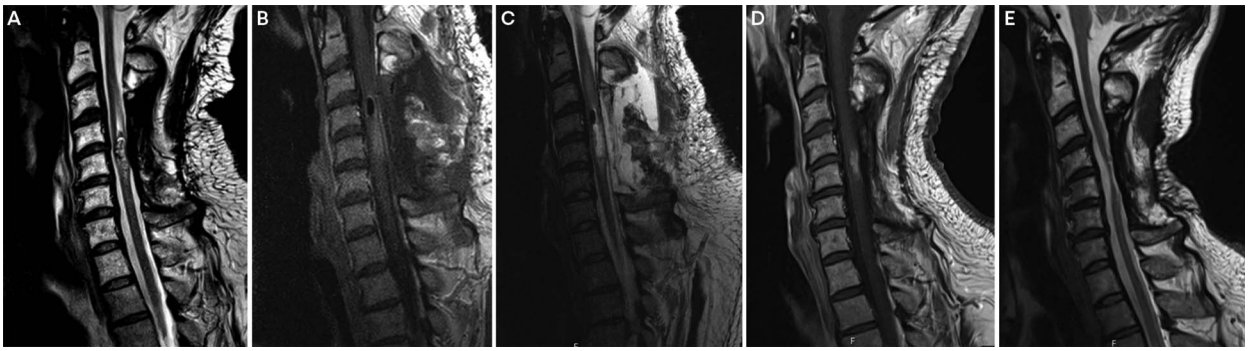

FIGURE 5-2
Imaging of the patient in CASE 5-1 with ependymoma. Intramedullary tumor with cystic component at first diagnosis of ependymoma on sagittal T2-weighted (*A*) and postcontrast T1-weighted (*B*) MRIs. Sagittal T2-weighted (*C*) and postcontrast T1-weighted (*D*) MRIs reveal tumor recurrence 7 years later and with progressive symptoms 2 years later not attributable to tumor but to tethering of the atrophic cord at C5 on sagittal T2-weighted MRI following radiation therapy (*E*).

COMMENT

This case illustrates the typical MRI findings of cyst and syrinx in a spinal cord ependymoma as well as the role of surgery at clinical progression and the resultant considerable disability, in this case proprioceptive dysfunction and pain. It also illustrates the propensity of ependymoma for local recurrence and subsequent spread through the neuraxis. This patient sustained surgical and radiation morbidities, with cord atrophy and a tethered cord. Although the indolent behavior over more than a decade is typical, recurrence is common both locally and through drop metastases. Diabetes complicated this patient's functional status as he likely had a superimposed distal sensory neuropathy.

enjoy long periods of minimal symptoms without surgical intervention (CASE 5-2, FIGURE 5-3). Specialized imaging of the spine, including diffusion-weighted imaging, diffusion tensor imaging, and fractional anisotropy, can be useful to map the extent of spinal lesions and to predict the outcome of surgical intervention, tracking fibers to visualize the integrity of white matter tracts.[18] Intraoperative monitoring adds to the safety of the surgical intervention.[19]

Prognostic factors for astrocytoma have been identified. In one series of 131 adults from the Surveillance, Epidemiology, and End Results Program

CASE 5-2

A 30-year-old woman first noted bandlike dysesthesia and occasional sharp neuralgic pains in the midthoracic region when she was 13 years of age, and a nonenhancing intraaxial mass in the thoracic spinal cord was first seen on imaging when she was 19 years of age. She was followed with stable MRI scans for more than 10 years (FIGURE 5-3), and her examination remained stable with mild hyperreflexia and allodynia over the T9 through T11 levels. In view of her clinicoradiographic stability, continued annual imaging was elected. She had no family history of neurofibromatosis type 1, neurofibromatosis type 2, or von Hippel-Lindau syndrome.

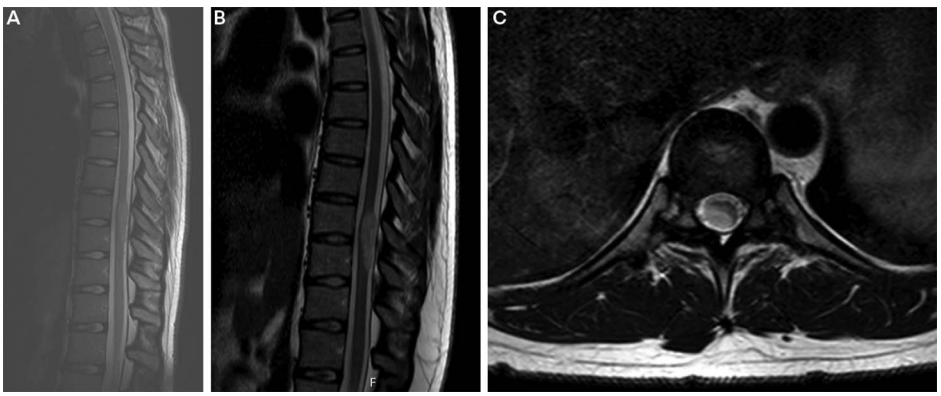

FIGURE 5-3
Imaging of the patient in CASE 5-2 with a nonenhancing intramedullary tumor. Sagittal T2-weighted images of the same tumor with a 14-year interval between *panel A* and *panels B* and *C*. Axial T2-weighted MRI shows the typical asymmetric location of this slow-growing astrocytic neoplasm.

COMMENT

Low-grade intramedullary spinal tumors account for 10% to 20% of all spinal tumors.[7] These tumors do not harbor the classic mutations associated with their intracranial counterparts; thus, for this patient, targeted therapeutic options are limited. Typical for astrocytomas, this tumor is nonenhancing and appears as a T2 hyperintensity on sagittal views (FIGURES 5-3A and 5-3B) that involve one-half of the cord (FIGURE 5-3C). MRI characteristically shows no enhancement in over 50% of low-grade astrocytomas, in contrast to high-grade glial neoplasms of the spine.[8]

CASE 5-3

A 28-year-old man presented with shortness of breath and was found to have a cardiac ejection fraction of 15%. Coronary angiography was normal, but MRI done because of dysphagia and right facial numbness showed a nonenhancing medullary lesion. Because of hemodynamic instability and tumor location, no biopsy was done, and he was treated empirically with proton therapy. He did well, with no dysphagia or hemodynamic instability for 9 months before presenting again with numbness below the nipples, urinary retention, and recurrent facial numbness. Repeat MRI showed a relatively stable brainstem tumor but also a T6 intramedullary lesion (FIGURE 5-4A). Within a month, dramatic spread of leptomeningeal enhancement was seen (FIGURE 5-4B). This area was biopsied, and H3 K27M astrocytoma was diagnosed. The patient's disease progressed too rapidly to permit enrollment in a clinical trial.

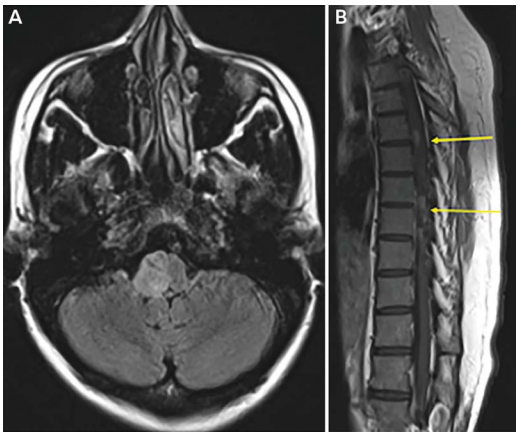

FIGURE 5-4
Imaging of the patient in CASE 5-3 with H3 K27M-mutant midline glioma presenting with medullary symptoms. *A*, Axial fluid-attenuated inversion recovery (FLAIR) MRI shows diffuse expansion of the right side of the medulla by a nonenhancing intramedullary lesion. One year later, the patient had developed paraparesis from this aggressive tumor. *B*, Sagittal postcontrast T1-weighted MRI obtained 1 year after the initial imaging shows diffuse contrast-enhancing metastases throughout the thoracic spine.

COMMENT

This tumor in the medulla, which presented unusually as takotsubo syndrome, did not behave like a low-grade brainstem glioma. Repeat imaging showed an enhancing intramedullary lesion in the thoracic region, and the patient rapidly developed paraplegia. The suspicion was that the biological behavior was that of a high-grade H3 K27M glial neoplasm. The cord lesion also was deemed inaccessible to safe biopsy, so diagnosis was made by biopsy of the cauda equina; treatment was radiation to a wide field of the spinal cord. The patient died before having access to developing targeted therapy, such as imipridone ONC201. The prognosis for these high-grade cord tumors is poor; this patient died 15 months after onset of symptoms.

(SEER) database, overall survival was 85.5% at 1 year, 71% at 3 years, 64.1% at 5 years, and 55% at 10 years.[20] Younger age at diagnosis, tumor grade, and larger extent of resection were each associated with worse long-term prognosis. This study is consistent with prior literature that also noted better survival with thoracic astrocytomas compared to cervical region tumors.[21]

Primary spinal high-grade gliomas (WHO grade IV, glioblastoma) account for only 7.5% of all intramedullary spinal cord gliomas.[22] The mean age at diagnosis is 39 years, with males outnumbering females by more than 3 to 1.[22] Median overall survival of patients with high-grade glial spinal neoplasms is 10 to 13 months. Recognized for the first time in the 2016 WHO classification of tumors is the WHO grade IV diffuse midline glioma, H3 K27M mutant, previously called diffuse intrinsic pontine glioma. Median survival was 48.5 months for H3 K27M–positive cases, compared to 1 month for those with *TERT* promoter mutation and 77 months for those harboring neither.[7] Median survival for cases with *TP53* mutations was 11.5 months and for those with *PPM1D* mutations was 84 months. These statistics suggest that high-grade infiltrating gliomas of the spinal cord in adults represent a heterogeneous group of tumors, the prognosis of which can be predicted by genetic profiling.

The H3 K27M mutation and *EGFR* or genetic alterations offering a better prognosis are mutually exclusive. Mutations conferring a better prognosis include the *IDH1*, *IDH2*, 1p/19q codeletion, and *BRAF* mutations seen in oligodendrogliomas and low-grade astrocytomas.

Like high-grade gliomas elsewhere in the nervous system, the H3 K27M mutation is associated with *TP53* expression, *ATRX* loss, and monosomy 10. In one series, the tumors of six of 13 patients with high-grade spinal cord gliomas harbored this mutation.[7] Most H3 K27M-mutant diffuse midline gliomas occur in the thalamus and brainstem, but brainstem cases can extend to the spinal cord and show a propensity for intramedullary drop metastases and leptomeningeal dissemination (CASE 5-3).[19,23,24] Although making the diagnosis through biopsy is hazardous because of location, it is important to attempt definitive diagnosis. In a 2017 phase 2 trial of patients with glioblastoma, treatment with imipridone ONC201, a selective antagonist of the G protein–coupled dopamine receptor D_2/D_3, produced a dramatic response in one patient with a H3 K27M mutation.[25-27] Based on this response, an expanded access program was initiated.[28] A 2019 report described 18 patients who received imipridone ONC201 after initial radiation therapy and at or before recurrence without leptomeningeal dissemination. Three adults among the 14 recurrent patients remained on treatment, with progression-free status at a median of 49.6 weeks (versus 14 weeks before the use of ONC201).[29] Referral to an ongoing open-label trial should be considered for patients with biopsy-proven H3 K27M mutations.

Better understanding of the molecular underpinnings of astrocytic tumors has led to some improvement in survival for another subset of patients. The *BRAF* V600E mutation has been infrequently reported in spinal cord tumors, although it is of prognostic and therapeutic significance in several types of low-grade intracranial gliomas such as pleomorphic xanthoastrocytomas, gangliogliomas, and pilocytic astrocytomas. Occasionally, this mutation is seen with higher-grade gliomas in both cord and brain.[10] Sustained responses to BRAF inhibitors have been reported in isolated instances.[8,11,30] For most symptomatic and incompletely resected primary spinal cord tumors, radiation therapy of 5040 cGy to 5400 cGy, depending on the grade of the tumor, is recommended.

KEY POINTS

- Ependymomas are the most common intramedullary primary spinal cord tumor in all age groups.
- Back, radicular, or central pain, often asymmetric and without motor involvement, is the most common symptom preceding the diagnosis of intramedullary neoplasm.
- Spinal glial tumors show no association between increasing grade of malignancy and patient age at diagnosis.
- Cellular ependymomas may be World Health Organization (WHO) grade II or grade III and arise from the intraspinal canal, usually in the cervical and thoracic regions; myxopapillary ependymoma, a WHO grade I tumor, is most frequently seen in the conus medullaris arising from the filum terminale, where they comprise 90% of tumors.
- Ependymomas are often well-demarcated isointense lesions that enhance with gadolinium.
- Gross total resection of astrocytomas is unlikely, but ependymomas, which are often encapsulated, are more amenable to total resection.
- Recognized for the first time in the 2016 WHO classification of tumors is the WHO grade IV diffuse midline glioma, H3 K27M mutant, previously called diffuse intrinsic pontine glioma.

Proton therapy is assuming a larger role in the radiation oncologic management of these tumors.[31]

Pilocytic astrocytomas of the spinal cord account for about 11% of pediatric spinal cord tumors.[2] These often are associated with neurofibromatosis type 1. Most are well circumscribed and WHO grade I. The majority have a fusion gene between the *BRAF* gene and *KIAA1549*. *BRAF* V600E also can be found. The most common location is the cervical spinal cord followed by thoracic spinal cord, but the tumor may be distributed throughout the cord. A limited role for radiation exists only in cases with definite radiographic or clinical progression.

Atypical Teratoid/Rhabdoid Tumor

Atypical teratoid/rhabdoid tumor (ATRT) is another WHO Grade I tumor that is seen primarily in children. The peak incidence is in children younger than

CASE 5-4

A 66-year-old man noted gradually progressive leg weakness over a 12-month period, during which he also experienced weight loss, fevers, and night sweats. MRI showed a single enhancing expansile abnormality in the cervical and thoracic cord (FIGURE 5-5), and brain MRI showed worsening confluent signal change in the corpus callosum and brainstem. Lumbar puncture showed protein of 169 mg/dL and a CD19-positive monoclonal B-cell population consistent with non-Hodgkin B-cell lymphoma. He was human immunodeficiency virus (HIV) negative, and Epstein-Barr virus was negative in the CSF. His CD4+ count was 293. He received rituximab, methotrexate, and temozolomide followed by hematopoietic stem cell transplantation nearly 2 years after onset of symptoms. Leg function returned, but he developed a persistent need to self-catheterize.

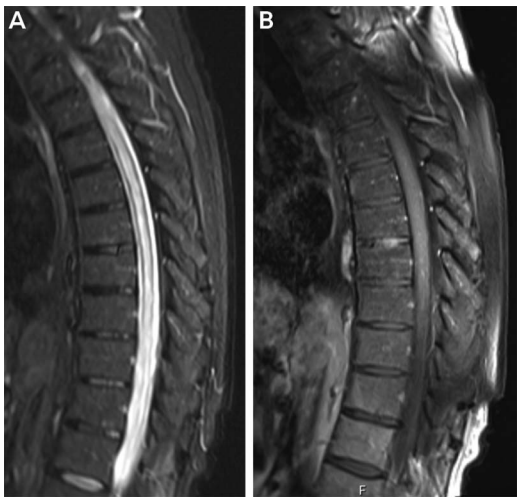

FIGURE 5-5
Imaging of the patient in CASE 5-4 with intramedullary lymphoma. *A*, Sagittal T2-weighted MRI shows an extensive area of intramedullary T2 signal abnormality. *B*, Sagittal postcontrast T1-weighted MRI shows diffuse homogeneous enhancement.

COMMENT

This patient had primary central nervous system lymphoma involving both brain and spinal cord, with the latter causing the predominant symptoms. He also had B (systemic) symptoms, although this is not typical of primary central nervous system lymphoma.

2 years of age, and ATRT is the most common CNS tumor in this age group. Localization of the primary tumor is nearly equally distributed between the supratentorial and infratentorial compartments. Data on spinal cord ATRT are limited to small numbers of patients included in series reporting on cerebral ATRT or published as isolated case reports. Recently, DNA methylation and gene-expression profiles disclosed three distinct epigenetic subgroups of ATRT (ATRT-MYC, ATRT-SHH, and ATRT-TYR), with distinguishing clinical features. In one series of 13 patients, long-term survival was achieved in some spinal cord ATRT patients with multimodality therapy (postoperative radiation and chemotherapy).[32]

Hemangioblastoma

Hemangioblastoma, a WHO grade I tumor, is rare except in von Hippel-Lindau syndrome, an autosomal dominant disorder characterized by chromosome 3p deletion; von Hippel-Lindau syndrome accounts for up to 30% of cases of hemangioblastoma.[33] Retinal hemangiomas, renal and pancreatic cysts, renal cell carcinoma, and pheochromocytoma are associated pathologies. Hemangioblastomas have a male predominance. Clinically, hemangioblastomas of the spinal cord are characterized by slowly progressive proprioceptive deficits. The location is more frequently cervical than thoracic, and neuroimaging shows a homogeneously enhancing mural nodule; cysts and a syrinx are additional common features. Hemangioblastomas are more vascular than ependymomas, and early draining veins may cause diagnostic confusion with a vascular malformation. The presence of a syrinx, uncommon with vascular malformations, is seen in up to one-half of hemangioblastomas.[3] Surgical resection may be curative. Tumor recurrence is common in patients with von Hippel-Lindau syndrome and case reports exist of tumor regression with treatment with bevacizumab, a vascular endothelial growth factor (VEGF) inhibitor.[33,34]

Primary Central Nervous System Lymphoma

Primary CNS lymphoma in the intramedullary or leptomeningeal compartments is rare. The majority of tumors arise from large B cells and comprise no more than 2% of all primary CNS lymphoma cases.[35] The tumors are often multifocal. Patients who are immunocompetent have a median age of 62 years, and patients with human immunodeficiency virus (HIV), who are organ transplant recipients, or who are otherwise immunocompromised are usually younger. Progressive myelopathy and radiculopathy are the most common presentations, and the clinical setting often raises the differential diagnosis of neuromyelitis optica spectrum disorder (NMOSD), multiple sclerosis, neurosarcoidosis, or another immune-mediated myelopathy syndrome (CASE 5-4).[35] Fludeoxyglucose positron emission tomography (FDG-PET) may show hypermetabolism in the lesion. Various systemic regimens based on rituximab, methotrexate, temozolomide, or combinations of drugs have been employed.

INTRADURAL-EXTRAMEDULLARY PRIMARY SPINAL CORD TUMORS

Intradural-extramedullary primary spinal cord tumors represent a diverse and important group of neoplasms, the treatment of which differs from intramedullary tumors in that these extramedullary neoplasms often are amenable to surgical resection. Many are associated with genetic syndromes, the identification and workup of which falls to the neurologic consultant (TABLE 5-2).

KEY POINTS

- Most H3 K27M-mutant diffuse midline gliomas occur in the thalamus and brainstem, but brainstem cases can extend to the spinal cord and show a propensity for intramedullary drop metastases and leptomeningeal dissemination.
- Pilocytic astrocytomas of the spinal cord account for about 11% of pediatric spinal cord tumors. These often are associated with neurofibromatosis type 1. Most are well circumscribed and WHO grade I.
- Hemangioblastoma, a WHO grade I tumor, is rare except in von Hippel-Lindau syndrome, an autosomal dominant disorder characterized by chromosome 3p deletion; von Hippel-Lindau syndrome accounts for up to 30% of cases of hemangioblastoma.

Meningioma

Meningiomas are the most common primary spinal cord neoplasm in adults, accounting for one-fourth of all primary spinal cord tumors. Eighty percent of patients with spinal cord meningioma are female, and 80% of the cases in females occur in the thoracic region, whereas spinal cord meningiomas in males are equally distributed between the cervical and thoracic cord.[36] The majority of spinal cord meningiomas are WHO grade I slow-growing tumors. Genetic predisposition (eg, in patients with NF2) and prior radiation are risk factors. Over 90% of spinal cord meningiomas are located in the intradural-extramedullary space, and only 6% are extradural.[36] On T1-weighted MRI, the tumors are isointense to hypointense and exhibit intense solid homogeneous enhancement postgadolinium; an accompanying dural tail may be seen. Radiosurgery is used for incomplete resection or recurrence, and protons are gaining a larger role in the treatment of spinal cord meningioma. No role for chemotherapy has been established, but intracranial meningiomas have been reported to respond to everolimus (a mammalian target of rapamycin [mTOR] inhibitor), sunitinib (a multi–tyrosine kinase inhibitor), and bevacizumab (a VEGF inhibitor). By extension of this experience, although without evidence from prospective trials, some of these agents may be considered for select patients with refractory spinal cord meningiomas (CASE 5-5).[36]

Patients with asymptomatic spinal cord meningiomas can be followed with serial MRIs. Surgery is the primary modality and can be curative. Conventional fractionated radiation therapy or proton therapy is a consideration at progression.

NERVE SHEATH TUMORS

Nerve sheath tumors include schwannomas and neurofibromas associated with genetic syndromes that also involve other neurologic abnormalities (TABLE 5-2). CASE 5-6 illustrates some of the management considerations for patients with neurofibromas.

TABLE 5-2 Spinal Cord Tumors Related to Genetic Syndromes[a]

Syndrome (genetic mutation)	Intracranial and systemic tumors	Spinal tumor
Neurofibromatosis type 1 (*NF1* gene on chromosome 17), autosomal dominant	Malignant nerve sheath tumors, optic gliomas, hamartomas	Neurofibroma, meningioma, schwannoma, ependymoma, glioma
Neurofibromatosis type 2 (*NF2* gene on chromosome 22), bilateral vestibular schwannomas	Cranial nerve schwannomas	Meningioma, schwannoma, ependymoma, glioma
Schwannomatosis (*SMARCB1* gene on chromosome 22, *LZTR1* gene on chromosome 22, somatic *NFR* mutation)	Schwannomas, meningiomas	Meningioma, schwannoma
Von Hippel-Lindau syndrome (*VHL* gene on chromosome 3)	Renal cell carcinomas, retinal angiomas, pheochromocytomas, hemangioblastomas of the central nervous system, endolymphatic sac tumors of middle ear, pancreatic tumors	Hemangioblastoma

[a] Modified with permission from Wu J, Ranjan S, Continuum (Minneap Minn).[4] © 2018 American Academy of Neurology.

Schwannoma

Schwannomas are benign nerve sheath tumors, the majority of which are WHO grade I. They represent nearly 30% of spinal root tumors, and multiple schwannomas can be found in patients with NF2 or schwannomatosis.[4] Patients with schwannomatosis typically present in their forties, usually with radicular pain and little motor involvement as the schwannomas develop primarily on spinal sensory roots. On MRI, the tumors often appear as heterogeneously enhancing paraspinous dumbbell-shaped masses. The tumors are considered cured after effective resection.

TRENDS

A word about spinal cord tumors resulting from "stem cell tourism" is in order. Berkowitz and colleagues[38] reported a case of a mixed spinal cord tumor arising

CASE 5-5

An 80-year old woman presented with a 6-month history of unsteadiness and leaning to the right. She reported that she sometimes felt that "food stays in my throat and goes down the wrong way." She worried that if she got any worse, she would not be able to be independent.

Her examination was notable for slight hyperreflexia in the lower limbs and minimal ataxia of the right arm. Her palate elevated midline, and her tongue was strong. Gag reflex was intact.

MRI showed a large, avidly enhancing extradural mass at the foramen magnum impinging on the cord (FIGURE 5-6).

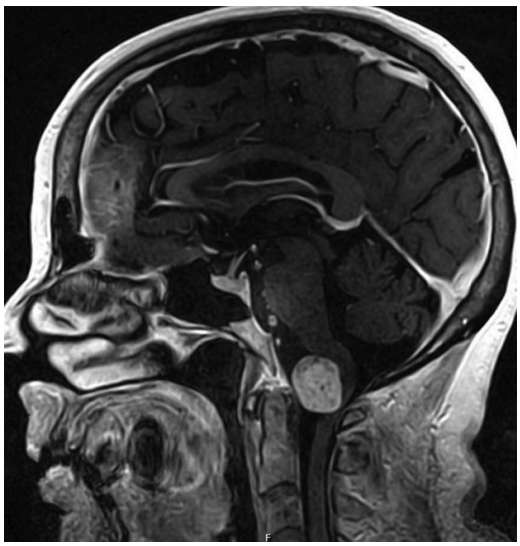

FIGURE 5-6
Imaging of the patient in CASE 5-5 with meningioma. Sagittal postcontrast T1-weighted MRI shows a large contrast-enhancing extramedullary lesion at the foramen magnum impinging on the upper cervical cord and lower brainstem.

COMMENT

This patient's MRI looked considerably worse than the patient's examination demonstrated, suggesting that the process had been slow. She had a foramen magnum meningioma, which is often heralded by lower cranial nerve findings. Her symptoms could not be improved, and some hazard existed in surgery. Systemic therapy options for unresectable meningioma are limited to investigational agents. For this older patient with stable symptoms, no systemic therapy would be recommended.

in a patient who underwent intrathecal infusions of what was represented to the patient as mesenchymal, embryonic, and fetal neural stem cells in commercial clinics in China, Argentina, and Mexico for treatment of deficits related to an ischemic stroke. When he subsequently developed back pain, paraplegia, and urinary incontinence, he had an MRI that revealed a lesion of the thoracic spinal cord. On neuropathologic review, it was shown to be a cellular highly proliferative primitive tumor with glial differentiation. This should represent a cautionary tale about such unsubstantiated treatments.

EXTRADURAL TUMORS

Numerically, extradural tumors represent the largest number of adult spinal cord neoplasms and are usually metastases from a systemic neoplasm.

CASE 5-6

A 28-year old woman with neurofibromatosis type 1 (NF1) presented with progressive neck pain, dysphagia, and evolving leg weakness. Multiple surgeries and tipifarnib systemic therapy for NF1-associated neurofibromas had failed. Cervical MRI was performed and showed enlarging neurofibromas at multiple cervical levels (FIGURE 5-7). She also had multiple neurofibromas caudal to the displayed level.

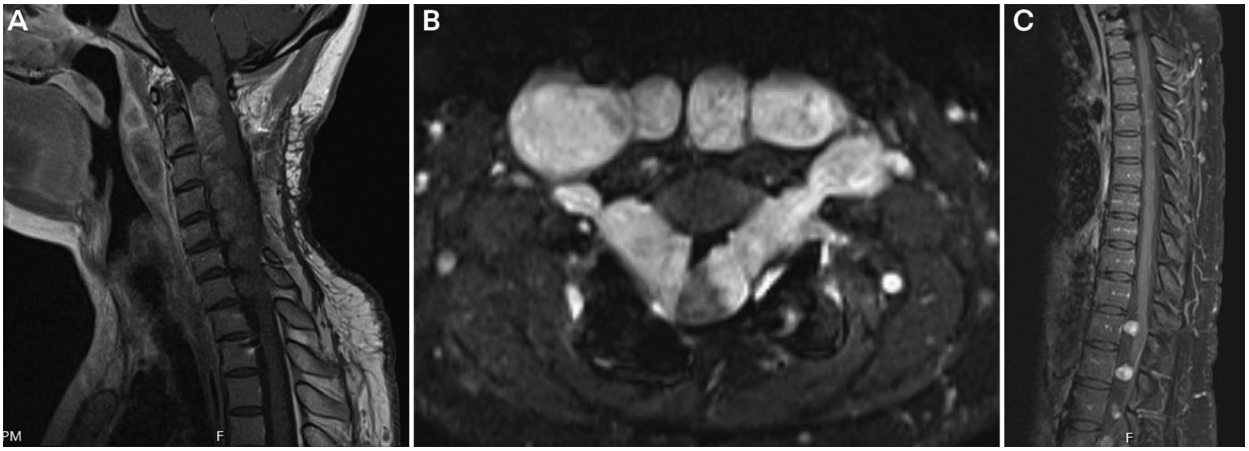

FIGURE 5-7
Imaging of the patient in CASE 5-6 with neurofibromatosis type 1. *A*, Sagittal postcontrast T1-weighted MRI shows multiple lesions throughout the extramedullary cervical spine. *B*, Axial postcontrast MRI shows the lesions more prominently. *C*, Sagittal postcontrast T1-weighted MRI of the thoracic spine shows additional lesions.

COMMENT

Surgery was not feasible for the patient in this case with multiple spinal neurofibromas. If possible, she should be offered a trial of systemic therapy. She is a candidate for selumetinib, which is a new development for the treatment of plexiform neurofibromas that has shown significant activity in large surgically hazardous tumors.[37]

Spinal Cord Metastases

Spinal intramedullary and leptomeningeal metastases are rare compared to their intracranial counterparts, but their effect on survival and quality of life is great. Tumors most frequently spreading to these compartments include some histologies for which new systemically administered targeted therapies are available (eg, lung cancer, breast cancer, melanoma). For example, second-generation (eg, ceritinib, alectinib) and third-generation(eg, brigatinib, lorlatinib) anaplastic lymphoma kinase (ALK) inhibitors have effected sustained remissions in non–small cell lung cancer.[39] Extradural metastases are most likely to occur from lung, breast, prostate, thyroid, and renal cancers, whereas leptomeningeal dissemination of solid tumors is most commonly seen from breast and lung cancers, melanoma, non-Hodgkin lymphoma, and gastrointestinal tumors.

Treatment of epidural cord compression is palliative, with the principle goals of pain relief, preservation of neurologic function, maintenance of spinal stability, and improvement in quality of life while avoiding the toxic consequences of radiation and chemotherapy. For selected patients, aggressive management can improve local control with two relatively new technologies that improve outcomes over simple laminectomy. The first, called separation surgery, involves dissecting the anterior sulcus in the spinal canal from the posterior edge of the vertebral body without affecting the vertebral body.[40-42] This causes dural decompression and restores the thecal sac circumferentially. It is coupled with the second technology, stereotactic body radiation therapy, also known as spinal stereotactic radiosurgery, as the physical separation of tumor from cord now improves spine stereotactic body radiation therapy dosimetry. High-dose radiation then ablates the remaining vertebral segment tumor, and vertebroplasty can be used to stabilize the bone. Integration of stereotactic body radiation therapy has fundamentally changed the indications and type of surgery performed for metastatic spine tumors. Protons can be used as well, but large-scale studies of outcomes are lacking. As these treatment decisions become more complex, a multidisciplinary approach involving neurologists, medical oncologists, radiation oncologists, spine surgeons, interventionalists, and pain specialists is required.[43]

Leptomeningeal Disease

Leptomeningeal carcinomatosis or neoplastic meningitis occurs when malignant cells gain access to the CNS either through hematogenous dissemination or by direct extension from parenchymal or bone metastases. This usually occurs at a time of advanced cancer dissemination. The most common cell types are breast, lung, and gastrointestinal cancers; melanoma; and non-Hodgkin lymphoma. Paresthesia, back pain, lower motor neuron weakness, and sphincter dysfunction are the most common symptoms. The cauda equina is typically involved, but the entire neuraxis should be scanned. Diagnosis is made by MRI or cytology, or both; MRI is better at visualizing solid tumors than lymphoma.[44] Epidural, brain parenchymal, and leptomeningeal involvement can coexist.

Progressive hydrocephalus may require repetitive lumbar punctures or shunting, and acetazolamide can be used to control intracranial pressure. Primary brain tumors can also spread to the spinal canal, usually late in the course, in which case they can have both intramedullary and leptomeningeal involvement (TABLE 5-1).

Intramedullary spinal cord metastases are much less common than epidural metastatic disease. More than half are from lung cancer, followed by breast

KEY POINTS

- Meningiomas are the most common primary spinal cord neoplasm in adults, accounting for one-fourth of all primary spinal cord tumors. The majority of meningiomas are WHO grade I slow-growing tumors. Genetic predisposition (neurofibromatosis type 2) and prior radiation are risk factors.
- Radiosurgery is used for incomplete resection or recurrence of spinal meningioma, and protons are gaining a larger role in the treatment of spinal meningioma. No role for chemotherapy has been established, but intracranial meningiomas have been reported to respond to everolimus, sunitinib, and bevacizumab.
- Schwannomas are benign nerve sheath tumors, the majority of which are WHO grade I. They represent nearly 30% of spinal root tumors, and multiple schwannomas can be found in patients with neurofibromatosis type 2 or schwannomatosis.
- Extradural metastases are most likely to occur from lung, breast, prostate, thyroid, and renal cancers, whereas leptomeningeal dissemination of solid tumors is most commonly seen from breast and lung cancers, melanoma, non–Hodgkin lymphoma, and gastrointestinal tumors.

cancer and renal cell cancer, melanoma, and lymphoma. The cervical cord is the most frequently involved region. Hematogenous spread or carcinomatous meningitis can occur concurrently, possibly by direct extension through nerve roots. Two radiographic signs of intramedullary spinal cord metastases may be seen: rim and flame. A thin rim of peripheral enhancement and a flame-shaped appearance in the region of enhancement at the superior and inferior margins should suggest a non-CNS metastatic intramedullary tumor rather than one of primary spinal cord origin.[45,46] The flame-shaped ovoid lesion is hypointense on T2-weighted sequences with a hyperintense rim with enhancement (FIGURE 5-8).

RADIATION-RELATED MYELOPATHY

Despite careful attention to dosimetry, the risk of permanent myelopathy from radiation remains possible and frequently is devastating. Early symptoms of radiation toxicity include paresthesia with the Lhermitte sign occurring 2 to 4 months after treatment, which may respond to a brief corticosteroid course. Less readily reversible signs and symptoms, such as paresthesia, pain, sphincter dysfunction, and weakness, can develop later. MRI shows hyperintensity on T2-weighted sequences with or without enhancement. At later stages, spinal cord atrophy predominates. Many treatment interventions have been attempted for these disabling symptoms, including high-dose corticosteroids, hyperbaric oxygen, anticoagulation, and bevacizumab (CASE 5-7).[47] Another complication of radiation therapy, cavernous malformations (which have been well described intracranially) can also be found in the spinal cord and may cause sudden paraplegia due to hemorrhage.

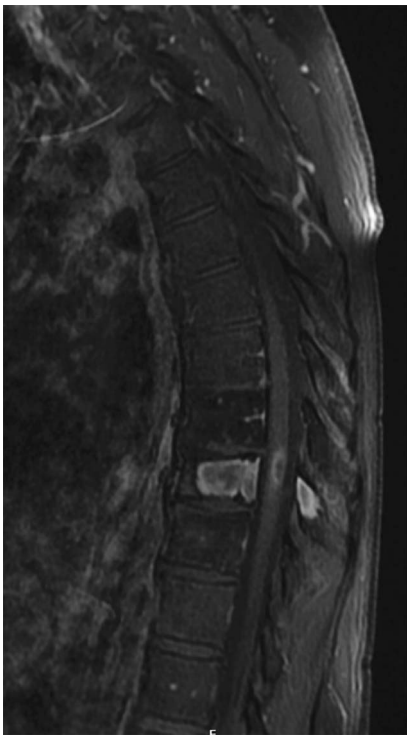

FIGURE 5-8
Intramedullary metastasis. Sagittal postcontrast T1-weighted MRI shows a flame-shaped enhancing lesion due to intramedullary metastasis from lung cancer. The associated vertebral body change is radiation related.

CHEMOTHERAPY-RELATED MYELOPATHY

Both intrathecally and systemically administered cytotoxic agents can infrequently result in a longitudinally devastating myelopathy. The most frequently implicated agents are methotrexate and cytarabine. The onset is often rapid; sometimes after a first dose, recovery is possible, although it is often incomplete (CASE 5-8).

EXTRADURAL PRIMARY SPINAL CORD TUMORS

Rarely, schwannomas and meningiomas may be predominantly in the extradural compartment. Meningiomas in this location are often en plaque. This pattern can mimic extradural metastatic tumors (such as those of breast, lung, or prostate origin) or primary dural lymphoma, a

low-grade B-cell marginal zone lymphoma. Myxopapillary ependymomas also can have an extradural component.

NON-NEOPLASTIC SPINAL CORD NEOPLASM MIMICS

Spinal cord enlargement seen on imaging with or without contrast enhancement can have diverse causes, and it often falls to the neurologic consultant to generate an appropriate differential diagnosis. Although cord enlargement from the above-discussed intramedullary tumors is always on the diagnostic list, the physician must also consider the consequences of radiation and adverse effects of cancer therapies. The differential of cord pathology is broad and includes many non-neoplastic entities, many of which can be excluded based on the timing of symptom onset and demographic features. However, it is always prudent to at least consider various non-neoplastic disease categories (FIGURE 5-1).

This section briefly covers some of the many processes that can mimic spinal cord neoplasm. Since cord biopsy is often a hazardous undertaking, recognition of processes that do not warrant invasive procedures is a valuable contribution to patient care. Certain situations should raise concern for spinal cord neoplasia.

Enhancement can persist for months to years after spinal cord compression, such as from cervical spondylosis, often taking the shape of pancake enhancement.

Acute demyelinating disease, including aquaporin-4-IgG–seropositive NMOSD and myelin oligodendrocyte glycoprotein (MOG) antibody–associated disorder, can produce longitudinally extensive, sometimes enhancing spinal cord abnormalities. In the context of neoplasm-associated myelopathic processes, demographic features suggestive of paraneoplastic myelopathies, including those with an NMOSD phenotype, should be recognized.[48,49] In one series, five of 156 patients had paraneoplastic NMOSD and these authors included 12 previously reported patients with paraneoplastic NMOSD in their series. Adenocarcinoma of lung and breast accounted for five cases each. Compared with patients with non-paraneoplastic NMOSD, patients with paraneoplastic NMOSD were older at symptom onset (median age 55 compared to 40) and more frequently male. Thus, older patients presenting with NMOSD, particularly if male, should be investigated for neoplasia.[49] The development of longitudinally extensive transverse myelitis in an older patient should prompt investigation for an occult tumor.

NMOSD-related myelopathy has also emerged recently in the setting of immune checkpoint inhibitor use. The anti–programmed cell death protein 1 (PD1) antibody nivolumab and others are now standard treatment for non–small cell lung cancer and melanoma. Such patients may harbor paraneoplastic antibodies, and aquaporin-4-IgG–seropositive NMOSD has emerged after just one or two cycles of PD1 inhibitor chemotherapy.[50] Other paraneoplastic antibody–associated spinal cord syndromes have also been reported to emerge in the setting of PD1 therapy.[51] Reported antibodies include antineuronal nuclear antibody type 1 (ANNA-1/anti-Hu), collapsin response mediator protein-5 (CRMP-5)/anti-CV2, and aquaporin-4 IgG. Immune checkpoint inhibitor treatment may correlate with ANNA-1/anti-Hu levels.[52] Kunchok and colleagues[53] reported CRMP-5 IgG–associated paraneoplastic myelopathy with the programmed death ligand 1 (PD-L1) inhibitor atezolizumab. These immune checkpoint inhibitor toxicities differ from their non–immune checkpoint

KEY POINTS

- Treatment of epidural cord compression is palliative, with the principle goals of pain relief, preservation of neurologic function, maintenance of spinal stability, and improvement in quality of life while avoiding the toxic consequences of radiation and chemotherapy.
- A thin rim of peripheral enhancement and a flame-shaped appearance in the region of enhancement at the superior and inferior margins should suggest a non–central nervous system metastatic intramedullary tumor rather than one of primary spinal cord origin.
- Compared with patients with nonparaneoplastic neuromyelitis optica spectrum disorder (NMOSD), patients with paraneoplastic NMOSD are older at symptom onset and more frequently male. Thus, older patients presenting with NMOSD, particularly if male, should be investigated for neoplasia.
- In the context of immune checkpoint inhibitor treatment, paraneoplastic antibody–associated spinal cord syndromes have emerged. Reported antibodies include anti-Hu/ANNA-1, CRMP-5/anti-CV2, and aquaporin-4 IgG.

CASE 5-7

A 62-year-old woman with kappa light chain multiple myeloma developed back pain and was treated with local radiation to lytic lesions at T5 and T7 in 10 daily fractions to 3000 cGy. She received multiple other chemotherapy regimens but had progressive plasmacytomas in many bony sites. Nine months after the radiation, she developed progressive back pain and left leg weakness along with new lytic fractures at T12, L2 through L4, and S1 that were treated with vertebroplasty. Her gait was further impaired by significant peripheral neuropathy from bortezomib and pomalidomide as well as proximal weakness from multiple extended corticosteroid courses. MRI showed enhancement of the spinal cord from T7 through T10 without mass lesion (FIGURE 5-9) and was felt to be most consistent with radiation myelitis. She also had chronic compression fractures at multiple levels.

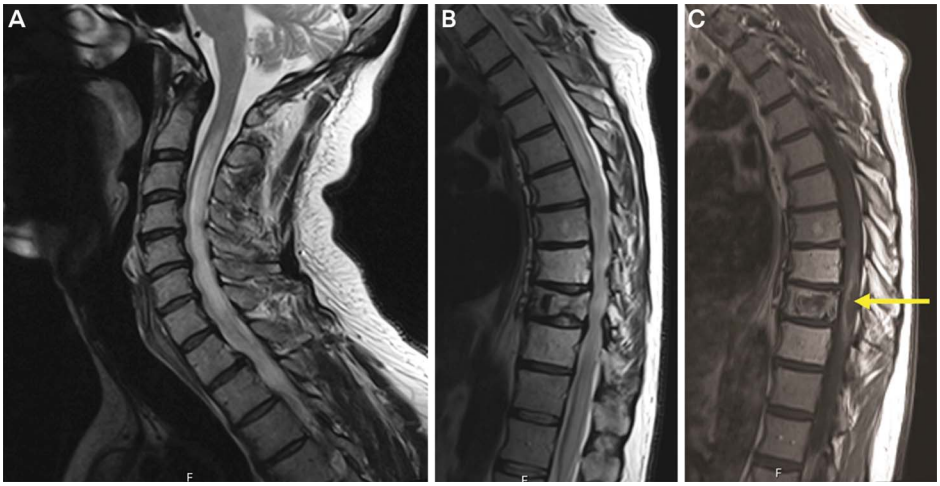

FIGURE 5-9
Imaging of the patient in CASE 5-7 with myeloma and multiple bone lesions presenting with rapidly progressive leg weakness. The T2 signal abnormality extends beyond the radiation fields on sagittal T2-weighted cervical (*A*) and thoracic (*B*) spine images, but the area receiving the largest dose of radiation shows an expansile enhancing lesion on sagittal postcontrast T1-weighted image (*C*, *arrow*).

COMMENT

This case illustrates the spread of bone tumor to the spinal canal, causing weakness and pain and complicated by radiation myelitis, chemotherapy-associated peripheral neuropathy, and corticosteroid-related myopathy. Multiple comorbidities must be considered when a patient has been treated with radiation and neurotoxic chemotherapy but also has evidence of advancing disease. Vertebroplasty can be an effective palliative maneuver.

inhibitor–associated counterparts in that they appear after therapy has begun and in close association with use of immune checkpoint inhibitors. The high doses of steroids necessary to control these syndromes may reduce the antineoplastic efficacy of immune checkpoint inhibitors. With the ever-widening indications for these drugs, other antibody-mediated syndromes are likely to emerge.

Neurosarcoidosis can produce both leptomeningeal and intramedullary spinal cord pathology that can mimic neoplastic processes radiographically and in the associated CSF formula of lymphocytic meningitis, CSF hypoglycorrhachia, and

CASE 5-8

A 47-year old woman had stage IV breast cancer, diagnosed when she was found to have thoracic compression fractures in the course of a back-pain evaluation. She was treated systemically with denosumab, letrozole, and palbociclib. Initial CSF cytology was positive, and she received seven intrathecal methotrexate treatments. She continued to have increasing back pain, which was treated with spinal radiation and fusion. Nine months later, she had progressive leg spasms and progressive right footdrop as well as urinary retention and within 48 hours developed paraplegia. MRI showed extensive posterior fossa and spinal cord leptomeningeal enhancement as well as developing hydrocephalus. Repeat CSF cytology was again positive.

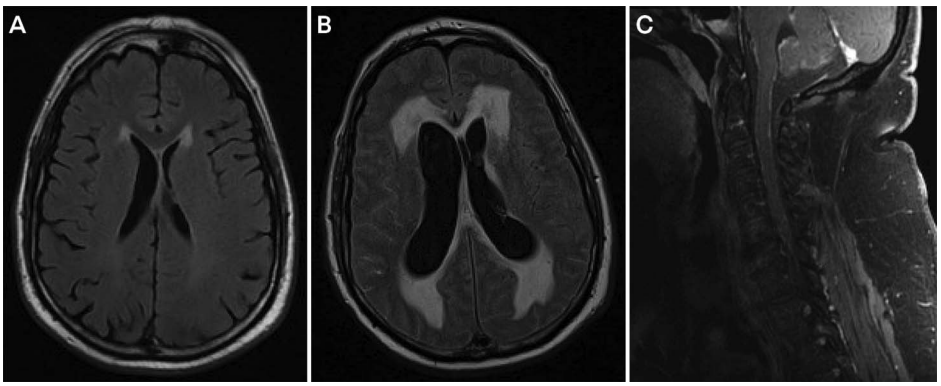

FIGURE 5-10
Imaging of the patient in CASE 5-8. Axial fluid-attenuated inversion recovery (FLAIR) MRI (*A*) and axial FLAIR MRI 1 month later (*B*) reflect a rapid rise in intracranial pressure and transependymal flow of CSF, with impaired CSF resorption and development of hydrocephalus. The posterior fossa and cervical spine leptomeningeal enhancement are visible on sagittal postcontrast T1-weighted MRI (*C*), consistent with carcinomatous meningitis.

COMMENT

This case illustrates multiple complications of advanced breast cancer. MRI showed both the original bone metastases and holocord involvement, which could be from either carcinomatous meningitis or intrathecal methotrexate, the latter being less likely because of the interval from treatment (FIGURE 5-10).

elevated protein. Longitudinally extensive and sometimes enhancing lesions in various compartments can be caused by infection. Some of the most frequently implicated offending pathogens are *Mycobacterium tuberculosis*, *Toxoplasma gondii*, *Schistosoma*, cytomegalovirus (cauda equina involvement), and West Nile virus.

Numerous toxic/metabolic states can produce cord swelling seen on imaging with or without gadolinium enhancement.

Although uncommon, posterior reversible encephalopathy syndrome (PRES) can, at times, involve the spinal cord and may be longitudinally extensive, sometimes in association with aquaporin-4 IgG.[54,55]

Tarlov cysts, large arachnoid cystic lesions usually in the lumbosacral area, are often felt to be incidental findings; however, at times they can produce lumbar and sacral radicular symptoms (including incontinence) and thus should be evaluated for possible surgical intervention.[56]

CONCLUSION

Early recognition of signs and symptoms of spinal cord tumors leads to expeditious neuroimaging that can define the compartment involved and focus the differential diagnosis with excellent accuracy among different histologies. Pain is the predominant symptom of spinal cord tumors and may not be alleviated with surgical resection. Surgery is the first-line treatment of symptomatic primary spinal cord tumors and is more effective for control of ependymomas than for astrocytomas. The histologic grade of the tumor and extent of resection are important determinants of outcome. Newer techniques, including separation surgery and stereotactic radiosurgery, offer better chances of quality survival in patients with spinal cord metastasis from systemic malignancies. The H3 K27M mutant diffuse midline glioma has been recently recognized, and some targeted therapies may have efficacy. Experience with chemotherapy for recurrent spinal cord tumors is limited, although successes with intracranial counterparts of similar histology may suggest potentially helpful agents.

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