

Adult Primary Intradural Spinal Cord Tumors: A Review

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Abstract Primary spinal cord tumors constitute 2% to 4% of all central nervous system neoplasms and are characterized based on their location as intramedullary, intradural extramedullary, and extradural. A contemporary literature review of primary intradural spinal cord tumors was performed. Among intramedullary tumors, ependymomas are more common and often can be surgically resected. However, astrocytomas infiltrate the spinal cord and complete resection is rare. Intradural extramedullary tumors include schwannomas, neurofibromas, and meningiomas and are usually amenable to surgical resection. Radiotherapy is reserved for malignant variants and recurrent gliomas, whereas chemotherapy is administered for recurrent primary spinal cord tumors without surgical or radiotherapy options. Early recognition of the signs and symptoms related to primary spinal cord tumors facilitates timely discovery, treatment, potentially minimizes neurologic morbidity, and may improve outcome. Treatment consists of surgical resection, and predictors of outcome include preoperative functional status, histologic grade of tumor, and extent of surgical resection.

Keywords Primary spinal cord tumors · Intradural intramedullary · Intradural extramedullary · Extradural tumors · Gliomas · Low-grade glioma · High-grade glioma · Glioblastoma · Ependymoma · Hemangioblastoma · Spinal cord parenchymal metastasis · Meningioma · Peripheral nerve sheath tumor · Neurofibroma · Schwannoma ·

Extradural metastasis · Resective surgery · Biopsy · Radiotherapy · Chemotherapy · Alkylator-based chemotherapy · Temozolomide · Platinoids · Etoposide · Bevacizumab

Introduction

Primary tumors of the spinal cord are ten to 15 times less common than primary intracranial tumors and overall represent 2% to 4% of all primary tumors of the central nervous system (CNS). There are estimated 850 to 1,700 new adult cases of primary spinal cord tumors diagnosed each year in the United States [1•]. The histology of spinal cord tumors is similar to their intracranial counterparts; however, unlike primary intracranial tumors, spinal cord tumors show no association between increasing grade of malignancy and age at diagnosis. The majority of primary spinal cord tumors are classified as low grade (grades I and II) according to the World Health Organization (WHO) pathology classification. In a recent study of 70 patients with intramedullary spinal cord tumors (IMSCTs), the median age at presentation was 41 years with a range of 18 to 47 years [1•].

Primary spinal cord tumors are divided into three categories based upon anatomic location: intramedullary, intradural extramedullary, and extradural [2]. Extradural tumors primarily consist of systemic cancer metastases, result in epidural spinal cord compression, and are not discussed further in this review of primary intradural spinal cord tumors. IMSCTs constitute 8% to 10% of all primary spinal cord tumors with the majority comprised of gliomas (80% to 90%), of which 60% to 70% are ependymomas and 30% to 40% are astrocytomas [3]. Overall, 15% of all primary intradural spinal cord tumors are ependymal in origin and include one of three histopathologic subtypes: ependymoma, subependymoma, and myxopapillary ependymoma. The third most common IMSCT is hemangioblastoma, representing approximately 3% to 8% of all

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IMSCTs, of which 15% to 25% are associated with von Hippel-Lindau (VHL) syndrome [4]. Intramedullary metastases originating from a systemic cancer can occur throughout the length of the spinal cord and are exceedingly rare. The incidence of intramedullary spinal cord metastasis ranges from 0.1% to 2% of all spinal cord tumors [5]. Primary spinal cord lymphomas are extremely rare and relative to intracranial primary CNS lymphoma. In contrast to the histologic variety of IMSCT, intradural extramedullary spinal cord tumors are predominantly either meningiomas (50%) or peripheral nerve sheath tumors (50%) [1, 2, 6].

The clinical presentation of primary spinal cord tumors is determined in part by the location of the tumor, and in nearly all clinical instances pain is the predominant presenting symptom (Table 1). In a recent series of IMSCTs, pain was the most common presenting symptom (72%) and may manifest as back pain (27%), radicular pain (25%), or central pain (20%). Motor disturbance was the next most common presenting symptom (55%) followed by sensory loss (39%; dermatomal, saddle, or segmental level). Sphincter disturbance was the least common presenting symptom seen in only 15% of all patients [6]. Diagnosis of a primary spinal cord tumor requires a high index of suspicion based upon clinical signs and symptoms as well as spine-directed MRI (Fig. 1).

Intramedullary Tumors

Astrocytomas and ependymomas as mentioned above represent the most common intramedullary neoplasms. It is estimated that the intracranial to spinal ratios for astrocytomas and ependymomas are 10:1 and 3:1 to 20:1 (depending on the histologic variant), respectively [3]. The clinical presentation of an intramedullary tumor is variable, but pain and a mixed sensorimotor tract disturbance (segmental sensory level, upper motor neuron signs) are

Table 1 SEER data: survival outcome of spinal cord gliomas

Tumor histology	5-year overall survival,%
Glioma	
Grade 1	82
Grade 2	70
Grade 3	28
Grade 4	14
Ependymoma	
Grade 1	100
Grade 2	98
Grade 3	64

Data from Milano et al. [50••]

SEER surveillance, epidemiology, and end results

usually present. A syringomyelic syndrome, characterized by disassociation between pain/temperature sensation and proprioception, as well as motor neuron dysfunction and myelopathy may occur as well.

MRI of the spine is the diagnostic modality of choice; however, patients unable to undergo MRI may require CT myelography (Fig. 1). An intramedullary tumor is radiographically recognized by focal, and sometimes holocord, spinal cord expansion with associated T2-weighted (T2W) and fluid-attenuated inversion recovery (FLAIR) image hyperintensity, T1-weighted (T1W) hypo- or isointensity, variable contrast enhancement, and occasional tumor-associated syrinx [7•].

Ependymoma

Ependymomas are the most frequent IMSCTs in adults [1•]. Histologically, there are two distinct pathologic types: cellular (WHO grades 2 and 3) and myxopapillary (WHO grade 1). Cellular (classic) ependymoma arises from the intraspinal canal of the cervical and thoracic cord. Myxopapillary ependymomas arise from the filum terminale and occur almost exclusively at the conus medullaris. The treatment and prognosis for spinal cord ependymomas is often excellent as these tumors may be resected completely and in such instances manifest a low recurrence risk (Table 2) [6, 8, 9].

Ependymomas by MRI appear as a focal enlargement of the cord and hyperintense on T2W and FLAIR images and hypo- or isointense to normal spinal cord on T1W images with heterogeneous contrast enhancement [7•]. These tumors may also be associated with cystic changes, hemosiderin suggestive of previous hemorrhage, and syrinx.

Ependymomas most often are low grade with a benign indolent course, although malignant histologic subtypes (anaplastic ependymoma; WHO grade 3) rarely occur. Surgery is the most effective treatment with complete surgical resection yielding reported local control rates of 90% to 100%, although gross total resection is not achieved in the majority of patients [9, 10••]. Intraoperative monitoring of motor and somatosensory-evoked potentials is often used to assist in achieving a more safe and complete resection [11]. Involved-field external beam radiotherapy at a dose of 45 to 54 Gy is indicated for partially resected WHO grade 2 ependymomas or malignant WHO grade 3 tumors [12, 13]. Overall, spinal cord ependymomas are associated with prolonged progression-free and overall survival with a median 82 and 180 months, respectively [14].

Data are very limited regarding chemotherapy for adults with spinal cord ependymomas (Fig. 1). Chemotherapy for ependymomas outside of a clinical trial is therefore reserved for patients in whom surgery or radiotherapy is not an option or has been previously administered. A prospective phase 2 study of ten consecutive patients with recurrent ependymoma reported a partial response in two

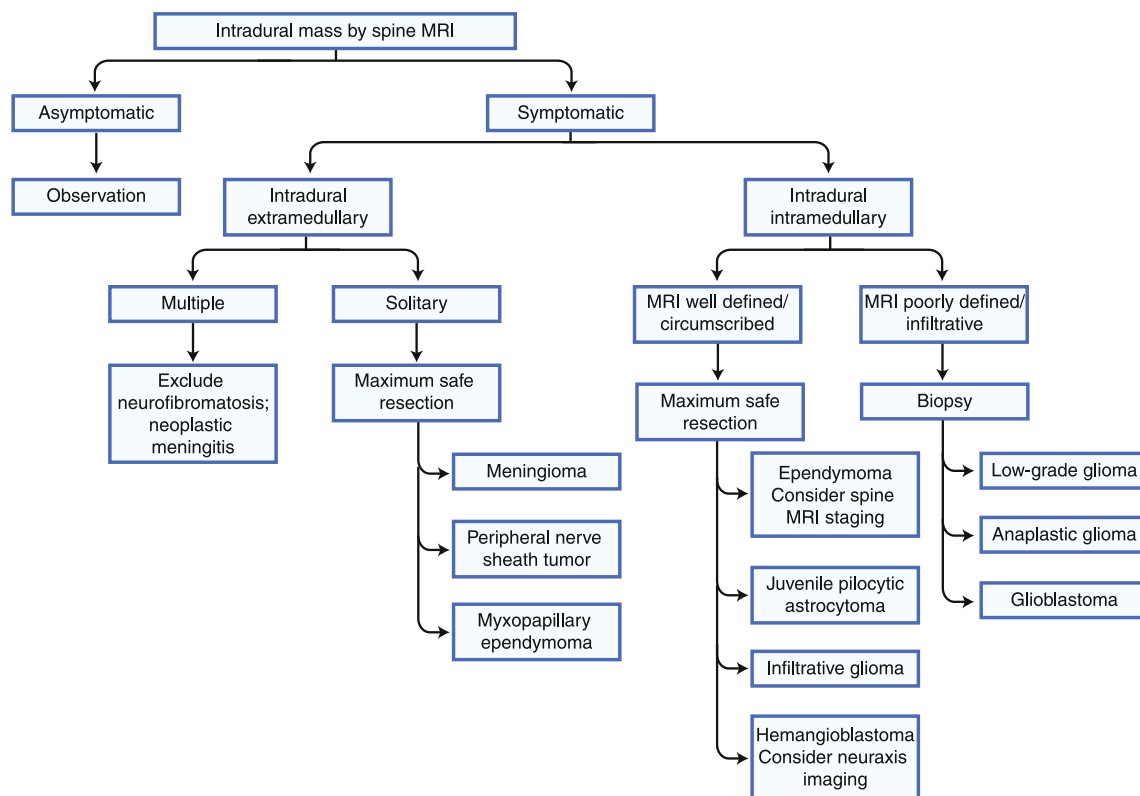


Fig. 1 An algorithm for primary spinal cord tumors

and stable disease in five after one cycle of etoposide. The median stable disease duration and overall survival were 15 and 17.5 months, respectively [15]. Either etoposide, a topoisomerase 2 inhibitor, or platinum salts are generally considered the agents most active for intracranial ependymomas and, by extrapolation, for spinal cord ependymomas. A recent study of 25 adult patients with recurrent spinal cord WHO grade 2 ependymoma assessed response to temozolomide (TMZ; a common DNA-damaging agent used to treat all grades of intracranial gliomas) in patients previously treated with surgery, radiotherapy, and platinum-based chemotherapy [16•]. Time to tumor progression ranged from 1 to 7 months (median, 2 months), survival ranged from 2 to 8 months (median, 3 months), and progression-free survival at 6 and 12 months was 2% and 0%, respectively. TMZ used in this dose and schedule (150–200 mg/m²/d for 5 days every 4 weeks) appeared to have little activity in recurrent spinal cord ependymoma following failure of platinum-based chemotherapy. A small retrospective study recently suggested recurrent refractory intracranial ependymoma respond to the angiogenic inhibitor bevacizumab, and perhaps by extension similar activity may be seen in spinal ependymomas [17•]. Another recent prospective pediatric trial of children with recurrent brain tumors suggested anti-ependymoma activity with the epidermal growth factor receptor type 2 antagonists lapatinib [18••].

Astrocytoma

Approximately 40% of IMSCTs are astrocytomas. The majority (75%) are low-grade (WHO grade 2) fibrillary astrocytomas with 5-year survivorship exceeding 70% (Table 2) [6, 19]. Histology is the most important prognostic variable [20•, 21]. High-grade spinal cord gliomas (WHO grades 3 and 4; 25%) are less common and associated with a poor survival. Regardless of WHO grade, spinal cord astrocytomas are infiltrative and associated with poorly characterized boundaries and consequently are typically biopsied only. However, a recent case report of corpectomy has yielded survival of greater than 15 months in one patient [22•].

Astrocytomas appear on MRI as fusiform expansion of the cord and occasionally a cystic component [7•]. Associated edema or syrinx (seen in 40%) may be present. The tumor is hypo- to isointense on T1W images, hyperintense on T2W and FLAIR images, with variable contrast enhancement. In general, the distinction between astrocytomas and ependymomas by magnetic resonance (MR) is not possible.

Initial treatment consists of maximal safe surgical resection or biopsy followed by observation or external beam radiotherapy (Fig. 1). Because spinal cord gliomas are infiltrative, gross total resection is rarely accomplished (in ~12% of WHO grade 2 and 0% of grades 3 or 4

Table 2 Primary spinal cord tumors

Tumor	Incidence	Location	Radiology MR	Treatment	Prognosis
Intramedullary					
Ependymoma	Most common	Cervical >thoracic	Expansile T2-hyper Contrast enhancing Cyst and/or syrinx	Surgery; RT/CT if unresectable	Good
Myxopapillary	Rare	Filum/conus Extramedullary	Expansile T2-hyper Contrast enhancing Hemosiderin	Surgery	Excellent
Subependymoma	Rare	Cervical >thoracic	T2-hyper Variable enhancing	Biopsy/observe/resection	Excellent
Astrocytoma	2nd most common	Cervical >thoracic	Expansile T2-hyper Variable enhancing	Biopsy/resection; RT/CT	Fair
Pilocytic astrocytoma	Rare	Cervical >thoracic	T2-hyper Variable enhancing	Biopsy/resection	Good
Anaplastic/glioblastoma	Rare	Cervical >thoracic	T2-hyper Contrast enhancing	Biopsy/observe; RT/CT?	Poor
Hemangioblastoma	Rare except in VHL	Cervical >thoracic	Mural nodule Cyst and syrinx common	Resection	Excellent
Ganglioglioma	Rare	Cervical >thoracic	T1-hypo T2-hyper Variable enhancing	Resection	Good
Lymphoma	Rare	Primary vs metastasis	T2-hyper Variable enhancing	Intrathecal CT	Poor
Melanoma	Rare	Primary vs metastasis		Biopsy/resection/CT	Poor
Extramedullary					
Meningioma	50%	Cervical > thoracic > lumbar women > men	T1-hypo T2-hyper Contrast enhancing	Resection	Good
Schwannoma	25%	NF	Solid T1-iso T2-hyper Contrast enhancing	Resection	Excellent
Neurofibroma	25%	NF	Solid or plexiform T1-iso T2-hyper Contrast enhancing	Resection	Excellent
MPNST	Rare	NF	Rapid growth on serial MR Contrast enhancing	Resection/RT/CT	Poor

CT chemotherapy, MPNST malignant peripheral nerve sheath tumor, MR magnetic resonance, NF neurofibromatosis, RT radiotherapy, T2-hyper T2-weighted hyperintensity, T1-hypo T1-weighted hypointensity, T1-iso T1-weighted isointense, VHL von Hippel Lindau syndrome

astrocytomas) [6]. The optimal extent of surgical resection and need for postoperative radiotherapy are controversial. Tumor histology, extent of resection, and functional status at time of presentation appear to be the primary determinants of outcome [6]. Nonetheless, radiotherapy is indicated for patients with high-grade histology, biopsied-only tumors, and those with progressive disease (Fig. 1). A retrospective study of 136 consecutive patients

found that postoperative radiotherapy improved survival for patients with infiltrative astrocytomas (WHO grades 2–4), but not those with pilocytic tumors (WHO grade 1) [20]. As such, patients with pilocytic astrocytomas should receive radiotherapy only in instances with definite clinical or radiographic progression. Although rare in adults, the majority of spinal cord pilocytic astrocytomas can be completely resected (up to 80%) [6]. In a

retrospective study of 57 patients with spinal cord astrocytoma, postoperative radiotherapy prolonged progression-free survival but not overall survival in those with low-grade astrocytomas [23].

It is recommended that low-grade spinal cord astrocytomas be treated up to a total tumor dose of 5,040 cGy in 180-cGy fractions over 28 treatment days and high-grade astrocytomas treated to a total dose of 5,400 cGy in 180-cGy fractions [12]. Involved fields (one vertebral body level above and below the tumor mass) are used because survival is short and local failure is the dominant pattern as in intracranial astrocytomas.

At recurrence, radiotherapy is the preferred treatment if not already utilized (Fig. 1). Re-irradiation may be used particularly if normal tissue-sparing methods can be employed (Cyberknife [Accuray, Sunnyvale, CA], heavy particle beam, or tomo-radiotherapy). Chemotherapy is reserved for patients with progression of disease following surgery and radiotherapy with no other treatment options. Literature regarding chemotherapy for recurrent astrocytomas is extremely limited. In one series of 22 adults with low-grade spinal cord gliomas treated with TMZ, 150 to 200 mg/m², per day for 5 consecutive days every 4 weeks, four had partial response and 12 had stable disease after two cycles [24•]. Median time to progression and overall survival were 14.5 and 23 months, respectively. In a retrospective review of eight patients with high-grade glioma treated with various TMZ schedules (TMZ: 150–200 mg/m²/d for 5/28 days; 150 mg/m² 7 days on/7 days off schedule; and 50 mg/m²/d), three patients experienced radiographic improvement, two had stable disease, two had progressive disease, and one discontinued treatment for myelosuppression after two cycles [25•]. However, this trial did not comment on duration of response. Other agents that have been used in children include lomustine, carboplatin, vincristine (PCV [procarbazine, lomustine, vincristine] chemotherapy), and 8-in-1 chemotherapy. Based on a limited literature, none of these chemotherapy agents appear to be highly effective, but may occasionally benefit individual patients. The utility of bevacizumab for recurrent spinal cord glioblastoma was recently reported in a small cohort of adults ($n=6$) all having failed prior therapy with surgery and TMZ-based chemoradiotherapy and post-radiotherapy chemotherapy [26•]. Similar to the experience with bevacizumab in patients with recurrent intracranial supratentorial glioblastoma, a palliative benefit was seen with a median survival of 9 months. There clearly is an unmet need for larger studies of chemotherapy or targeted therapy for recurrent spinal cord astrocytomas. Most often in patients with high-grade gliomas of the spinal cord, adjuvant alkylator-based chemotherapy (ie, TMZ) is used based on data in treating similar tumors of the intracranial compartment.

Hemangioblastoma

Hemangioblastomas, the third most common IMSCT, are rare vascular tumors that occur as a solitary tumor or as part of VHL syndrome [4]. Approximately 10% to 30% of patients with hemangioblastoma of the spinal cord have VHL syndrome, an autosomal-dominant disorder caused by a deletion on chromosome 3p. Other tumors associated with VHL include retinal hemangiomas, renal and pancreatic cysts, pheochromocytomas, and renal cell carcinomas. Whether solitary or associated with VHL, the clinical and histopathologic characteristics of hemangioblastomas are identical. There is a male predominance and presentation is usually in the fourth decade.

The majority of hemangioblastomas arise from the dorsal portion of the spinal cord. As such, presenting symptoms are usually sensory, especially slowly progressive proprioception deficits. There may also be other long tract signs and radicular symptoms. Rarely, patients present with subarachnoid or intramedullary hemorrhage.

On MR, hemangioblastoma appear as a homogeneously enhancing hypervascular nodule with associated cyst or syrinx and peritumoral edema [27]. Spinal angiography demonstrates enlarged feeding arteries, intense nodular stains, and early draining veins [7•]. Hemangioblastoma can be differentiated from ependymoma by the vascular abnormalities on MRI and the presence of tumor hypervascularity. Hemangioblastoma is differentiated from a spinal cord vascular malformation by an associated syrinx and tumor enhancement on MR.

Surgical resection is the primary treatment because there are often well-defined margins allowing for a complete resection and thus the potential to achieve long-term local cure. Excessive intraoperative bleeding, obscuring the operative field, is the limiting factor for subtotal resection [27]. In contrast to posterior fossa hemangioblastomas, preoperative embolization is usually not performed as complications have been reported [28]. Serial MRI should be obtained because de novo lesions can appear in patients with VHL. There is a limited role for radiotherapy and experience with chemotherapy is almost nonexistent. Stereotactic radiosurgery is an option for patients with recurrent or unresectable tumors [29]. In small case series of surgery and radiation, refractory spinal cord hemangioblastoma, angiogenic inhibitors such as SU5416 (semaxanib), and bevacizumab have demonstrated clinical and radiographic response [30, 31•].

Ganglioglioma

Ganglioglioma is a glial-neuronal tumor that usually occurs in the brain, but may arise from the intramedullary spinal cord. The tumor is typically slow growing, but rarely may have an aggressive course. Adult cases of spinal cord ganglioglioma are rare and paraparesis and radicular pain are the most common presenting symptoms [8].

On T1W MR the tumor is hypointense or has mixed signal characteristics, homogenous or heterogeneous hyperintensity on T2W/FLAIR images, with variable contrast enhancement. Tumor cysts, scoliosis, and bone erosion/scalloping may be present [32].

Maximal surgical resection is the optimal treatment for spinal cord gangliogliomas. Complete or near complete resection is associated with excellent long-term survival and minimal morbidity [8, 32]. Postoperative radiotherapy is not recommended, even in patients who undergo a subtotal resection. Despite the apparent benign nature, the progression-free survival rate in the largest case series (56 pediatric patients) was only 67% [8]. Rarely, there is transformation to a higher grade tumor (ie, anaplastic ganglioglioma). One author suggested that adjuvant radiotherapy may increase the risk of malignant transformation based on experience with benign supratentorial gangliogliomas [33]. At recurrence, reoperation should be considered, but radiotherapy is also an option. There are no data regarding treatment with chemotherapy in the recurrent setting aside from extrapolation from recurrent intracranial gangliogliomas that may respond to alkylator-based chemotherapy (ie, TMZ or PCV).

Lymphoma

Primary CNS lymphoma rarely (<1% of all CNS lymphomas) presents as an isolated spinal cord intramedullary tumor [34•]. On MR, lymphoma appears as single or multifocal, ill-defined T2W/FLAIR hyperintense lesions with homogenous contrast enhancement on T1W images. Because of high cell tumor density, diffusion-weighted MRI often demonstrates restriction and correspondingly hyperintensity. Following histologic diagnosis, a careful search for other sites of CNS disease (including slit lamp eye examination, brain MRI, total spine MRI, and cerebrospinal fluid [CSF] flow cytometry/cytology) should be performed. Because CNS lymphoma is a diffuse disease most often affecting the entire neuraxis, treatment should include high-dose methotrexate-based chemotherapy similar to regimens used with CNS lymphoma involving the brain [35].

Germinoma

Germinoma may present as an IMSCT. Age at presentation is between 10 and 40 years old. Craniospinal axis imaging and CSF cytology should be obtained to look for other sites of disease. Because germinoma is usually radiosensitive and chemosensitive, treatment includes biopsy followed by radiotherapy alone or in combination with platinum-based chemotherapy [36•]. The majority of intracranial germinoma are treated with cisplatin or carboplatin in addition to etoposide, although experience with spinal cord germinoma

is sufficiently limited that no evidenced-based recommendations can be made.

Melanoma

Melanoma can arise and be isolated to the intramedullary spinal cord region. Clinical presentation is similar to other intramedullary tumors, but often evolves more rapidly compared with ependymomas or astrocytomas.

On MRI, melanoma is usually hyperintense on T1W images, iso- or hypointense on T2W/FLAIR images, and with mild contrast enhancement [37]. Intratumoral hemorrhage is common at presentation and may lead to the erroneous diagnosis of cavernous angioma or other vascular malformation. The MR features are variable depending on intratumoral bleeding and melanin content. Because there is no reliable MR method to differentiate primary spinal cord melanoma from metastatic tumor, a careful examination of skin, squamous mucosa, and eyes should be performed as well as contrast-enhanced CT imaging of the chest, abdomen, and pelvis.

Surgery establishes the diagnosis and may provide long-term palliation if the tumor is resected completely. Because complete resection is rarely achieved, most patients receive postoperative radiotherapy. Chemotherapeutic agents used for systemic melanoma, with good CNS penetration (ie, DTIC [dacarbazine] or TMZ), can be considered following radiotherapy. The disease course of primary intramedullary melanoma may be more indolent than with metastatic melanoma.

Others

Other rare primary IMSCTs include primitive neuroectodermal tumor (PNET), paraganglioglioma, teratoma, dermoid cyst, epidermoid cyst, lipoma, and hamartoma [18••]. Treatment following maximal safe resection is similar to that of intracranial counterparts and in most instances surgery (PNET being the exception) suffices as primary therapy.

Intradural Extramedullary Tumors

Schwannomas, neurofibromas, and meningiomas are the most common intradural extramedullary spinal cord tumors (Fig. 1). Less common entities include paragangliomas, metastases, lipomas, spinal nerve sheath myxomas, sarcomas, and vascular tumors [7•].

Schwannoma

Schwannomas are nerve sheath tumors that arise from the dorsal nerve root. They are considered benign tumors, although malignant subtypes exist (ie, malignant schwan-

noma). Presentation is usually in the 4th through 6th decades. There is an increased incidence in patients with neurofibromatosis type II (NF2). Adolescents and young adults with NF2 often have multiple schwannomas and have a higher risk for malignant transformation.

Patients harboring schwannomas may be asymptomatic and the lesions are found incidentally on imaging studies. However, most patients present with mild sensory symptoms consisting of shooting pain or paresthesias with nerve palpation; spontaneous pain can occur, but is uncommon.

On MRI, schwannomas appear as solid tumors in the dorsal sensory root region, with displacement of the spinal cord, conus medullaris, or filum terminale [7•]. They are isointense on T1W MRI and hyperintense on T2W/FLAIR images. Contrast enhancement varies from intense homogeneous to faint enhancement, especially if a cystic component is present. Topographically, spinal cord nerve sheath tumors are located in the upper cervical region (16%), cervical cord (31%), thoracic cord (22%), conus medullaris (7%), and cauda equina (24%) [38]. Melanocytic schwannomas have also been reported and usually demonstrate a hypointense region on T2W images.

If asymptomatic, schwannomas may be followed with serial MR given their usual benign behavior. Symptomatic or radiographically enlarging tumors should undergo maximal safe resection. Surgery has minimal morbidity, improves symptoms, and may be curative. No adjuvant therapy is recommended and incompletely resected tumors should be followed given the benign growth of the majority of these tumors. Stereotactic radiosurgery is an option for poor surgical candidates [39•]. Malignant schwannoma should be treated with postoperative radiotherapy, even if total resection was achieved. At present there are no compelling data to suggest a role for either chemotherapy or targeted therapy, notwithstanding recent reports of response of vestibular schwannomas to bevacizumab and epidermal growth factor receptor inhibitors (ie, erlotinib).

Neurofibroma

Neurofibromas are benign tumors that arise from peripheral sensory nerves. Two types are recognized: solitary and plexiform. Solitary neurofibromas are discretely localized, globular, or fusiform nodules. Plexiform neurofibromas are characterized by redundant loops of nerve fiber bundles and tumor tissue intermixed in a disorganized pattern that extends over multiple nerve roots. In contrast to schwannomas, neurofibromas encase nerve roots rather than displacing them. Spontaneous pain (rather than induction by palpation) and dysesthesias are the most common presenting symptoms. Patients with neurofibromatosis type I (NF1) may have multiple spinal cord neurofibromas that often increase in number with age. Patients with NF1

should be followed closely with serial imaging studies because there is a higher incidence of malignant transformation. On imaging, neurofibromas appear as rounded or fusiform tumors that are isointense on T1W images and hyperintense on T2W/FLAIR images [7•]. Intense MR enhancement is usually seen post contrast. However, there are no MR characteristics that differentiate malignant transformation of neurofibromas and consequently a high index of suspicion is required in concert with radiographic findings such as rapidity of tumor growth.

Patients with symptomatic or enlarging solitary neurofibromas should undergo surgical resection. Complete resection with minimal morbidity is usually achieved and minimally invasive techniques may be employed [40]. The clinical results following resection of a plexiform neurofibroma associated with NF1 are poor because complete resection is rarely achieved. Plexiform neurofibromas may undergo malignant transformation (malignant peripheral nerve sheath tumor [MPNST]). Radiotherapy or chemotherapy is almost never employed for benign neurofibromas. Patients with NF1 may be at risk for malignant degeneration following radiotherapy [41]. Chemotherapy use is limited to MPNSTs and is usually adriamycin-based as with other soft tissue sarcomas.

Meningioma

Meningiomas are dural-based tumors that arise from arachnoid cap cells and consequently can be found in any location that dura is present. Approximately 25% of all primary spinal cord tumors are meningiomas. More than 80% of spinal cord meningioma patients are women, of which 80% occurs in the thoracic region. In men, spinal cord meningiomas are equally distributed between the cervical and thoracic cord. Overall, 15% of spinal cord meningiomas occur in the cervical spine, 81% in the thoracic spine, and 4% in the lumbar spine. Most are slow-growing low-grade tumors (WHO grade 1). Genetic predisposition (NF2) and prior exposure to ionizing radiation are the only definite risk factors. Common presenting symptoms include back pain (70%), motor dysfunction (60%), sensory disturbance (40%), and incontinence (40%) [42–44].

By imaging, meningiomas appear as solid, well-circumscribed lesions with an attachment to the dura [7•]. The tumor is iso- to hypointense on T1W MRI and slightly hyperintense on T2W/FLAIR images. Meningiomas display intense, homogenous contrast enhancement and 94% of all spinal cord meningiomas are intradural extramedullary whereas 6% are extradural.

Asymptomatic patients with spinal cord meningioma can be followed clinically with serial imaging studies. If treatment is indicated, surgery is the primary modality and can be curative with complete resection (5- and 10-year recurrence rates 3% and 6%, respectively) [42, 43].

Conventional external beam fractionated radiotherapy or stereotactic radiosurgery is used for patients with incomplete resection or recurrence [42, 45]. There is no established chemotherapy for spinal cord meningiomas, but somatostatin analogues, hydroxyurea, interferon- α , PTK787, and sunitinib appear to have efficacy for patients with recurrent intracranial meningioma and may by extrapolation be administered to patients with recurrent surgery and radiotherapy refractory spinal cord meningiomas, although there are no specific studies of chemotherapy in spinal cord meningiomas [46, 47•, 48•, 49•].

Conclusions

Early recognition of the signs and symptoms of primary spinal cord tumors facilitates early diagnostic evaluation and treatment, potentially minimizes neurologic morbidity, and may improve outcome (Fig. 1). Pain is the predominant symptom of spinal cord tumors and often persists after treatment. Primary treatment of primary spinal cord tumors is surgical resection and predictors of outcome include preoperative functional status (limited to no neurologic deficit predicts for better outcome), histologic grade of tumor (lower grade predicts for improved survival), and extent of surgical resection (image-verified complete resection improves survival). Symptom management can be challenging with spinal cord tumors, particularly intramedullary tumors with quality-of-life disrupting pain and motor, sensory, and autonomic function. The role for chemotherapy for recurrent spinal cord tumors is still poorly defined. In general, principles and therapies used for tumors of similar histology in the intracranial compartment are used for spinal cord tumors, although the literature to support this approach is sparse.

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- Of major importance

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