Intramedullary Spinal Cord Tumors

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Opinion statement

The three most common types of intramedullary spinal cord tumors are low-grade astrocytomas, ependymomas, and high-grade astrocytomas. Surgical extirpation is the necessary and sufficient primary treatment for most intramedullary spinal cord tumors. Radiation therapy may also have a role in the management of persistent, recurrent, or progressive low-grade astrocytomas and ependymomas. The current treatment of spinal cord high-grade astrocytomas, which includes surgical debulking, radiation therapy, and possibly chemotherapy, is clearly inadequate. Chemotherapy may have a potential role for certain progressive spinal cord tumors, but the role is undefined at present. Recent reports have described the use of stereotactic radiosurgery for extramedullary spinal tumors, and stereotactic radiosurgery may someday be useful in the management of intramedullary spinal cord tumors. Rehabilitation programs are an important component of the multidisciplinary care of patients with spinal cord tumors. Finally, more work, especially the inclusion of adults and children with intramedullary spinal cord tumors into prospective clinical trials, is needed to improve the therapy of intramedullary spinal cord tumors and rehabilitation after diagnosis of a spinal cord tumor.

Introduction

Tumors of the spinal cord account for 6% to 8% of central nervous system tumors in children and adults, which is approximately the same proportion of mass of the spine compared with the central nervous system. Most intramedullary spinal cord tumors, such as ependymomas and astrocytomas, are of glial origin. Non-glial tumors are common, however (Table 1). Intramedullary spinal cord tumors may be located throughout the spine, and have a variety of tumor histologies, degrees of surgical resectability, and prognoses.

The purpose of this report is to summarize the most common types of primary intramedullary spinal cord tumors, current treatment strategies for these tumors, and their prognoses. Because of their rarity, there has never been a randomized clinical trial comparing two therapies for spinal cord tumors. As a result, nearly all of the currently existing literature cited in this paper is Class III evidence.

PRESENTING SYMPTOMS AND DIAGNOSIS

Spinal cord tumors have no typical clinical presentation. Furthermore, presenting signs and symptoms of a spinal cord tumor may occur with the sudden onset of severe symptoms after an apparently trivial injury or occur very gradually over many years; for example, the duration of symptoms ranged from 14 days to 9 years in one large series [1••]. Presenting signs and symptoms can include the following: localized back or radicular pain, extremity weakness, sensory disorders, paresthesias, dysesthesiae, torticollis, Brown-Sequard syndrome (weakness in one leg, loss of pain sensation in the contralateral leg, and gait changes), spasticity, and urinary dysfunction. In children, the loss of acquired developmental milestones or kyphoscoliosis may be the first presenting symptom of a spinal cord tumor.

The differential diagnosis for a patient with new complaints of focal back and radicular pain, extremity

Table 1. Histology of intramedullary spinal cord tumors [34]

Low-grade astrocytoma
Ependymoma and myxopapillary ependymoma
Pilocytic astrocytomas
High-grade astrocytoma
Oligodendroglioma
Mixed glioma
Polar spongioblastoma
Ganglioglioma, gangliocytoma, and ganglioneuroblastoma
Neurofibroma
Schwannoma
Lipoma
Epidermoid
Dermoid
Teratoma
Hemangioma
Hemangioblastoma
Cysts and tumor-like lesions—epidermoid and dermoid
Germ cell tumors—teratoma and germinoma
Primitive neuroectodermal tumor
Carcinomatous tumor metastases

weakness, sensory deficits, spasticity, and urinary dysfunction includes intramedullary spinal cord tumors, primary extramedullary or metastatic spinal tumors, inflammatory lesions, demyelinating processes, and vascular insults (Table 2). Intramedullary spinal cord tumors may be focal, involving a few centimeters of the cord or cauda equina, or sometimes diffusely along the length of the cord. The holocord spinal astrocytoma, more commonly occurring in pediatric patients, may extend from the medulla to the conus.

Conventional radiographs are frequently normal, especially in adults. Sometimes children with a long-standing intramedullary spinal cord tumor will have a diffusely widened spinal canal with relatively localized erosion or flattening of the pedicles. Usually, the most informative and sufficient diagnostic study for intramedullary spinal cord tumors is via magnetic resonance imaging (MRI) studies [2]. Magnetic resonance imaging precisely locates and defines the characteristics of the tumor in multiple planes. A complete examination requires T1- and T2-weighted images and T1-weighted gadolinium-enhanced studies. Historically, myelography was the standard radiographic method of imaging spinal cord tumors, and it is mostly used for patients with severe scoliosis and in patients with metal implants who may not be appropriate candidates for MRI.

PROGNOSIS

The most important prognostic factor for adult and childhood intramedullary spinal cord tumors is tumor histology, which is closely associated with the ability to achieve a complete surgical resection [1••,3,4,5••, Class III]. Patients with low-grade astrocytomas and ependymomas may be completely resected and have tumor stability for long intervals, and they may possibly be cured. However, patients with high-grade astrocytomas share a similar poor prognosis as cerebral high-grade astrocytomas [6]. Also, although there has been no definitive evidence that adjuvant radiation therapy or chemotherapy significantly and independently improves the outcome of individuals with intramedullary spinal cord tumors, the prognostic importance of complete surgical resection is not questioned. Patients with well-circumscribed ependymomas and low-grade astrocytomas are more likely to have them completely resected, and these patients subsequently have a relatively good prognosis [7–9, Class III]. Because of the strong correlation between extent of surgical resection and survival for patients with ependymomas, an attempted second surgery to achieve complete resection may be acceptable if postoperative MRI reveals residual tumor.

Radiation therapy after incomplete resection or biopsy of spinal cord tumors is somewhat controversial. Despite the lack of a randomized, prospective study to evaluate its use after surgical resection or biopsy of spinal cord tumors, postoperative radiation therapy is generally advocated for incompletely resected ependymomas, low-grade astrocytomas, and all high-grade astrocytomas. The dose of radiation therapy may possibly correlate with patient survival for these tumors [7]. Several reports of different chemotherapy regimens have demonstrated activity against recurrent intramedullary spinal cord tumors, especially low-grade astrocytomas, which have recurred or progressed after surgery and radiation therapy [10–13, Class III].

The duration of symptoms before diagnosis of a spinal cord tumor also correlates with survival [5••]. This observation is likely a result of the close correlation of a long duration of symptoms before diagnosis with a lower-grade tumor histology. Finally, there are reports that patients who are younger than 40 years old at diagnosis of an intramedullary spinal cord tumor have an improved survival [3,7].

INTRAOPERATIVE MONITORING

Many patients with newly diagnosed intramedullary spinal cord tumors have neurologic deficits from their tumors. Furthermore, surgery to excise an intramedullary spinal cord tumor invariably puts remaining spinal cord function at risk of additional injury. Continuous intraoperative neurophysiologic monitoring of somatosensory evoked potentials and motor-evoked potentials (MEPs) during spinal cord surgery has been demonstrated to predict postoperative functional performance status. Their use has been hypothesized to

Table 2. Differential diagnosis of spinal cord tumors [35]

Metastatic extradural tumors
Carcinomas (lung, breast, prostate, kidney)
Myeloma
Lymphoma
Intradural spinal tumors
Neurofibromas
Meningiomas
Leptomeningeal spread of primary brain tumors
Inflammatory lesions (sarcoidosis)
Demyelinating diseases
Infections (such as schistosomiasis)
Vascular malformations

reduce postoperative neurologic morbidity [14,15, Class III]. To measure MEPs, electrodes placed on the scalp are stimulated to induce transcranial activation of the cerebral cortex. Electrodes are also placed on upper and lower limb muscles or in the epidural space located cranial and caudal to the tumor to record MEPs of the neuromuscular junction or the corticospinal tract, respectively. The loss of muscle MEPs or reductions in peak-to-peak amplitude of epidural MEPs by greater than 50% from baseline are considered significant.

STEREOTACTIC RADIOSURGERY

Stereotactic radiosurgery delivers a limited fraction, a high dose of radiation to a tumor volume or vascular malformation, while limiting the dose to radiation to adjacent normal structures. Recently, the availability of improved immobilization, the integration of imaging into treatment planning, and advances in treatment planning software have allowed for the exploration of the use of stereotactic radiosurgery for spinal cord tumors [16,17, Class III]. To date, small numbers of patients with spinal cord tumors, including meningiomas, spinal metastases, and schwannomas, have been treated with stereotactic radiosurgery. The radiation doses that have been used range from 1600 to 2500 cGy in one to five fractions as outpatients with minimal morbidity [17]. At present, its reported use has primarily been for extramedullary spinal cord tumors, but there may soon be reports of the use of stereotactic radiosurgery for intramedullary spinal cord tumors. The uncertainty regarding the effectiveness and safety of stereotactic radiosurgery for spinal cord tumors is a result of the very short duration of patient follow-up.

CONCLUSIONS

Patients with spinal cord tumors may suffer permanent sequelae as a result of their spinal cord tumor or its treatment, including neurologic injury, scoliosis, kyphosis, and hydrocephalus [1••]. In general, patient's immediate postoperative functional status is usually equal to their preoperative status, and is rarely improved or worse [5••,9,18]. Most patients have improved functional status after treatment [8]. In one study, half of the nonambulatory patients regained the ability to ambulate, and one third of patients without progressive tumor had improved functional status [5••].

Rehabilitation is important component of spinal cord tumor therapy [19••]. Rehabilitation is a multidisciplinary process that involves the patient, physical medicine and rehabilitation specialists, nurses, physical and occupational therapists, psychologists, dietetics, social services, and recreational therapists. The primary objectives of rehabilitation of patients with spinal cord tumors include the relief of symptoms, improvement in quality of life, improvement in functional independence, and prevention of further complications. Patients with spinal cord tumors share many of the same rehabilitation issues as those with traumatic spinal cord injury, including mobility, activities of daily living, neuropathic bowel, neuropathic bladder (prevention of urinary tract infections), skin care, pain management, spasticity management, and psychologic support. In general, however, patients with spinal cord tumors suffer less severe neurologic impairment, more incomplete motor lesions, and more paraplegia than tetraplegia compared with patients with traumatic spinal cord injury [20].

The ideal and sufficient treatment for most intramedullary spinal cord tumors is, when possible, complete surgical resection. For incompletely resected low-grade astrocytomas and ependymomas, radiation therapy may be able to provide prolonged tumor stability and survival. Regardless of therapy, most patients with high-grade astrocytomas of the spinal cord soon die of their cancer. Multidisciplinary rehabilitation programs are necessary in the postoperative care of patients with spinal cord tumors. Finally, more work, especially the inclusion of adults and children with intramedullary spinal cord tumors into prospective clinical trials, is needed to improve the therapy of intramedullary spinal cord tumors.

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Treatment

Surgery

- Surgery is therapeutic in most instances and provides necessary histologic diagnosis.
- Complete resection of low-grade astrocytomas of the spine is ideal and sufficient treatment [1••,8,21,22, Class III].
- Complete resection of ependymomas of the spine is ideal and sufficient treatment [1••,9,23,24, Class III].
- Complete resection of spinal myxopapillary ependymomas is ideal and sufficient treatment [25, Class III].
- Intraoperative ultrasonography may improve the ability to attain a complete tumor resection [26,27, Class III].
- Monitoring of MEPs can predict postoperative functional status and may reduce neurologic morbidity after spinal cord tumor surgery [14,15].

Tumor resection

Standard procedure	Depends on anatomic location.
Contraindications	Medical comorbidity, coagulopathy, and active infection.
Complications	Infection, bleeding, nerve injury, and spinal fluid leak.
Main side effects	Pain.
Cost/cost effectiveness	No data available.

Radiation therapy

	Adjuvant radiation therapy is recommended for incompletely resected low-grade astrocytomas [28••]. The 10-year overall survival rate is 40% to 91% for low-grade astrocytomas after surgery and radiation therapy. The predominant pattern of treatment failure is local [28••]. Adjuvant radiation therapy is recommended for incompletely resected ependymomas [29–32, Class III]. The 10-year overall survival rate is 62% to 100% for ependymomas after surgery and radiation therapy. The predominant pattern of treatment failure is local [28••]. Adjuvant radiation therapy is recommended for all high-grade astrocytoma [4,30,33–35].
Standard procedure	50 to 60 cGy in 1.8 to 2 Gy fractions over 6 weeks.
Contraindications	Previous radiation therapy in field.
Complications	Radiation myelopathy, delayed radiation necrosis, spinal kyphosis or subluxation, and the development of a second malignant neoplasm.
Main side effects	Impaired wound healing, spinal cord edema, and radionecrosis.
Cost/cost effectiveness	No data available.

Chemotherapy

Standard procedure	Chemotherapy has activity against progressive low-grade astrocytomas of the spinal cord after radiation therapy [6]. Chemotherapy regimens that are reported to have activity against intramedullary spinal cord tumors include procarbazine, lomustine, and vincristine [10], carboplatin and vincristine [11,12], and the "eight-in-one" chemotherapy regimen [13].
Contraindications	Abnormal hematopoietic and renal or hepatic dysfunction.
Complications	Myelosuppression and risk of life-threatening sepsis.
Main side effects	Nausea and vomiting; nephrotoxicity and ototoxicity (platinum agents).
Special points	Chemotherapy needs to be administered with vigorous hydration (platinum agents) and anti-emesis prophylaxis.
Cost/cost effectiveness	No data available.

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