

Spinal cord gliomas

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Introduction

Primary tumors arising from the spinal cord, spinal nerve roots, and dura are rare compared to neoplasms in intracranial locations. Spinal cord gliomas account for the majority of primary intramedullary spinal tumors, and have many unusual features which distinguish them from their intracranial counterparts.

Characteristics of spinal cord gliomas

Spinal cord gliomas comprised 20% of intraspinal tumors of all types in a large surgical series (Table 1) [1]. These tumors share several characteristics with cerebral gliomas. Spinal gliomas use the same histopathological classification as gliomas of the cerebral hemispheres, such as astrocytoma and ependymoma. Determination of tumor grade is useful in predicting clinical behavior [2]. Diffuse fibrillary astrocytomas of the spinal cord are infiltrative, with significant limitations for resectability, whereas pilocytic astrocytomas and ependymomas are well-circumscribed lesions.

Beyond these similarities, however, lie several interesting differences. Astrocytomas of the spinal cord do not show the correlation between increasing grade and increasing age at diagnosis that is so prominent with cerebral diffuse astrocytomas. High-grade gliomas of the spinal cord have a noted tendency to undergo leptomeningeal spread, a feature which is rare with gliomas of

the brain. Hydrocephalus is not unusual with spinal cord astrocytomas. In the case of low-grade tumors, this may be associated with a syrinx reaching up into the region of the obex of the medulla producing obstruction, whereas with high-grade spinal cord astrocytomas, hydrocephalus is often related to leptomeningeal spread of tumor.

Although the mechanisms by which intramedullary spinal cord tumors produce neurological dysfunction are not precisely known, the effects of pressure and edema on axonal conduction probably play a key role. The best evidence for this is the improvement in function that can follow surgical resection of the tumor or drainage of a syrinx. With respect to syrinx formation, the flow of normal cerebrospinal fluid (CSF) in the central canal of the cord is disrupted by the presence of the mass lesion. This mechanical explanation probably accounts for the fact that tumor-associated syringes are typically rostral to the tumor.

Spinal cord astrocytoma

Astrocytomas of the spinal cord are rare neoplasms, occurring with an incidence of 0.8 to 2.5 per 100 000 per year, which makes them over 10 times less common than astrocytomas of the brain [3]. The average age at diagnosis in large surgical series is between 35 and 40 years.

Neuropathology

Spinal cord astrocytomas are graded according to the same WHO criteria used for cerebral astrocytomas, and grade is a strong prognostic indicator [4,5]. Low-grade astrocytomas (WHO grade II/IV) comprise about 75–90% of tumors, with the remainder being high-grade astrocytomas (WHO grades III/IV and IV/IV). Tumors typically involve a focal segment of the cord, and have a fairly even incidence along its length, but rarely may involve a large portion of the cord in a condition called ‘holocord’ astrocytoma. The tumor may grow in a diffuse manner with indistinct margins between tumor and the adjacent normal spinal cord tissue, and can extend along spinal nerve roots. Pilocytic astrocytomas have discreet margins.

An important feature is the presence of a tumor-associated syrinx, which occurs in about 40% of patients with astrocytomas of the spinal cord [1,6]. Syringes are more common with low-grade than high-grade astrocytomas, are more frequent the further rostral the tumor lies along the cord and they appear to favor the rostral

Table 1. Frequencies of primary spinal tumors

Tumor type	Frequency (%)
Schwannoma	29
Meningioma	25
Glioma	22
Sarcoma	11.9
Vascular malformations*	6.2
Chordoma	4.0
Epidermoid, dermoid, teratoma, and cyst	1.4

*Not neoplasms, but included by the authors in this tabulation. Data from [1].

aspect of cord above the tumor [6]. Syringes may be less common with astrocytomas than with ependymomas.

Clinical presentation and differential diagnosis

While midline back pain, with or without radicular pain at the level of the tumor, is the most common initial symptom of spinal cord tumors, leg weakness and sensory changes are the symptoms that bring patients to diagnostic evaluation. Autonomic dysfunction affecting bowel and bladder control are late symptoms, although many patients have these by the time the tumor is diagnosed. The presence of a Brown-Sequard syndrome, in which there is vibration sensory loss and weakness in one leg and loss of pain sensation in the other leg, is suggestive of an intramedullary lesion rather than an extramedullary one.

The rate at which symptoms and signs progress correlates fairly well with the grade of the lesion. Symptoms from low-grade spinal cord astrocytomas may progress slowly over a period of years, whereas high-grade tumors produce symptoms over a period of weeks or months. The duration of symptoms also correlates with survival [2,7].

The differential diagnosis of a spinal cord astrocytoma includes other tumors such as intramedullary metastases, inflammatory lesions (such as sarcoidosis), demyelinating disease, infection (such as schistosomiasis), and vascular lesions [8]. Leptomeningeal metastasis may infiltrate into the cord parenchyma to produce an intramedullary mass lesion.

Therapy and prognosis

Aggressive surgical resection should be considered, particularly in patients with low-grade diffuse astrocytomas and pilocytic astrocytomas. With the advent of the operating microscope, surgical resection often leads to improvement in the neurological deficits. The value of aggressive resection in high-grade spinal cord astrocytomas is unclear. Compared to the more circumscribed ependymoma, however, the infiltrative nature of spinal cord astrocytomas frequently limits the extent of resection. Tumor-associated syringes should be decompressed if they appear to be symptomatic. Patients with symptoms suggestive of intracranial metastasis or hydrocephalus, and those with high-grade tumors, should undergo imaging of the brain.

The value of radiation therapy remains unclear because of the rarity of spinal cord astrocytomas. However, it should be considered for tumors with high-grade histopathology, for clinically progressive lesions and for tumors in which a substantial resection cannot be achieved.

Chemotherapy can be considered in patients with progression of disease after radiation therapy. There

are a number of case reports and small series indicating chemotherapy responses in pediatric and adult spinal cord astrocytomas [9–12].

It is difficult to obtain accurate survival data from the literature on spinal cord astrocytomas [4,5,13–15]. Many surgical series describe survival from the time of surgery at the reporting institution, not from the initial surgery. They often combine all grades of tumors into the outcome measurement and use varying measures of outcome. The overall 5-year survival for patients with spinal cord astrocytomas is approximately 50%. 5-year survival is 70–90% with low-grade tumors, and 30% with high-grade tumors [2].

Prognostic factors for patients with spinal cord astrocytoma include histological grade and duration of symptoms prior to diagnosis. Patients with glioblastomas usually have survival measured in months, and those with high-grade tumors in the cervical cord have the worst prognosis.

Failure is almost always due to tumor growth at the original tumor site [2], although the possibility of simultaneous tumor dissemination throughout the neuraxis should be also considered, especially with high-grade tumors [16].

Spinal cord ependymoma

Ependymomas of the spinal cord are slightly more common than spinal cord astrocytomas [1,3]. The average age of patients is between 35 and 45 years, an age which is higher than that for intracranial ependymomas.

Neuropathology

Spinal ependymomas are thought to arise from ependymal cells lining the central canal. Cellular ependymomas are distributed evenly along the length of the spinal cord, whereas myxopapillary ependymomas occur almost exclusively at the filum terminale and occasionally the conus medullaris [17]. Tumors may extend over several spinal segments, and may have a substantial exophytic component. Holocord lesions are rare. Syringes or tumor-related cysts may be more common with ependymomas than with astrocytomas of the spinal cord. The lesions are usually well circumscribed.

Histopathological classification includes myxopapillary ependymoma (WHO grade I/IV), ependymoma (WHO grade II/IV) and anaplastic ependymoma (WHO grade III/IV). The two low-grade lesions are more common than anaplastic ependymoma. Anaplastic ependymomas may be associated with leptomeningeal spread, although this complication occurs with the lower grade lesions as well. Ependymomas, including those arising from the spinal cord, have the unusual propensity to spread

outside of the neuraxis. This is particularly true for subcutaneous myxopapillary tumors that arise over the sacrococcygeal region. Metastasis to lung, skin and kidney have been documented.

Clinical presentation and differential diagnosis

As with spinal astrocytomas, local back pain is the most common initial manifestation of spinal cord ependymomas. Low back pain with radiation into the lower extremities is a common symptom in patients with myxopapillary ependymomas. Leg weakness, gait changes, sensory changes and disturbances of bowel and bladder function follow pain in the progression of symptoms. There are no specific symptoms that allow ependymomas to be differentiated clinically from other spinal cord tumors. The differential diagnosis of spinal cord ependymoma is similar to that of spinal cord astrocytoma, as discussed above.

Therapy and prognosis

The well-circumscribed, encapsulated nature of spinal cord ependymomas often permits an aggressive surgical resection, even when the lesions extend over substantial segments of the cord. Thus, a gross total resection should be the primary treatment goal for patients with this tumor. Tumors should be removed *en bloc* when possible, in order to decrease the theoretical risk of spreading tumor cells via the CSF pathways. High-grade ependymomas may exhibit a more infiltrating character, making gross total resection more difficult and increasing the risk of worsened neurological function. Tumor associated syringes should be decompressed if they appear to be symptomatic.

As with the case for astrocytomas, it has been difficult to quantitate the value of radiation therapy for spinal cord ependymomas [18,19]. Small series have suggested improved local control rates in patients with subtotal resections, but treatment-decision bias could also account for any differences. However, radiation therapy should be considered for spinal ependymomas in which a gross total resection cannot be achieved, in the presence of progressive neurological symptoms due to tumor growth and for anaplastic ependymomas. Patients with high-grade ependymomas should be considered for craniospinal irradiation due to the higher risk of tumor growth in the CSF pathways. Chemotherapy can be administered in patients with progression of disease after radiation therapy, since ependymomas demonstrate some responsiveness to chemotherapy.

Low-grade ependymomas of the spinal cord are usually slowly growing lesions with little tendency to undergo anaplastic progression to higher grades of histology or more aggressive biological behavior. Recurrence is almost always due to tumor growth at the original tumor site,

although the possibility of simultaneous tumor dissemination throughout the neuraxis should be also considered, especially with anaplastic lesions and tumors [19].

Prognostic factors include histological grade and post-operative neurological function. Overall survival rates of series of patients with low-grade ependymomas of the spinal cord are in the range of 85% 5-year survival. Survival rates are even higher in patients with myxopapillary ependymomas and are significantly lower in patients with anaplastic ependymomas.

Conclusion

Astrocytomas and ependymomas are the most common gliomas of the spinal cord. Their epidemiology, clinical presentation, diagnosis and treatment are unique from intracranial gliomas. Like other tumors of the central nervous system, however, they can produce devastating neurological dysfunction without early diagnosis and appropriate intervention.

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