

# Spinal cord astrocytomas: Rare but life-threatening tumors in children

Though usually benign, these tumors require early surgical intervention to preserve neurologic function and quality of life for pediatric and adolescent patients.

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**S**olid tumors of the spinal cord are a rare but serious diagnosis in pediatric patients, accounting for only 4% to 10% of all CNS tumors in that population;<sup>1</sup> 25% to 40% of spinal cord tumors are intramedullary, or intrinsic to the spinal cord.<sup>2,3</sup> Most intramedullary spinal cord tumors (IMSCTs) are classified as either astrocytomas or ependymomas, with the former comprising 60% to 80% of pediatric IMSCTs.<sup>3,4</sup> Although most pediatric IMSCTs are benign,<sup>2,5</sup> 10% to 15% of intramedullary astrocytomas are malignant and carry a poor prognosis.<sup>4,6</sup> Early surgical intervention is essential to preserve neurologic function and quality of life for children and adolescents. This article discusses the background, clinical presentation, and diagnostic evaluation of intramedullary spinal cord astrocytomas in pediatric patients as well as current treatment strategies and the long-term complications of such treatments.

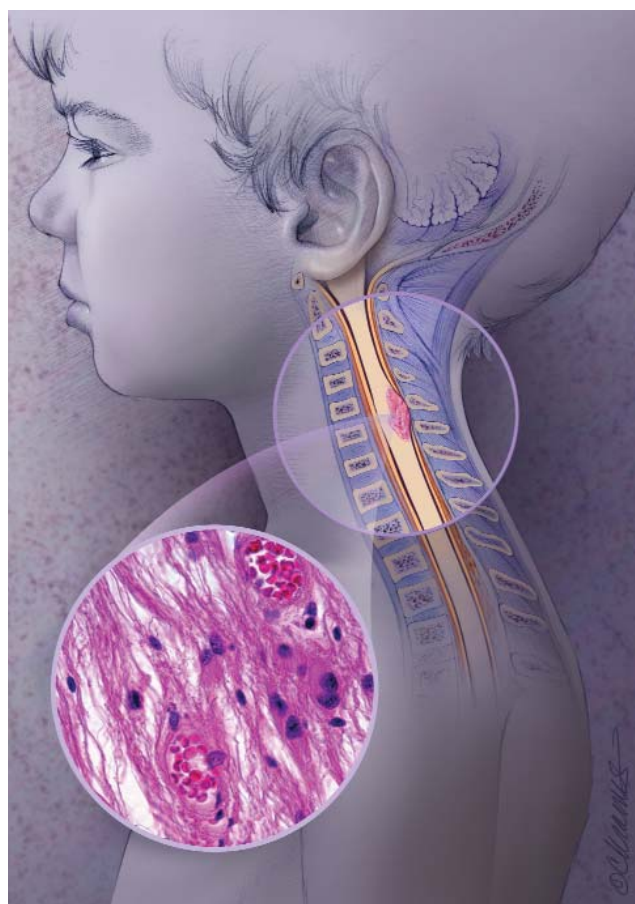
## BACKGROUND AND EPIDEMIOLOGY

IMSCTs occur most often in children between the ages of 1 and 5 years, with an equal prevalence in males and females.<sup>3,4</sup> Although the overall incidence of spinal cord astrocytomas is low (0.8-2.5 per 100,000 population per year),<sup>7</sup> these tumors are the most common IMSCT in the pediatric population.<sup>4</sup> Spinal cord astrocytomas are usually located in the cervical or thoracic spine, with 75% found in these regions. Only 20% are found in the distal spinal cord, while a rare 5% are found in the filum terminale.<sup>4</sup>

Although no specific risk factors for astrocytomas have been clearly identified,<sup>8</sup> associations have been made with such inherited conditions as Li-Fraumeni syndrome, Turcot syndrome, tuberous sclerosis, and neurofibromatosis. In rare cases, previous radiation for other neoplasms has been associated with the development of astrocytoma of the spinal cord.<sup>4</sup>

## CLINICAL PRESENTATION

Astrocytomas are initially asymptomatic. Development of symptoms depends on the grade of the tumor, with high-grade lesions causing more rapid symptom progression.<sup>7</sup> Localized, midline back pain is the presenting symptom in



An astrocytoma (inset) in the cervical spine

70% of children with intramedullary spinal cord astrocytomas.<sup>1</sup> Patients frequently complain of dull, shooting pain that wakes them from sleep.<sup>2,9</sup> The exact mechanism by which astrocytomas of the spinal cord cause pain is unknown;<sup>7</sup> possible explanations include direct pressure on the dura by the enlarging spinal cord, nerve-root impingement, or abnormal muscle innervation.<sup>7</sup> Nocturnal pain is thought to be due to increased pressure on the spinal cord from venous congestion that occurs when lying down.<sup>5,9</sup> Other sensory complaints include paresthesias and changes in perception of pain and

Illustration: © Christy Kramers; Histology image: Molecular Expressions

temperature.<sup>4,7</sup> Dysesthesias—uncomfortable sensations of numbness and tingling or hot and cold—are also described.<sup>5</sup>

As the tumor grows and impinges on motor neurons, the child may experience motor dysfunction manifested by weakness, clumsiness, gait disturbance, and frequent falls.<sup>2,4,5,7</sup> Younger children may exhibit regression of motor function, such as reverting to crawling after having learned to walk.<sup>5</sup> Altered sphincter tone leading to changes in bowel or bladder function is a sign of advanced disease.<sup>1,4,5,7</sup>

Physical examination of the child reveals abnormal neurologic findings, including hyperreflexia, spasticity, decreased sensation, and decreased proprioception.<sup>4,5,7</sup> Muscle atrophy may be noted as a consequence of prolonged weakness.<sup>3</sup> One-third of children with astrocytoma of the spinal cord will present with a spinal cord deformity, such as scoliosis or torticollis.<sup>2,5</sup> Scoliosis is the most common presenting sign in patients with thoracic lesions.<sup>1</sup> Rarely, patients will present with hydrocephalus due to tumor cells in the subarachnoid space.<sup>5,7</sup>

### DIAGNOSIS

MRI with or without contrast is the imaging study of choice for spinal cord tumors.<sup>2</sup> Astrocytomas appear heterogeneous and asymmetric with poorly defined borders on MRI<sup>4</sup> and enhance with gadolinium contrast on T1-weighted imaging.<sup>7</sup> Also visible on MRI are surrounding spinal cord edema, scoliosis, hemorrhage, and areas of infarction.<sup>2,7</sup> Cysts associated with the tumor, which are present in 40% of cases, do not enhance with contrast<sup>2</sup> but are visible on T2-weighted imaging.<sup>5</sup> If MRI is contraindicated because of previous surgery with metal implants, CT myelography is the diagnostic test of choice.<sup>5</sup>

Because spinal cord malignancy is rare and the differential diagnosis of back pain in children is broad, the workup often begins with plain radiographs.<sup>3</sup> Nonspecific findings, such as spinal canal enlargement or scoliosis, may be noted on the plain radiographs from the initial evaluation.<sup>7</sup> If a lumbar puncture is performed, CSF analysis may show increased protein levels. This is also a nonspecific abnormality; lumbar puncture is not useful in the diagnosis of CNS tumors.<sup>7</sup>

The final diagnostic evaluation of spinal cord astrocytomas is based on histologic tumor grading. The grading of astrocytomas is based on the World Health Organization (WHO)

scale. Low-grade astrocytomas include WHO grade I (*pilocytic*) and grade II (*diffuse*) tumors. Pilocytic astrocytomas are the most common grade diagnosed in children.<sup>4</sup> WHO grade III (*anaplastic*) and IV tumors (*glioblastoma multiforme*) are considered high-grade and show increased cellularity, anaplasia, and vascular proliferation.<sup>4,8,10</sup> In the pediatric population, high-grade tumors make up only 7% to 25% of astrocytomas.<sup>7</sup>

**Differential diagnosis** The differential diagnosis of astrocytomas includes other types of spinal cord tumors as well as benign conditions that cause back pain (see Table 1), which as previously noted is a common presenting symptom of astrocytomas in children. Back pain can be due to trauma or musculoskeletal strain (for example, from carrying a heavy backpack).<sup>11</sup> Trauma to the back can lead to disk herniation, vertebral fractures, or epidural hematomas. Less common causes of back pain include osteomyelitis, diskitis, epidural abscess, urinary tract infection, or sickle cell crisis. Chronic back pain can be caused by inflammatory disorders, such as juvenile rheumatoid arthritis or ankylosing spondylitis.<sup>11</sup> Careful history-taking from the child or parents is needed to determine if trauma has occurred or if the child is at risk for other causes of back pain. A history of acute or subacute onset of back pain with nighttime symptoms in the absence of trauma or a history of back pain that is prolonged or unremitting with conservative treatment raises suspicion for a neoplastic etiology.

Spinal cord tumors that differ histologically from astrocytomas include gangliomas, ependymomas, meningiomas, primitive neuroectodermal tumors, and nerve-sheath tumors.<sup>3</sup> Although diagnosed by biopsy or excision, these lesions also have MRI characteristics that distinguish them from astrocytomas. Extramedullary malignancies that cause back pain include osteoid osteoma, osteoblastoma, Ewing's sarcoma, leukemia, and lymphoma.<sup>11,12</sup>

### TREATMENT

Spinal cord astrocytomas are treated primarily by surgical resection.<sup>2,4</sup> The addition of chemotherapy and/or radiation therapy for high-grade tumors is still under investigation.<sup>1</sup> The current recommendation is that adjunct therapy should be used only in select high-grade tumors or for tumor recurrence after surgical resection.<sup>5</sup>

### KEY POINTS

- Localized, midline back pain is the presenting symptom in 70% of children with intramedullary spinal cord astrocytomas. Tumor progression can lead to weakness, clumsiness, gait disturbance, and frequent falls. Altered sphincter tone leading to changes in bowel or bladder function is a sign of advanced disease.
- Primary treatment is surgical resection. Radiation therapy is reserved for high-grade lesions in which surgical resection is difficult or impossible. Chemotherapy may be considered in very young children with low-grade tumors or after surgery and radiation have failed.
- All treatment modalities of spinal cord astrocytomas have long-term side effects. Surgery carries a high risk of neurologic injury, including paralysis, CSF leak, and wound dehiscence. Radiation therapy can damage the bone or nervous system and may lead to delays in normal growth and development. Side effects of chemotherapy include myelosuppression, renal insufficiency, and neurotoxicity.
- The best predictor of survival in patients with astrocytoma is the histologic grade of the tumor as well as the preoperative neurologic status of the patient. Early-stage diagnosis is necessary to preserve neurologic function. Death from high-grade astrocytomas usually occurs within 2 years of diagnosis.

**Surgical resection** The surgical treatment for infiltrating spinal cord tumors has improved significantly with advancements in technology. Intraoperative ultrasound visualization of the spinal cord and monitoring of motor and sensory function during the procedure have led to improved outcomes.<sup>2</sup> Because complete resection of astrocytomas is difficult, the goal of surgery is to reduce tumor burden while preserving neurologic function.<sup>2,4</sup> For low-grade tumors, treatment with surgical resection may be curative.<sup>1</sup>

Corticosteroid therapy is used perioperatively to control edema. Preoperative management includes methylprednisolone, 64 mg every 6 hours for 24 hours prior to surgery. At the time of surgery, the dosage is increased to 125 mg every 6 hours followed by a slow taper over 4 to 5 days.<sup>8,13</sup>

During surgery, the spinal cord is exposed by laminectomy or osteoplastic laminotomy,<sup>2</sup> and a midline incision is made into the dura. Myelotomy, an incision into the spinal cord, is performed to visualize the astrocytoma, which is gray to yellow in color. The lesion is biopsied, and specimens are sent for histologic evaluation and grading.<sup>2</sup> The tumor is then resected in piecemeal fashion using ultrasonic aspirator or laser techniques, starting in the center of the lesion and progressing toward the poles.<sup>2,7</sup> During the procedure, electrocautery is avoided; bleeding is controlled by packing the wound with hemostatic agents.<sup>7</sup>

Throughout the procedure, ultrasound imaging is used to determine the extent of tumor infiltration and to minimize vertebral and spinal cord disruption.<sup>4</sup> Intraoperative monitoring of neurologic status includes the use of motor-evoked potentials (MEPs) to monitor the corticospinal tracts<sup>2</sup> as well as somatosensory-evoked potentials (SSEPs) to monitor dorsal column function.<sup>4</sup> The procedure is stopped if signs of spinal cord injury or excess traction on the cord are evident on monitoring.<sup>4</sup> Constantini and colleagues recommend continuing with resection as long as MEPs are greater than 50% of original amplitude. If MEPs fall below 50%, surgery should be stopped.<sup>14</sup> To allow for MEP and SSEP monitoring during the procedure, anesthesia is achieved with propofol and fentanyl, with the addition of short-acting muscle relaxants only during intubation.<sup>5</sup>

Postoperatively, MRI should be performed to evaluate the extent of tumor resection.<sup>7</sup> Unfortunately, because of the infiltrative nature of astrocytomas, residual microscopic foci of tumor may remain in the spinal cord following resection.<sup>2</sup> A second surgery is recommended at a later date if the first procedure was stopped due to spinal cord injury or if residual tumor growth occurs.<sup>7</sup>

**Radiation therapy** A multicenter, retrospective study of 183 patients with spinal cord gliomas compared treatment with surgery followed by daily radiation therapy versus surgery alone.<sup>15</sup> Of the 57 patients in the study with intramedullary astrocytomas, 39 received postoperative radiation therapy. More than half the patients in the radiation group went on to develop disease progression, and 19 of the 39 died of their disease. Although there was a statistically significant improvement in outcome for patients with low-grade tumors who re-

ceived radiation, the authors concluded that this improvement was probably due to the extent of surgical resection rather than to any benefit of radiation.

The side effects of radiation therapy, especially in young children, limit the use of this modality in the pediatric population. Therefore, radiation therapy in the setting of pediatric spinal cord astrocytomas is reserved for high-grade lesions in which surgical resection is difficult or impossible.<sup>4</sup>

**Chemotherapy** A review of the literature revealed limited data on chemotherapy specifically for spinal cord astrocytomas. Chemotherapy with carboplatin and vincristine has been shown to benefit patients with grade I or II astrocytomas of the brain;<sup>1</sup> however the same therapy in spinal cord astrocytoma has an uncertain outcome. In a small retrospective study that evaluated 10 children with spinal cord astrocytoma, carboplatin and vincristine appeared to be beneficial to three of the children with low-grade lesions. The fourth child to receive this regimen did not benefit from chemotherapy.<sup>1</sup>

A study of 52 patients with high-grade CNS astrocytomas showed a statistically significant improvement in survival rates in patients who received postoperative treatment with ifosfamide, etoposide, methotrexate, cisplatin, and cytarabine when compared with lomustine, vincristine, and cisplatin.<sup>10</sup> Only two patients in this study had tumors located in the spinal cord. Another study, published by the American Cancer Society, showed no significant improvement in survival rates of 102 children whose high-grade astrocytomas of the brain were treated with high-dose chemotherapy compared with those who received conventional treatment using lower doses of chemotherapy.<sup>16</sup>

Although chemotherapy is not currently the standard of care for spinal cord astrocytomas,<sup>4</sup> it may be considered in very young children with low-grade tumors or after surgery and radiation have failed. Newer studies with the use of

**TABLE 1. Causes of back pain in children and adolescents**

Common
Muscle strain
Herniated disk
Spondylolysis
Spondylolisthesis
Scoliosis
Uncommon
Sickle cell crisis
Infection (osteomyelitis, diskitis)
Tumor
Pyelonephritis
Vertebral fracture
Data from Bernstein RM and Cozen H. <sup>11</sup>

**TABLE 2. Complications of treatment for spinal cord astrocytoma**

Treatment modality	Complications
Surgical resection	Paralysis, transient motor deficit, wound dehiscence, CSF leak, spinal deformity, meningitis
Radiation therapy	Growth delay, bone damage, myelitis, endocrine dysfunction, alopecia, cerebral necrosis, necrotizing leukoencephalopathy
Chemotherapy	Myelosuppression, gonadal dysfunction, renal insufficiency, pulmonary toxicity, neurotoxicity, hearing loss

Data from Townsend N et al,<sup>1</sup> Jallo GI et al,<sup>2</sup> Rossi A et al,<sup>3</sup> Kothbauer KF,<sup>5</sup> Roonprapunt C and Hooten JK,<sup>7</sup> Sandersen SP and Cooper PR,<sup>8</sup> Constantini S et al,<sup>14</sup> and Burzynski SR.<sup>17</sup>

temozolomide as a chemotherapeutic agent have shown promising results in phase 2 trials.<sup>17</sup>

**Complications of treatment** The treatment of spinal cord astrocytomas is not without complications. Surgery, chemotherapy, and radiation therapy all have long-term side effects that must be considered when choosing a treatment strategy. Treatment complications are summarized in Table 2.

Surgical resection of infiltrative astrocytomas carries a high risk of neurologic injury.<sup>8,14</sup> Postoperative motor paralysis, a worrisome complication of spinal cord surgery, is closely associated with preoperative state.<sup>2</sup> A retrospective study including 76 patients with astrocytomas revealed increased surgical morbidity in patients who had poor preoperative motor function. The majority of patients in the study, however, experienced either no change or improvement in neurologic function after surgery.<sup>14</sup> In patients with no preoperative motor dysfunction, the risk of postoperative paralysis is less than 1%.<sup>2</sup> Up to one-third of patients will experience a transient decrease in neurologic function postoperatively due to edema at the surgical site. Sensory function returns first, with improvement in both sensory and motor function in the following weeks to months.<sup>2,7</sup>

Patients who have previously undergone chemotherapy or radiation therapy are at risk for wound dehiscence and CSF leak.<sup>2,5,8</sup> Meningitis is also possible with wound dehiscence.<sup>8</sup>

An estimated two-thirds of patients will develop scoliosis or kyphosis after surgical resection.<sup>2</sup> Deformity most commonly occurs in the cervical spine as a result of laminectomy or weakness of spinal musculature.<sup>8</sup> Osteoplastic laminotomy with replacement of the laminar roof is preferred over complete laminectomy to preserve the normal vertebral anatomy and reduce the incidence of postoperative scoliosis.<sup>4</sup> Postoperative radiographs are recommended to evaluate for spinal deformity.<sup>9</sup>

Radiation therapy carries many risks, including damage to bone or the nervous system, delays in normal growth and

development, endocrine abnormalities, vasculopathies, and alopecia.<sup>1,2,4,17</sup> Toxic effects of radiation include cerebral necrosis and necrotizing leukoencephalopathy causing permanent neurologic damage.<sup>17</sup> Additionally, radiation therapy has been estimated to carry a 25% risk of secondary tumor development over 30 years.<sup>6</sup> Current recommendations call for the use of radiation only for malignant tumors or in cases of incomplete tumor resection or regrowth after initial resection.<sup>2,5</sup> Craniospinal radiation is no longer used; instead radiation should be localized to the tumor and to 2-cm margins on either side of the tumor. Because radiation therapy has such toxic effects, it is not recommended for children younger than 3 years.<sup>17</sup>

Side effects of chemotherapy include myelosuppression and increased risk of infection, renal insufficiency, neurotoxicity, gonadal dysfunction, pulmonary toxicity, and hearing loss. Young children who receive chemotherapy are at risk of psychological and cognitive impairment as well.<sup>17</sup>

**Prognosis** Unfortunately, tumors of the CNS are the leading cause of pediatric cancer deaths.<sup>17</sup> The outcome of spinal cord astrocytomas is primarily dependent on the histologic tumor grade (WHO classification) as well as the preoperative neurologic status of the patient.<sup>4</sup> Because the child's condition at the time of surgery is the best indicator of surgical outcome,<sup>7</sup> early-stage diagnosis of spinal cord astrocytoma is necessary in order to preserve neurologic function and improve prognosis.<sup>14</sup>

The best predictor of survival in patients with astrocytoma is the histologic grade of the tumor.<sup>7</sup> The five-year survival rate for low-grade astrocytomas ranges from 60% to 90%,<sup>8</sup> while high-grade lesions are associated with a worse prognosis.<sup>18</sup> In a study of 231 children with high-grade astrocytomas of either the brain or spinal cord treated with a combination of surgery, radiation, and chemotherapy, the 5-year survival rate was only 36.6%.<sup>18</sup> The 5-year survival rate in the previously noted retrospective study of 10 patients was significantly higher (68%).<sup>1</sup> This was a smaller study, involving eight patients with low-grade lesions and two with high-grade lesions. Death from high-grade astrocytomas usually occurs within 2 years of diagnosis due to disease progression or dissemination into the leptomeninges (pia mater and arachnoid mater). Tumor progression often leads to hydrocephalus or respiratory failure from paralysis, and 58% of patients with grade III or grade IV tumors will die of hydrocephalus or leptomeningeal metastases. Other causes of death include pulmonary embolism and pneumonia secondary to prolonged immobility.<sup>7,8</sup>

**CONCLUSION**

Although rare overall, astrocytoma is the most commonly diagnosed IMSCT in the pediatric population. Most intramedullary astrocytomas occur in the cervicothoracic spine. Symptoms include back pain, sensory and motor dysfunction, and spinal cord deformity. The diagnosis is made by contrast and noncontrast MRI as well as tumor biopsy.

Surgical intervention is the treatment of choice, although it is difficult to completely resect the solid tumor because of the infiltrative nature of astrocytomas. Adjunct therapies, including radiation and chemotherapy, have also been studied for use in the treatment of astrocytomas. However, more research is needed to determine the role of these therapies in children. The prognosis of astrocytomas is dependent upon the histologic tumor grade as well as the child's functional status at diagnosis. Unfortunately, the prognosis of high-grade astrocytomas is poor. As clinicians, we must consider spinal cord astrocytoma in the differential diagnosis of any child with back pain, as diagnosis at an earlier stage improves survival and functional outcome. [JAAPA](#)

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#### DRUGS MENTIONED

Carboplatin (Paraplatin, generics)	Lomustine (CeeNU)
Cisplatin (Platinol, generics)	Methotrexate
Cytarabine (Cytosar-U, DepoCyt, generics)	Propofol (Diprivan, generics)
Etoposide (Etopophos, VePesid, generics)	Temozolomide (Temodar)
Fentanyl (Sublimaze, generics)	Vincristine (Oncovin, Vincasar)
Ifosfamide (Ifex)	

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