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Spinal Cord Astrocytomas: Presentation, Management, and Outcome

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Gliomas of the spinal cord have historically been one of the most challenging lesions of the central nervous system to treat. Surgery was once reserved exclusively for diagnosis, but it is now emerging as one of the most effective treatments for most of these tumors. Primary glial tumors of the spinal cord include astrocytomas, ependymomas, and gangliogliomas, which together comprise greater than 85% of all intramedullary tumors in pediatric and adult patients [1–3]. In this article, we review the literature and our experience with the current management of spinal cord astrocytomas. Reports of long-term follow-up on series of patients who have undergone surgery for spinal astrocytomas have now been published and reveal several factors that can influence outcome [4–6]. First, histologic grade is the most significant predictor of survival. Second, the most important prognostic indicator is the patient's condition at the time of surgery. Third, there is a trend that the extent of resection of low-grade astrocytomas in some series (but not all) correlates with better outcome.

Epidemiology and pathologic findings

Astrocytomas are common glial neoplasms of the central nervous system, but only 3% of cases are found in the spinal cord [7]. Astrocytomas of the spinal cord have a reported incidence of 0.8 to 2.5 per 100,000 per year [8]. These tumors can affect individuals of all ages, although rarely presenting before 2 years of age or after 60 years of age. Astrocytomas are the most common spinal cord tumors in children, and they are second only to ependymomas in adults. They are the most frequent histologic type of intramedullary spinal cord tumor encountered in the pediatric population, representing 59% of the lesions reported in a survey of the literature [3]. In adult series, the proportion of astrocytomas varies but is generally slightly less than that of ependymomas [9]. There is a slight male predominance in the occurrence of astrocytomas [10,11].

Although astrocytomas may present anywhere throughout the spine, approximately 60% localize to the cervical and upper thoracic areas [1]. These tumors commonly span multiple spinal levels (Fig. 1). In 40% of cases, there is an associated tumoral cyst or syrinx, which may cause significant mass effect. Rarely, the entire spinal cord may be involved with tumor or cyst components. Such lesions have been termed *holocord tumors* and are most commonly of low histologic grade (Fig. 2) [3,12].

Spinal cord astrocytomas have routinely been categorized using the Kernohan grading scheme [13]. More recently, the World Health Organization (WHO) criteria have gained acceptance as the primary standardized grading scheme. Although adult intracranial astrocytomas are generally high-grade tumors (WHO grades III and IV), adult spinal cord astrocytomas are usually low-grade lesions (WHO grades I and II). High-grade lesions in the spinal cord account for 7% to 25% of spinal astrocytomas in children and 10% to

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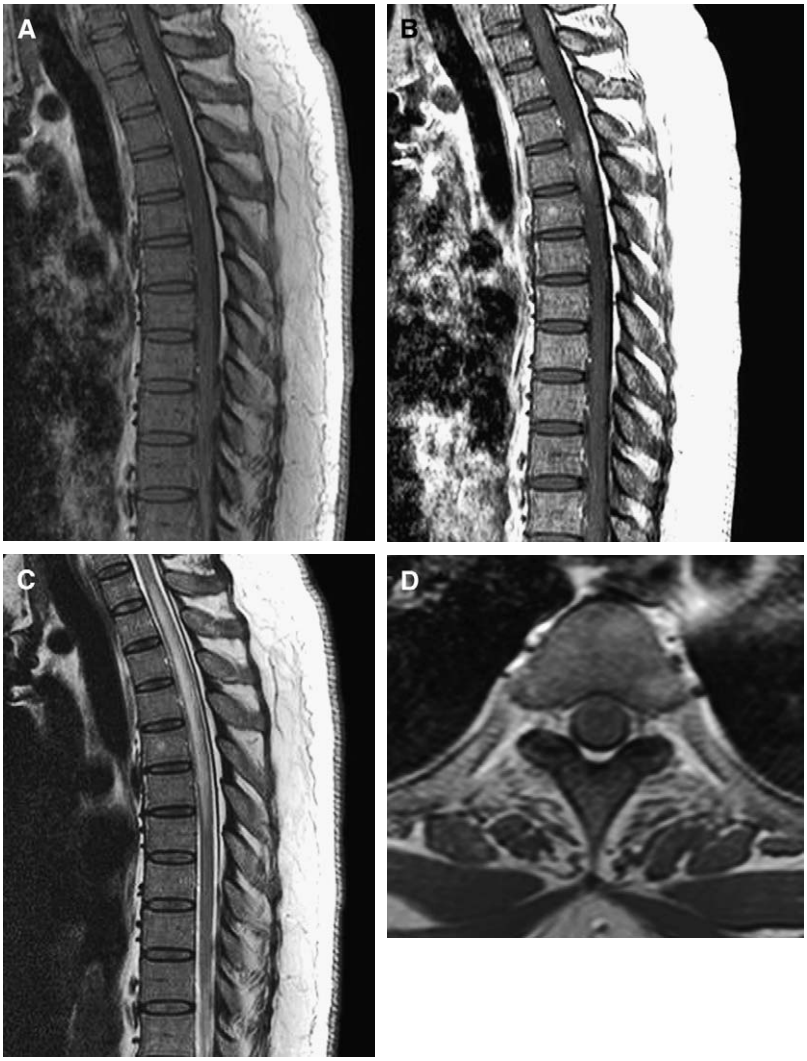

Fig. 1. Thoracic spinal astrocytoma in an adult. (*A*) Sagittal T1-weighted (T1W) image. (*B*) Sagittal T1W image with gadolinium administration. (*C*) Sagittal T2-weighted image. (*D*) Axial T1W image. (*E*) Axial T1W image with gadolinium administration.

30% of those in adults [14–18]. Astrocytomas are a heterogeneous histopathologic group, including low-grade pilocystic and fibrillary astrocytomas, intermediate grade anaplastic astrocytomas, and high-grade glioblastomas. Juvenile pilocytic astrocytomas are generally well circumscribed from the surrounding tissue, and they are typically associated with a better prognosis. These tumors are common in young children but rare in adults, who mostly present with low-grade fibrillary astrocytomas [1,19]. Anaplastic astrocytoma and glioblastoma of spinal cord are more aggressive variants [19]. Astrocytomas of the spinal cord may be associated with neurofibromatosis type 1 (NF1) [20].

Presentation

The predominance of benign histopathologic subtypes translates into a usual indolent prodromal course. Patients generally report symptoms that have been present for months to years.

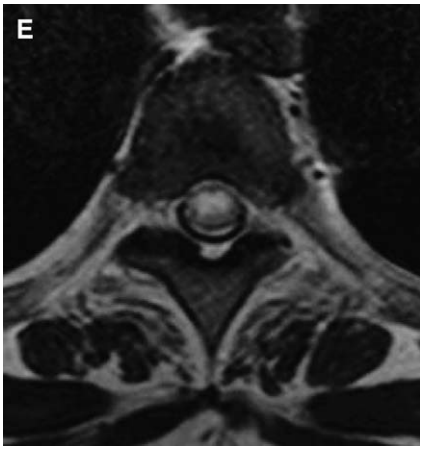

Fig. 1 (*continued*)

As would be anticipated, the rarer high-grade astrocytomas demonstrate a more rapid symptom progression. The lack of a characteristic pattern of symptoms often leads to a delay in diagnosis. With the prevalence of MRI, these tumors are now being diagnosed earlier.

Paravertebral pain is the most common symptom, although radicular pain may be experienced in some cases [11]. The ways in which an intramedullary spinal cord tumor can cause back pain are diverse and not entirely understood. Back pain may be the result of direct pressure on the surrounding dura, an innervated structure, by the expanded spinal cord. Musculoskeletal pain may be caused by derangement of the paraspinal muscle innervation. Impingement on or involvement of a nerve root may result in radicular pain. Radicular pain may mimic other etiologies; for example, thoracic pain may mimic angina, and lower thoracic roots may trigger pain similar to that of diverticulitis, cholelithiasis, or appendicitis.

Other frequent presenting complaints relate to impingement on the motor neurons or white matter tracts of the spinal cord. These symptoms include extremity weakness or clumsiness, gait difficulty, and abnormal sensory perception. Bowel, bladder, or sexual dysfunction is typically a feature of more advanced disease; however, in tumors of the conus medullaris, such dysfunction may be part of the initial symptomatology.

Sensory disturbances other than pain may consist of dysesthesias, loss of pain and temperature sense, and loss of proprioception. Centrally situated intramedullary tumors destroy the crossing segmental fibers from the spinothalamic tract,

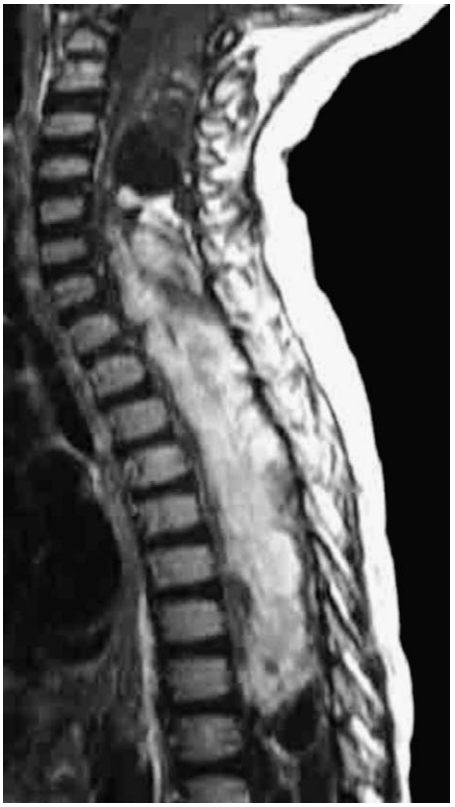

Fig. 2. Pediatric holocord tumor. Sagittal T1-weighted image with gadolinium administration. (Courtesy of G. Jallo, MD, Baltimore, MD.)

resulting in impaired pain and temperature sensation. Sacral sparing may occur, given the outermost location of the lumbosacral spinothalamic fibers. Proprioceptive impairment from dorsal column impingement or invasion may be suggested by difficulty with fine tasks, such as buttoning one's shirt or typing.

Motor deficits are a common presenting complaint. These tumors are centrally located in the spinal cord, and when they occur in the cervical region, the weakness in the upper extremities precedes that in the lower as the motor representation in the spinal cord places hand fibers medially and leg fibers laterally. In young children, in whom verbal complaints are not articulated, pain is also identified as the most common first symptom, but gait deterioration, motor regression, torticollis, and kyphoscoliosis are also significant presenting findings [18,21]. In malignant tumors presenting with symptoms of pain, rapid deterioration of motor function follows,

resulting in significant disability in 3 to 5 months [14,18].

Hydrocephalus may be present in patients with intramedullary spinal cord tumors and is most often seen in the pediatric population [22,23]. The cause of hydrocephalus may be increased protein in the cerebrospinal fluid (CSF) or from dissemination of tumor cells in the subarachnoid space. Tumors near the cervicomedullary junction may produce thickening of the leptomeninges, which results in outflow obstruction from the fourth ventricle.

Lumbar puncture rarely provides a diagnosis. Typically, CSF analysis is nonspecific, usually revealing increased protein. CSF cytology rarely yields malignant cells, even in instances in which there has been frank leptomeningeal dissemination [24].

Diagnostic imaging

Plain radiographs

Plain radiographs usually contribute little to the diagnosis of spinal cord astrocytomas in adults. In long-standing tumors, plain radiographs may reveal an enlarged spinal canal with scalloping of the vertebral bodies, medial pedicle erosion, and thinning of the laminae. In children with astrocytomas, however, neuromuscular scoliosis is common. An interesting finding in many of these patients is that the apex of the curvature is to the left rather than to the right as in idiopathic scoliosis.

MRI

MRI with and without intravenous administration of gadolinium is the imaging technique of choice for the evaluation of spinal cord tumors. MRI also allows for assessment of associated findings, such as edema, infarct, hemorrhage, cysts, syringomyelia, and cord atrophy. Evaluation for flow voids, nerve roots, and relation of tumor to avenues of safe surgical approach is invaluable in preoperative planning. Additionally, cranial imaging is an important adjunct to rule out intracranial lesions or hydrocephalus.

Astrocytomas widen the spinal cord from their mass effect and associated edema. Although sometimes difficult, MRI with and without gadolinium may distinguish between astrocytomas and intramedullary ependymomas of the spinal cord. Both lesions are isointense or hypointense to the spinal cord on T1-weighted imaging and hyperintense on T2-weighted imaging. Both enhance with contrast in spite of low histologic grade, although astrocytoma enhancement is usually more intense [25]. Ependymomas may have distinctive hemosiderin patterns at the rostral and caudal poles of the tumor, which are a result of local areas of hemorrhage. Astrocytomas of the cord are generally more infiltrative and have less well-defined margins compared with ependymomas. For either tumor, a clear tumor margin on MRI may not guarantee the presence of a surgical cleavage plane at the time of surgery.

Cysts are present in at least 40% of cases and may appear indistinguishable from solid tumors on T2-weighted studies as a consequence of the high protein content of the cyst fluid. Astrocytomas demonstrate tumor cysts more frequently, whereas ependymomas are commonly associated with reactive cysts. Contrast can help to distinguish a cyst from a tumor, because cysts do not enhance. Astrocytomas frequently appear eccentric on axial views, whereas ependymomas are almost always centrally located, consistent with their assumed origin in the ependymal lined central canal.

CT Myelography

Since the introduction of MRI, CT myelography is mainly relevant for patients in whom MRI is contraindicated because it provides limited indirect information about intramedullary spinal cord tumors. The most significant finding on CT myelography is widening of the spinal cord, although it cannot reliably distinguish between an intramedullary spinal cord tumor and other nonneoplastic causes of spinal cord swelling, such as syringomyelia. In instances in which MRI cannot be performed, delayed CT scanning can sometimes be used to demonstrate uptake of water-soluble contrast within the center of the spinal cord, typical of tumor-associated cysts and syringomyelia.

Surgical goals and preoperative patient selection

Surgery is the primary diagnostic and treatment modality because it allows for procurement of tissue for histopathologic staging and debulking or full resection of the tumor. The goals of intramedullary spinal cord tumor surgery are to obtain a tissue diagnosis and to maintain or improve neurologic function. Unlike other intramedullary tumors, astrocytomas are infiltrative

and may not demonstrate a clear plane of demarcation from the normal spinal cord. This may not be readily apparent on preoperative MRI. As a result, the risk of subtotal resection must be balanced against the risk of neurologic impairment. Patient selection and intraoperative technique are of paramount importance.

The best surgical candidates are those for whom functional independence may be prolonged by forestalling the development of severe motor deficit. Some patients with significant deficit may still benefit from surgery if sphincter function or the ability to position in bed is preserved. Patients with few medical comorbidities generally have a better postoperative course with fewer complications. Those with complete neurologic deficits or extensive tumor dissemination are not appropriate surgical candidates [26].

The decision to proceed to surgery in patients with a slowly progressive minor motor or sensory deficit is difficult, particularly if imaging studies suggest the presence of an infiltrating astrocytoma, which may not be removed without significant risk of neurologic deficit. One rational strategy in such cases is to follow the patient with serial neurologic assessments and MRI scans until there is tumor progression with functional deterioration. Some surgeons, however, take a more aggressive stance, noting that ''watchful waiting'' may occasionally allow a tumor in an individual with a potentially curable lesion to become unresectable. There is now evidence suggesting that the better the patient's preoperative clinical status is, the better is the postoperative outcome [5,27].

Intramedullary surgical techniques

Technologic advances, such as the operating microscope, intraoperative ultrasound [28], Cavitron surgical aspirator [29,30], and motor and somatosensory evoked potential monitoring [31,32], have improved the safety and effectiveness of surgery. Accordingly, patients demonstrating a solitary intraspinal mass, good neurologic function, and tumor growth are considered for early surgical intervention. Operative techniques have been well described elsewhere [1,33,34], and some salient features are summarized here.

Laminectomy is the standard approach in adults. Excessive removal of the lamina is avoided to protect against the development of spinal deformity. For children, osteoplastic laminotomy is considered if a multilevel exposure is required. Although osteoblastic laminotomies may not always prevent deformity, there is reossification of the bony segments, which can avoid the cosmetic deformity frequently seen with multilevel laminectomies [35].

The location of the tumor and any associated cysts is confirmed using ultrasound. A midline myelotomy is performed using the neodymium: yttrium-aluminum-garnet (Nd:YAG) laser [36] so as to avoid injury to the posterior columns. The myelotomy is deepened and lengthened by spreading the posterior columns using microforceps, a plated bayonet forceps [37], and the Nd:YAG laser. On gross inspection, astrocytomas often appear yellow and gray, whereas ependymomas appear red and gray. It is important to minimize retraction of surrounding neural tissue during resection. The tumor is removed piecemeal using a combination of suction aspiration and the ultrasonic aspirator. Tumor debulking and dissection are achieved by working from the inside outward. The Nd:YAG laser is sometimes helpful in removing small amounts of tumor at the margins or in tight confines. Bleeding is controlled with packing and hemostatic agents. Cautery is to be avoided at the margins of the tumor because it frequently results in injury to surrounding tissue. Tissue specimens are always sent early for frozen section analysis. If the lesion is identified as a high-grade tumor, the operation is generally curtailed, because there has been no proven benefit to surgical debulking of these aggressive tumors.

Postoperative care and adjuvant therapies

Neurologically, the patient's preoperative symptoms may be transiently or permanently worsened after surgery. For that reason, special care needs to be taken during the initial phase of recovery. Transient neurologic changes have been attributed to changes in spinal microcirculation, ischemia, and postoperative edema, which peaks within 48 hours.

For low- to intermediate-grade spinal astrocytomas, there have been minimal improvements in the long-term survival of patients directly attributed to adjuvant therapy. In fact, the spinal cord has a lower tolerance for irradiation. Some studies have shown that postoperative radiation therapy improves survival and recurrence rates [10,38]. There is disagreement, however, on whether it should be used if gross total resection is achieved because it may complicate reoperation for

recurrence [14]. Given the significant advances in surgery of intramedullary tumors, second surgery has become a viable option. Indications for second surgery have included (1) delayed recurrent growth in the solid or cystic component of the tumor, resulting in new symptoms, and (2) early re-exploration after the original subtotal resection was halted prematurely because of transient intraoperative injury confirmed by monitoring. The goal of these reoperations is identical to that of the first operation (ie, sufficient debulking of the tumor so as to lessen symptoms without causing progression in neurologic deficits). It has not been established whether there is any role for chemotherapy in the treatment of spinal cord astrocytomas [39]. High-grade spinal astrocytomas cannot be fully resected. As a result, adjuvant therapies, such as spinal irradiation [40] and chemotherapy [41], for high-grade tumors have been attempted without significant clinical improvement.

Outcome

The outcome for intramedullary spinal cord astrocytoma is significantly worse than that for ependymoma and is predicted by pathologic grade. Low-grade tumors (WHO grades I and II) may recur and result in death. Sandler and colleagues [42] report a 5-year survival of 57% in a series of 21 patients, of whom 18 had a pathologic grade of I or II, and Cooper [15] presented a series of 11 patients with grade I or II astrocytomas, of whom 4 of 11 died within the follow-up period and only 4 were not neurologically worse in functional grade. In addition, we have seen tumors nitially found on pathologic examination as low-grade astrocytomas that have progressed to higher grade tumors.

Younger age is a positive prognostic factor; Sandler and colleagues [42] found that younger patients had a substantially increased length of time to recurrence. This observation may be related to the fact that low-grade tumors in pediatric patients are usually the pilocytic histologic subtype, which has a more favorable prognosis [10].

Although numerous studies have attempted to assess the likelihood of recurrence with respect to extent of tumor resection, a convincing relation has yet to be demonstrated [10,42–45]. Postoperative MRI is necessary to determine objectively any residual tumor. The absence of an enhancing tumor does not always ensure complete resection, especially with regard to high-grade lesions.

Preoperative neurologic function is the best prognostic indicator for functional outcome [17,45]. In the immediate postoperative period, transient neurologic deterioration from the preoperative baseline is typically seen [14,43]. Recovery generally occurs over a period of days to months, with improvement in sensory loss earlier than improvement in motor deficits. Those with severe long-standing neurologic deficits, however, are unlikely to have any improvement.

The prognosis of high-grade astrocytomas is extremely poor, with disease progression, widespread leptomeningeal dissemination, and hydrocephalus frequently seen [46]. Improvement of neurologic function as a result of surgery is unlikely [14]. Previous reports of survival after surgery averaged 6 months in adults and 13 months in children [46,47]. The immediate cause of death is typically pulmonary embolus and pneumonia or respiratory failure from direct tumor extension into the cervicomedullary region.

Summary

Although advances in imaging and surgical instrumentation have improved the diagnosis and management of intramedullary spinal cord astrocytomas, they remain a great challenge to the clinician. Generally, these are infiltrating tumors that cannot be entirely resected. The pilocytic subtype, however, is similar to those astrocytomas occurring in the posterior fossa in that they usually occur in the pediatric age group, may be resected, and have a favorable prognosis. MRI with and without contrast is the imaging modality of choice. The functional outcome of surgery correlates well with the preoperative condition. The surgical objective is resection to the extent possible so as to allow preservation of function. Outcome correlates with histologic grade. Patients with low-grade astrocytomas have a worse prognosis that those with ependymomas. As is the case for intracranial astrocytomas, the outcome for high-grade astrocytomas is extremely poor.

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