Spinal cord astrocytoma: pathological and treatment considerations

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Seventy-nine patients underwent surgery, with or without radiation therapy, for astrocytoma of the spinal cord. There were 43 tumors (54%) classified as pilocytic astrocytoma and 25 (32%) as diffuse fibrillary astrocytoma. Eleven tumors (14%) could not be classified other than as astrocytoma, “type not otherwise specified.” The 10-year overall survival rate for all 79 patients was 50% but significantly differed by histological type: 81% for patients with pilocytic astrocytoma compared to 15% for those with diffuse fibrillary astrocytoma. Tumor grade by the Kernohan, et al., or St. Anne–Mayo methods was also a significant predictor of survival in patients with diffuse fibrillary astrocytoma. The extent of surgical resection (biopsy vs. subtotal resection vs. gross total resection) did not significantly impact survival among patients with pilocytic or nonpilocytic astrocytomas of the spinal cord, although there was a trend toward poorer survival in patients undergoing some degree of resection as opposed to biopsy. Postoperative radiation therapy improved survival but did so more for diffuse fibrillary astrocytoma than pilocytic astrocytoma.

In this series, histological type was the most significant predictor of survival in patients with astrocytoma of the spinal cord. The survival rate was highest in patients who underwent biopsy followed by postoperative radiation therapy.

Key Words • spinal cord • astrocytoma • pilocytic astrocytoma • resection • radiation therapy

Intramedullary spinal cord astrocytomas represent only 6% to 8% of spinal cord tumors.2,17 Relatively little data exist on the pathological diagnosis, biological behavior, prognostic factors, and treatment results for these tumors. Existing clinicopathological series have failed to distinguish pilocytic from nonpilocytic (that is, diffuse fibrillary) spinal cord astrocytomas, which is so important in the case of intracranial astrocytomas.9,20 Other important and presently unsettled issues include the impact of the extent of surgical resection on local control and survival,3,7,8 and the value of postoperative radiation therapy.1,6,10,14,16,21 This review consists of a detailed analysis of 79 patients with histologically confirmed and characterized astrocytic spinal cord tumors.

Clinical Material and Methods

Between the years 1958 and 1988, 92 patients were pathologically diagnosed with spinal cord astrocytoma at the Mayo Clinic. After careful review of the histological specimens, 13 patients were excluded because the diagnosis could not be confirmed. Of the 13 patients excluded, five patients were found to have a ganglioglioma, two gliotic cyst, two ependymoma, one subependymoma, one pineal parenchymal tumor, one hemangiopericytoma, and one an oligodendroglioma. The remaining 79 patients form the basis of this review.

During the 30-year study period, no uniform policy was in place regarding preoperative diagnostic workup and postoperative treatment. A detailed neurological history and examination were completed on each patient. Similarly, all patients underwent myelography. Twenty-one also underwent computerized tomography. The extent of surgery included incisional biopsy in 55 (70%) patients, subtotal resection in 20 (25%), and gross total resection in only four (5%). Of the 79 patients, three (4%) died within 1 month of surgery as a result of postoperative complications.

Of the 79 patients under study, 64 (81%) received postoperative radiation therapy. The total radiation dose, calculated at cord depth, ranged from 1310 to 6660 cGy (median 4984 cGy). Dose per fraction ranged from 144 to 250 cGy (median 180 cGy). The most common radiation treatment field arrangement was that of a single posterior field encompassing the area of the tumor with a two-vertebral body margin above and below the tumor. Only 11 patients were treated with multiple fields, usually a posterior field in combination with opposed lateral fields.
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Fifteen patients did not receive radiation therapy, eight because it was not advised by the surgeon or radiotherapist, usually in patients who underwent gross total resection; four because of poor neurological condition; and three who did not survive postoperatively.

Pathological Review

All surgical specimens were promptly fixed in 10% neutral buffered formalin, routinely processed for light microscopy, and stained with hematoxylin and eosin. Microsections were reviewed by a single pathologist who was unaware of the patient’s clinical outcome. All specimens were histologically classified into the two principal subtypes, pilocytic astrocytoma and diffuse fibrillary astrocytoma. A “not otherwise specified” (NOS) designation was applied in a minority of cases, usually ones in which a small specimen permitted the diagnosis of a low-grade astrocytic neoplasm but precluded its further classification. All tumors were graded according to the scale of Kernohan, et al., which, as originally devised and historically applied by Kernohan, et al., did not distinguish between histological subtypes of astrocytoma. The St. Anne–Mayo grading method was applied to diffuse fibrillary astrocytomas because the clear definition of its four parameters (presence or absence of nuclear atypia, mitoses, endothelial proliferation, and necrosis) permits simple, reproducible specimen assessment. Furthermore, its elements form the basis of the present World Health Organization scheme. General histological features included tumor cellularity, nuclear atypia, nuclear pseudo-inclusions, multinucleation, rosette arrangement of nuclei, mitoses, glomeruloid vessels, hyalinized vessels, endothelial proliferation, necrosis, Rosenthal fibers, granular bodies (protein droplets), microcysts, macrocysts, calcification, hemosiderin deposition, inflammation, gliosis, and infiltration of brain parenchyma.

The following nonpathological patient characteristics were also analyzed: sex, age, preoperative symptoms (including neurological deficit), symptom duration, presence of neurofibromatosis, tumor location, number of vertebral segments involved, myelographic findings, extent of surgery, radiation dose, and length of radiation field. Patient follow-up information was obtained through a review of patient histories, correspondence with the local physician(s), and by direct telephone contact with patients. For living patients, the median follow-up time was 6.3 years (range 1 month to 24 years). Actuarial survival was calculated from the date of tissue diagnosis. Survival analyses used the method of Kaplan and Meier. Potentially significant survival differences were assessed utilizing the Wilcoxon test. There were too few patients and events to perform a multivariate analysis.

Results

Patient Characteristics

Table 1 outlines the patient characteristics according to histological tumor type. There were 43 pilocytic astrocytomas (54%), 25 diffuse fibrillary astrocytomas (32%), and 11 astrocytic tumors (14%) of the NOS type. Several differences were observed between patients with pilocytic and diffuse fibrillary tumors. The latter were more common than pilocytic or NOS types only in patients younger than 20 years of age. Patients with diffuse fibrillary tumors exhibited a distinct sex predilection, with a 3:1 ratio of males to females. The duration of symptoms prior to tissue diagnosis ranged from 1 day to 126 months (median 8 months). Symptom durations of less than 60 days were more common in diffuse fibrillary tumors (28%) than in the case of pilocytic astrocytomas (12%). The most common symptom at diagnosis was motor deficit, which occurred in 87% of patients. Other common signs and symptoms included pain, radiculopathy, sensory deficit, and bladder or bowel incontinence. Only the incidence of radiculopathy differed significantly between the groups, occurring with more than twice the frequency in diffuse fibrillary tumors (76%) as in pilocytic astrocytoma (28%). Neurofibromatosis was present in one patient who had a pilocytic astrocytoma.

No differences were observed when comparing tumor location with histology. All but one lesion involved either cervical and/or thoracic levels. Seven percent of cervical or thoracic tumors extended into the thoracic or lumbar cord, respectively. Most tumors spanned fewer than four
vertebral segments. Pilocytic astrocytomas were the most likely to extend four segments or more.

Pathological Characteristics

A summary of the histopathological findings is presented in Table 2. As previously noted, there were 43 pilocytic (54%), 25 diffuse fibrillary (32%), and 11 astrocytomas of the NOS type (14%). The majority (89%) of specimens were classified as low grade according to the Kernohan method. None of the diffuse fibrillary tumors was considered Grade 1 in either grading system, whereas approximately one-third of these tumors were considered high grade according to the Kernohan method and one-half on the basis of the St. Anne–Mayo method. Histological features that were significantly more common in pilocytic astrocytomas included +1 atypia, nuclear inclusions, Rosenthal fibers, granular bodies, glomeruloid vessels, hyalinized vessels, and hemosiderin deposition. Features significantly more characteristic of diffuse fibrillary spinal cord astrocytomas were +3 to +4 cellularity, +2 to +3 atypia, absence of Rosenthal fibers, mitoses, necrosis, and parenchymal infiltration.

Treatment by Histological Type

There were no significant differences between the histological subtypes with regard to the extent of surgery performed or total dose of radiation administered (Table 3).

Survival Rates

The survival rate for all 79 patients with spinal cord astrocytoma was 55% at 5 years and 50% at 10 years (Fig. 1). Patients with pilocytic tumors had significantly improved survival rates compared to those with diffuse fibrillary tumors. Both the 5- and 10-year survival rates were 81% for patients with pilocytic astrocytoma versus 15% for those with diffuse fibrillary tumors (Fig. 2). The patients with tumors not amenable to histological subtyp-
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Ing (type NOS) had survival rates that were better than those with diffuse fibrillary tumors (Fig. 2), although the difference was not statistically significant. Survival rates by grade and histological type are shown in Fig. 3. The Kernohan grading system (Fig. 3 left) was used to separate survival differences between pilocytic tumors of Grades 1 and 2, because of variation in cellularity and nuclear atypia. The St. Anne–Mayo grading method (Fig. 3 right) better distinguished lower-grade (1 + 2) from higher-grade (3 + 4) nonpilocytic tumors than the Kernohan system.

Prognostic Factors

Patient characteristics found to be prognostic for increased survival by univariate analysis included ages greater than 20 years at diagnosis, a greater than 180-day time interval from first symptoms to diagnosis, and lesion location in the thoracic spinal cord. Improved survival rate in patients with thoracic tumors was independent of histology, because no difference in the incidence of the three histological subtypes was observed among thoracic tumors. None of the patient characteristics was of prognostic significance for decreased survival.

Pathological characteristics found to be prognostically important and associated with increased survival by univariate analysis were pilocytic histology, Kernohan Grade 1, low (+1) cellularity, lack of nuclear atypia, presence of Rosenthal fibers, and presence of hyalinized vessels. Only seven histological specimens classified as pilocytic astrocytoma on the basis of cytology and histological pattern did not exhibit Rosenthal fibers. These seven patients had a 5-year survival rate of 45% compared to 85% for the 36 patients with Rosenthal fiber–containing pilocytic tumors (p < 0.001).

Treatment Results

The extent of tumor resection did not have an impact on patient survival (Fig. 4). Indeed, there was a trend toward poorer survival in patients who underwent more aggressive resection compared to those who underwent biopsy alone (p = 0.081).

Patients who did not receive radiation therapy had poorer survival rates than patients who did (Fig. 5). Although this difference was apparent among patients with both pilocytic and diffuse fibrillary tumors, it was only statistically significant in the case of nonpilocytic tumors. Radiation dose in cGray (≥ 5000 compared to < 5000) did not result in increased survival.

Discussion

This review provides new information regarding patient and pathological characteristics, prognostic factors, and treatment results for patients with astrocytic tumors of the spinal cord. In our series, such tumors most commonly occurred when the patient was in middle age, had a 1.3:1 male sex predilection, occurred with equal frequency in the thoracic and cervical spinal cord, usually involved fewer than four vertebral segments, and most often pro-
duced signs and symptoms consisting of pain, radiculopathy, sensory or motor deficits, and incontinence. These findings are consistent with those of Rossitch and colleagues who reviewed 12 children with spinal cord astrocytomas.

Arriving at a specific pathological diagnosis of spinal cord lesions is fraught with difficulty, because lesion biopsies are often small and exhibit frozen section artifacts. It can be difficult, for example, to distinguish an astrocytoma from a gliotic syrinx, the cavity surrounding a hemangioblastoma, an ependymoma with predominantly glial features, or even demyelinating disease. Only patients whose lesions were clearly neoplastic and astrocytic in nature were included in the present study. Such tumors were subclassified into pilocytic, diffuse fibrillary, and NOS types, their ratio being approximately 3:2:1, respectively. Pilocytic tumors were associated with significantly improved survival rates; this observation is similar to those in our previously published experience with cerebellar astrocytic tumors, and that of Hulshof, et al., with spongioblastomas of the spinal cord. When the specimen could not be specifically subclassified, the lesion was assigned to the NOS category. The prognosis of patients with such tumors was more closely correlated with that of diffuse fibrillary astrocytoma than pilocytic astrocytoma (Fig. 2).

Not only did more aggressive resection not improve patient survival rates, it was associated with a somewhat less favorable outcome, although not a statistically significant one (Fig. 4). Whereas other investigators have advocated aggressive surgical management, our review does not support the use of extensive surgery. It must be stated, however, that the majority of the patients in the present analysis were operated on prior to the development of the ultrasonic surgical aspirator, intraoperative electromyographic monitoring, and the development of neurosurgical techniques that permit more effective resection of intramedullary tumors. It remains to be seen whether magnetic resonance imaging definition of tumor extent and newer monitoring methods will materially change survival and postoperative outcome in this subset of patients. Furthermore, more modern studies will be required to determine more definitively the role of aggressive surgery.

The use of postoperative radiation therapy for patients with intramedullary spinal cord tumors has been considered the standard of care. This review supports the continued use of radiation therapy for astrocytic spinal cord tumors. Survival was better among patients with all histological subtypes of astrocytoma who underwent radiation treatment and was significantly improved for those with nonpilocytic astrocytoma. It is of note, however, that in the present study, the outcomes of patients who did not receive radiation therapy were negatively biased, as four of 12 postoperative survivors did not receive radiation therapy because of their poor neurological condition. Nonetheless, our results are consistent with those of Rauhut and colleagues, who reviewed 10 cases of Grade 1 spinal cord astrocytoma that received neutron irradiation. Lack of a correlation between increasing radiation dose and improved patient survival was noted in our study as well as several other published series.

Conclusions

Tumor subtype and histological grade are the most important prognostic factors in spinal cord astrocytomas. There are two major groups, those with the prognostically favorable pilocytic tumors and those with the less favorable diffuse fibrillary tumors. Both the Kernohan and St. Anne–Mayo grading systems separate patients with diffuse fibrillary astrocytomas into histologically low- and high-grade populations that differ significantly in terms of survival. Although it is not standard practice to grade pilocytic astrocytoma, the Kernohan grading method was originally applied to such tumors and can be used to distinguish between tumors that are most and least prognostically favorable types. More aggressive surgical removal does not appear to be associated with improved survival of patients with spinal cord astrocytomas of both pilocytic and nonpilocytic types, whereas the addition of postoperative radiation therapy results in a modest increase in survival. Further studies of spinal cord astrocytomas, again separating patients on the basis of histological tumor subtype, pilocytic versus nonpilocytic, are still needed to address the issue of extent of resection and its effect on prognosis.

References


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