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Clinical Investigation: Pediatric

Management of Pediatric Spinal Cord Astrocytomas: Outcomes With Adjuvant Radiation

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Summary

Primary pediatric spinal cord astrocytomas vary widely in presentation and clinical course. This study reports the outcomes in pediatric patients with spinal cord astrocytomas treated at a tertiary care center. Patients with low-grade tumors experienced excellent disease control and long-term survival compared to those with high-grade tumors. This report suggests that the judicious application of radiation therapy in this sensitive patient population may enhance tumor control with an acceptably low risk of long-term sequelae.

Purpose: Pediatric intramedullary spinal cord tumors are exceedingly rare; in the United States, 100 to 200 cases are recognized annually, of these, most are astrocytomas. The purpose of this study is to report the outcomes in pediatric patients with spinal cord astrocytomas treated at a tertiary care center.

Methods and Materials: An institutional review board-approved retrospective single-institution study was performed for pediatric patients with spinal cord astrocytomas treated at our hospital from 1990 to 2010. The patients were evaluated on the extent of resection, progression-free survival (PFS), and development of radiation-related toxicities. Kaplan-Meier curves and multivariate regression model methods were used for analysis.

Results: Twenty-nine patients were included in the study, 24 with grade 1 or 2 (low-grade) tumors and 5 with grade 3 or 4 (high-grade) tumors. The median follow-up time was 55 months (range, 1-215 months) for patients with low-grade tumors and 17 months (range, 10-52 months) for those with high-grade tumors. Thirteen patients in the cohort received chemotherapy. All patients underwent at least 1 surgical resection. Twelve patients received radiation therapy to a median radiation dose of 47.5 Gy (range, 28.6-54.0 Gy). Fifteen patients with low-grade tumors and 1 patient with a high-grade tumor exhibited stable disease at the last follow-up visit. Acute toxicities of radiation therapy were low grade, whereas long-term sequelae were infrequent and manageable when they arose. All patients with low-grade tumors were alive at the last follow-up visit, compared with 1 patient with a high-grade tumor.

Conclusion: Primary pediatric spinal cord astrocytomas vary widely in presentation and clinical course. Histopathologic grade remains a major prognostic factor. Patients with low-grade tumors tend to have excellent disease control and long-term survival compared to those with high-grade tumors. This experience suggests that radiation therapy may enhance tumor control with an acceptably low risk of long-term sequelae in this sensitive patient population.

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Introduction

Pediatric intramedullary spinal cord tumors are rare, with only 100 to 200 cases recognized annually in the United States (1). Of these, low-grade astrocytomas and other primary glial neoplasms account for the majority (2-4). In the pediatric population, the majority of spinal cord astrocytomas are low grade (5).

The presenting symptoms of intramedullary spinal cord tumors generally arise slowly and progress insidiously. They can be general or localized and may include pain, paresthesia, weakness, spinal deformity, motor regression, incontinence, and torticollis (6).

Interventions for spinal cord astrocytomas include surgery, radiation, and chemotherapy. Although surgery is the cornerstone of pediatric spinal cord astrocytoma management, the benefit of gross total resection (GTR) for low-grade astrocytomas is not clear, and higher-grade tumors are more infiltrative; therefore, a GTR is difficult to obtain (7). Radiation alters the disease course, yet is often deferred or avoided because of concerns about long-term sequelae for the pediatric patient (8). Although published reports about the use of chemotherapy are limited, it may emerge as an alternative or adjunct to surgery in an effort to delay radiation therapy (RT) in children to minimize late sequelae (7, 9).

The purpose of this study is to report the outcomes in pediatric patients with spinal cord astrocytomas treated at our institution.

Methods and Materials

An institutional review board-approved retrospective single-institution study was performed for pediatric patients with spinal cord astrocytomas treated at our institution from 1990 to 2010 identified from a pathology database. The inclusion criteria included age <25 years at diagnosis, intramedullary spinal cord tumor, and a tissue diagnosis of astrocytoma. All pathology reports were re-reviewed at our institution if they had been obtained from an outside institution. All World Health Organization (WHO) grades (1-4) were included and categorized as low (WHO 1-2) or high (WHO 3-4) grade.

The extent of surgical resection was determined by analysis of the operative report and postoperative radiographic imaging. GTR was defined as 90% resection or no visible tumor remaining at the end of surgery. Subtotal resection (STR) was defined as 50% to 90% resection, partial resection (PR) was defined as <50% resection, and biopsy was defined as a very limited resection intended only to reveal a histopathologic diagnosis.

Progression-free survival (PFS) was defined as the time elapsed from diagnosis to progression or recurrence. Disease control was defined as the lack of radiologic or clinical progression or recurrence at the most recent record. Patient records were assessed for the development of radiation-related toxicities. Adverse events were evaluated by the Common Terminology Criteria for Adverse Events, version 3.0 (10).

Overall survival and PFS were estimated by the Kaplan-Meier product limit method. Observations were censored at the last follow-up visit in the absence of progression or death. PFS was stratified by various covariates and compared with a log-rank test. The Cox proportional hazards method was applied to identify predictors of PFS (11). An initial model was created by adjustment for age, sex, grade, chemotherapy, radiation, and degree of resection. A final parsimonious model was generated by use of backward selection, removing 1 variable at each step and comparing the nested models using the likelihood ratio test and Akaike information criterion (12, 13). The reported P values in the results are 2-sided and considered significant when <.05. All analysis was performed with Stata Statistical Software: Release 9 and IBM SPSS Statistics, version 20 (14, 15).

Results

Demographics

There were 29 patients identified for the study. The demographic and treatment characteristics are shown in Table 1. Twenty-four patients had low-grade tumors, and 5 had high-grade tumors (including 1 glioblastoma [GBM]). Of the 29 astrocytomas, 9 were cervical, 7 were cervicothoracic, 11 were thoracic, and 2 were holocord. The median age at diagnosis was 7.1 years (range, 1.3-21.2 years). The median follow-up time was 52 months (range, 1-215 months). Patients with low-grade tumors had a longer median follow-up time of 55 months (range, 1-215 months) compared with high-grade tumor patients, who had a median follow-up of 17 months (range, 10-52 months).

Pain was the most common presenting symptom, affecting 12 patients. Other prominent symptoms included weakness in 9 patients, headache in 3 patients, and urinary incontinence, torticollis, or paresthesia in 2 patients. There were 3 patients who had leptomeningeal involvement, 2 at presentation and 1 at recurrence. There were 6 patients who experienced intracranial involvement, 2 at presentation and 4 at recurrence.

Surgery, chemotherapy, and radiation therapy

All patients underwent surgical intervention at initial presentation. Fifteen patients had GTR, 4 had STR, and 9 received PR or

Table 1 Patient demographics

Characteristic	n	%
Sex		
F	9	31.0
M	20	69.0
Pathology		
Low-grade	24	82.8
AA	4	13.8
GBM	1	3.4
Surgery		
PR/biopsy	9	31.0
STR	4	13.8
GTR	15	51.7
Unknown	1	3.4
Radiation therapy		
None	15	51.7
Focal	8	27.6
CSI	2	6.9
Unknown	2	6.9
Chemotherapy		
Received	13	44.8

Abbreviations: AA = anaplastic astrocytoma; CSI = craniospinal irradiation; GBM = glioblastoma multiforme; GTR = gross total resection; PR = partial resection; STR = subtotal resection.