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Outcome of children with primary intramedullary spinal cord tumors*

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Abstract. The influence of clinical and treatment factors on the outcome of children with primary intramedullary spinal cord tumors (PST) was evaluated by reviewing the records of 26 children diagnosed during the 15-year period 1970–1984. Five-year survival was 39%, but 5-year event-free survival (EFS) was only 14%. Eighteen-month EFS was 53% (9/17) among children with low-grade astrocytoma, 100% (2/2) with ependymoma, and 0 of 7 with anaplastic astrocytoma or ganglioglioma. There was no significant difference in the 18-month EFS by location of tumor, duration of symptoms, or extent of surgical removal. Five of 9 children with locally recurrent PST had a second operation, and 4 were alive a median of 56 months later. PST disseminated to the leptomeninges or the III ventricle in 5 children: 2 at diagnosis, 2 as the first sign of disease relapse, and 1 after local recurrence. Given the poor outcome of our children, different methods of treatment for children with tumors in this location should be evaluated.

Key words: Spinal cord neoplasms – Children – Outcome.

Primary intramedullary spinal cord tumors (PST) account for approximately 5% of central nervous system tumors in children [1, 11]. The conventional approach to therapy is biopsy or partial resection of the tumor, followed by radiation therapy (RT) of the tumor site [6, 7]. Recently it was reported that gross total removal of extensively infiltrating PST may result in a higher rate of event-free survival [2, 3, 5]. Postoperative RT after gross total removal of PST is thought possibly to improve outcome [8]. However, the duration and rate of response of patients treated more conventionally has not been well documented.

We reviewed records of 26 children with PST who were diagnosed and treated either at the Children's Hospital of Philadelphia or at another hospital in the Greater Delaware Valley. Data were analyzed to evaluate response to therapy. Other factors such as duration of symptoms prior to diagnosis, microscopic diagnosis, and extent of surgical resection were also analyzed to evaluate their effect on outcome.

Materials and methods

Records of the Greater Delaware Valley Pediatric Tumor Registry and of the Division of Neurosurgery of The Children's Hospital of Philadelphia (CHOP) were reviewed to ascertain all children under 20 years of age living in the 31-county region of Philadelphia who had a diagnosis of PST during 1970 through 1984. Twenty-six children were identified, all of whom had surgery and a biopsy-proven tumor. We excluded 56 children with other types of primary spinal tumors: lipoma (50), epidermoid cyst (3), and hamartoma (3). Hospital medical records were reviewed, and all available surgical and autopsy specimens were reviewed microscopically to confirm the diagnosis.

Survival was calculated by subtracting the date of initial surgery for tumor from the date of last encounter, which was no later than 31 December 1985. *Event-free survival* was defined as survival without radiographic, cytologic or clinical evidence of relapse. *Clinical relapse* or *recurrence* was defined as worsening or deterioration of clinical status in the absence of other explanations such as sepsis or scoliosis.

Results

The average age at diagnosis of the 26 children was 9 years and 6 months (range: 1 year and 2 months to 19 years and 7 months). Sixteen patients (62%) were male and 10 (38%) female. Fifteen children were diagnosed between 1970–1979, accounting for 3% of the 446 children who were diagnosed with central nervous system (CNS) tumors during that same period [9]. Based on the 1970 census population of children under 15 years old in the Greater Delaware Valley, the annual incidence of PST is 7 per 10 million.

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Preoperative course

Pain was the initial symptom in 11 (42%) children. The most frequent location of pain was the back (6), but it also was located in the head (2), neck (1), extremity (1), or abdomen (1). Five children (19%) had weakness of one extremity; 8 (31%) had weakness of more than one extremity; 2 (8%) had unilateral numbness. Two children initially complained of both pain and weakness. Six (27%) of the 22 children with only pain or only weakness developed the combination of both symptoms 1 month to 10 years later. Vomiting, cranial nerve paresis, or urinary incontinence were noted later in the course of 10 (39%) children.

The clinical diagnosis was correct for 17 children (65%). Among the other 9 (35%) mistaken diagnoses included 2 for cerebral palsy: 1 each for muscular dystrophy, Guillain-Barré syndrome, brachial plexus neuropathy, scoliosis, and hydrocephalus; 2 for syringomyelia syndrome associated with either scoliosis or an abnormally low position of the IV ventricle (Chiari type II malformation).

Radiographic diagnosis

Spine radiographs were available for 13 children: 7 had widened spinal canal; 3 had scoliosis; 3 children had normal results. Myelogram in 23 children disclosed spinal cord enlargement or blockage of the spinal canal in each case. Computed tomography of the head (HCT) showed a posterior fossa mass in 3 children who did not have a myelogram, 1 of whom was confirmed to have cervicomedullary tumor by magnetic resonance imaging.

Postoperative course

Surgery was performed in all 26 children (Table 1). Seventeen patients (65%) had low-grade astrocytoma; 6 (23%) had anaplastic astrocytoma; 2 (8%) had ependymoma; 1 (4%) had ganglioglioma. Local RT was given to 21 (81%) children, the doses ranging from 2,000 to 5,580 rad (mean 4,455 rad). An 8-cycle course of vincristine chemotherapy was administered after RT to the child with ganglioglioma.

Table 1. Initial treatment of 26 children with PST

Category	Number (%)
Extent of surgical removal	
Biopsy	17 (65)
Partial	5 (19)
Subtotal	3 (12)
Gross total	1 (4)
Postoperative therapy	
Radiation therapy	20 (77)
Chemotherapy and RT	1 (4)
Neither RT nor chemotherapy	5 (19)

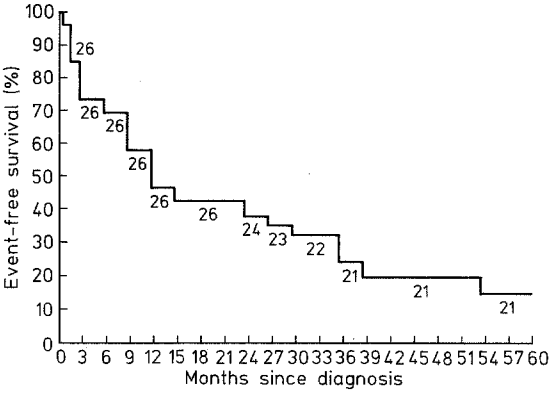

Fig. 1. Event-free survival among 26 children with primary intramedullary spinal cord tumor. The *number under the bar* indicates the number followed during each interval

Outcome

All 26 children survived at least 1 month after diagnosis. Fourteen are still alive and have been followed from 1 to 14 years (median 4 years and 8 months). Eight have been in continuous remission from 24 to 174 months after diagnosis, and 6 are alive after relapse from 4 months to 6 years after diagnosis. Twelve children died of progressive tumor growth, confirmed in the 5 who had a necropsy. Seven of the children who died were never in remission; 3 had a relapse 1–6 years after remission; and 2 died 12 and 13 months, respectively, after developing disseminated tumor.

Five-year survival is 39% (7/18) for the total group. However, 5-year event-free survival (EFS) (Fig. 1) is only 14% (3/21). Eighteen-month EFS in the total group is 42% (11/26): 53% (9/17) among children with low-grade astrocytoma, 100% (2/2) with ependymoma, and 0% (0/7) with anaplastic astrocytoma or ganglioglioma. Neither the location of tumor nor the duration of symptoms before surgery bears a significant relationship to survival. Moreover, extent of surgical resection has no relationship to outcome as 18-month EFS was 41% among 17 children with only biopsy and 38% among 8 with partial or subtotal removal. One child with gross total removal had a relapse 12 months later.

Initial therapy of five children did not include RT: two with anaplastic astrocytoma died without remission 3 and 10 months, respectively, after diagnosis; two with low-grade astrocytoma developed locally recurrent disease after 12 and 15 months, respectively; one with low-grade astrocytoma developed disseminated tumor 11 months after diagnosis.

There was remission of symptoms in 19 children, but 9 (47%) then had local recurrence. Six children with low-grade astrocytoma had local recurrence 4–39 months (median 13) after diagnosis. Two children with ependymoma had local relapse after 42 and 75 months, respectively. One child with ganglioglioma had local recurrence 13 months after remission.

Table 2. Treatment of 12 children with recurrent PST

Extent of relapse	Number				Total group (months survival)	
	Total	Surgery	RT	Chemotherapy[a]	Range	Median
Local	9[b]	5	1	1	1–161	37
Disseminated	2	0	2	2	10– 11	10

[a] Vincristine (3), chloroethylcyclohexylnitrosourea (2), and methotrexate (1)
[b] Three had a second relapse: two local and one disseminated

Tumor disseminated to the leptomeninges or the III ventricle in five patients: three with low-grade astrocytoma and two with anaplastic astrocytoma. Two patients, one with low-grade astrocytoma and one with anaplastic astrocytoma, had disseminated tumor at the time of diagnosis. The child with low-grade astrocytoma received RT, but both died within 3 months. Two children developed dissemination as the first sign of disease relapse. The fifth child had low-grade astrocytoma, which disseminated 6 months after local relapse and surgery.

Treatment after relapse

Five of nine children with local relapse (three with low-grade astrocytoma and two with ependymoma) had a second operation: one had biopsy; three had partial removal (one followed by chemotherapy); one had subtotal removal followed by RT (Table 2). Four were alive a median of 56 months (range 19–161) later, but one died 10 months after the second operation. The second biopsy in one child with low-grade astrocytoma disclosed a ganglioglioma; in another with ependymoma the second biopsy appeared to be an oligodendroglioma. Each of the three children with low-grade astrocytoma had a second relapse: one had biopsy of a locally recurrent low-grade astrocytoma and died during RT; another had gross total resection of locally recurrent astrocytoma and is alive 107 months later; the third had disseminated tumor, was given chemotherapy, and relapsed a third time after 32 months.

Two children had disseminated tumor at relapse; both were given RT and chemotherapy. One of these two had anaplastic astrocytoma and died 11 months later; the other had a low-grade astrocytoma and died 10 months later.

Four children were not treated after local relapse: two with low-grade astrocytoma died 2 and 76 months later, respectively; one with low-grade astrocytoma is alive after 6 months; one with ganglioglioma is alive 84 months after relapse.

Discussion

The annual incidence of PST among children is approximately one per million, and PST accounts for 3% of childhood central nervous system tumors. Overall 5-year survival is 39% in our series, which is less than the 69% survival among children with all grades of astrocytomas reported by Reimer and Onofrio [10]. This Mayo Clinic series and our series include children with tumors that relapsed even after 5 years of survival. Event-free survival among children with this rare tumor is discouragingly low, and EFS does not show a plateau of survival. In our series only 14% enjoy a 5-year EFS. Eighteen-month EFS is higher among the children with low-grade astrocytoma or ependymoma than among children with anaplastic astrocytoma; however, the two children with ependymoma had recurrence after several years of remission. Eighteen-month EFS is independent of the extent of surgical removal, duration of initial symptoms, or the location of tumor. Since the majority of patients in our series received RT, we can draw no conclusion regarding its efficacy; however, those few patients not irradiated relapsed within 15 months after diagnosis. Repeated surgery may prolong survival among children who have recurrent low-grade astrocytoma or ependymoma. Four of five children who had a second operation after local relapse are alive one or more years later; one child who relapsed a second time had gross total removal and is alive 8 years later.

Intramedullary astrocytoma, whether low grade or anaplastic, may be disseminated throughout the leptomeninges or intraventricularly at diagnosis or as the first sign of disease relapse. Dissemination of low-grade astrocytoma arising in the cerebrum, cerebellum, or brain stem is exceptionally uncommon; it would be peculiar indeed if those arising in the spinal cord displayed a different biological behavior. It is possible that those children who on biopsy were thought to have a low-grade astrocytoma actually had a more anaplastic tumor, that is, the biopsy was obtained from the more mature portion of the neoplasm and hence was not representative of the lesion. On the other hand, one child came to necropsy whose spinal cord tumor was unquestionably of low-grade malignancy but who nevertheless had disseminated tumor. Given the poor outcome of patients treated with only local RT, we have begun giving craniospinal RT to patients with anaplastic PST. It has been suggested that children with anaplastic cerebral glioma benefit from addition of chloroethylcyclohexylnitrosourea, vincristine, and prednisone after radiotherapy [4]; this type of chemotherapy may be of benefit for children with anaplastic PST.

Gross total resection of PST, when possible, is optimal surgical management [2, 3, 5], and extensive surgical resection has been enhanced recently by utilizing the

operative microscope and Cavitron ultrasonic surgical aspiration. Our series includes patients who had surgery either before or after introduction of these innovations but, although similar in size to other reported series of children with astrocytomas of the spinal cord [3, 4], our results do not confirm improved survival after extensive surgical removal of the tumor compared with limited removal or biopsy alone. Given the poor survival of children treated with conventional therapy, new avenues of treatment should be pursued in these patients.

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