Journal of Neuro-Oncology **9**: 211–217, 1990.

Clinical Study

External beam radiotherapy for primary spinal cord tumors

Ha Chung Chun, Rupert K. Schmidt-Ullrich, Aaron Wolfson, Oscar F. Tercilla, Robert H. Sagerman[1] and Gerald A. King[1]

Department of Radiation Oncology, Medical College of Virginia, Box 58 – MCV Station, Richmond, VA 23298;[1] Division of Radiation Oncology, State University of New York, Health Sciences Center, Syracuse, NY 13210, USA

Key words: radiotherapy, spinal cord tumors

Summary

Of 34 evaluated patients with primary spinal cord tumors, 32 were irradiated at our institutions between 1969 and 1983. The results are reported of 32 patients, 16 with ependymoma and 16 with astrocytoma, who were treated with postoperative external beam radiotherapy following biopsy or subtotal resection.

Twenty-nine patients received 45–55 Gy megavoltage beam irradiation in five to six weeks, and the remaining three patients received less than 40 Gy. The minimum follow-up was five years. Five- and ten-year actuarial survival rates for the entire group of patients were 73% (22/30) and 50% (8/16), respectively, including three patients who were salvaged by surgery after radiotherapy failures. Corresponding five- and ten-year relapse-free survival rates were 60% (18/30) and 32% (6/19), respectively. Of the 29 patients who received more than 45 Gy, relapse-free survival at five years was 63% (17/27). Treatment failed in 13 patients, and all of those failures were within the irradiated portals. Patients with ependymomas have significantly better relapse free survival than those with astrocytomas, 80% vs. 40% ($p < 0.05$). There was a significant difference in survival between patients with tumors involving the cervical spine and those with tumors in the other locations, 45% vs. 89% ($p < 0.05$). There was no significant difference in survival between patients with cauda equina tumors and those with tumors of the spinal cord, 100% vs. 68% ($p > 0.05$). No radiotherapy-related neurological deficit was noted with a maximum 20 year follow-up. This study confirms that external beam radiotherapy is a safe and effective treatment modality for primary spinal cord tumors.

Introduction

Primary spinal cord tumors are rare. Only 4% of central nervous system neoplasms are intraspinal, and the incidence of spinal cord gliomas is approximately 23% of all tumors arising in the spinal canal [1, 2]. It has been well documented that no further therapy is required for tumors that were completely excised using microsurgical techniques [3–7]. Recently, Hermann *et al.* [8] reported that microscopic CO_2 laser resection is a safe and reliable alternative to achieve complete removal of intramedullary tumors, in particular those that were previously considered unresectable with standard microsurgical techniques. Postoperative external beam radiotherapy following incomplete surgical resection, such as biopsy or subtotal resection, has shown the potential benefit in the management of primary spinal gliomas; however, there are no clear guidelines with respect to radiotherapeutic management due to the small number of patients in each series and relatively short follow-up of reported cases. This retrospective study analyzes our experience with 32 patients treated for cure with ex-

ternal beam radiotherapy and compares the treatment results with those in other series [9–16].

Materials and methods

Thirty-six patients with primary spinal cord tumors were seen at our institutions between 1969 and 1983. One patient refused treatment, and one was treated elsewhere. Non-Hodgkin's lymphomas were found in two patients who were excluded from this study. We report the results on the remaining 32 patients. Patient evaluation consisted of history, physical examination and laboratory studies, including cytology in cerebrospinal fluid (CSF). Spine x-rays and myelogram were performed routinely, and computed tomography (CT) of the spine with contrast material was added after 1975. Presenting symptoms in decreasing order were motor weakness, pain in the back or neck, sensory changes, urinary frequency and muscular atrophy.

The patient distribution according to age is shown in Table 1. The highest incidence is in the third decade with a median age of 26 years and a range from two to 66 years. The study group is comprised of 16 patients with ependymomas and 16 patients with astrocytomas. In all patients the histopathological diagnosis was established by surgical procedures such as decompression biopsy or subtotal resection. Three of the 16 patients with astrocytoma were found to have high-grade tumors. Eighteen patients, 13 with astrocytoma and five with ependymoma, underwent decompression biopsy only, and in 14 patients, three with astrocytoma and 11 with ependymoma, subtotal resections were performed. Twenty-seven of the neoplasms originated within the spinal cord, and five involved the conus medullaris and cauda equina. Cervical spine (C-spine) involvement was found in 11 of 32 patients. Statistical significance was determined by the chi-square test.

All patients were treated with megavoltage equipment, Cobalt-60 and 4-MeV or 12-MeV linear accelerators. In all cases, treatment planning was initiated approximately two to three weeks following surgery. Patients were treated in the prone position, if feasible.

Twenty-three patients were treated with a 3 cm craniocaudal margin around the tumor volume, which was defined by radiographic criteria from myelograms or CT myelograms. The remaining nine patients were treated with margins of two vertebral bodies above and below the spine involved with tumor. The doses delivered are summarized in Table 2. Three patients received less than 40 Gy; two, due to poor medical conditions, received 20 Gy, and one 38 Gy. Twenty-one patients received 45–50 Gy in five to six weeks, and six patients were treated to doses in excess of 50 Gy. Daily fraction sizes of 1.8 or 2.0 Gy were given through single posterior portals, and the dose usually was prescribed at a depth of 5 cm. Where feasible, two posterior oblique fields were used with wedges. The fields were not routinely reduced for boost irradiation.

The follow-up period ranges from five to 20 years. Patients were seen at one and three months after irradiation, then at three- to four-month intervals for three years, and thereafter at six-month

Table 1. Patient distribution according to age (median age = 26)

Age	Number of patients
1–10	3
11–20	6
21–30	8
31–40	1
41–50	4
51–60	4
61–70	6
Total	32

Table 2. Patient distribution according to dose

Dose (cGy)	Number of patients
2000–3800	3
4500–5000	21
5001–5500	6
Total	32

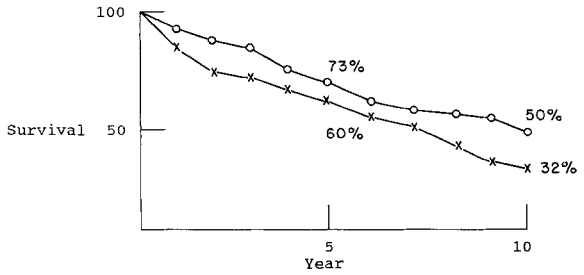

Fig. 1. Entire group of patients (32 patients). o = Actuarial survival; x = Relrelapse free survival.

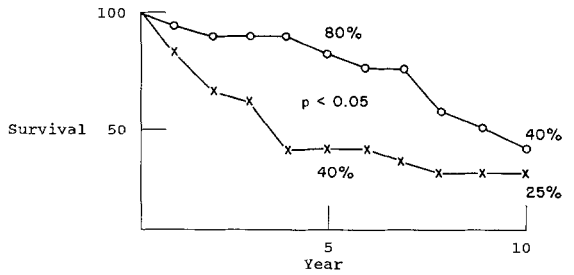

Fig. 2. Relapse free survival (Ependymoma vs. astrocytoma). o = Ependymoma (16 patients); x = Astrocytoma (16 patients).

or one-year intervals by both the radiation oncologist and the neurosurgeon.

History and careful neurological examinations were relied upon for evaluation of tumor control. Spine x-ray, myelogram, CT myelogram, and magnetic resonance imaging studies were obtained for asymptomatic patients once a year or whenever clinical signs and symptoms indicated possible recurrence.

Results

For the entire group of 32 patients, survival rates at five and 10 years were 73% and 50%, respectively. The corresponding five- and ten-year relapse-free survival rates were 60% and 32% (Fig. 1). Patients with ependymomas have significantly better relapse-free survival than those with astrocytomas, 80% vs. 40% at five years ($p < 0.05$) (Fig. 2). For 16 patients with ependymomas, five- and ten-year actuarial survival rates were 87% and 67% and corresponding relapse-free survival rates were 80% and 43%, respectively. One patient who experienced recurrence one year following radiotherapy was salvaged by surgery and is currently alive without recurrent disease at six years. For 16 patients with astrocytomas, the survival rates at five and 10 years, respectively, were 60% and 40%, with corresponding relapse-free survival rates of 40% and 25%. Two patients were salvaged by surgery after radiotherapy failure. One patient experienced a local recurrence at 18 months and was salvaged by surgery until she died of rectal cancer 11 years later. The second patient failed locally seven months after radiotherapy, was salvaged by surgery, and remains free of disease five years following irradiation.

Table 3. 5 year actuarial survival according to location of the tumor

Cervical spine involved	Other locations	
5/11 (45%)	17/19 (89%)	$p < 0.05$
Canda equina involved	**Other locations**	
5/5 (100%)	17/25 (68%)	$p > 0.05$

The tumor arose in, or involved, the C-spine in 11 of 32 patients. Eight of the 11 tumors were astrocytomas. C-spine involvement represents an important adverse prognostic factor, as survival of these patients was significantly worse relative to those with tumors in other locations (45% vs. 89%, $p < 0.05$) (Table 3). Five patients with tumors originating from the cauda equina were found to have ependymomas and experienced a 100% actuarial survival at five years. All of these patients had presented with ependymomas. For the 27 patients without cauda equina involvement, the five-year survival rate was 68%. This difference was not statistically significant. For ependymoma patients with involvement of other portions of the spinal cord, the five-year survival rate was 80%, compared with 100% in patients with tumors located in

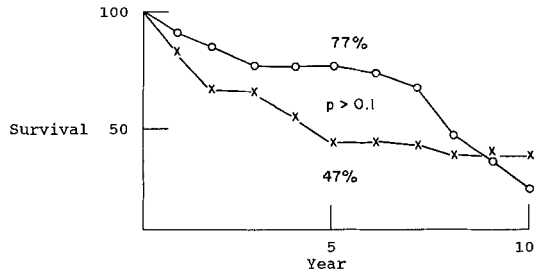

Fig. 3. Relapse free survival (Subtotal resection vs. biopsy only). o = Subtotal resection (14 patients); x = Biopsy only (18 patients).

the cauda equina ($p > 0.05$). In contrast, the survival at five years was 60% in patients with astrocytomas involving spinal cord; none of the astrocytomas presented in the cauda equina.

Three patients received less than 40 Gy; two of these patients received 20 Gy in 13 fractions secondary to medical conditions. One patient died of recurrent disease at ten months, and the other patient died at five years from recurrent disease, which had developed four years following radiotherapy. The third patient received 38 Gy in 21 fractions and remains alive without recurrence at seven years.

For the 29 patients who received more than 45 Gy, the relapse-free and overall survival rates at five years were 53% and 78%, respectively. With a 20 year maximum follow-up, no radiotherapy-related neurological deficits were noted, although in six patients, the spinal cord was irradiated to doses greater than 50 Gy. Four patients with ependymomas were treated to radiation doses between 52 and 55 Gy; three are free of disease without radiation sequelae, one is alive with recurrent tumor at 14 years. In contrast, both patients, two patients receiving 52 and 54 Gy for astrocytomas died of recurrent disease within 18 months after treatment.

Treatment failed in nine of 16 patients with astrocytomas and in four of 16 with ependymomas. All those failures were within the irradiated portals. There were no marginal failures irrespective of how much margin was given. We saw no evidence of intracranial failure or CSF seeding.

In our analysis, the extent of surgical resection had no significant impact on ultimate tumor control. The five-year relapse-free survival rates in patients who underwent biopsy *vs.* subtotal resection were 47% *vs.* 77%, respectively (Fig. 3). This difference was not statistically significant ($p > 0.1$). Of patients with ependymoma, five and 11 underwent decompression biopsies and subtotal resections, respectively. In contrast, 13 of 16 patients with astrocytoma had biopsies only, and three underwent subtotal resections.

Discussion

Approximately 50% of intramedullary ependymomas can be completely removed by microsurgical technique, as reviewed by Garcia [15]. In contrast, only 6% of intramedullary astrocytomas can be removed completely even with the use of microsurgical technique. It is well documented that complete surgical excision alone of primary spinal cord tumors using microsurgical technique can result in excellent local control and survival rates [3–9]. Fischer *et al.* reported on 14 of 16 patients surviving after complete removal of intramedullary ependymomas [5]. Therefore, postoperative adjuvant radiotherapy is not recommended for most of those patients who undergo complete surgical removal.

Several authors reported that postoperative radiotherapy resulted in improved long-term survival rates for those patients who underwent incomplete surgical removal such as decompression biopsy or subtotal resection [9–16]. Schwade *et al.* showed that all 12 patients with ependymomas are alive without recurrence with a minimum follow-up of three years, and five of the six patients with low-grade astrocytomas survived longer than three years [10]. Garcia reported 70% and 58% respective five- and ten-year actuarial survivals for patients treated with surgery and postoperative irradiation [15]. According to Kopelson *et al.*, local control was achieved in eight of nine patients after subtotal resection and radiation therapy and in five of eight patients after biopsy and radiotherapy [11]. This study reports actuarial five- and ten-year survival rates of 58% and 23%, respectively, for patients with astrocytoma and of 100% and 73% for

patients with ependymoma. Five- and ten-year actuarial survival rates in our studies are comparable to these, being, respectively, 73% and 50% for the entire group of patients, 87% and 67% for patients with ependymoma, and 60% and 40% for those with astrocytoma. As reported by several other authors [10, 11, 15] patients with ependymoma had significantly better relapse-free survival rates at five years than did patients with astrocytoma (80% *vs.* 40%). However, for both types of tumors a significant number of late failures between five and ten years were seen as was also noted in another recent report [17].

Shaw *et al.* reported that the extent of surgical removal did not significantly affect disease-free or overall survival in patients with intraspinal ependymoma [16]. According to Reimer *et al.*, there was a significantly lower rate of survival at seven years for patients who underwent decompression and biopsy only, as compared to those who had subtotal removal (42% *vs.* 60%), and they suggested that more radical resection may be associated with increased survival [7]. In our analysis, relapse-free survival rates at five years for patients who underwent biopsy alone *vs*, subtotal resection were 47% *vs.* 77%, respectively ($p > 0.1$). This suggests improved survival for the latter group of patients but has not reached statistical significance. The impact of the extent of surgical resection on survival remains controversial. Table 4 summarizes the results of different series and their recommended dose.

Most of the authors recommended doses of 40–45 Gy for ependymomas and 50 Gy for astrocytomas. Shaw *et al.* suggested that improved control can be achieved safely with doses greater than 50 Gy and recommended localized treatment to lesions, following surgical removal, with a shrinking field technique delivering a total dose of 55 Gy for ependymomas [16]. Based on our failure rates and excellent tolerance of radiotherapy (45–55 Gy), we recommend 45 Gy for ependymomas at either the spinal cord and/or cauda equina and 50 Gy for astrocytomas. In selected cases, doses in excess of 50 Gy may improve local control with excellent tolerance. Since all recurrences were within the radiation portals and none were outside or at the edge of the field, we believe that the shrinking field technique is not necessary as a routine, and that radiation fields with margins of 2–3 cm around the carefully assessed tumor volume are sufficient to achieve optimal local control. Given the failure patterns of primary spinal cord tumors, local tumor control is most critical for the overall treatment outcome. Improvement of local tumor control by irradiation is challanging because

Table 4. Literature review

Author	Number of patients	Histology	Survival	Recommended dose
Schwade *et al.* (1950–1975)	27	12 E; 6 A; 9 Unknown	E = 100%; A = 67%; Unknown = 56%	45–50 Gy
Kopelson *et al.* (1962–1979)	23	11 E; 10 A; 2 Mixed	E = 100%; A = 58%	40–45 Gy for E 45–50 Gy for A
Garrett *et al.* (1958–1980)	41	41 E	E = 83%	50 Gy
Shaw *et al.* (1963–1983)	22	22E	E = 95%	55 Gy
Garcia (1954–1979)	37	18 E; 15 A; 3 Unknown; 1 Lymphoma	70% for entire group	40–45 Gy for Cauda Equina Tumor 45–50 Gy for Intramedullary Tumor
Chun *et al.* (1969–1983)	32	16 E; 16 A	E = 87%; A = 60%	45 Gy for E 50–55 Gy for A

E = Ependymoma; A = Astrocytoma.

of the narrow margin between tumor control and the potential complications of spinal cord injury. This can be estimated to be 20% at doses of 57 Gy and to increase rapidly as doses are escalated [18]. Given the benefitial effects of hyperfractionated irradiation in differentiating between late-reacting normal and tumor tissues it is worth exploring the value of altered fractionation schemes with fraction sizes of 1.1 to 1.2 Gy twice-a-day [19, 20]. Based on animal studies, the tolerance of the spinal cord to radiation doses between 1.0 and 2.0 Gy is overestimated by the linear quadratic model and appears to more accurately predicted by the incomplete repair model [21, 22]. More data on the repair kinetics of spinal cord tissue is required until hyperfractionated irradiation can be used clinically [21].

Garcia showed that anatomic location of the tumor was the most important predictor of both survival and neurological function. Patients with tumors of the cauda equina had a significantly better survival than those with tumors at other sites (75% *vs.* 50% at ten years) [15]. In that study, one of 11 cauda equina tumors was an astrocytoma, and ten were ependymomas. In contrast, 13 and 8 of 26 tumors in other parts of the spinal cord were astrocytomas and ependymomas, respectively. Since patients with ependymoma generally have a better prognosis, the apparently better treatment outcomes of cauda equina tumors is most likely due to the high rate of ependymomas in that location.

In our experience, there was no significant difference in actuarial survival between patients with tumors of the cauda equina and those with tumors at other sites (100% *vs.* 68% $p > 0.05$). However, there was a significant difference in actuarial survival between patients with tumors of the C-spine (three ependymomas and eight astrocytomas) and those with tumors at other sites (13 ependymomas and eight astrocytomas). This may be due to the fact that, in our study, the majority of tumors in the C-spine were astrocytomas (8/11) relative to the other portions of the spine (8/21).

Our analysis confirms that external beam radiotherapy with or without debulking surgery is a safe and effective treatment modality for primary spinal cord tumors.

References

1. Farwell JR, Dohrmann GJ, Flannery JT: Central nervous system tumors in children. Cancer 40: 3123–3132, 1977
2. Slooff J, Kerohan J, MacCarty C: Primary Intramedullary Tumors of the Spinal Cord and Filum Terminale. Saunders, Philadelphia, 1964, p 5
3. Greenwood J: Intramedullary tumors of spinal cord: A follow-up study after total surgical removal. J Neurosurg 20: 665–668, 1963
4. Malis LI: Intramedullary spinal cord tumors. Clin Neurosurg 25: 512–539, 1978
5. Fischer G, Mansuy L: Total removal of intramedullary ependymomas: Follow-up study of 16 cases. Surg Neurol 14: 243–249, 1980
6. Cooper PR, Epstein F: Radical resection of intramedullary spinal cord tumors in adults. J Neurosurg 63: 492–499, 1985
7. Reimer R, Onofrio BM: Astrocytomas of the spinal cord in children and adolescents. J Neurosurg 63: 669–675, 1985
8. Hermann H, Neuss M, Winkler D: Intramedullary spinal cord tumors resected with CO_2 laser microsurgical technique. Neurosurgery 22: 518–522, 1988
9. Scott M: Infiltrating ependymomas of the cauda equina: treatment by conservative surgery plus radiotherapy. J Neurosurg 4: 446–448, 1974
10. Schwade JG, Ward WM, Sheline GE, Sorgen S, Wilson CB: Management of primary spinal cord tumors. Int J Rad Onc Biol Phys 4: 389–393, 1978
11. Kopelson G, Linggood RM, Kleimann GM, Douchette J, Wang CC: Management of intramedullary spinal cord tumors. Radiology 135: 473–479, 1980
12. Marks JE, Adler SJ: A comparative study of ependymomas by site of origin. Int J Rad Onc Biol Phys 8: 37–43, 1982
13. Peschel RE, Kapp DS, Cardinale F, Manuelidis EE: Ependymomas of the spinal cord. Int J Rad Onc Biol Phys 9: 1093–1096, 1983
14. Garrett PG, Simpson WJK: Ependymomas: results of radiation treatment. Int J Rad Onc Biol Phys 9: 1121–1124, 1983
15. Garcia DM: Primary spinal cord tumors treated with surgery and postoperative irradiation. Int J Rad Onc Biol Phys 11: 1933–1939, 1985
16. Shaw EG, Evans RG, Scheithauer BW, Ilstrip DM, Earle JD: Radiotherapeutic management of adult intraspinal ependymomas. Int J Rad Onc Biol Phys 12: 323–327, 1986
17. Linstadt DE, Wara WM, Leibel SA, Gutin PH, Wilson CB, Sheline GE: Postoperative radiotherapy of primary spinal cord tumors. Int J Rad Onc Biol Phys 16: 1397–1403, 1989
18. Marsa GW, Goffinet DR, Rubinstein LR, Bagshaw MA: Megavoltage irradiation in the treatment of glioma of the brain and the spinal cord. Cancer 36: 1681–1689, 1975
19. Fowler JF: The linear-quadratic formula and progress in fractionated radiotherapy. Brit J Radiol 62: 679–694, 1989
20. Thames HD, Withers HR, Peters LJ, Fletcher GH: Changes in early and late radiation responses with altered dose fractionation: implications of dose-survival relationships. Int J Rad Onc Biol Phys 8: 219–226, 1982

21. Thames HD, Ang KK, Stewart FA, van der Schueren E: Does incomplete repair explain the apparent failure of the basic LQ model to predict spinal cord and kidney responses to low doses per fraction? Int J Radiat Biol 54: 13–19, 1988
22. Bentzen SM, Thames HD, Travis EL, Ang KK, van der Schueren E, Dewit L, Dixon DO: Direct estimation of latent time for radiation injury in late-responding normal tissues: gut, lung, and spinal cord. Int J Radiat Biol 55: 27–43, 1989

Address for offprints:
R. Schmidt-Ullrich,
Department of Radiation Oncology,
Medical College of Virginia,
Box 58 – MCV Station,
Richmond, VA 23298-0058, USA