External Beam Radiotherapy for Primary Spinal Cord Tumors

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

Twenty-nine patients received 45~55 Gy megavoltage beam irradiation in 5~6 weeks and the remaining three patients received less than 40 Gy. Spinal cord was in the irradiated field for six patients who received more than 50 Gy. The minimum follow-up was five years. Five and ten year acturaial survival rates for entire group of patients were 73% (22/30) and 50% (8/16), including three patients who were salvaged by surgery after radiation failures. Corresponding five and ten year relapse free survival rates were 60% (18/30) and 32% (6/19), respectively. Of the 29 patients who recived 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 in the irradiated portal. Patients with ependymomas have significantly better relapse free survival than those with astrocytomas, 80% vs. 40% ($p<0.05$). There was significant difference in survival between patients with tumors involving the cervical spine and those with tumors in the other loactions, 45% vs. 89% ($p<0.05$). There was no significant differnece in survival between patients with cauda equina tumors and those with tumors at 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.

Key Words: Radiotherapy, 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 which were completely excised using microsurgical techniques[3~7].

Recently, Hermann et al reported that microscopic CO_2 laser resection is a safe and reliable alternative for compete removal of intramedullary tumors, in particular those that previously were thought to be unresectable with standard microsurgical techniques[8]. 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 clean 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 external 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 Medical College of Virginia between 1969 and 1983. One patient refused the treatment and one was treated elsewhere. Non-Hodgkin's lymphoma was 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 were motor weakness, pain in the back or neck, sensory changes, urinary frequency and muscular atrophy

in decreasing order.

The patient distribution according to age is shown at 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. Histopathological diagnosis was established by surgical procedures such as decompression biopsy or subtotal resection in all patients. Sixteen patients each with ependymomas and astrocytomas were diagnosed. 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 neoplasm 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 2~3 weeks folowing surgery. Patients were treated in prone position, if feasible.

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	30

Twenty-three patients were treated with a 3 cm craniocaudal margin around the tumor volume, which was defined by radiographic studies such as myelograms or CT myelograms. The remaining nine patients were treated with two vertebral body margin from the involved level of spine. The doses delivered are summarized in Table 2. Three patients received less than 40 Gy (two 20 Gy, one 38 Gy). Twenty-one patients received 45~50 Gy in 5~6 weeks and six patients were treated to doses in excess of 50 Gy. Spinal cord was in the treated field in all six patients. Daily fraction sizes were 1.8 Gy or 2.0 Gy. Single posterior portals were most commonly employed and the dose was usually prescribed at 5 cm depth. If feasible, two posterior oblique fields were employed 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 or one year intervals by both the radiation oncologist and the neurosurgeon.

Histroy and careful neurological examinations were relied upon for evaluation of tumor control. Spine X-ray, myelogram, computed tomography 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%, respecively. The corresponding five and ten year relapse free survival rates were 60% and 32% (Fig. 1). For 16 patients with ependymomas, five and ten year acturaial survival rates were 87% and 67% and corresponding relapse free survival rates were 80% and 43%, respectively. One patient who experienced recurrence one year folowing radiotherapy was salvaged by surgery and is currently alive without recurrent disease at six years following irradiation. For 16 patients with astrocytomas, survival rates were 60% and 40%, respectively. Corresponding relapse free survival rates were 40% and 25%, repectively. Two patients were salvaged by surgery after radiotherapy failure. One patient had local recurrence at 18 months and was salvaged by surgery until she died of rectal cancer 11 years following radiotherapy. The second patient had a

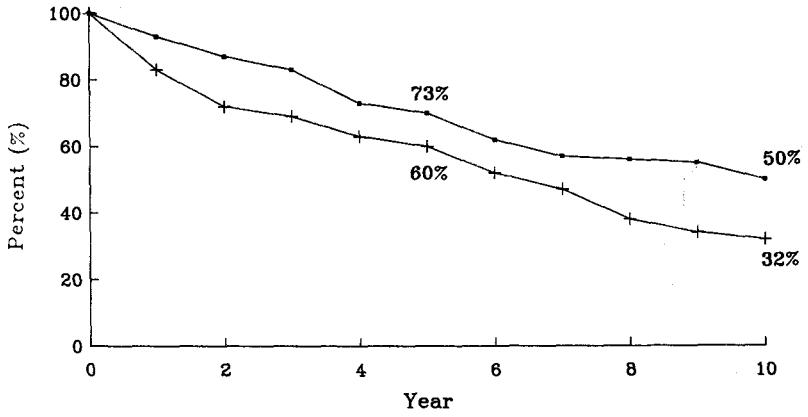

Fig. 1. Entire Group of Patients (32 Patients)
· =Actuarial Survival + =Relapse Free Survival

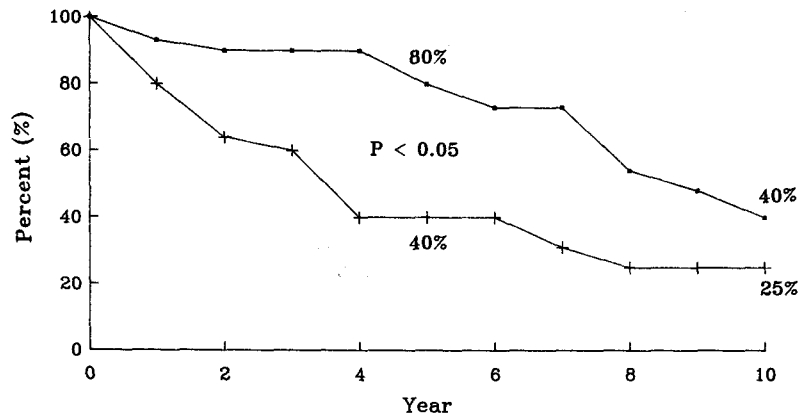

Fig. 2. Relapse Free Survival (Ependymoma vs. Astrocytoma)
· =Ependymoma (16 patients) + =Astrocytoma (16 patients)

local failure at seven months which was salvaged by surgery. This patient remains NED (no evidence of disease) currently five years and two months following irradiation. Patients with ependymomas have significantly better relapse free survival than those with astrocytomas, 80% vs. 40% at fie years ($p<0.05$) (Fig. 2).

The tumor arose in or involved the C-spine in 11 of 32 patients. C-spine involvement represents an important prognostic factor as there was a significant difference in survival between patients with tumors involving the C-spine and those with tumors at other locations (45% vs. 89%, $p<0.05$) (Table 2). Five patients with tumors originating from the cauda equina had an acturarial survival 100% at five years. All these patients presented with ependymomas. For those 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 spinal cord, the five year survival rate was 80%, compared with 100% in patients with tumor located in the cauda equina ($p>0.05$). The survival was 60% in patients with astrocytoma involving spinal cord and none of the astrocytoma patients presented with cauda equina lesions.

Three patients received less than 40 Gy; two of these patients received 20 Gy in 13 fractions, one patient died of recurrent disease at ten months, and the other patient died at four years and eight months from recurrent disease, which had developed four years following radiotherapy. The third patient recived 38 Gy in 21 fractions and is still alive without recurrence at seven years.

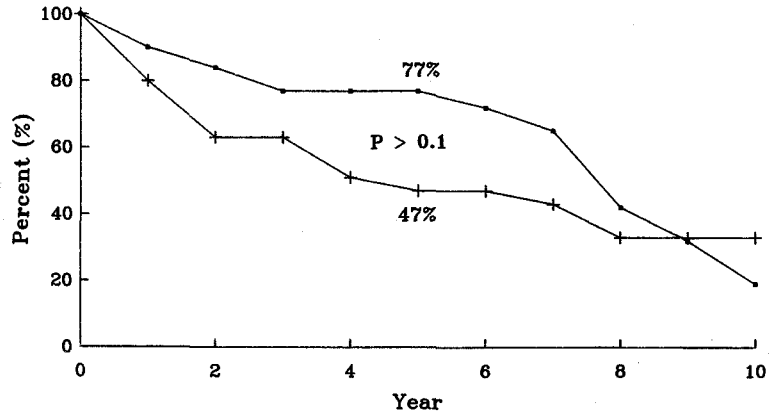

Fig. 3. Relapse Free Survival (Subtotal Resection vs. Biopsy Only)
· =Subtotal Resection (14 patients) + =Biopsy Only (18 patients)

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 deficit was noted, although the spinal cord was irradiated in six patients who received more than 50 Gy. One patient received 55 Gy for ependymoma at T10-S2 and is currently alive with normal neurological function at six years. One patient did receive 54 Gy for a high grade astrocytoma involving C1-C6; she developed local failure and died of recurrent disease at one year and four months. Four patients, one with astrocytoma and three with ependymoma, received 52 Gy. Of those four patients, one died of recurrent disease and one is alive with disease at 13 years and nine months. The remaining two patients are alive and free of disease at 13 and five years, respectively, without complications related to radiotherapy.

Table 3. 5 Year Actuarial Survival According to Location of the Tumor

Cervical Spine Involved	Other Locations	
5/11 (45%)	17/19 (89%)	$p < 0.05$
Cauda Equina Involved	**Other Locations**	
5/ 5 (100%)	17/25 (68%)	$p > 0.05$

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; 2Mixed	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	22 E	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 (1969–1983)	32	16 E; 16 A	E=87%; A=60%	45 Gy for E 50–55 Gy for A

E : ependymoma A : astrocytoma

Treatement failed in nine of 16 patients with astrocytomas and in four of 16 with ependymomas. All of those failures were within the irradiated portals. No failure noted at the margin of the radiation field. The margins of the vertebral bodies or the 3 cm were associated with same in-field failure rates. We found no evidence of intracranial failure or CSF seeding.

Five and 11 patients with ependymoma underwent decompression biopsy only and subtotal resections. Of 16 astrocytoma patients, 13 were biopsied only and three underwent subtotal resection. Five-year relapse free survival rates of all tumors for the patients who underwent biopsy only vs. subtotal resection were 47% vs. 77%, respectively, (Fig. 3). This difference was not statistically significant ($p>0.1$) and, therefore, extent of surgical resection was not the important prognostic factor for ultimate tumor control.

DISCUSSION

Approximately 50% of intramedullary ependymoma can be completely removed by microsurgical trchnique as reviewed by Garcia[15]. On the contrary, only 6% of intramedullary astrocytomas can be removed completely even using the microsurgical trchnique. 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 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 underwent 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% 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 only and radiation therapy[11]. This study reports actuarial five and ten year survival rates of 58% and 23% for astrocytoma and of 100% and 73% for patients with ependymoma, respectively. Five and ten year actuarial survival rates in our studies are comparable to these with 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 ependyma had significantly better relapse free survival at five years than patients with astrocytoma (80% vs. 40%).

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 significantly lower rate of survival st seven years for patients who underwnet decompression and biopsy only, as compared to those who did 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 significance. The impact of extent of surgical resection on survival remains controversial. Table 4 summarizes the results of different series and their recommended dose. 40 ~45 Gy were recommended for ependymomas and 50 Gy for astrocytomas by most of the authors.

Shaw et al, suggested imporved control can be achieved safely with doses greater than 50 Gy and recommended localized treatment to lesions following surgical removal with 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 to ependymomas at either spinal and/or cauda equina and 50 Gy to astrocytomas. In selected cases, dose more than 50 Gy may improve local control with excellent tolerance. Since all recurrences were within radiation portal and no recurrence at the outside or the edge of the field, we believe the shrinking field technique is not necessary and radiation field with a margin (2~3 cm) from the carefully assessed tumor volume is sufficient to achieve optimal local control.

Garcia showed that anatomic location of the tumor was the most improtant 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 astrocytoma and ten of those tumors were ependymoma. On the contary, 13 and 8 of 26 tumors in spinal cord were astrocytomas and ependymomas. Since patients with ependymoma generally have a better prognosis than those with astrocytoma, better prognosis of cauda equina tumors is most likely to be due to the high rate of ependymomas in that location.

In our experience, there was no significant difference in acturarial 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 significant difference in acturarial survival between patients of tumors with C-spine (three ependymoma and eight astrocytoma) and those with tumors at other sites (13 ependymoma and eight astrocytoma). This may well be due to the fact that tumors at C-spine has higher rate of astrocytoma (8/11) than tumors at other locations (8/21) in our study.

This study confirms that external beam radiotherapy is a safe and effective treatemnt modality for primary spinal cord tumors.

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국문초록 =

척수종양의 방사선 치료

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전 하 정

1969년부터 1983년까지 버지니아 의대부속 병원에서 방사선 치료를 받은 34예의 원발성 척수암중, 조직검사 또는 아절제술을 시행한후 수술후 방사선 요법으로 치료 받은 32예(Astrocytoma 16, ependymoma 16)에 대한 치료실적을 보고하고자 한다.

29예에서는 45~55 Gy를 5내지 6주간에 조사받았으며 나머지 3예에서는 40 Gy 이하의 선량을 조사받았다. 50 Gy 이상 조사된 6예는 모두 척수가 조사야에 포함되었다.

본 연구의 최저 추적 기간은 5년이었다. 방사선 치료 실패후 재수술로 치료된 3예를 포함하여, 모든 예에서 생존율은 5년과 10년에서 각각 73%와 50%이었다. 각각의 투병생존율은 60%와 32%이었다. 45 Gy 이상의 선량을 받은 29예에서는 5년 무병생존이 63%이었다. 13예에서 치료실패를 경험했으며 치료실패는 조사야에서만 관찰되었다.

Ependymoma가 astrocytoma보다 통계적으로 유의하게 무병생존율이 높았다 (45% : 89% ($p<0.05$)). 원발부위에 있어 경추가 포함된 예에서 그렇지 않은 예보다 생존율이 저하되었다.

원발부위의 cauda equina 포함여부는 예후에 영향이 없었다. 최고 20년간 추적결과 방사선 치료에 의한 신경성 합병증은 관찰되지 않았다. 본 연구는 원발성 척수암의 치료에 있어서 방사선 치료가 안전하고 효과적임을 확인하였다.