Postoperative Radiotherapy for Intracranial Meningioma

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Purpose : To evaluate the effectiveness and tolerance of postoperative external radiotherapy for patients with intracranial meningiomas.

Materials and Methods : The records of thirty three patients with intracranial meningiomas who were treated with postoperative external irradiation at our institution between Feb, 1988 and Nov, 1999 were retrospectively analyzed. Median age of patients at diagnosis was 53 years with range of 17 to 68 years. Sites of involvement were parasagital, cerebral convexity, sphenoid ridge, parasellar and tentorium cerebelli. Of 33 evaluated patients, 15 transitional, 10 meningotheliomatous, 4 hemangiopericytic, 3 atypical and 1 malignant meningioma were identified. Four patients underwent biopsy alone and remaining 29 patients underwent total tumor resection. A dose of 50 to 60 Gy was delivered in 28-35 daily fractions over a period of 5 to 7 weeks. Follow-up period ranged from 12 months to 8 years.

Results : The actuarial survival rates at 5 and 7 years for entire group of patients were 78% and 67%, respectively. The corresponding disease free survival rates were 73% and 61%, respectively. The overall local control rate at 5 years was 83%. One out of 25 patients in benign group developed local failure, while 4 out of 8 patients in malignant group did local failure ($p<0.05$). Of 4 patients who underwent biopsy alone, 2 developed local failure. There was no significant difference in 5 year actuarial survival between patients who underwent total tumor resection and those who did biopsy alone. Patients whose age is under 60 showed slightly better survival than those whose age is 60 or older, although this was not statistically significant. There was no documented late complications in any patients.

Conclusion : Based on our study, we might conclude that postoperative external beam radiotherapy tends to improve survival of patients with intracranial meningiomas comparing with surgery alone.

Key Words : Meningioma, Radiotherapy

INTRODUCTION

Meningiomas consist of approximately 15% of all intracranial neoplasms and they usually have a dural attachment and are primarily benign, slow growing, well circumscribed.[1, 2] Surgical excision provides the mainstay of management. Radiation therapy is usually reserved for the treatment of residual disease or unresectable tumors, for recurrent disease following surgery and for tumors of malignant histology.[3, 5 7, 11, 14 19]

Reported crude recurrence rates of benign meningiomas following complete resection range from 0% to 11%.[1, 3, 4] However, crude recurrence rates may underestimate the long-term risk which is more reliably expressed on actuarial basis. This has been recently emphasized by Mirimanoff et al.[2] who reported 32% 15-year actuarial recurrence rate 145 patients following complete resection, crude recurrence rate was only 11%. Also Jaaskelainen et al.[4] reported continuing risk of relapse up to 25 years with median time to recurrence of 7.5 years following complete surgical removal.

Historically meningiomas have been considered to be radioresistant and the role of radiotherapy has been controversial. We retrospectively analyzed the records of patients with intracranial meningiomas to evaluate the effectiveness and tolerance of postoperative radiotherapy for these tumors.

Submitted December 1, 2000 accepted April 11, 2001

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MATERIALS AND METHODS

Thirty three patients with intracranial meningiomas who were treated with postoperative external irradiation at our

institution between February, 1988 and November, 1999 were reviewed. Median age of patients at diagnosis was 53 years with range of 17 to 68 years. Twenty two patients were under the age 60 and 11 patients were 60 or older. Sixteen patients were male and remaining 17 patients were female with male to female ratio of 0.94. Distribution of patients according to site of involvement is shown in Table 1. Sites of the involvement were parasagital, cerebral convexity, sphenoid ridge, parasellar and tentorium cerebelli in decreasing order.

Histological diagnosis was available in all of the patients. Of the 33 patients in this study, 15 transitional, 10 meningotheliomatous, 4 hemangiopericytic, 3 atypical and 1 malignant meningioma were identified. Tumors which showed increased mitosis, vessel proliferation, brain necrosis, invasion into brain, deformity of architecture were classified as atypical and malignant type. Transitional and meningotheliomatous histologic types were considered to be benign group, while hemangiopericytic, atypical and malignant histologic types were considered to be malignant group. Therefore 25 patients consisted of benign group and remaining 8 patients consisted of malignant group.

Of 33 patients, four patients underwent biopsy alone. Remaining 29 patients underwent total tumor resection and were referred for radiotherapy either because of uncertainty about complete excision or because of aggressiveness of the tumor. Of 4 patients who underwent biopsy alone, 3 were malignant group and one was benign group.

Table 1. Patient Characteristics

	No. of patients
Age	
Median	53 (17 68)
<60	22
>60	11
Male : Female	16:17
Site of Involvement	
Parasagittal	12
Cerebral convexity	11
Sphenoid Ridge	4
Parasellar	4
Tentorium Cerebelli	2
Histology	
Transitional	15
Meningotheliomatous	10
Hemangiopericytic	4
Atypical	3
Malignant	1

All patients were treated with megavoltage photon irradiation mostly with 6 MeV linear accelerator except few with Cobalt 60 units, delivering uniform dose to a target volume encompassing the preoperative extent of tumor with approximately 2 cm margin. A dose of 50 to 60 Gy was delivered in 28 35 daily fractions over a period of 5 to 7 weeks. Distribution of the patients according to delivered dose is shown in Table 2. Usually parallel opposed 2 lateral fields were employed with appropriate blocks. Follow- up period ranged from 12 months to 8 year with median follow up of 37 months. Patients were followed by us or their referring neurosurgeons at regular interval after completion of radiotherapy. Survival was calculated from day one of radiotherapy and actuarial survival probability was used to define the rate of survival.

RESULTS

The actuarial survival rates at 5 and 7 years for entire group of patients were 78% and 67%, respectively. The corresponding disease free survival rates were 73% and 61%, respectively. The actuarial and disease free survival rates for

Table 2. Distribution of Patients according to Delivered Dose

Dose	No. of Patients
<53 Gy	5
54 56 Gy	26
>57 Gy	2
Total	33

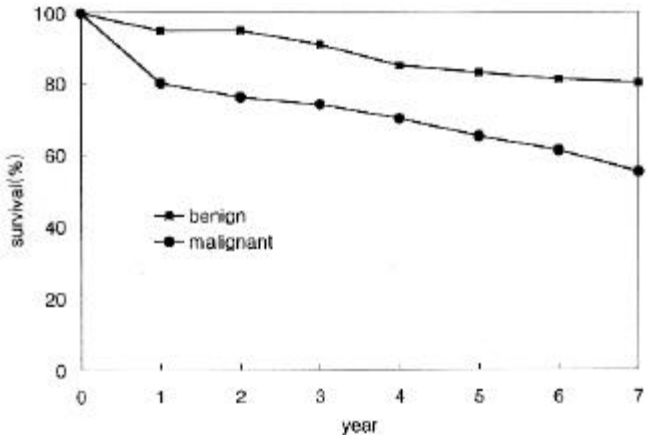

Fig. 1. Actuarial survival rates for benign and malignant group.

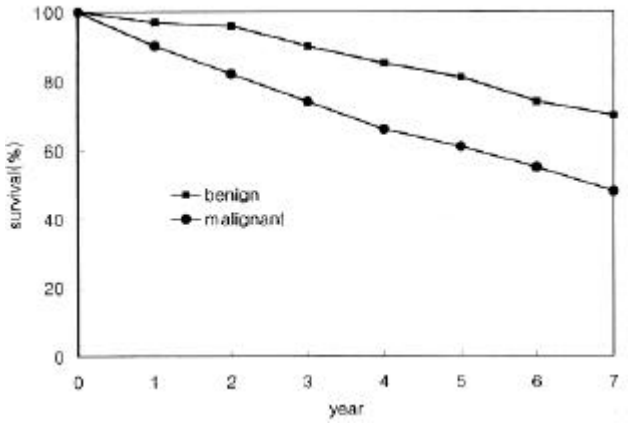

Fig. 2. Disease free survival rates for benign and malignant group.

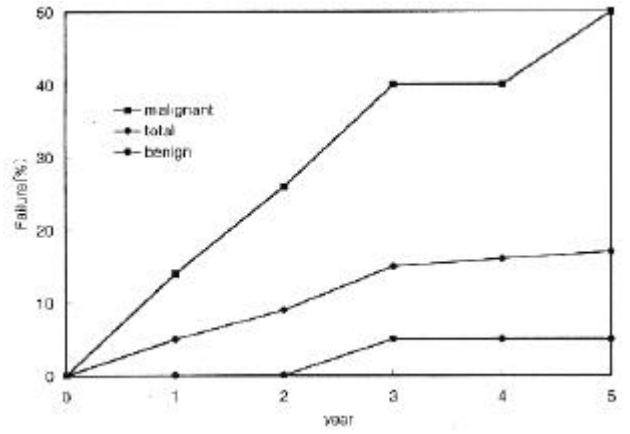

Fig. 3. Cumulative local failure rate.

entire group of patients are shown in Fig. 1 and Fig. 2.

The overall local control rate at 5 years was 83%. Cumulative local failure rate is shown in Fig. 3. Five patients developed local recurrences, of which two were hemangiopericytic, one was transitional, one was atypical and remaining one was malignant histology. One out of 25 patients in benign group developed local failure, while 4 out of 8 patients in malignant group did local failure ($p<0.05$). One patient who failed in benign group was treated with total tumor resection and postoperative radiotherapy. Of 4 patients who underwent biopsy alone, 2 developed local failure. Of these 2 failed patients, one patient died of disease at 2 years after the treatment and the other was alive with disease at the time of follow-up. On the contrary, 3 out of 29 totally resected patients developed local failure (Table 3).

There was no significant difference in 5 year actuarial

Table 3. Local Failure according to Histobgy and Extent of Surgery

	Biopsy alone	Total Resection
Benign	0/ 1	1/ 24
Malignant	2/ 3	2/ 5

survival rates between patients who underwent total tumor resection and those who did biopsy alone (80% vs 75%). Patients whose age is under 60 showed better survival than those whose age is 60 or older (80% vs 69%, $p>0.05$). However, this was not statistically significant. This result was probably due to the small number of patients in each group.

Twelve patients complained of mild to moderate headache during the treatment and 6 patients presented with generalized fatigue. None of the patients had to have treatment break because of acute reactions. There was no documented late complications in any patients.

DISCUSSION

This report describes the results of treatment of intracranial meningioma with megavoltage photon irradiation. Because surgery was considered by the referring neurosurgeons to be definitive and enough treatment for completely resected benign meningiomas, it is important to emphasize that the patients in this study represent a population with adverse prognostic factors.

The role of postoperative radiotherapy for incompletely resected meningioma has not yet been addressed by a prospective randomized trial and therefore comparative studies have employed historical controls. Wara et al.[8] in Northern California reported results of treatment in 118 patients with subtotally resected meningioma. The 5-year crude recurrence free rate was 76% in 58 patients who received postoperative irradiation compared with 29% in 34 patients treated surgery alone. These results were supported by Taylor et al.[9] in which 10-year relapse free survival was 82% in 23 patients who were irradiated following subtotal tumor resection.

However, relapse free survival in 19 non-irradiated patients was only 18%. In our study, we report 5 and 7 year disease free survival rates of 73% and 61%, respectively and this is similar to other series.

The results of postoperative radiotherapy for malignant meningiomas was disappointing, with a high probability of

death from disease progression or recurrence of tumor. Review of the literature reveals large variation in results of treatment of these malignant meningiomas which is probably due to the small number of cases in each series. Carella et al.[10] reported 8 of 11 disease free survivors over 1 to 10 years follow up after radiotherapy. Similarly, Wara et al.[8] reported 2 of 3 long term survivors with malignant tumors. In contrast, several other groups have reported poor long term survival despite postoperative radiotherapy.[7, 12, 13]

The results of postoperative radiotherapy for these tumors may be unsatisfactory even after so called complete surgical removal. In our study, three out of eight patients with malignant group underwent biopsy alone and four out of eight malignant patients developed local failure.

Although patients under 60 showed better survival than those over 60, this was not statistically significant.

Because majority of patients in our study received 54 to 56 Gy, dose dependence of the tumor in terms of survival or local recurrence was not evaluated. The importance of fraction size specifically in relation to brain tolerance has been emphasized by Pezner et al.[20] who has documented brain tolerance unit based upon historical data from literature. The isoeffective dose was found to have greater dependence on fraction size rather than overall treatment time. The excellent tolerance with low incidence of late complication in our study probably resulted from daily tumor dose 1.6 to 1.8 Gy per fraction.

As mentioned above, Taylor et al.[9] reported only 18% of relapse free survival in non-irradiated patients following subtotal tumor resection. Also Wara et al.[8] documented 29% of recurrence free rate in patients treated with surgery alone. Comparing with these historical data, survival rates of irradiated patients in our study tend to be higher. Based on these results, we suggest that postoperative radiotherapy is likely to improve survival of the patients with intracranial meningioma. Radiation tumor dose of not more than 1.8 Gy per fraction results in minimal late morbidities. Therefore, we might conclude that postoperative external beam radiotherapy is safe and effective treatment for patients with intracranial meningiomas.

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국문 초록

뇌수막종 환자의 수술 후 방사선치료

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목 적 : 뇌수막종 환자에서 수술후 방사선치료의 효과를 평가하고 최적의 방사선치료 방법을 알아보고자 함이 본 연구의 목적이다.

대상 및 방법 : 1988년 2월부터 1999년 11월까지 본원에서 뇌수막종으로 수술후 방사선치료를 받은 33명의 환자를 후향적으로 분석하였다. 환자의 나이는 17세부터 68세이었고 중앙값은 53세이었다. 조직학적 분류는 33명의 환자중 이행성이 15명, 수막성이 10명, 혈관주위세포성이 4명, 이형성이 3명, 악성이 1명이었다. 4명은 조직검사만을, 29명은 완전절제술을 시행하였다. 5 7주에 걸쳐 50 60 Gy를 28 35회에 나누어 조사하였다. 추적기간은 12개월 8년이었다.

결 과 : 전체 환자에서 5년 및 7년 실질 생존율은 각각 78% 및 67%이었다. 5년 및 7년 무병생존율은 각각 73% 및 61%이었다. 국소제어율은 5년에 83%이었다. 25명의 양성군 환자중 1명만이 국소재발을 나타내었고, 8명의 악성군 환자중 4명이 국소재발을 나타내었다. 조직검사만을 시행한 환자에서 2명이 재발하였고 완전절제술을 시행한 29명의 환자에서 3명이 재발하였다. 조직검사만을 시행한 환자와 완전절제술을 시행한 환자의 생존율은 유의한 차이가 없었다. 60세 미만의 환자가 60세 이상의 환자보다 나은 생존율을 나타내었으나, 이는 통계적으로 유의하지 않았다.

결 론 : 수술만을 시행한 환자와 비교하여 수술후 방사선치료를 시행한 환자에서 생존율이 향상됨을 알 수 있었고 뇌수막종 환자에서 수술 후 방사선치료가 안전하고 효과적인 치료방법이라 평가하였다.

핵심용어 : 뇌수막종, 방사선치료