의학석사 학위논문

Postoperative Radiotherapy for Intracranial Ependymoma

– Long-Term Results from a Single Institution –

두개강내 상의세포종에서 수술 후 방사선치료

– 단일기관 장기 추적 결과 –

2013년 8월

서울대학교 대학원

의학과 방사선종양학 전공

장 원 일

Postoperative Radiotherapy for Intracranial Ependymoma

– Long-Term Results from a Single Institution –

지도교수 김 일 한

이 논문을 의학석사 학위논문으로 제출함

2013년 4월

서울대학교 대학원

의학과 방사선종양학 전공

장 원 일

장원일의 의학석사 학위논문을 인준함

2013년 6월

위 원 장 _____ (인)

부 위 원 장 _____ (인)

위 원 _____ (인)

Abstract

Postoperative Radiotherapy for Intracranial Ependymoma

– Long-Term Results from a Single Institution –

Won Il Jang

Radiation Oncology

Department of Medicine

Seoul National University

The purpose of this study is to analyze long-term outcome and to evaluate the efficacy of salvage treatment in the patients who received surgery and postoperative radiotherapy (RT) for intracranial ependymoma.

From January 1979 through June 2006, 70 patients with intracranial ependymoma received RT with definitive aim at our institution. The median age was 9 years (range,

1~62 years). Seven patients (10%) had craniospinal metastasis at initial diagnosis. Differentiated and anaplastic ependymoma were found in 57 and 13, respectively. All patients received postoperative RT to a median total dose of 54 Gy (range, 44.7~61.2 Gy). Craniospinal RT was used in 40 patients (57%).

The median follow-up duration was 52 months (range, 3~228 months). The 5-year and 10-year overall survival (OS) rates for all patients were 86.2% and 62.9%, respectively. By univariate analysis, age ($p=0.04$) and extent of resection ($p<0.01$) were significant prognostic factors for OS. Mulvariate analysis showed that age was a significant prognostic factor for OS ($p=0.02$, relative risk 0.262, 95% confidence interval 0.088–0.777). Thirty-four patients (49%) had failure as follows: local in 25 patients, craniospinal in 2, and local plus craniospinal in 7. In patients with anaplastic ependymoma, there was no craniospinal failure. Twenty-eight of 34 patients with failure had salvage treatment and 22 patients were successfully salvaged.

Age and extent of resection were identified as major prognostic factors in patients with intracranial ependymomas. The major pattern of failure of ependymoma was local

failure. Aggressive salvage treatment for the patients with treatment failure results in high salvage rates. The new treatment strategies are required to improve the probability of local control.

Key words: Ependymoma, Surgery, Radiotherapy

Student Number:: 2007-21968

Contents

List of Tables

List of Figures

Introduction

Intracranial ependymoma are relatively uncommon tumor, comprising 2% to 6% of all intracranial neoplasm (1). The current standard of treatment for intracranial ependymoma usually includes maximal surgical resection followed by postoperative radiotherapy (RT) and chemotherapy is reserved for recurrent tumors. However, for very young children with age less than 3 years, chemotherapy has been used to delay or avoid RT. Recent clinical trials in the children with high-grade tumors include chemotherapy as a component of initial therapy with surgery and RT (2, 3). Ependymoma arise from the ependymal lining of the ventricular system. They can occur at any site within the ventricular system or in the spinal canal, so the children with infratentorial or high-grade tumors have received prophylactic craniospinal radiotherapy (CSRT). However, there was no evidence to support the use of extended field or CSRT (4-7). As a result, the current recommendation for patients with ependymoma is limited-field radiation.

Although several studies have revealed that postoperative RT improves control and survival, the optimal management has been debated and is based mainly on single institution experiences (8-11). Until now, age at presentation, tumor location, histologic grade, craniospinal metastasis, postoperative RT, and the extent of resection have been identified as important prognostic factors (4-14). Radiation dose, the duration of RT, and the interval between surgery and RT have been reported as prognostic factors (7, 15-17). However, controversies exist concerning the prognostic factors because of inconsistency among reported studies. Actually, most of studies were small, comprising a heterogeneous mix of tumor parameter and prognostic factors, including extent of resection and grade.

We performed a retrospective review of our institutional experience for 27 years. The purpose of the present study is to analyze long-term outcome and to evaluate the efficacy of salvage treatment in the patients who received surgery and postoperative RT for intracranial ependymoma.

Materials and Methods

1. Materials

Medical records of 70 patients with intracranial ependymoma who received RT with definitive aim at Seoul National University Hospital between January 1979 and June 2006 were reviewed retrospectively. Patient and tumor characteristics of analyzed patients are shown in Table 1. The median age of patients at the time of initial treatment was 9 years (range, 1-62 years) (Figure 1). There were 41 male patients (59%) and 29 female patients (41%). The patients had adequate radiographic studies for craniospinal area, such as computed tomography (CT), magnetic resonance imaging (MRI), or cerebral angiography. Seventeen patients (24%) had only CT and 53 patients (76%) had MRI. The majority of patients (83%) had infratentorial tumor. Seven patients (10%) had M+ disease. All patients had pathological confirmation of the diagnosis. Differentiated and anaplastic ependymoma were found in 57 and 13 patients, respectively.

Table 1. Patient and tumor characteristics (n=70)

		Number of patients (%)
Age	Median	9 years
	Range	1–62 years
Sex	Male	41 (59)
	Female	29 (41)
ECOG PS	0, 1	44 (63)
	2, 3, 4	26 (37)
Location	Supratentorial	12 (17)
	Infratentorial	58 (83)
Tumor grade	Differentiated	57 (81)
	Anaplastic	13 (19)
Image at diagnosis	CT	17 (24)
	MRI	53 (76)
Craniospinal metastasis	Negative	63 (90)
	Positive	7 (10)

Abbreviation: ECOG PS, Eastern Cooperative Oncology Group Performance Status; CT, computed tomography; MRI, magnetic resonance imaging

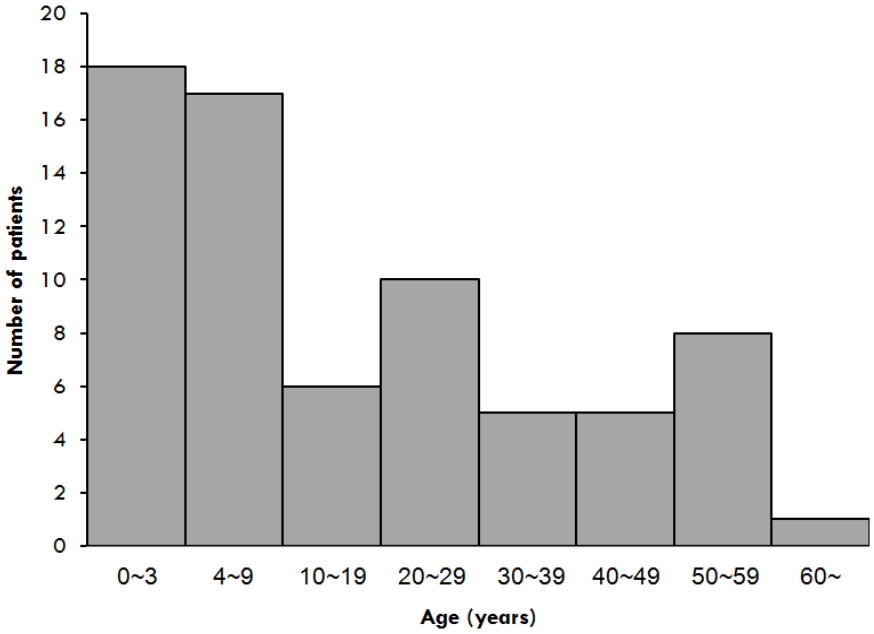

Figure 1. Age distribution of the patients with intracranial ependymoma (n=70)

2. Methods

(1) Treatment

Our general recommendation for the management of an intracranial ependymoma is maximum surgical resection followed by postoperative RT. Gross total resection (GTR) was achieved in 21 patients (30%), near total resection (NTR) in 14 (20%), subtotal resection (STR) in 29 (41%), partial resection (PR) in 4 (6%), and biopsy only in 2 (3%). All patients received underwent microneurosurgery. The extent of resection was based on through review of the surgeon`s operative note.

All patients received postoperative RT to a median total dose of 54 Gy (range, 44.7~61.2 Gy). The median duration of RT was 48 days (range, 37~104 days). CSRT was used in 40 patients (57%). The indication of CSRT varied over the treatment era. From 1979 to 1998, the patients who had high grade, infratentorial location, or craniospinal metastasis received CSRT. From 1999 to 2003, the patients who had high grade or craniospinal metastasis received CSRT. Only patients who had craniospinal metastasis received CSRT since 2004. A median total dose of CSRT was 30 Gy (range,

18~42 Gy). The RT techniques were 2-dimensional in 57 patients (81%), 3-dimensional in 11 (16%), and intensity modulated in 2 (3%), respectively

Twelve patients (17%) received chemotherapy. Of these patients, 10 patients received chemotherapy to delay or avoid RT and the others as a component of initial therapies with surgery and RT for high-grade tumors (Table 2).

Table 2. Treatment characteristics (n=70)

		Number of patients (%)	
Extent of resection	Gross total	21	(30)
	Near total	14	(20)
	Subtotal	29	(41)
	Partial	4	(6)
	Biopsy only	2	(3)
Radiation dose	≤ 54 Gy	45	(64)
	> 54 Gy	25	(36)
Radiation duration	≤ 50 days	45	(64)
	> 50 days	25	(36)
Radiation field	Craniospinal	40	(57)
	Local	30	(43)
Radiotherapy technique	2 dimensional	57	(81)
	3 dimensional	11	(16)
	IMRT	2	(3)
Chemotherapy	Yes	12	(17)
	No	58	(83)

Abbreviation: IMRT, intensity modulated radiation therapy

(2) Follow-up and Statistical anaylsis

Treatment response was evaluated using Response Evaluation Criteria in Solid Tumor (RECIST) version 1.1 and toxicity was evaluated using National Cancer Institute Common Terminology Criteria for Adverse Effect (NCI-CTCAE) version 3.0. Fisher`s exact test or Pearson`s chi-square test was used to compare the distribution of various clinical and pathological characteristics. Overall survival (OS), progression-free survival (PFS), and craniospinal progression-free survival (CSPFS) rates were calculated using Kaplan-Meier method and the difference were compared using log-rank test. All important factors including any factor that influenced prognosis in univariate analysis were subjected to multivariate analysis using a Cox proportional hazards regression model with a backward, stepwise procedure to determine whether factors acted independently. Follow-up time was calculated from the date of the start of definitive treatment to the date of the last contact or death. Time-to-failure was calculated from the date of the start of definitive treatment to the date of the relevant event. A level of 0.05 was considered statistically significant. All calculations were

performed using the SPSS 12.0.1 for Windows (SPSS Inc. Chicago, IL USA) statistical software package.

Results

1. Treatment outcome

For all patients, the median duration of follow-up was 52 (range; 3-291 months).

The 5- and 10-year OS rates 86.2% and 62.9%, respectively. The 5- and 10-year PFS rates were 46.3% and 34.9, respectively (Figure 2). By univariate analysis, age and extent of resection were significant prognostic factors for OS (Table 3). The 5- and 10-year OS rates were 70.6% and 34.9% in the patients with age equal or less than 4 years compared to 91.8% and 75.8% in those with age more than 4 years (p=0.04) (Figure 3). For 63 patients without craniospinal metastasis, there were no significant differences in OS, PFS and CSPFS rates between the patients with CSRT and those without CSRT. Mulvariate analysis showed that age was a significant prognostic factor for OS (p=0.02, relative risk 0.262, 95% confidence interval 0.088–0.777).

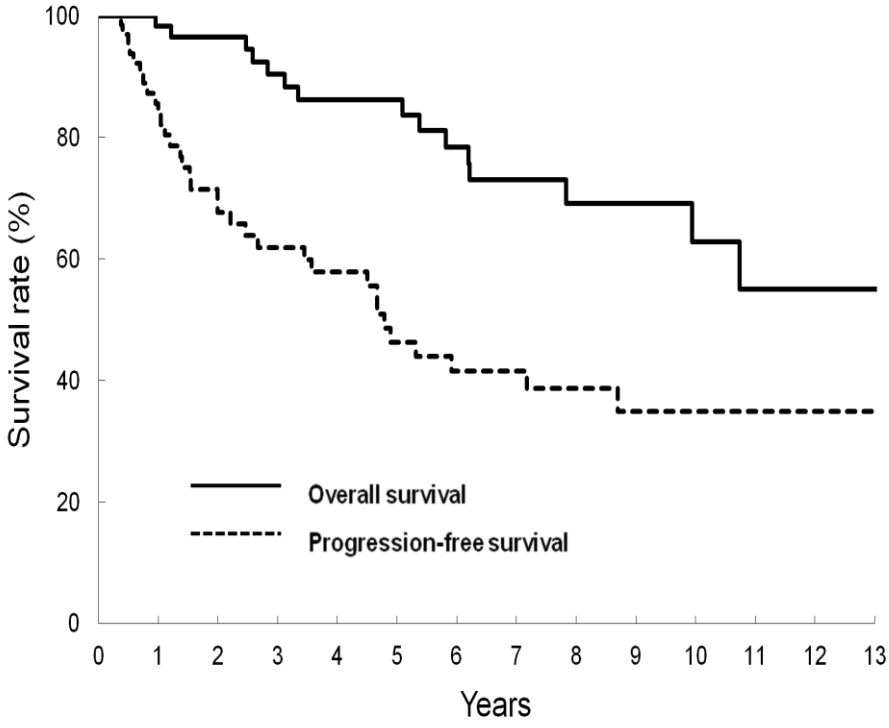

Figure 2. Overall survival and progression-free survival of all patients (n=70)

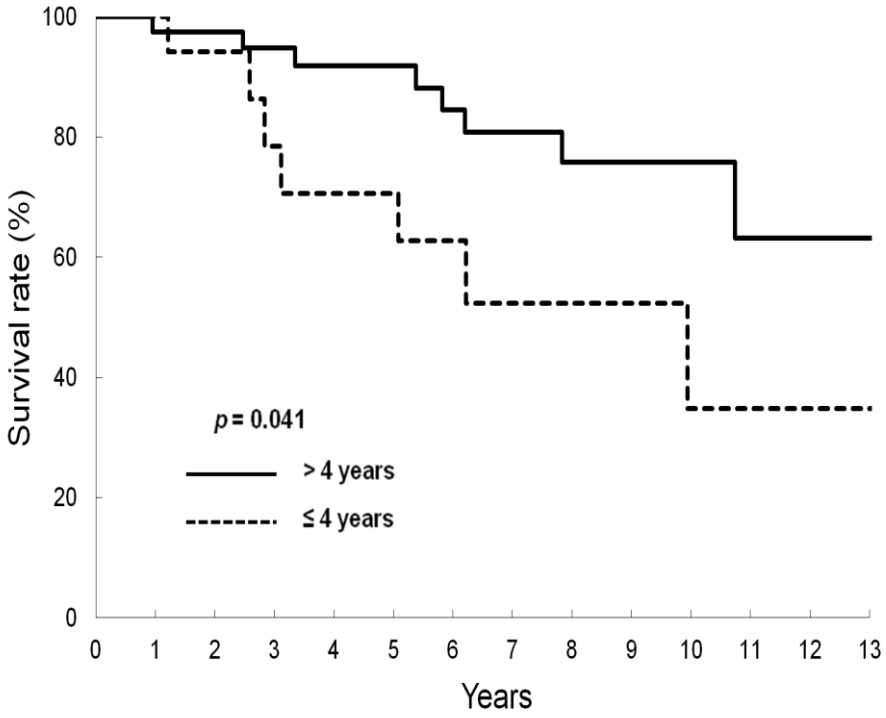

Figure 3. Overall survival according to age (n=70)

Table 3. Prognostic factors of intracranial ependymoma with surgery followed by postoperative radiotherapy: univariate analysis (n=70)

		5-yr OS	*p*-value	5-yr PFS	*p*-value
Age	0–4 years	70.6	0.04	39.2	0.14
	> 4 years	91.8		49.6	
Sex	Male	86.7	0.26	45.3	0.98
	Female	85.7		48.5	
ECOG PS	0– 1	87.0	0.76	39.9	0.32
	2– 4	84.9		56.1	
Location	Supratentorial	88.9	0.28	37.9	0.83
	Infratentorial	85.6		48.2	
Tumor grade	Differentiated	85.4	0.32	47.1	0.98
	Anaplastic	90.0		43.0	
Image as diagnosis	CT	100.0	0.66	56.3	0.22
	MRI	83.1		44.5	
Metastases	M0	88.6	0.12	43.1	0.37
	M+	68.6		83.3	
Extent of resection	GTR, NTR	86.3	<0.01	50.6	0.18
	STR	89.6		50.4	
	PR, Biopsy	66.7		0.0	

Radiation dose	≤ 54 Gy	83.4	0.70	44.1	0.40
	> 54 Gy	89.6		43.2	
RT duration	≤ 50 days	81.2	0.81	38.4	0.20
	> 50 days	94.4		56.1	
RT field	Craniospinal	84.5	0.49	45.4	0.79
	Local	88.2		47.0	
RT technique	Conventional	83.8	0.84	46.4	0.45
	3D or IMRT	100.0		56.1	
Chemotherapy	Yes	77.1	0.57	50.0	0.72
	No	88.2		45.4	

Abbreviation: OS, overall survival; PFS, progression-free survival; ECOG PS, Eastern Cooperative Oncology Group Performance Status; CT, computed tomography; MRI, magnetic resonance imaging; RT, radiotherapy; GTR, gross total resection; NTR, near total resection; STR, subtotal resection; PR, partial resection; 3D, 3 dimensional; IMRT, intensity modulated radiation therapy

2. Patterns of failure

Of the all patients, 34 (49%) had treatment failure. The patterns of failure were as follows: local failure in 25 patients (73%), craniospinal failure in 2 (6%), and local plus craniospinal failure in 7 (21%). Of the 7 patients with local plus craniospinal failure, 6 patients had developed local failure as the first failure. One patient who developed crainospinal failure as the first failure presented with craniospinal metastasis at diagnosis

Of the 63 patients without craniospinal metastasis at initial diagnosis, 32 (51%) had treatment failure as follows: local failure in 25 patients (78%), craniospinal failure in 2 (6%), and local plus craniospinal failure in 5 (16%). Of the 7 patients with craniospinal metastasis, two had treatment failure in crainospinal area and nobody experienced treatment failure in local area (Table 4). In the 13 patients with WHO grade III ependymoma, there was no craniospinal failure.

Table 4. Patterns of failure according to initial craniospinal metastasis (n=70)

Patterns of failure	Initial craniospinal metastasis		
	Negative	Positive	Total
Local failure	25	0	25
Craniospinal failure	2	0	2
Local & craniospinal failure	5	2	7
Total	32	2	34

3. Salvage treatment

Of the 34 patients with treatment failure, 28 had salvage treatment. Twenty-three patients were treated with surgery, 4 with radiosurgery, 1 with RT. Of the 23 patients with surgery as salvage treatment, 4 received combined treatments with radiosurgery, 9 with RT, and 3 with both radiosurgery and RT. Twelve patients received chemotherapy. The response to salvage treatment was complete remission in 10 patients, partial remission in 2, stable disease in 10, and progressed disease in 6, respectively

4. Toxicity

Hematologic toxicity was the most common of the treatment-related toxicity. Severe anemia, leukopenia, neutropenia, and thrombocytopenia developed in 4, 17, 10, and 6 patients. The patients with CSRT experienced more hematologic toxicity, compared to those without CSRT ($p<0.01$). In the patients without CSRT or chemotherapy, severe hematologic toxicity developed in only one patient (grade 3 anemia). Short stature developed in 7 patients and 4 of these 7 patients received CSRT. Memory disturbance

developed in 4 patients and 3 of these 4 patients received CSRT. Scoliosis and cognitive dysfunction developed in 1 and 1 patients, respectively and these two patients received CSRT (Table 5).

Table 5. Complication* according to radiation field (n=70)

Complication	Radiation field			
	Craniospinal field		Local field	
	Grade 1,2	Grade 3,4	Grade 1,2	Grade 3,4
Anemia	30	1	6	3
Leukopenia	26	13	1	4
Neutropenia	17	6	0	4
Thrombocytopenia	28	2	0	4
Short stature	4	0	3	0
Scoliosis	1	0	0	0
Memory disturbance	3	0	1	0
Cognitive dysfunction	1	0	0	0

*National Cancer Institute Common Terminology Criteria for Adverse Effect (NCI-CTCAE) version 3.0

Discussion

Intracranial ependymoma are relatively uncommon tumor and there is no randomized controlled trial. Existing outcome and prognostic factors were mainly reported by single institution-based retrospective analysis. Therefore, there was little consensus with regard to outcome and prognostic factors. The present study was performed to analyze long-term outcome and to evaluate the efficacy of salvage treatment in the patients who received surgery and postoperative RT for intracranial ependymoma. This study is one of the larger studies in the literatures.

In our study, 5-year OS and PFS rates after surgery and postoperative RT, 86.2% and 46.6%, respectively. These results is comparable with those of previous other studies (4-15). By univariate analysis, age and extent of resection were significant prognostic factors for OS. Sala et al reported that survival was significantly lower for children under 4 years. They concluded that age has the strongest prognostic relevance in childhood intracranial ependymomas, while the effect of tumor location on survival

may be related to the high incidence of lateral recess ependymomas in younger children (18). Duffner et al reported that in the patients with age < 3 years and ≥ 3 years, 5-year survival rates were 25.7% and 63.3%, respectively. They interpreted that the most likely reason for the difference in survivals between the two age groups relates to the timing of radiation following chemotherapy. And they suggested an alternative but less likely hypothesis is that ependymomas in the younger children have a more aggressive biology (19). Most studies reported that extent of resection was a prognostic factor for local control, progression-free survival, and overall survival (6, 8-12). In our study, patients with GTR, NTR, or STR had improved outcome compared with those with PR or biopsy. The relatively low PFS rate in the patients with GTR may be caused by the difference of the GTR definition. The definition of GTR has evolved over time into more stringent definition based on surgeon`s reports and immediate postoperative imaging (8). We were unable to evaluate the extent of resection with MRI on patients who were treated in the early eras of our study. In some patients, the extent of resection may be less than GTR on the basis of MRI.

In case of the patients with postoperative RT, radiation dose have been reported as a prognostic factor (7, 15-17). Garret et al reported a dose-response relationship in intracranial ependymoma. For the patients with radiation dose ≤ 45 Gy, crude survival rate was 28%, in contrast to 67% for the patients with radiation dose > 45 Gy (20). Stuben et al reported the significant difference in PFS between the patients with radiation dose ≤ 45 Gy and > 45 Gy (7). On the other hand, in the series by Chiu et al, 5-year survival rates in the patients with radiation dose ≤ 50 Gy and > 50 Gy were 33% and 58%, respectively and they reported a dose-response relationship for >50 Gy versus ≤ 50 Gy (16). In our study, we did not observe a dose-response relationship in intracranial ependymoma. Perhaps it may be because all patients received postoperative RT with radiation dose more than 44.7 Gy and the majority of patients (89%) received postoperative RT with radiation dose more than 50 Gy. Recently, there is some evidence that dose escalation reaching 59.4 Gy or more improve outcome. Merchant et al reported that the 7-year local control, event-free and overall survival for pediatric intracranial ependymoma were 83.7%, 69.1%, and 81%, respectively. In that

study, more than 80% of patients received GTR and RT with 59.4 Gy. The high rates of local tumor control, event-free and overall survival highlight the importance of gross-total resection and the management strategy to administer high-dose postoperative radiation therapy. (21).

In our study, for 63 patients without craniospinal metastasis, there were no significant differences in OS, PFS and CSPFS rates between the patients with CSRT and those without CSRT. Vanuystel et al reported that 5-year PFS rates in the patients with local RT and CSRT were 38% and 46%, respectively (15). Oya et al reported that there was no difference for craniospinal metastasis between the patients who received local RT and CSRT (22). In a recent prospective trial, Merchant et al showed that limited volume RT achieves high rates of disease control and results in stable neuro-cognitive outcome. In that study, the patients received 3-dimensional conformal RT to 54-59.4 Gy using a 1 cm clinical target volume margin surrounding the tumor bed or residual tumor (23). In previous literatures, there was no evidence to support the use of extended field or CSRT (4-7, 13-16, 22).

In our study, local failure was predominant pattern of failure. Of the 7 patients with local plus craniospinal failure, 6 patients had developed local failure as the first failure. These results are comparable with those of previous studies (4-7, 13-16, 22, 24). In the current German HIT group trials, 40 patients received CSRT for high-grade intracranial ependymoma and 25 of these patients had treatment failure, predominantly local failure (22/25) (25). Considering the patients` age with intracranial ependymoma and the possibility of considerable toxicity in the patients with CSRT, we need to establish strict indications of CSRT. In this study, the indication of CSRT varied over the treatment era and only patients who had craniospinal metastasis receive CSRT at present.

In our study, 12 patients received chemotherapy as a component of initial treatment with surgery and RT and 12 patients received chemotherapy as salvage treatment for recurrent disease. Bloom et al reported that chemotherapy improved survival in high grade tumor (26). The other series reported that a significant proportion of children with ependymoma can avoid or delay with prolonged chemotherapy (27, 28). A

prospective trial (Head Start III) reported that intensive induction and consolidation chemotherapy in deferring RT appears ineffective in children with infratentorial ependymoma in the absence of RT (29). In our study, the major indication of chemotherapy was very young age and these patients had delayed RT. Although the patients with chemotherapy had more adverse prognostic factors, there was no difference for outcome between the patients with chemotherapy and without chemotherapy. We couldn`t conclude the role of chemotherapy in high grade tumor because of the relatively small number of the patients with high grade tumor and further study is needed.

The patients with treatment failure had aggressive salvage treatment. Of the 34 patients with treatment failure, 28 had salvage treatment and better response more than stable disease developed in 22 patients. Merchant et al reported that patients with locally recurrent ependymoma experience durable local control after salvage treatement such as surgery or re-RT (30). Stafford et al reported that the median survival was 3.4 years and 3-year LC rate was 68% after radiosurgery for recurrent intracranial ependymoma

(31). Bouffet et al reported that re-irradiation (re-RT) is an effective treatment that may change the natural history of recurrent ependymoma in children (3-year OS rate 7% without re-RT and 81% with re-RT) (32). These studies confirmed the efficacy of aggressive salvage treatment in patients with recurrent intracranical ependymoma. Further data and longer follow-up is needed to evaluate the long-term efficacy and toxicity.

Major limitations of this study are unavoidable selection biases in retrospective study, the relatively small number of the patients with high grade tumor, no central pathology review, and the change of treatment strategies over the era.

In conclusion, our study showed that age and extent of surgery are significant prognostic factors for OS. The major pattern of failure of ependymoma is local failure. Aggressive salvage treatment for the patients with treatment failure results in high salvage rates. The treatment strategies, such as radiation dose escalation, radiosurgery, proton therapy, heavy charged particle therapy, combined radiosensitizer, or increasing extent of resection, are required to improve the probability of local control..

References

1. Greenberg HS, Chandler WF, Sandler HW. Posterior fossa tumors. In: Greenberg HS, Chandler WF, Sandler HW, editors. Brain tumors. New York: Oxford University Press. 1999;201-236.

2. Evans AE, Jenkin DT, Sposto R, et al. The treatment of medulloblastoma: The results of a prospective randomized trial of radiation therapy with and without CCNU, vincristine, and prednisone. J Neurosurg 1990;72:572-582.

3. Tait DM, Thornton-Jones H, Bloom HJG, et al. Adjuvant chemotherapy for medulloblastoma: The first multi-centre control trial of the International Society of Pediatric Oncology(SIOP-I). Eur J Cancer 1990;26:464-469.

4. Rousseau P, Habrand JL, Sarrazin D, et al. Treatment of intracranial ependymomas of children: Review of a 15-year experience. Int J Radiat Oncol Biol Phys 1994;28:381-386.

5. Pollack IF, Gerszten PC, Martinez AJ, et al. Intracranial ependymomas of childhood:

Long-term outcome and prognostic factors. Neurosurgery 1995;37:655-666.

6. Mansur DB, Perry A, Rajaram V, et al. Postoperative radiation therapy for grade II and III intracranial ependymoma. Int J Radiat Oncol Biol Phys. 2005;61:387-91.

7. Stuben G, Stuschke M, Kroll M, et al. Postoperative radiotherapy of spinal and intracranial ependymomas: Analysis of prognostic factors. Radiother Oncol 1997;45:3-10.

8. Metellus P, Barrie M, Figarella-Branger D et al. Multicentric French study on adult intracranial ependymomas: prognostic factors analysis and therapeutic considerations from a cohort of 152 patients. Brain. 2007;130::1338-1349

9. Swanson EL, Amdur RJ, Morris CG et al. Intracranial ependymomas treated with radiotherapy: long-term results from a single institution. J Neurooncol. 2011;102):451-457

10. Koshy M, Rich S, Merchant TE et al. Post-operative radiation improves survival in children younger than 3 years with intracranial ependymoma. J Neurooncol. 2011;105:583-590.

11. Tamburrini G, D'Ercole M, Pettorini B, et al. Survival following treatment for intracranial ependymoma: a review.. Childs Nerv Syst. 2009;25:1303-1312.

12.. Pi JH, Wang KC, Park SH, et al. Pediatric infratentorial ependymoma: prognostic significance of anaplastic histology. J Neurooncol. 2012;106:619–626.

13. Paulino AC,Wen BC, Buatti JM, et al. Intracranial ependymomas: An analysis of prognostic factors and patterns of failure. Am J Clin Oncol 2002;25:117-122.

14. Schild SE, Nisi K, Scheithauer BW, Wong WW, et al. The results of radiotherapy for ependymomas: the Mayo Clinic experience. Int J Radiat Oncol Biol Phys. 1998;42:953-958.

15. Vanuytsel LJ, Bessell EM, Ashley SE, et al. Intracranial ependymoma: Long-term results of a policy of surgery and radiotherapy. Int J Radiat Oncol Biol Phys 1992;23:313-319.

16. Chiu JK, Woo SY, Ater J, et al. Intracranial ependymoma in children: Analysis of prognostic factors. J Neurooncol 1992;13:283-290.

17. Paulino AC, Wen BC. The significance of radiotherapy treatment duration in

intracranial ependymoma. Int J Radiat Oncol Biol Phys 2000;47:585-589.

18. Sala F, Talacchi A, Mazza C, et al. Prognostic factors in childhood intracranial ependymomas: the role of age and tumor location. Pediatr Neurosurg. 1998 ;28:135-142.

19. Duffner PK, Krischer JP, Sanford RA, et al. Prognostic factors in infants and very young children with intracranial ependymomas. Pediatr Neurosurg. 1998 ;28:215-222.

20. Garrett PG, Simpson WJ. Ependymomas: Results of radiation treatment. Int J Radiat Oncol Biol Phys 1983; 9:1121-1124.

21. Merchant TE, Li C, Xiong X et al. Conformal radiotherapy after surgery for paediatric ependymoma: a prospective study. Lancet Oncol. 2009;10):258-266.

22. Oya N, Shibamoto Y, Nagata Y, et al. Postoperative radiotherapy for intracranial ependymoma: Analysis of prognostic factors and patterns of failure. J Neurooncol 2002;56:87-94.

23. Merchant TE, Mulhern RK, Krasin MJ, et al. Preliminary results from a phase II

trial of conformal radiation therapy and evaluation of radiation-related CNS effects for pediatric patients with localized ependymoma. J Clin Oncol. 2004;22:3156-3162.

24. Merchant TE, Haida T, Wang M, et al. Anaplastic ependymoma: Treatment of pediatric patients with or without craniospinal radiation therapy. J Neurosurg 1997;86:943-949.

25. Timmermann B, Kortmann RD, Kuhl J, et al. Combined postoperative irradiation and chemotherapy for anaplastic ependymomas in childhood: Results of the German prospective trials HIT 88/89 and HIT 91. Int J Radiat Oncol Biol Phys 2000;46:287-295.

26. Bloom HJG, Glees J, Bell J, et al. The treatment and long-term prognosis of children with intracranial tumors: A study of 610 cases, 1950-1981. Int J Radiat Oncol Biol Phys 1990;18:723-745.

27. Grundy RG, Wilne SA, Weston CL, et al.; Children's Cancer and Leukaemia Group (formerly UKCCSG) Brain Tumour Committee. Primary postoperative chemotherapy without radiotherapy for intracranial ependymoma in children: the

UKCCSG/SIOP prospective study. Lancet Oncol. 2007;8:696-705.

28. Grill J, Le Deley MC, Gambarelli D, et al.; French Society of Pediatric Oncology. Postoperative chemotherapy without irradiation for ependymoma in children under 5 years of age: a multicenter trial of the French Society of Pediatric Oncology. J Clin Oncol. 2001;19:1288-1296.

29. Venkatramani R, Ji L, Lasky J, et al. Outcome of infants and young children with newly diagnosed ependymoma treated on the "Head Start" III prospective clinical trial. J Neurooncol. 2013;113:285-291.

30. Merchant TE, Boop FA, Kun LE, et al. A retrospective study of surgery and reirradiation for recurrent ependymoma. Int J Radiat Oncol Biol Phys. 2008;71:87-97.

31. Stafford SL, Pollock BE, Foote RL, et al. Stereotactic radiosurgery for recurrent ependymoma. Cancer. 2000;88:870-875.

32. Bouffet E, Hawkins CE, Ballourah W, et al. Survival benefit for pediatric patients with recurrent ependymoma treated with reirradiation. Int J Radiat Oncol Biol Phys.

2012;83:1541-1548.

국문초록

두개강내 상의세포종에서 수술 후 방사선치료

– 단일기관 장기 추적 결과 –

장원일

방사선종양학 전공

의학과

서울대학교

본 연구의 목적은 수술, 방사선치료를 받은 두개강내 상의세포종 환자들을 대상으로 장기추적 결과을 분석하고, 구제치료의 효과에 대해 평가하는 것이다.

1979년 1월부터 2006년 6월까지 서울대학교병원에서 근치적 목적으로 방사선치료를 받은 두개강내 상의세포종 환자 70명에 대해 후향적 분석을

시행하였다. 대상 환자들의 연령은 1-62세(중앙값, 9세)다. 진단 당시에 7명(10%)에서 뇌척수 전이가 있었다. 분화된 상의세포종이 57명, 역형성 상의세포종이 13명이었다. 모든 환자들은 수술 후 방사선치료를 받았으며, 방사선량의 중앙값은 54 Gy (범위, 44.7~61.2 Gy)였다. 40명의 환자들은 전뇌척수 방사선치료를 받았다.

전체 환자에서 추적관찰 기간은 3-228개월(중앙값, 52개월)이었다. 5년 및 10년 전체 생존율은 각각 86.2% 및 62.9%였고, 5년 및 10년 무진행 생존율은 각각 46.3% 및 34.9%였다. 단변량 분석에서 나이 ($p=0.04$)와 절제 정도 ($p<0.01$)가 전체 생존율에 대해 의미있는 예후인자였다. 다변량 분석에서는 나이 만이 전체 생존율에 대해 의미 있는 예후 인자였다($p=0.02$, 상대 위험도 0.262, 95% 신뢰구간 0.088-0.777). 전체 환자 중 34명이 추적관찰 기간 중에 치료 실패가 있었다. 치료 실패 양상은 25명이 국소 실패, 2명이 뇌척수 실패였으며, 7명에서는 국소 실패와 뇌척수 실패가 같이 있었다. 역형성 상의세포종 환자에서는 뇌척수 실패가 발생한 환자는 없었다. 치료 실패가 있었던 34명의 환자 중에 28명은

구제치료를 받았으며, 22명이 성공적으로 구제되었다.

본 연구에서 나이와 절제 정도가 두개강내 상의세포종 환자에서 주요 예후인자로 나타났다. 치료 재발 양상의 대부분은 국소 재발이었다. 치료 실패가 있는 환자에서 적극적인 구제 치료를 통해 높은 구제율을 얻을 수 있다. 국소 제어율을 높이기 위한 새로운 치료방법이 요구된다.

주요어: 상의세포종, 수술, 방사선치료

학번: 2007-21968