Postoperative Radiation Therapy of Craniopharyngioma

Kyung Hwan Shin, M.D., Hyong Geln Yun, M.D.,** Il Han Kim, M.D.
Charn Il Park, M.D. and Byung Kyu Cho, M.D.*

Department of Therapeutic Radiology, Department of Neurosurgery, College of Medicine, Seoul National University, Seoul, Korea*
*Department of Therapeutic Radiology, Korea Cancer Center Hospital, Seoul, Korea***

Between December 1979 and September 1989, 23 patients with craniopharyngioma who underwent surgery and postoperative radiation therapy were retrospectively evaluated to assess the efficacy of this management at the Department of Therapeutic Radiology, Seoul National University Hospital. Total removal of tumor was attempted in all patients. Of these, surgeons tried total removal in eight patients, but revealed residual mass by postoperative CT, and partial removal was done in 15 patients. The morphology of tumor on the operative finding was grouped into three types: cystic 13 (57%), solid 4 (17%), and mixed 6 (26%). Cystic type was predominant in≤20 years old group. Actuarial overall survival rates at 5 and 10 years were 95% and 81% respectively and actuarial tumor control rates were 74% and 50%. Surgical extent was not related to the survival rates ($p=0.41$). Pediatric and adolescent patients (age of≤ 20 years) had a trend of better survival than that of adult patients ($p=0.10$). The results indicated that limited surgical excision followed by radiation therapy is recommended when total excision is not possible.

Key Words: Craniopharyngioma, Radiation therapy, Survival rate.

INTRODUCTION

Craniopharyngiomas are histologically benign intracranial tumors that arise from remnants of Rathke's pouch. They are usually slow-growing and not invasive. But suprasellar extension may induce hypothalamic or thalamic damage because of anatomical situation. Craniopharyngioma may extend anteriorly to the optic chiasm leading to visual impairment, posteriorly to the pituitary gland or hypothalamus leading to hormonal deficiencies, or superiorly to the third ventricle or foramen of Monro leading to hydrocephalus or neurologic deficit. Therefore, the endpoint of treatment is improving the quality of life as well as survival.

The managements of craniopharyngioma have still been debated. Some neurosurgeons[1~4] have preferred total removal. Other authors have advocated more limited surgery, for example, subtotal removal or aspiration biopsy, usually followed by postoperative radiation therapy. The reliability of this treatment has been controversial in neurosurgical practice, but recently, it has been more generally accepted that patients with residual craniopharyngioma receiving radiation therapy have a better outcome, in terms of survival and also quality of life[5].

This study attempts to evaluate the role of postoperative radiation therapy in the management of craniopharyngioma. In addition, a variety of clinical, radiologic and pathologic characteristics are evaluated for prognostic significances.

METHODS AND MATERIALS

Between December 1979 and September 1989, 28 patients with craniopharyngioma were treated in the Department of Therapeutic Radiology, Seoul National University Hospital. Five of these patients were excluded from this analysis for the following reasons: Three had received incomplete radiation therapy and two were lost to follow-up immediately after the completion of radiation therapy.

The age of 23 remaining patients ranged from 6 to 58 years with a median of 27 years. Eight (35%) patients were included in≤20 years old group and 15 (65%) were>20 years old group. There were 12 males and 11 females. The patients were followed from 31 months to 134 months (median 68 months).

1. Presenting Symptoms and Signs

All patients had a complete history, physical

This work was partly supported by 1991 SNUH Research Fund

Table 1. Presenting Symptoms and Signs (N=23)

	No. of patients (%)
Visual	
Visual field defect	16 (70)
Decreased visual acuity	12 (52)
Papilledema	5 (22)
Diplopia	1(4)
Neurologic	
Headache	18 (78)
Nausea or Vomiting	9 (39)
Somnolence	5 (22)
Lower extremity paresis	2 (9)
Hormonal	
Diabetes insipitus	16 (70)
Panhypopituitarism	6 (26)
Primary amenorrhea	2 (9)
Decreased height	2 (9)
Obesity	2 (9)
Precocious puberty	1 (4)

Table 2. Preoperative CT Findings (N=21)*

	No. of patients (%)		
	≤ 20 years	> 20 years	*p* value
Hydrocephalus			
positive	4 (50)	2 (15)	
negative	4 (50)	11 (85)	*NS***
Calcification			
positive	8 (100)	9 (69)	
negative	0 (0)	4 (31)	*NS*
Size			
> 3 cm	5 (63)	3 (23)	
≤ 3 cm	3 (37)	10 (77)	*NS*

**CT was not performed in initial two patients.*

***NS*: not significant

examination including neurologic examination, fundoscopic examination, and visual field mapping, and a complete hormonal profile. The majority of patients had significant symptoms and signs prior to treatment (Table 1).

Of the visual symptoms, visual field defect was the presenting finding in 16/23 (70%), decreased visual acuity 12/23 (52%), papilledema 5/23 (22%) and diplopia 1/23 (4%). Headache was the most frequent neurologic symptom (78%). Other neurologic findings were as follows: nausea or vomiting, somnolence and lower extremity paresis. The endocrine function most severely compromized was consistant with panhypopituitarism (26%). Other hormonal changes observed were: Diabetes insipitus (70%), Primary amenorrhea (9%), Decreased height (9%), Obesity (9%) and Precocious puberty (4%).

Table 3. Operation and Tumor Morphology on Operative Findings

	No. of patients (%)		
	≤ 20 years	> 20 years	Total
Operation			
Total removal*	4 (50)	4 (27)	8 (35)
Partial removal	4 (50)	11 (73)	15 (65)
Morphology			
Cystic	6 (75)	7 (46)	13 (57)
Solid	9 (0)	4 (27)	4 (17)
Mixed	2 (25)	4 (27)	6 (26)

*All patients showed small residuals on postop. CT findings.

2. Computed Tomography (CT) Evaluation at Initial Presentation

As shown in table 2, CT findings were available in 21 patients. Six (29%) patients showed hydrocephalus, which consisted of 4/8 (50%) patients in ≤ 20 years and 2/13 (15%) patients in > 20 years. There noted calcifications in 17/21 (81%) patients. Among these, all ≤ 20 years old patients showed calcifications. The tumor size measured on CT findings was grouped into > 3 cm and ≤ 3 cm : 8/21 (38%) in > 3 cm and 13/21 (62%) in ≤ 3 cm. Initial presenting symptoms and signs such as hydrocephalus, calcification and large tumor size in ≤ 20 years old group were shown more prevalent than those in adult patients, but it was not statistically significant.

3. Tumor Morphology

We analyzed the tumor morphology in all patients as shown in table 3. Cystic tumors in 13 (57%), purely solid tumors in four (17%), and mixed cystic and solid tumors in six (26%) were noted. In ≤20 years old group, the cystic type was 75% and no solid one, but of 15 over 20 years old group, cystic type in 7 (46%), solid 4 (27%) and mixed one

4 (27%) were found.

4. Surgery

The surgical approach was performed at SNUH in an attempt at total removal of the tumor in all patients. The craniotomy was performed in 22 patients and aspiration following transsphenoidal approach was performed in one patient.

A total removal of tumor, as determined by the surgeon's impression, was achieved in eight of 23 patients (Table 3), but they had small residuals with calcifications on postoperative CT. So the postoperative radiation therapy was mandatory, and they were included in this analysis. The patients showing no residual tumors on postoperative follow-up CT didn't receive radiation therapy and were excluded from this study.

Partial removal was performed in 15 patients. Of these patients, two were recurrent cases. One was treated with radiation therapy alone and the other was reoperated and irradiated.

5. Radiation Therapy

Radiation therapy was delivered with 6 or 10 MV linear accelerator or cobalt-60 teletherapy unit. Field arrangements were used lateral two opposed fields in 11 patients, opposed two laterals with an anterior field boost at the end of treatment in 12 and three fields of opposed two laterals along with an anterior field in one. The field size was usually from 4×4 cm to 6×6 cm depending on tumor size. The doses ranged 5000-6000 cGy during the period of 5-7 weeks in 180-200 cGy per fraction (median: 5580 cGy).

6. Follow-up

All patients were regularly followed and the follow-up period ranged from 31 to 134 months (median: 68 months). They were checked up with every two or three months for initial two years after the completion of radiation therapy, two or three times a year for next three years, and after then, once or twice a year. All patients were periodically examined for hormonal change and neurologic examination as well as serial CT scans.

7. Progression and Statistics

The patients were scored as having failure if they developed symptoms of progressive disease (e.g., headache, progressive visual loss, nausea and vomiting, papilledema, etc.), or they had evidence of an enlarging mass by radiologic studies.

Overall survival was calculated from the date of surgery to the date of last follow-up or the time of death. Tumor control was measured from the date of surgery to the date of detecting the progressive disease in tumor-progression patients and last follow-up in tumor-control patients.

Survival calculation was performed using Kaplan-Meier method[6], and Log-Rank test[7] was used for univariate analysis, which were provided through the statistical package, SAS.

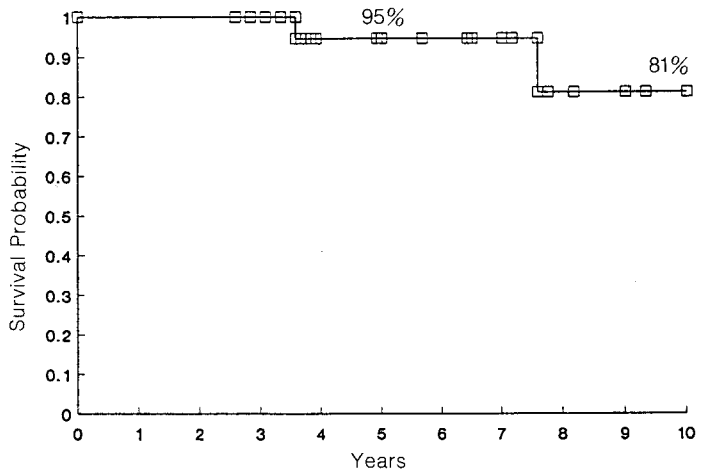

Fig. 1. Overall survival for total patients (N=23).

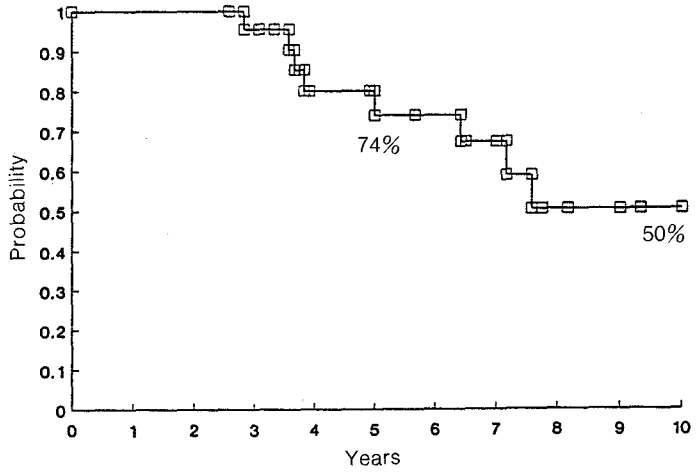

Fig. 2. Tumor control for total patients (N=23).

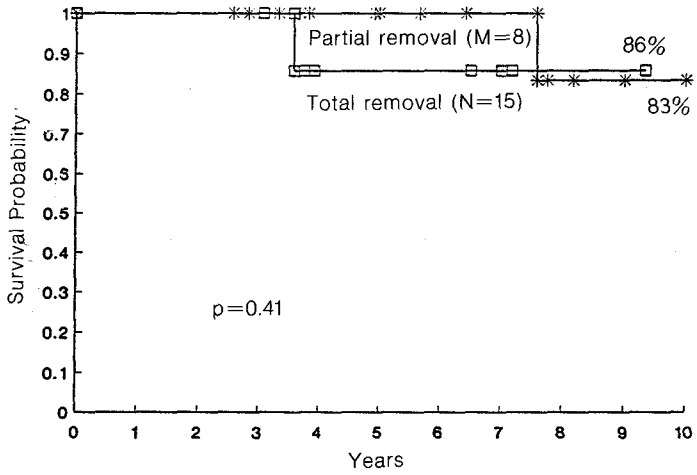

Fig. 3. Overall survival by type of surgery.

RESULTS

1. Overall Results

The actuarial overall survival and tumor control for the entire group of 23 patients are shown in Figure 1 and 2. Two patients were dead of unknown cause at the time of data analysis. Actuarial overall survival rates were 95% and 81% at 5 and 10 years and tumor control was achieved in 74% and 50% at 5 and 10 years.

2. Prognostic Factors

An univariate analysis of prognostic factors including sex, age, tumor size on CT findings, type of surgery and radiation therapy field was performed to determine their impact on prognosis as shown in table 4.

Survival rates or tumor control rates according to type of surgery are shown in Figure 3 and 4. The actuarial 5- and 10-year survival rates in partial removal group were 69% and 49% compared to 85% and 43% in total removal group (p=0.73). The tumor control rate was 83% in partial removal group and 86% in total removal group at 10 years (p=0.41). There were no significant statistical differences in overall survival rate or tumor control rate between two groups.

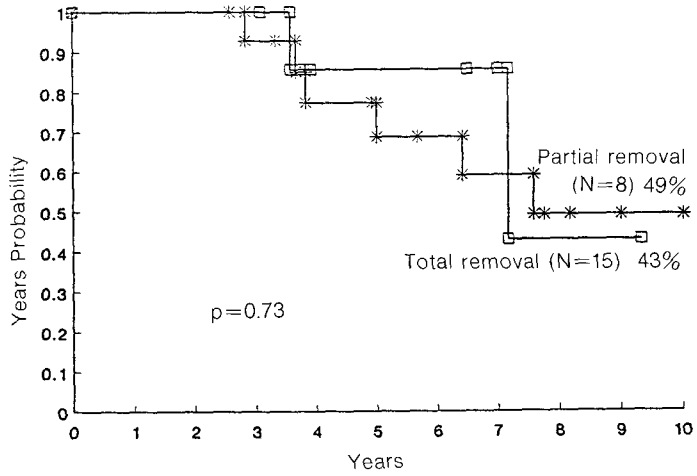

Fig. 4. Tumor control by type of surgery.

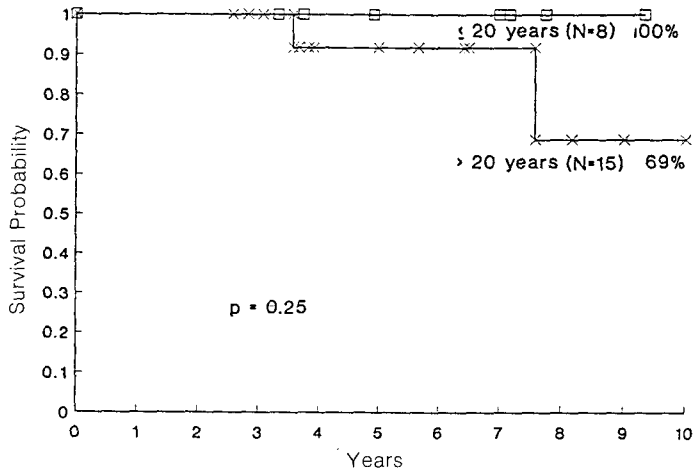

Fig. 5. Overall survival by age.

The pediatric and adolescent patients had a better result than the adult patients (Figure 5, 6). All of the pediatric and adolescent patients survived at 5 and 10 years, but the adults survived 92% at 5 years and 69% at 10 years ($p=0.25$). In tumor control rate, 75% of the pediatric and adolescent tumors were controlled at 10 years, but only 38% of the adult tumors were controlled ($p=0.10$). But it was not statistically significant.

In view of sex, radiation therapy field, and tumor size on preoperative CT finding, there showed no significant correlation with prognosis (Table 4).

DISCUSSION

A variety of methods have been used to treat craniopharyngiomas. These include total removal, partial removal alone, partial removal followed by radiation therapy, and radiation therapy alone.

Some surgeons[1~4] insist that total removal should be attempted in every patient with craniopharyngioma, because the dissecting microscope and high resolution CT and MRI scans make this approach relatively safe, and because the availability of total pituitary replacement makes the morbidity tolerable. Unfortunately, it is often difficult to achieve complete removal of the tumor without

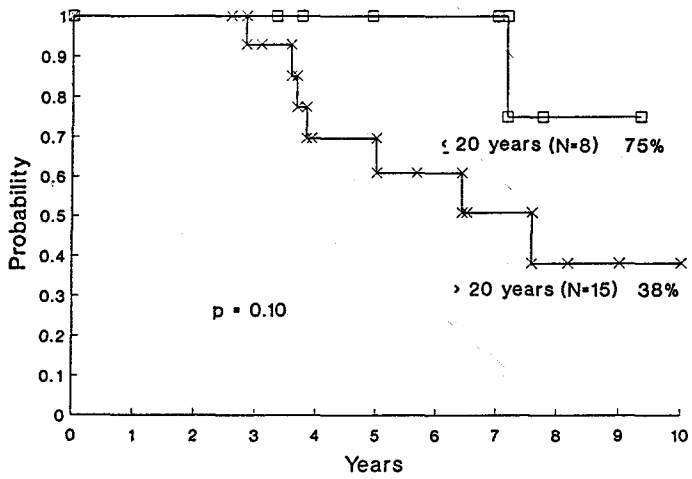

Fig. 6. Tumor control by age.

Table. 4. Prognostaic Significance of Clinical and Radiologic Characteristics

Parameters	No. of patients	Tumor control at 10 year (%)	Overall survival at 10 year (%)
Sex			
Male	12	66	100
Female	11	44	71
p value		0.67	0.23
Age			
≤ 20 yr	8	75	100
> 20 yr	15	38	69
p value		0.10	0.25
Tumor size on CT*			
≤ 3 cm	8	71	86
> 3 cm	11	44	75
p value		0.91	0.71
Type of surgery			
Total removal	8	43	86
Partial removal	15	49	83
p value		0.73	0.41
RT field			
≤45 cm^2	13	63	77
>45 cm^2	10	27	100
p value		0.27	0.43

*Tumor sizes were not measured in two patients.

significant morbidity. These tumors are often densely adherent to the optic chiasm, pituitary stalk, and internal carotid artery. They may extend close to the posterior communicating artery, and often invade the region of the third ventricle. The literatures show mortality rates ranging from 7%[8] to 41%[9] and developing major complication rates 30-40%[10]. In fact, eventhough surgeons attempted to resect the tumors completely at SNUH, patients having residual tumors on postoperative CT, e.g., residual calcification, following not only partial removal but also apparent total removal were routinely treated with postoperative radiation therapy.

Other surgeons[8] have advocated limited surgery without postoperative radiation therapy. But Wen et al.[10] reported only 15% of tumor control rate with incomplete removal without postoperative radiation therapy, and the results of many authors do not support this mode of treatment[2,4,10~15].

Most of radiation oncologists advocate limited surgery followed by radiation therapy[16~20], and there is strong evidence that less aggressive surgery is associated with preservation of endocrine function. In this report, overall 5-and 10-year tumor control rates revealed 74% and 51% respectively, with a median follow-up of 5.7 years. The value of incomplete removal and postoperative radiation therapy is well documented in the review of the Table 5.

The question arises as to whether radiation therapy alone is adequate to control craniopharyngiomas. It is difficult to answer this question, because of scant data. Wen et al.[10] showed that six of seven patients treated for gross disease had

Table 5. Tumor Control by Treatment Type on Literature Review*

Authors (year)	Surgery only			Incomplete removal & RT
	Complete resection	Incomplete removal**	Total	
Kramer et al.[18] (1961)	–	–	–	10/12
Katz[2] (1975)	25/34	1/6	26/40	–
Onoyama et al.[21] (1977)	–	–	–	25/32
Hoffman et al.[11] (1977)	17/17	6/29	23/46	0/2
Shapiro et al.[4] (1979)	17/22	2/9	19/31	18/29
Bloom[16] (1982)	–	–	–	76/112
Richmond et al.[12] (1980)	5/8	2/4	7/12	14/20
Thomsett et al.[13] (1980)	10/14	1/11	11/25	14/17
Sung et al.[14] (1981)	19/37	7/37	26/74	24/32
Danoff et al.[17] (1983)	–	–	–	12/14
Fischer et al.[22] (1985)	3/5	–	3/5	25/32
Amendola et al.[15] (1985)	8/14	5/16	13/30	–
Wen et al.[10] (1989)	10/20	3/20	13/40	8/8
Weiss et al.[23] (1989)	12/18	0/11	12/29	4/5
Total (%)	126/189 (67)	27/143 (19)	153/332 (46)	230/315 (73

*From Wen BC, et al: Int J Radiot Oncol Biol Phys 16:17-24, 1989-Modified

**Includes subtotal removal, partial resection, cyst aspiration, and biopsy

long-term tumor control with no further treatment. Thus it can be considered radiation therapy alone is adequate to control craniopharyngiomas. However, surgery is needed to confirm the diagnosis histologically, and surgical decompression is probably indicated to control symptoms before radiation therapy is delivered.

The factors such as the patient's age, the size of the tumor, and the extent of surgery are believed to influence the prognosis in craniopharyngioma. Although there has been no detailed study focusing on the influence of these variables, it has been discussed by some authors. Hoff and Patterson[1] reported that postoperative radiation therapy delayed recurrence, especially in adults. Conversely, other authors have stated that the survival and tumor control rates were better in childhood and adolescence[14,21]. Our analysis revealed that surgery plus radiation therapy was of more advantage to pediatric and adolescent patients than to adults, but the difference was not statistically significant ($p=0.10$), and it might be due to the small number of patient. Hoffman et al.[11] reported that radiation therapy decreases cyst fluid formation. Shapiro et al.[4] commented that radiation therapy was most beneficial in patients with predominantly cystic tumors. Thus, it could be inferred that because cystic histology was predominant in ≤ 20 years old group, they had a trend of better outcome in our result. Onoyama et al.[21] reported that the survival rate of males was superior to that of females, but our analysis did not show a sexual difference.

Dose was not related to survival or tumor control in our study. Onoyama et al.[21] found that patients who received less the 5000 cGy fared less well than patients who received more than 5000 cGy. Hoff and Patterson[1] had suboptimal results using low doses of 2750-4500 cGy and orthovoltage equipment. Sung et al.[14] reported a 33% recurrence rate in patients treated with < 5000 cGy and only a 13% failure rate over 5500 cGy. We currently recommend 5400-5600 cGy in 180-200 cGy per fraction in case of residual lesion on postoperative CT and medically inoperable patients.

CONCLUSION

A comparison of patients undergoing an attempt of total removal plus radiation therapy with those receiving radiation therapy after partial

removal shows that the outcome for these two groups is similar. Moreover, the outcome of total removal alone is similar to our results in spite of increasing the major complications. So the strategy of limited excision plus radiation therapy is recommended when total excision is not possible, and our policy for the management of craniopharyngioma is limited surgery, followed by radiation therapy.

REFERENCES

1. **Hoff JT, Patterson RH Jr:** Craniopharyngiomas in children and adults. J Neurosurg 36:299-302, 1972
2. **Katz EL:** Late results of radical excision of craniopharyngiomas in children. J Neurosurg 42:86-90, 1975
3. **Matson DD, Crigler JF:** Management of craniopharyngioma in childhood. J Neurosurg 30:377-390, 1969
4. **Shapiro K, Till K, Grant DN:** Craniopharyngiomas in childhood: A rational approach to treatment. J Neurosurg 50:617-623, 1979
5. **Amacher AL:** Craniopharyngioma: The controversy regarding radiotherapy. Childs Brain 6:57-64, 1980
6. **Kaplan E, Meier P:** Nonparametric estimation from incomplete observations. J Am Stat Assoc 53:457 -481, 1958
7. **Peto R, Pike MC, Armitage P, et al:** Design and analysis of randomized clinical trial requiring prolonged observaiton of each patient. 11. analysis and examples. Br J Cancer 35:1-39, 1977
8. **Kahn EA, Gosch HH, Seeger JF, et al:** Forty-five years experience with the craniopharyngiomas. Surg Neurol 1:5-12, 1973
9. **Kerr AS:** Craniopharyngioma. J Neurol Neurosurg Psych 31:646, 1968
10. **Wen BC, Hussey DH, Staples J, et al:** A comparison of the roles of surgery and radiation therapy in the management of craniopharyngiomas. Int J Radiat Oncol Biol Phys 16:17-24, 1989
11. **Hoffman HJ, Hendrick EB, Humphreys RP, et al:** Management of craniopharyngioma in children. J Neurosurg 47:218-227, 1977
12. **Richmond IL, Wara WM, Wilson CB:** Role of radiation therapy in the management of craniopharyngiomas in children. Neurosurgery 6(5):513-517, 1980
13. **Thomsett MJ, Conte FA, Kaplan SL, et al:** Endocrine and neurologic outcome in childhood craniopharyngioma: Review of effect of treatment in 42 patients. J Pediatr 97(5):728-735, 1980
14. **Sung DI, Chang CH, harisiadis L, et al:** Treatment results of craniopharyngiomas. Cancer 47:847 -852, 1981
15. **Amendola BE, Gebarski SS, Bermudez AG:** Analysis of treatment results in craniopharyngioma. J Clin Oncol 3(2):252-258, 1985
16. **Bloom HJG:** Intracranial tumors: Response and resistance to therapeutic endeavers, 1970-1980. Int J Radiat Oncol Biol Phys 8:1083-113, 1982
17. **Danoff BF, Cowchock FS, Kramer S:** Childhood craniopharyngioma: Survival, local control, endocrine and neurologic function following radiotherapy. Int J Radiot Oncol Biol Phys 9:171-175, 1983
18. **K amer S, McKissock W, Concannon JP:** Craniopharyngiomas: Treatment by combined surgery and radiation therapy. J Neurosurg 18;217-226, 1961
19. **Lichter AS, Wara WM, Sheline GE, et al:** The treatment of craniopharyngiomas. Int J Radiot Oncol Biol Phys 2:675-683, 1977
20. **Manaka S, Teramoto A, Takakura K:** The efficacy of radiotherapy for craniopharyngioma. J Neurosurg 62:648-656, 1985
21. **Onoyama Y, Ono K, Yabumoto E, et al:** Radiation therapy of craniopharyngiomas. Radiology 125: 799-803, 1977
22. **Fischer EG, Welch K, Belli Ja, et al:** Treatment of craniopharyngiomas in children: 1972-1981. J Neurosurg 62:496-501, 1985
23. **Weiss M, Sutton L, Marcial V, et al:** The role of radiation therapy in the mangement of childhood craniopharyngioma. Int J Radiot Oncol Biol Phys 17:1313-1321. 1989

국문초록 =

두개인두종의 수술후 방사선치료 성적

서울대학교 의과대학 치료방사선과학교실, 신경외과학교실*
원자력병원 치료방사선과**

신경환 · 윤형근** · 김일한 · 박찬일 · 조병규*

1979년 12월부터 1989년 9월까지 서울대학병원 치료방사선과에서 두개인두종으로 수술 및 수술후 방사선치료를 시행받은 23명의 환자에 대해 적정 치료원칙을 제시하기 위하여 후향적 분석조사를 시행하였다. 모든 환자에서 근치적 수술을 시도하였으나 수술후 전산화단층촬영 소견상 종양이 남아있는 전절제군 8예 및 부분절제군 15예가 이분석에 포함되었다. 수술소견상 낭형 13예(57%), 고형 4예(17%), 혼합형이 6예(26%)로 나타났고 20세이하군에서는 낭형이 더 많은 수에서 나타났다. 5년 및 10년 생존율은 각각 95%, 81%를 보였고, 5년 및 10년 종양 조절율은 각각 74%, 51%였다. 수술정도에 따른 결과의 차이는 보이지 않았고 소아 및 청소년군에서 성인군보다 좀더 나은 결과를 보였으나 통계적으로 유의하지는 않았다. 두개인두종에 있어서 완전절제술이 시행되기 어려운 경우 부분절제술후 방사선치료가 유용한 것으로 사료된다.