Radiotherapy Results of Pineal Tumors

Kyu Young Chai, M.D., Woo Yoon Park, M.D., Doo Ho Choi, M.D.
Woong Ki Chung, M.D., Il Han Kim, M.D. and Sung Whan Ha, M.D.

Department of Therapeutic Radiology, College of Medicine, Seoul National University, Seoul, Korea

A retrospective analysis was performed on 23 patients with pineal region tumors treated with radiation from 1979 through 1985 at the Department of Therapeutic Radiology, Seoul National University Hospital. Histologic confirmation was done in only one case by surgical removal, and in the remaining 22 patients, the diagnosis was based on clinical and radiological findings. The radiation volume was the primary tumor site in 1 case, whole brain in 14 cases, and the whole craniospinal axis in 8 cases. The overall 5 year survival was 71.5%. The 5 year survival was 69.3% for whole brain treated group and 73.3% for craniospinal axis treated group. The survival for the two groups did not differ significantly. In two cases sites of recurrence were detected, one in supratentorial area, and the other in the lung. The results from this retrospective analysis and the review of other reports indicate that routine use of prophylactic spinal irradiation is not warranted in pineal region tumor, and the craniospinal irradiation is recommended in cases with high risk for subarachnoid seeding such as positive CSF cytology, surgical removal or biopsy.

Key Words: Radiotherapy, Pineal tumors

INTRODUCTION

Primary pineal tumors comprise only 0.5 to 3% of intracranial tumors with geographic variation, and more than 50% of all pineal tumors are found in patients under 20 years of age[1~3].

Due to their location and infiltrative nature, surgical extirpation of pineal tumor is difficult to achieve. Though recent advance in microsurgical or stereotactic technique reduced surgical morbidity and mortality[3~5], the advantage of direct surgery is still considered to be evident only in benign, encapsulated or radioresistant tumor, and such tumors comprise about 20-25% of pineal tumors[3,6,7]. So, irradiation with or without draining procedure is considered the treatment of choice for pineal tumor. But the heterogeneity in tumor behaviour, frequent lack of histologic diagnosis make the optimal radiation treatment design difficult. In this retrospective analysis, we are going to discuss the optimal radiation treatment for pineal tumor based on our experience and result of others.

METHODS AND MATERIALS

Twenty seven patients with pineal tumor were treated at the Dept. of Therapeutic Radiology, Seoul National University Hospital from 1979 were eliminated from this study: 2 patients because of spinal metastasis at the beginning or early stage of radiotherapy, and the other 2 patients because of incomplete treatment. So 23 patients were analyzed in this retrospective study. Two patients were lost to follow up at 39 and 44 months respectively. Median follow up periods were 39 months(1-81Mo) for all patients, and 46 months(24-81 Mo) for survivors.

Male to female ratio was 3.5 to 1, and about 65% of patients were under age of 20 years. Histologic verification was done in only one case of germinoma. In the remaining 22 cases, the diagnosis was based on clinical or radiological findings (Table 1).

Table 2 shows initial clinical presentation of patients. Symptoms due to increased intracranial pressure such as headache or vomiting, and visual disturbance were most commo: clinical manifestation. Upward gaze disturbance was present in 8 patients. The tumor mass in pineal region was confirmed by CT scan in all patients. Angiography was performed in only one patient. CSF was studied in 19 patients, and all specimens were negative for malignant cells (Table 3). Serum marker study was done in 13 patients. β-HCG levels were elevated in 5 patients, α-FP levels were elevated in 2 patients, and in the remaining 6 patients the marker levels were within normal limits (Table 4).

Sixteen patients underwent ventricular shunting, through 1985. Among these 27 patients 4 patients

Table 1. Patient Characteristics

Characteristics	No. of pts (%)
Sex	
Male	18 (78.3)
Female	5 (21.7)
Age (years)	
0 – 9	2 (8.7)
10 – 19	13 (56.5)
20 – 29	4 (17.4)
30 – 39	1 (4.4)
40 – 49	0 (0.0)
50 –	3 (13.0)
Base of Diagnosis	
Histologic Dx.	1 (4.4)
Clinical Dx.	22 (95.6)

Table 2. Presenting Symptoms and Signs

	No. of patients (%)
Symptoms	
Headache	15 (65.2)
Vomiting	11 (47.8)
Conciousness change	6 (26.1)
Polyuria & Polydipsia	4 (17.4)
Visual distrubance	13 (56.5)
Ataxic gait	4 (17.4)
Seizure	1 (4.3)
Signs	
Papilledema	5)21.7)
Upward gaze disturbance	8 (34.8)
Nystagmus	1 (4.3)
Hemiparesis	2 (8.7)

Table 3. Diagnostic Study

Study	Positive Results
CT	23/23
Angiography	1/ 1
CSF cytology	0/19
Tumor marker	7/13

Table 4. Tumor Marker Study (Serum)

Result	No. of patients
Normal	6
Elevated	7
α-FP	2
β-HCG	5
Not checked	10

and surgical resection was attempted in only one patient. Radiation treatment was given using Co 60 gamma ray. The radiation treatment volume was the primary tumor site in 1 patient, whole brain in 14 patients and whole craniospinal axis in 8 patients. There were no differences in tumor extensions or radiation responsiveness among each groups. In local area only treated patient, 50 Gy was irradiated to primary tumor area. In whole brain treated patients, 40 Gy was irradiated to whole brain followed by 10 to 15 Gy boost to primary tumor site, and in whole craniospinal axis treated patients, brain treatment was same as in whole brain treated patients and 20 to 25 Gy was irradiated to whole spine.

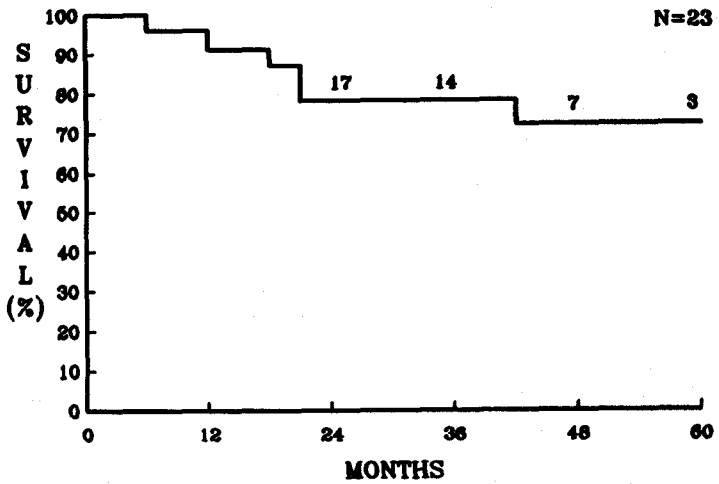

Fig. 1. Overall actuarial survival for all patients.

RESULTS

Fig. 1 shows the survival for all patients. The 5 year survival for all patients was 71.5%. Among 16 survivors, 15 patients were alive without evidence of disease until the time of follow up, and only one patient was alive with uncontrolled disease. Fig 2 shows survival according to treatment volume. The 5 year survival was 69.3% for whole brain treated patients, 73.3% for whole craniospinal axis treated patients. There was no statistical significance between two groups. One patient treated at primary site only is alive well with disease free state for 81 months.

Serum tumor marker seemed to correlate with the prognosis. All 6 patients with normal marker level were disease free at the time of follow up. One patient died of traffic accident. Among 5 patients with elevated β-HCG, 3 patients were alive without evidence of disease, and 2 patients died, one due to extraneural metastasis, the other due to uncontrolled primary disease. α-FP was elevated in two patients, one was alive, the other died of uncontrolled disease (Fig. 3).

Recurrence was detected in two patients; one in supratentorial area, the other in the lung. Supratentorial recurrence developed at 59 month, and the patient died one month later. The recurrent site was within the primary site boost field, and the tumor dose was 50 Gy. Initial β-HCG level was high(7,500 mIU/ml) in patient who developed lung metastasis suggesting choriocarcinoma. Lung metastasis developed 2 months after completion of radiotherapy, and he died 16 months later.

DISCUSSION

The pineal tumors are classified into four categories according to originating component: germ cell tumor, pineal parenchymal tumor, glial tumor and benign cyst. Among these, germ cell tumors account for at least 50% of pineal tumors[3,7].

Traditionally reported operative morbidity and mortality for pineal tumors ranged from 30% to 70 %. So surgical extirpation in this area has been abandoned by most of neurosurgeons. In spite of such trends, some authors advocated the necessity of tissue diagnosis by surgical approaches for planning effective therapy according to tumor histology[3~5,7,12]. However, treatment result of patients undergoing irradiation alone and that of patients undergoing tumor excision followed by irradiation did not differ[2,5,11,13~15]. So prevailing attitude has been the use of radiotherapy as the initial therapeutic modality in pineal tumors.

For planning effective treatment without histology confirmation, it would be of value to predict the tumor characteristics on the basis of clinical, biochemical, and radiological studies. Jooma[3] and Rich[14] suggested some criteria for differentiating various tumor type on the basis of clinical behaviours. On the other hand, Packer[12] claimed unreliability of clinical parameters as discriminating index.

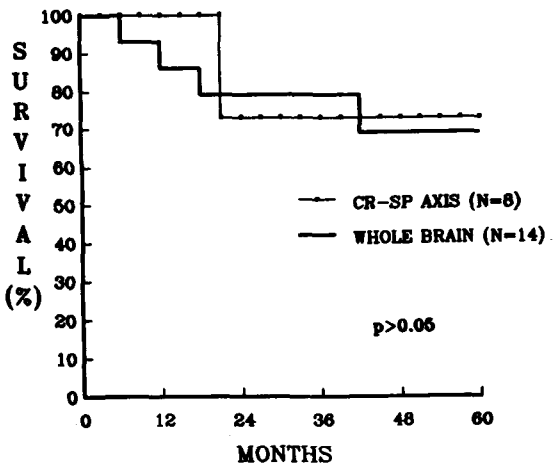

Fig. 2. Actuarial survival according to treatment volume.

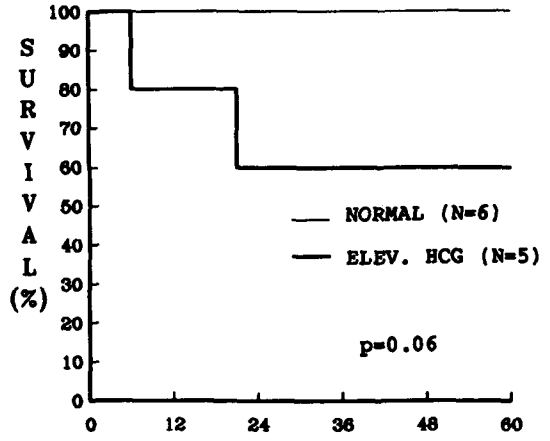

Fig. 3. Actuarial survival according to status of tumor marker.

Main debating issue in radiotherpy for pineal tumors is selective criteria for spinal irradiation. Most authors do not warrant routine prophylactic spinal irradiation in every patient with germinoma due to lack of effective salvage treatment in case of spinal failure. Griffin et al[20] also recommended spinal irradiation to all the highly radioresponsive tumors at an early stage of treatment. The reported incidence of subarachnoid seeding in pineal tumors generally ranges from 5% to 20%[15,19,21~25]. Wide variation has also been reported[11,16]. Although the incidence of positive spinal fluid cytologic finding has been reported as being 6 to 55%, the correlation between CSF cytology and metastasis to spinal cord is unclear. The presence of malignant cells in the CSF does not necessarily indicate the presence of subarachnoid seeding[26], and also subarachnoid seeding may occur with negative cytology[3,4,11,27]. In one report, the actuarial incidence of spinal metastasis was 37% in the cases of positive CSF cytology without spinal irradiation[14]. It seems that cytologic test is more useful in detecting post-treatment recurrence or metastasis.

Since Sung et al[11] reported 57% incidence of subarachnoid seeding in biopsied pineal tumor, it has been generally accepted that surgical approach is critical factor for subarachnoid seeding, and many reports support this[3,21,25,28,29]. But recently, such concept is challenged by several authors[3,18,19,30]. Such reports make the spinal irradiation in biopsied tumor controversial. Recently, Linstadt et al[18] reported the combined result of spinal irradiation from several reports separating unbiopsied cases and biopsied cases. In biopsied cases, about 15% of patients benefit from spinal irradiation; 23% spinal failure without spinal irradiation and 8% spinal failure with spinal irradiation.

In unbiopsied cases, no benefit was detected with spinal irradiation; 9% spinal failure without spinal irradiation and 11% spinal failure with spinal irradiation. In current series, 22 patients were treated without biopsy confirmation, among these, 15 patients were treated with whole brain field, and 7 patients were treated with whole craniospinal axis field. There was no confirmed spinal failure in both groups, and also, survival difference was not detected. This result agrees with collected data. From current result and other reports, it seems likely that routine prophylactic spinal irradiation is not warranted in pineal tumors, and craniospinal irradiation is recommended in cases with high risk for subarachnoid seeding such as positive CSF cytology, or surgical extirpation.

Five year survival for pineal tumors treated with radiotherapy ranges from 44% to 78% with average of approximately 65%[32], and 71.5% in current report is comparable with worldwide results. The incidence of intracranial recurrence ranges from 6 % to 40% with average of 25% depending on radiation dose or technique[2,25,33]. By Sung et al intracranial recurrence rates for patients receiving 50 Gy or more was 10%[11]. In current series, one case of intracranial recurrence developed (4.3%). But real incidence may be higher because more intracranial failure may be detected in the dead with unknown cause of death.

Tumor marker study for serum or CSF has been used as noninvasive diagnostic indicators of tumor histology, and there is good correlation between CSF or serum tumor marker and histologic category of tumors[22]. The presence of biomarker in intracranial germ cell tumor has been shown to be a grave prognostic sign as in patients with testicular germ cell tumor[34~36]. But it is controversial whether β-HCG production by germinoma alters prognosis of patients[22,37,38]. In current series, among 13 patients underwent marker study 7 patients showed positive results and the survival was worse in these patients than in patients with negative results. Hematogenous metastasis to lung in patients with high level of serum β-HCG correlate well with characteristics of choriocarcinoma. Extraneural metastasis is very rare with pineal tumors. Of the eight known cases reviewed by Sakata et al, all were pulmonary metastasis[31].

Nongerminomatous germ cell tumor respond poorly to radiotherapy, so chemotherapy may be combined with radiotherapy. The absence of blood brain barrier in the pineal gland may enhance the effect of chemotherapy[7,22]. The effect of chemotherapy on pineal parenchymal tumor or glial tumor is not yet clear. Neo-adjuvant chemotherapy was tried for primary intracranial germ cell tumor by Allen et al[39]. The objectives for this trial was to reduce the late sequelae of radiotherapy by reducing the dose without compromising treatment result for germinoma, and to increase the local control rate for nongerminomatous germ cell tumor. The result was promising for germinomas, but it was not so for nongerminomatous germ cell tumor.

REFERENCES

1. **Araki C, Matumoto S:** Statistical re-evaluation of

pinealoma and related tumors in Japan. J Neurosurg 30:146-149, 1969
2. **Abay EO, Laws ER, Grado GL, et al:** Pineal tumors in children and adolescents. Treatment by CSF shunting and radiotherapy. J Neurosurg 55:889-895, 1981
3. **Jooma R, Kendall BE:** Diagnosis and management of pineal tumors. J Neurosurg 58:654-665, 1983
4. **Chapman PH, Linggood RM:** The management of pineal area tumors-a recent reappraisal. Cancer 46:1253-1257, 1980
5. **Sano K, Matsutani M:** Pinealoma treated by direct surgery and postoperative radiotherapy. A long-term follow-up. Childs Brain 8:81-97, 1981
6. **Stein BM:** Surgical treatment of pineal tumors. Clin Neurosurg 26:490-510, 1979
7. **Neuwelt EA, Glasberg M, Frenkel E, et al:** Malignant pineal region tumors: A clinico-pathological study. J Neurosurg 51:597-607, 1979
8. **Kunicki A:** Operative experiences in 8 cases of pineal tumor. J Neurosurg 17:815-823, 1960
9. **Poppen JL, Marino R Jr:** Pinealomas and tumors of posterior portion of third ventricle. J Neurosurg 28:357-364, 1968
10. **Rand RW, Lemmen LJ:** Tumors of posterior portion of third ventricle. J Neurosurg 10:1-17, 1953
11. **Sung DI, Harisiadis L, Chang CH:** Midline pineal tumors and supraselar germinoma: highly curable by irradiation. Radiology 128:745-751, 1978
12. **Packer RJ, Sutton LN, Rosenstck JG, et al:** Pineal region tumors of childhood. Pediatrics 74:97-102, 1984
13. **Rao YTR, Medini E, Haselow RE, et al:** Pineal and ectopic pineal tumors: The role of radiation therapy. Cancer 48:99-107, 1987
14. **Rich TA, Cassady JR, Strand RD, et al:** Radiation therapy for pineal and suprasellar germ cell tumors. Cancer 55:932-940, 1985
15. **Salazar O, Castro-Vita H, Bakos RS, et al:** Radiation therapy for tumors of pineal region. Int J Radiat Oncol Biol Phys 5:491-499, 1979
16. **El-Mahdi A, Phillips E, Log S:** The role of radiation therapy in pinealoma. Radiology 103:407-412, 1972
17. **Wara WM, Fellows CF, Sheline GE, et al:** Radiation therapy for pineal tumors and suprasellar germinomas. Radiology 124:221-223, 1977
18. **Linstadt D, Wara WM, Edwards MSB, et al:** Radiotherapy of primary intracranial germinomas: The case against routine craniospinal irradiation. Int J Radiat Oncol Biol Phys 15:291-297, 1988
19. **Shibamoto Y, Abe M, Yamashita J, et al:** Treatment result of intracranial geminoma as a function of the irradiation volume. Int J Radiat Oncol Biol Phys 15:285-290, 1988
20. **Griffin BR, Griffn TW, Tong DYK, et al:** Pineal region tumors: Results of radiation therapy and indications for elective spinal irradiation. Int J Radiat Oncol Biol Phys 7:605-608, 1981
21. **Wara WM, Jenkin DT, Evans A, et al:** Tumors of pineal and suprasellar region. Childrens Cancer Study Group treatment results 1960-1975. Cancer 43:698-701, 1979
22. **Jennings MT, Gelman R, Hochberg F:** Intracranial germ cell tumors: Natural history and pathogenesis. J Neurosurg 63:155-167, 1985
23. **Rubin P, Kramer S:** Ectopic pinealoma: a radiocurable neuroendocrinologic entity. Radiology 85:512-523, 1965
24. **Bloom HJG:** Intracranial tumors: Response and resistance to therapeutic endeavors, 1970-1980. Int J Radiat Oncol Biol Phys 8:1083-1113, 1982
25. **Jenkin RDT, Sympson WJK, Keen CW:** Pineal and suprasellar germinomas. Results of radiation treatment. J Neurosurg 48:99-107, 1987
26. **De Girolami U, Schmidek H:** Clinicopathological study of 53 tumors of the pineal region. J Neurosurg 39:455-462, 1973
27. **Balhuizen JC, Bots GTAM, Schaberg A, et al:** Value of cerebrospinal fluid cytology for the diagnosis of malignancies in the central nervous system. J Neurosurg 48:747-753, 1978
28. **Suzuki J, Hori S:** Evaluation of radiotherapy of tumors in the pineal region by ventriculographic studies with iodized oil. J Neurosurg 30:595-603, 1969
29. **Waga W, Handa H, Yamashita J:** Intracranial germinomas: treatment and results. Surg Neurol 11: 167-172, 1979
30. **Sano K:** Pineal region tumors: Problems in pathology and treatment. Clin Neurosurg 30:59-91, 1983
31. **Sakata K, Yamada H, Sakai N:** Extraneural metastasis of pineal tumor. Surg Neurol 3:49-54, 1975
32. **Liebel SA, Sheline GE:** Radiation therapy for neoplasms of the brain. J Neurosurg 66:1-22, 1987
33. **Mincer F,Meltzer J,Botstein C:** Pinealomas-A report of twelve irradiated cases. Cancer 37:2713-2718, 1976
34. **Bosl GJ, Geller NL, Cirrincione C, et al:** Multivariate analysis of prognostic variables in patients with metastatic testicular cancer. Cancer Res 43:3403-3407, 1983
35. **Szymendera JJ, Zborzil J, Sikorowa L, et al:** Evaluation of five tumor markers (AFP, CEA, hCG, hPL, and SPI) in monitoring therapy and follow up of patients with testicular germ cell tumors. Oncology 40:1-10, 1983
36. **Germa-Lluch JR, Begent RHJ, Bagshawe KD:** Tumor marker levels and prognosis in malignant teratoma of the testis. Br J Cancer 42:850-855, 1980
37. **Mostofi FK:** Pathology of germ cell tumors of testis. A progress report. Cancer 45:1735-1754,

1980
38. **Bosman FT, Giard RWM, Nieuwenhuijen Kruseman AC, et al:** Human chorionic gonadotrophin and alphafetoprotein in testicular germ cell tumors: a retropspective immunohistochemical study. Histopathology 4:673-684, 1980
39. **Allen JC, Kim JH, Packer RJ:** Neoadjuvant chemotherapy for newly diagnosed germ cell tumors of the central nervous system. J Neurosurg 67:65-70, 1987

= 국문초록 =

송과선종의 방사선치료 성적

서울대학교 의과대학 치료방사선과학교실

채 규 영 · 박 우 윤 · 최 두 호
정 웅 기 · 김 일 한 · 하 성 환

1979년부터 1985년까지 서울대학교병원 치료방사선과에서 치료를 받은 송과선종 환자 23명에 대한 후향적 분석을 시행하였다. 종양에 대한 조직학적 진단은 1명에서만 이루어졌고, 나머지 22명의 환자에 있어서의 진단은 임상적 소견 및 방사선학적 검사결과에 의거하였다. 방사선조사는 1명에 있어서는 종양부위에 국한하였고, 14명에 있어서는 전 뇌부위, 8명에 있어서는 전뇌-척수부위에 대하여 시행하였다.

전 환자의 5년 생존율은 71.5%이었고, 전 뇌부위 치료 환자의 5년 생존율은 69.3%, 전뇌-척수부위 치료 환자의 5년 생존율은 73.3%이었다. 원발 부위 및 원격부위에서의 재발이 각각 한명씩 확인되었으며 척수부위에서의 치료실패는 확인된 경우가 없었다.

이상의 분석결과 및 기왕의 여러보고를 바탕으로 하여 송과선종의 방사선치료에 있어서 모든 환자에서 전척수 조사를 시행하는 것은 타당치 않으며 전척수 조사는 뇌척수액내에서 종양세포가 발견된 경우나 또는 종양의 제거나 생검을 위하여 외과적 시술이 시행되었던 경우 등에 국한되어야 할 것으로 결론지었다