Medulloblastoma: Radiotherapy Result with Emphasis on Radiation Dose and Methods of Craniospinal Treatment

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Twenty five patients with histologically proven medulloblastoma received craniospinal radiotherapy (CSRT) at the Seoul National University Hospital from 1979 to 1984.

The extent of tumor removal was biopsy only in 2 patients, partial in 18, and near total in 5. With orthogonal technique of CSRT, mainly 55 Gy was delivered to the posterior fossa (PF), 40 Gy to whole brain (WB), and 30 Gy to whole spine (WS). And with AP: PA technique, 50 Gy to PF, 45-50 Gy to WB, and 36 Gy to WS.

Complete remission was obtained in 84% of patients. Among 21 CR's 10 failures were observed, thus total failure rate was 56% (14/25). Of 14 faiure 13 had the primary failure, 11 failed in primary site alone, 1 failure was combined with ventricular seeding, and another 1 was combined with neck node metastasis. There was 1 isolated spinal failure. Actuarial overall survival rates at 3 and 5 years were 75% and 54%, and disease-free survival rates were 58% and 36%, respectively.

Better 5 year disease-free survival was noted in patients with 55 Gy to the posterior fossa than those with 50 Gy (62% vs 17%, $p<0.05$), in patients treated with orthogonal technique than those treated with AP:PA technique (87% vs 12%, $p<0.05$), and in patients with near total removal than those with partial or less removal of tumor (56% vs 30%, N.S.) Re-irradiation was not satisfactory. No severe late sequelae was noted among the survivors.

For the higher control of medulloblastoma, dose to posterior fossa should be at least 55 Gy with orthogonal CSRT to small tumor burden. And dose reduction in the subarachnoidal spaces might be safe, but optimal dose to the subarchnoidal spaces should be determined by the thorough tumor staging before radiotherapy.

Key Words: Medulloblastoma, Dose, Radiotherapy method

INTRODUCTION

Medulloblastoma is the most common brain tumor in children. Gloomy prognosis with surgical resection alone was dramatically changed after introduction of craniospinal radiotherapy (CSRT) which included not only the primary tumor site in the posterior fossa but cranial and spinal subarachnoidal spaces, because it was evident that radiotherapy only to the posterior fossa resulted in very poor survival and that subarachnoidal metastases were detected among newly diagnosed asymptomatic or recurred patients[1~9].

Thereafter, various techniques of CSRT were tried for better dose homogeneity through the neuraxis and for prevention of avoidable relapse in neuraxis[10~17]. And the search for the optimal radiation dose for higher tumor control and lesser sequelae has been continued but optimal preventive dose to the subdural areas is still undetermined[6,18~27].

In this study, treatment results of medulloblastoma were analyzed especially by the radiation dose to the neuraxis and the methods of craniospinal radiotherapy.

MATERIALS AND METHODS

Among the histologically proven medulloblastoma patients who got craniospinal radiotherapy (CSRT) at the Department of Therapeutic Radiology, Seoul National University Hospital from 1979 to 1984, 25 patients completed treatment and so were eligible in this analysis. All except 2 were followed up. and 11 NED patients were followed up for 28 to 72 months (median 55). During this period, CSRT was delivered with 2 different methods,

orthogonal and AP:PA, those will be described in detail, and differences in characteristics of patients treated with 2 different methods were negligible though not randomized.

There were 13 boys and 12 girls. Age ranged 6 months to 18 years, and 40% were in the range of 6 to 10 years (Table 1). Before CSRT, 7 patients had the performance status of 3 to 4 by ECOG scale. Extent of 17 tumors were confined in the cerebellum, largely in vermis, but 8 tumors extended to floor of the 4th ventricle or involved brainstem by CT or operative findings. Cytologic examination of cerebrospinal fluid by lumbar puncture or by ventricular drainage was done in 10 cases and malignant cells were found in 2 cases; one with tumor in the vermis had invasion to the floor of the 4th ventricle and were treated with the orthogonal method, the other with vermis tumor were treated with AP:PA methods. And in myelogram, done in some cases, gross involvement of spinal subarachnoidal spaces was not detected. And there were 3 cases of desmoplastic variant.

Tabel 1. Patient Characteristics

Characteristics	No. of Patients		
	Ortho.	AP : PA	Total
Sex			
Male	8	5	13
Female	7	5	12
Age			
– 5	2	3	5
6–10	7	3	10
11–15	2	3	5
16–20	4	1	5
Performance status			
ECOG 0–2	10	8	18
ECOG 3–4	5	2	7
Histology			
Classical	15	7	22
Desmoplastic	–	3	3
Tumor extent			
Cerebellum	10	7	17
Cerebellum + brainstem or V4 floor	5	3	8
Total	15	10	25

Table 2. Surgical Procedures

Procedure	No. of Patients		
	Ortho.	AP : PA	Total
Shunt			
(+)	7	6	13
(–)	8	4	12
Tumor resection			
Biopsy	1	1	2
Partial	12	6	18
Near Total	2	3	5
Total	15	10	25

Shunting procedure owing to hydrocephalus was done pre- or post-operatively in 13 cases. Major neurosurgical procedure was partial tumor removal (72%), and near-total removal was done in 20% of patients (Table 2). Six cases were referred from outside hospital.

Radiotherapy was usually applied within 4 weeks after operation. As was mentioned above, 2 methods of CSRT were used. With the first, AP:PA method, 10 patients were treated from 1979 to 1983. In this method the whole cranial contents and the whole spine were encompassed by spade-shaped posterior field from the top of brain to S2-S3 level. And brain was additionally treated by an anterior field which was tilted caudad to the direction of eyebrow to the tip of the mastoid process in order to include skull base. And then final boost was delivered to posterior fossa by lateral ports ususally (Fig. 1).

From 1981 to 1984, 15 patients were treated with the orthogonal method. Whole brain was treated by lateral ports and the whole spine from C2 to S2 level was treated by one or two ports according to the spine length. Lower margin of brain field abutted on the divergent upper margin of spine field at C2 level initially and shifted down 1 to 2 cm at accumulated dose of 10 Gy (Fig. 2). All the patients were treated with a telecobalt unit.

Usual radiation dose with orthogonal group was somewhat differed from that with AP:PA group (Table 3). By orthogonal method, mainly 55 Gy was delivered to the posterior fossa (PF), 40 Gy to the whole brain (WB), and 30 Gy to the whole spine (WS). By AP:PA methods, mainly 50 Gy to PF, 40 or 50 Gy to WB, and 36 Gy to WS. For a 6-month boy, 45 Gy was delivered to PF. As Table 3, while 67% of patients treated with orthogonal method had 55 Gy to PF, 30% of patients treated with AP:PA method had 55Gy to PF. Daily dose was 150~175 cGy for whole brain and 100~150 cGy for the whole spine. And during CSRT, CBC was checked at least twice a week to evaluate the degree of acute marrow

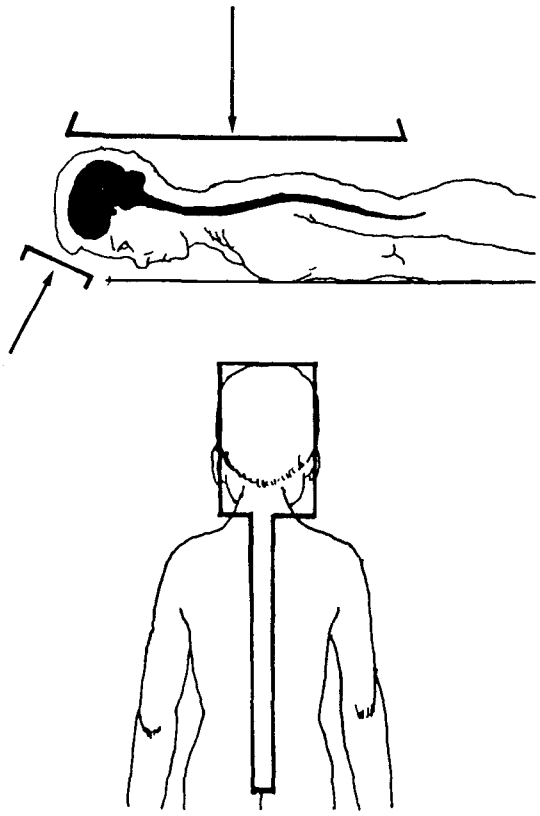

Fig. 1. AP : PA method of craniospinal radiotherapy, 1979–1983.

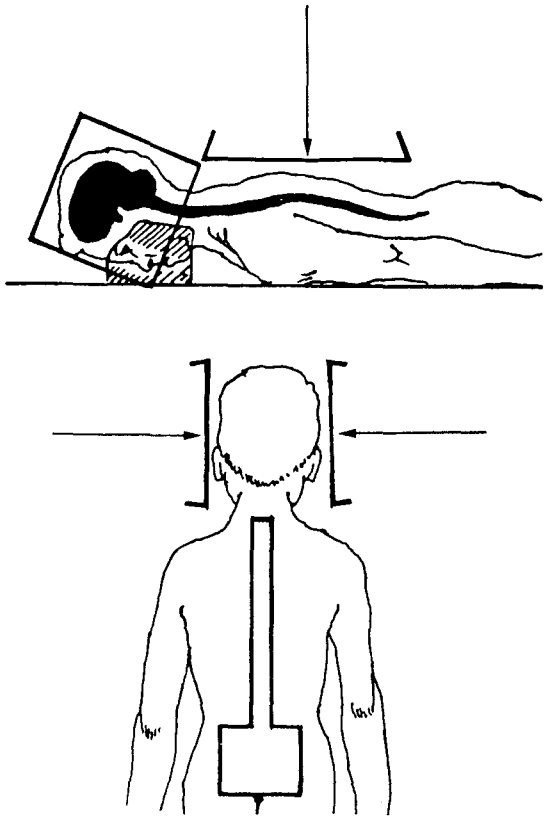

Fig. 2. Orthogonal method of craniospinal radiotherapy, 1981–1984.

Table 3. Radiation Dose

Site	Dose (cGy)	No. of Patients		
		Ortho.	PA : PA	Total
Posterior Fossa	4,500	–	1#	1
	5,000	5	6	11
	5,500	10	3	13
Whole Brain	4,000	10	4	14
	4,500	3	1	4
	5,000	2	5	7
Whole Spine	2,400	4	2	6
	3,000	8	2	10
	3,600	3	6	9

: 6 months of age

Table 4. Response to Treatment

Response	No. of Patients		
	Ortho.	AP : PA	Total
CR	13	8	21
PR	2	1	3
MR	–	1	1

reaction.

Response to radiotherapy was assessed by measuring tumor size in CT films at 1 month after completion of radiotherapy. And survival was calculated from the day of operation by the life table method and was analyzed by the logrank test. And Student's t test was used in comparison of NED rates.

RESULTS

Complete remission was obtained in 84% of all patients and PR rate was 12% (Table 4). CR rate was not influenced by extent of tumor removal, radiation dose, radiotherapy methods, or other

factors.

Of 21 CR cases, 10 failed during follow-up period from 6 to 56 months (median: 34 months). Thus total failure rate was 56% (14/25). Of 14 failure, analysis of failure pattern showed that all but 1 had the component of failure at the posterior fossa; 11 isolated, 2 combined (Table 5). One CR case relapsed in PF with periventricular seeding at 34 months. And another 1 PF failure, initially PR, was combined with neck node metastasis at 11 months after CSRT. This extraneural metastatic case had ventriculo-peritoneal shunt preoperatively and revision of shunt because of malfunction during CSRT but the CSF cytology was negative initially. There was 1 isolated spinal relapse at the level of L1 to L2 at 54 months.

Failure was influenced by extent of tumor removal; 63% (12/19) of patients with partial or less removal failed, but 33% (2/6) of failure was noted in near totally removed cases ($p<0.05$). And radiation dose to the posterior fossa affected failure rate; 31% (4/13) failed with 55 Gy, but 83% (10/12) failed with 50 Gy or less ($p<0.05$). And method of CSRT also significantly influenced treatment result; 33% (5/15) of patients with orthogonal method failed, while 90% (9/10) of cases with AP:PA method failed to radiotherapy ($p<0.05$). But it is impossible to discern the influence of radiation dose and treatment method, because 70% of patients who was treated by AP:PA method had 50 Gy or less to PF.

As for the relationship between PF dose and disease-free status in the primary site, dose effect was more definite. Of 13 patients who had 55 Gy to PF, 10 cases (77%) accomplished disease-free status at the primary site, but only 17% (2/12) with 50 Gy or less to PF had local tumor control ($p<0.05$, Table 6).

Among patients with the whole brain doses of 40, 45, and 50 Gy, respectively, 6/14, 3/4, and 2/7 were in the disease-free status.

As for the spinal failure, 1 out of 10 patients with spinal dose of 30 Gy failed as isolated spinal relapse, but none of 6 with 24 Gy or of 9 with 36 Gy relapsed at the spinal subarachnoidal space at all. Follow-up period of all 6 patients with 24 Gy to the whole spine was less than 3 years.

It was noteworthy that 3 of all desmoplastic cases failed and 50% (11/22) of patients with classical histology failed to treatment. Patients with ECOG 0~2 performance status or who had a rest during treatment showed a higher failure without significance. But age, sex, tumor extent, or whether patients were shunted or not did not affected the treatment outcome at all.

During craniospinal radiotherapy 9 patients experienced interruption of treatment for 1 to 6 weeks. Seven patients had a rest for 1 to 5 weeks due to leukopenia with or without fever, one for 6 weeks because of CSF leakage at the operation wound and fever, and another for 10 days for the revision of malfunctioning VP shunt.

Among 13 patients alive, for 28 to 75 months, some mild forms of late reactions were observed. Three patients had two reactions. There were slight memory disturbances (2), alopecia partialis (2), decrease in the visual acuity (2), obesity with short stature of unknown degree (1), primary amenorrhea (1), and disturbance in the intelligence (1). But profound disability was not noted at all.

In all 25 patients, actuarial survival rates were 75% and 54% and the disease-free survival (DFS) rates were 58% and 36%, at 3 and 5 years respectively (Fig. 3).

By the radiation dose to the posterior fossa survival was markedly affected, 5 year survival and disease-free survival rates were 77% and 62% with 55 Gy but were 26% and 16% with 50 Gy (Fig. 4; $p<$

Table 5. Patterns of Patients

Failure Site	No. of patients		
	Ortho. (n=15)	AP : PA (n=10)	Total
Posterior fossa	3	8	11
PF + Ventricles	1	–	1
PF + Extra-CNS	–	1	1
Spine alone	1	–	1
Total	5	9	14

Table 6. Dose to the Posterior fossa and NED in the Posterior Fossa

P.F. Dose (cGy)	NED patients in PF/Patients		
	Ortho.	AP : PA	Total
4,500	–	0/1#	0/ 1
5,000	2/ 5	0/6	2/11
5,500	9*/10	1/3	10/13

: case of 6 months of age

* : included 1 spine faliure alone

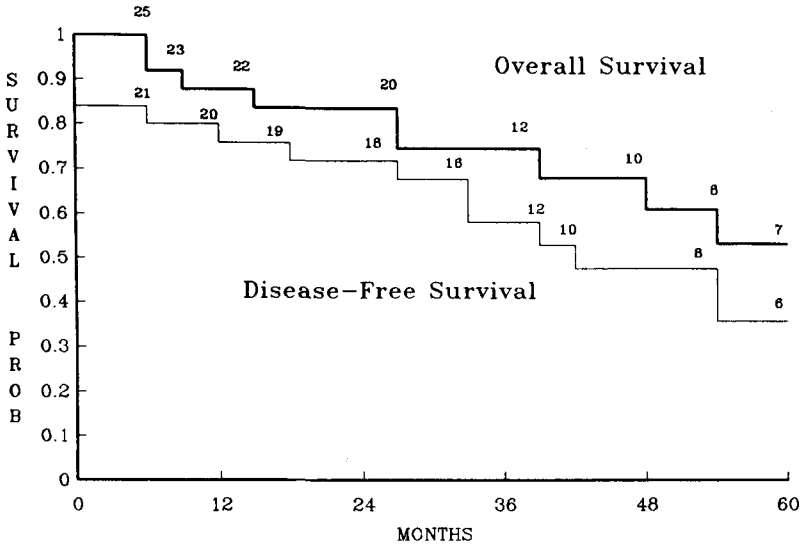

Fig. 3. Actuarial and disease-free survival of all 25 patiehts.

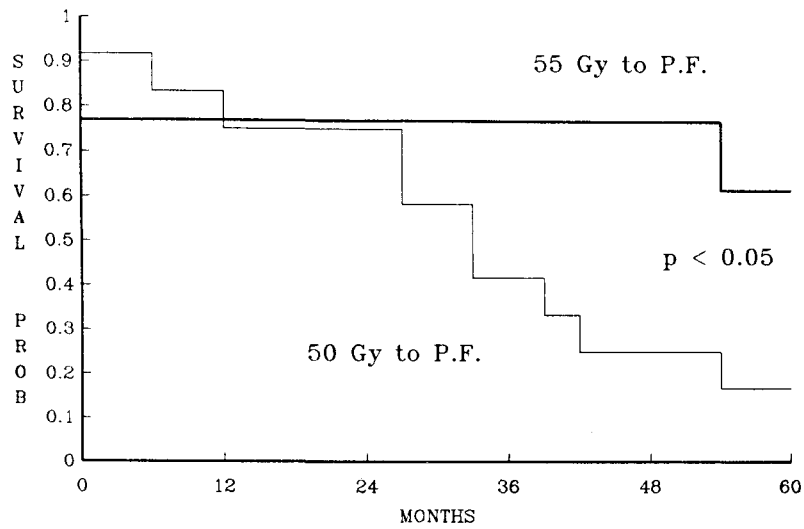

Fig. 4. Disease-free survival by the dose to the posterior fossa.

0.05). Five year disease-free survivals with 40 Gy and 50 Gy to the whole brain were 27% and 29%, but that with 45 Gy was 75% in small number of pathents (4 cases). And there was no difference in the survival data by the dose to the whole spine.

Also the survival was greatly influenced by the method of CSRT. Those who treated with orthogonal method had the better survival and DFS rates at 5 year than those with AP:PA method. With orthogonal method they were 87% and 58% but with AP:PA method they were 12% and 10% (Fig. 5; $p<0.05$).

Pre-radiotherapy tumor burden affected the survival too. Five year survival and DFS rates in patients whose tumor was resected near totally were 56% and 56%, but in patients with partial removal or less were 52% and 30%. But the difference in DFS was not significant (Fig. 6). Initial tumor

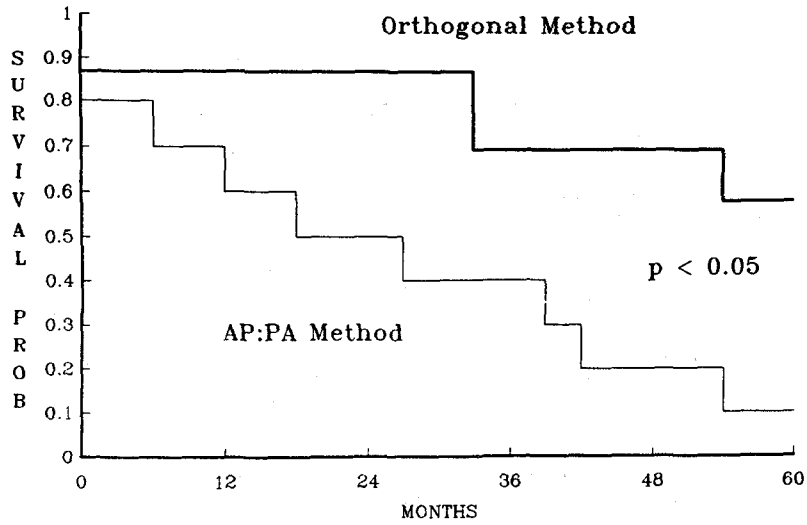

Fig. 5. Disease-free survival by the methods of craniospinal therapy.

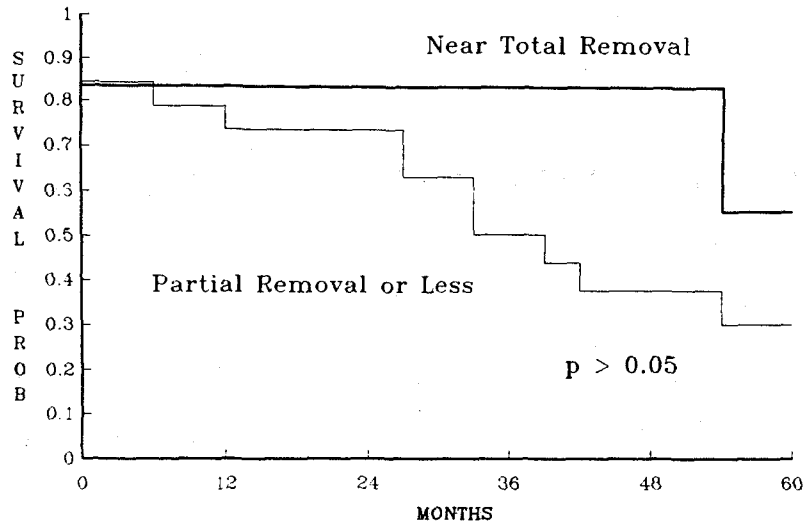

Fig. 6. Disease-free survival by the extent of surgical tumor removal.

involvement of brainstem or floor of the 4th ventricle, poor performance status, and shunt did not result in poor outcome. In the meanwhile, 44% 5 year DFS was obtained in the classical type but there was no survivor with desmoplastic type. And no patients who had a interruption of treatment of any reason survived, while 11 of 22 patients without interruption were in the disease-free status.

Re-irradiation in 3 cases, with or without combined chemotherapy, failed to get salvage effect. One with residual tumor after 5040 cGy had re-irradiation of 40 Gy to the posterior fossa at 22 months after the first treatment but died in 2 months. By re-treatment of 16 Gy, a recurrent case after 5040 cGy responed partially and died in 1 month, and another recurrent case with initial dose of 49 Gy to PF again but died in 6 months.

DISCUSSION

Recently accomplished better survival of medulloblastoma with 5 year survival of 60~70% is due

mainly to the improvements of radiotherapy such as use of megavoltage equipment, refinements of radiotherpay technique, delivery of higher dose especially to the posterior fossa and due partly to improvements in operation and anesthesia, more clarification of tumor burden, and use of combined modality therapy. But outcome of all children with medulloblastoma is not so good. By the population based data, 5 year survival rate was 38% during 1975~1977, 18% during 1962~1970, and was 27% during 1971~1974[26].

Medulloblastoma spread well to subarachnoidal spaces. Asymptomatic spinal involvement was detected in 36% of newly diagnosed patients before radiotherapy[3]. And extent of radiotherapy markedly affected the treatment result, so that 10 year survival rates were reported as 5%, 25%, and 53% when radiotherapy was done to the posterior fossa only, posterior fossa and the spine, and the whole CNS, respectively[6]. Similar results were reported by others[4,5,9].

Thus it was absolutely necessary to treat the whole neuraxis with maintaining homogeneity of dose and with adequate field arragement for the cure of medulloblastoma. There has been various techniques of craniospinal radiotherapy (CSRT) from orthovoltage period till now.

With modified methods of the original Patterson-Farr's technique, (what we called the AP:PA method), by which the brain and the spine were treated with single posterior port and the brain was treated additionally with anterior tilted port, many treatments have been reportd[9,10,18,28~32]. And their 5 year survival rates ranged from 32% to 51%.

Orthogonal method, seems to be largely used now, encompasses the brain and upper part of cervical cord in lateral ports and remained spine, usually C2 to S2, in posterior port(s) with shift of junction between ports[11,17~19,22,23,33~35]. Five-year survival with orthogonal method ranged 40% to 60 %. And some institutes modified the method for higher survival and therapeutic ratio[13~15,24,36]. Another method named as 'hockey stick' in which brain and spine were treated with single field by head turning to one side resulted in 5 year survival rate of 73% in small number of cases[16].

Better survival with orthogonal method in this paper can be explained by higher proportion of patients with 55 Gy delivered to the posterior fossa and better homogeneity. We now only use orthogonal method because it was less complicated and easy to set up in everyday treatment, could reduce the dose to the anterior part of head and neck, and so thus could lessen the degree of unwanted sequelae, in addition to better survival. But it was interesting to note that CR rates were nearly equal in 2 methods. And gradual increase in treatment outcome reported in the same institute as time went on was due mainly to adoption of better method or refinements in technique[28,29,30]. Although orthogonal method tended to give a better survival, sequence of treatment to the posterior fossa, brain, and spine did not affected the prognosis[18].

Concerning the radiation dose, two factors must be considered, tumor control and sequelae. Our result that higher dosage to the posterior fossa gave a great impact on the tumor control and survival was consistent with many other report but differed in the level of the dosage itself. Significant differences in survival were reported between patients treated with more dose than and with lesser dose than 40 Gy[37], 45 Gy[9,26], 50 Gy[22,23,38~41] or 52 Gy[18,34]. In a sense our dosage levels of 50 Gy and 55 Gy weren't clearly deviated from that of 52 Gy, but ours differed from results those obtained by doses below or above 50 Gy or from seemingly same results in which no survivor was observed below 50 Gy[24], because our patients were all treated with dose above 50 Gy except one under age 1.

Failure in the posterior fossa accounted for 70 ~75% in collected series[42,43]. In individual series, meanwhile, proportion of failure in the PF among the all failure ranged 14~25%[3,24,27,34,44] to 37~64 %[2,6,18,22,41]. In these variety of proportion, higher dose to the posterior fossa showed the lower portion especially in recent results. Proportion of the posterior fossa combined with failures at other sites ranged 36~44%[3,6,24,44] to 50~89%[18,22,27,34,37,41].

Contrary to the posterior fossa, optimal dose to the subarachnoidal spaces is still debated. To the brain, accepted dose of standard was 35~45 Gy[4,5,8,9,16,18~20,22~25,31,32,34,35,39,40,45], with dose reduction in younger children. But reports in 1980's recommended 30 Gy as the optimal and safe dose[3,6,15,20] or even 25 Gy for the patients with low risk[27]. But the optimal dose must be determined in the balance of supratentorial relapse rate and late sequelae. Reported proportion of supratentorial failure among the total failure was in the range of 6 to 25% and that of combined failure ranged 6% to 43%[2,3,6,18,24,27,34,41~44]. And 5% to 15% of all patients had cranial relapse alone with disease-free posterior fossa[7,8,43].

Usually reported sites in supratentorium were

frotal lobe, subfrotal/cribriform plate area, temporal lobe, basal cistern, and the anterior hemispheric fissure. Subfrotal/cribriform plate relapse, firstly noted in 1978, and temporal relapse were explained by inadequate covering of the floor of the temporal fossa and anterior or medial aspects of the floor of the anterior cranial fossa[28,46]. Survival improvement was reported using anterior electron boost therapy to overcome underdose of cribriform plate region[14].

Many data about late sequelae can be gathered. But it is not easy to discern late complication from direct effect of tumor or increase in intracranial pressure. Severe or total disability was reported in 11% to 20% among long-term survivors[4,18,19,47]. Other sequelae were impairment of growth or intelligence, mental retardation, behaviour disorder, subnormal scholastic integration, hearing impairment, growth hormon deficiency, delayed puberty, hypopituitarism, and hypothyroidism[4,8,19,25,31,32,38,40,45,48~52]. In general, it was severe in younger patients with higher dose. But there was a report that 83% of survivor were in normal performance status without episode of growth or mental retardation after delivery of 30 Gy[6].

Simple reduction of dose in infant or younger patients for fear of severe sequelae seems inadequate because probable cure with this reduced dose has been poor. Thus recent trial of postponement of radiotherapy till 2 to 4 years of age by starting and maintaining systemic chemotherapy after operation appears to be promising in infants or younger children who were assumed to have high risk[49].

There was no consensus on the optimal dose to the spinal subarachnoidal space, too. Dose of 30 ~40 Gy was largely used with reduction in the younger patients. But reduced dose of 20~25 Gy was recently suggested as safe and effective level[19,27]. No survival under 34 Gy[14,24] does not provide a rational back-up for necessity of higher dose because spinal dose itself is not related to overall survival but only to control of spinal disease of varying tumor burden.

Regarding this aspect, raise or reduction of spinal dose usually depended on the experiences of institutes. Some raised the dose to 40 Gy or more after high rate of overall failure[25,45], Contradictory results were not solved; higher rate of spinal metastasis with dose under 30 Gy (41% vs 20%)[26], vs better spinal disease-free status with dose of 20 ~25 Gy than with 30~36 Gy[21]. Thus precise assessment of tumor burden in the spinal subarachnoidal space before radiotherapy is mandatory to evaluate the result of treatment by dose. By this, optimal dose accoridng to the tumor burden can be delivered and treatment result will be better. Importance of CSF cytologic exam and myelography was confirmed in a report that better survival was noted in patients treated after doing them than in whom treated without doing[44]. After treatment, rate of spinal metastasis was 21~40% in all patients[1,2,7,26].

The proportion of the spinal failure of all the failure accounted for 12~43%, and the proportion of the spinal failure alone ranged from 3 to 25 %[3,6,8,18,22,24,27,32,34,41,42,44]. Our results of no difference in the rates of spinal failure among doses of 24, 30, and 36 Gy isn't considered as a rationale of safe reduction of spinal dose because patients with 24 Gy were not yet followed up till 5 years.

Radiation effect to bone, especially growing vertebra, was known from earlier days. The greater the inherent growth potential of affected bone, the more severe the radiation effect. And severe damage was related with the age at the time of irradiation (<2 or puberty) and the radiation dose (>20 ~25 Gy)[36,53,54]. Short stature, dysproportion of sitting and standing height, hypothyroidism, and hypoplastic mandible were reported as late sequelae of spinal radiotherapy[8,16,20,31,34,55,56]. But minimal incidence of sequelae was reported with reduced dose[9,12,68] or even with 30 Gy[6,40].

Electron therapy with 25~30 Gy has been recently tried to reduce the dose to vertebral body, to minimize and to prevent unwanted dose to the thyroid, heart, lung, mediastinum, and gonads[12,15,36]. These refinements are anticipated to enhance the therapeutic ratio by lowering the late sequelae.

Extraneural metastasis, 5~7% at the time of diagnosis, was considered as low but increased in the proportion of all failure after treatment. Of all patients 10~15% had it[8,57], but 5~40% of all failure was acknowledged to have it[2,8,18,22,24,27,34,41,42,44,58]. Bypassing of CSF such as VP shunt was proven to enhance extraneural metastasis greately in some reports, accepting or denying the efficacy of millipore filter[18,57]. Furthermore there were opinions of that shunting as routine procedure should be strongly resisted[8,28,29,57]. One extraneural metastasis to neck node in our case seemed to be related with shunt, because he had 2 shunting procedures.

Relapses were usually detected within 2 to 3 years after treatment, but 5~10% of failures were observed beyond 5 years[43]. Late relapses or

exceptions to Collins' period of risk were found[31,40,59,60]. Thus increase in the long-term survival owing to the improvements of treatment changed not only the traditional patterns of failure but the time to progression.

Strict surveillance must be kept for the earlier detection of relapse with low tumor burden that might increase the salvage rate. It will had better to check CSF polyamines, especially putrescine, that had high predictive value without false negative rate[43,61]. So relapse could be more easily differentiated from other conditions mimicking relapse such as subacute reaction or necrosis[62].

Results of various kinds of re-treatment for the relapsed cases were so poor that median survival of 11 to 13 months and diseasefree survival rate of 0~4% could be obtained[4,9,18,23,63,64]. And there were pros[35,63] and cons[34,64] for the effectiveness of additional chemotherapy to regimen for the relapsed.

Opinions varied in prognostication of demographic factors such as age and gender. Children under age 15 were said to have worse survival than adult[33,37,66]. And younger children, under age 4, 5, or 6, had poor survival by some results[8,18,67], but other reports showed that children under age 5 were poor in short-term survival but weren't in long-term survival[26,38], but still others couldn't find actual difference of survival between younger and older children[2,41]. We did not find any impact of age on the treatment outcome, too. Under this intermingled results must we see confounding factors that younger patients had higher percentage of disseminated disease, large tumor burden, and were usually treated with less aggressive method such as reduced-dose radiotherapy[1,49,67]. And better survival in female was general belief[19,66], but better survival in male[8] or equal results regardless of gender was also reported[38,41].

Medulloblastoma are now considered as a subclass of the primitive neuroectodermal tumor (PNET) and some histologic classification by the degree of differentiation were suggested[38,68], but there were debates on prognostic influence of differentiation degree[38,39,67]. Whether desmoplastic variants had poor survival or not was uncertain[8,66,67]. And no potential prognostication of histology was even reported[2]. The cause of all 3 failure of desmoplastic variants in this study is hard to be explained.

As the tumor burden was importantly accepted, efforts were made to establish a staging system. In 1969, a TM staging system was proposed by Chang et al. based on the pre- or operative findings of tumor extent[33]. Prognostic potential of Chang's staging was confirmed by some reports that 10 year survivals of T1, T2, T3 and T4 were 75%, 44%, 13% and 0, respectively, that T1, 2 was better than T3, 4, that M0, 1 was better than T3, 4 or M0 than M1, 2, 3 and that invlovement of brainstem or floor of the 4th ventricle badly impacted on outcomes[8,18,19,34,39,57]. But others couldn't find any significant differentials by T or TM[18,38].

Critical limit of Chang's staging lies on its dependence on pre- or operative tumor extent. Thus pre-radiotherapy tumor burden must be categorized. Patients with small tumor bulk after complete removal of tumor showed better survival[4,8,18,19,24,26,27,29,34,66], but extent of tumor resection did not result in the survival difference in some series[2,38~40,67]. Also we had a marginally better survival for the near total removal. So it can be concluded that complete removal of tumor might give a equal or better survival than partial or less. MAPS staging, proposed in 1985, included 4 factors; metastasis (M), age (A), pathologic grade (P), and surgery (S; postoperative residua)[69]. Although MAPS system advanced by incorporating postoperative tumor burden, its value must be assessed in large clinical trials because it included controversial factors, age and pathologic grade, too.

Anyway, more clarification of prognostic factors will enable us to set more accurate and practical staging system, by which treatment can be modified and higher therapeutic gain can be obtained because we can make efforts to reduce treatment-related complication in the good prognosis patients and to do more aggressive treatment toward survival improvement in high risk groups of patients. For doing this, it is mandatory to determine the extent of tumor by thorough work-up before radiotherapy.

Chemotherapy was delivered before radiotherapy for the high risk patients in some institutes[1,2,18,29,35,70,71]. In large study of SIOP, chemotherapy gave a marginal gain in ovarall survival but its main advantage was in the high risk patients with advanced stage (T3, 4), subtotal removal, involvement of brainstem, or under age 2[8,33]. CCSG is now under clinical trials to give '8 agents in 1 day' regimen to the poor prognosis groups.

In conclusion, best result was obtained with 55 Gy to the posterior fossa by orthogonal method. And pre-radiotherapy tumor burden gave a nearly significant impact on the result of treatment. As for

the dose to the subarchnoidal spaces, it may be haste to draw any affirmative conclusion for dose reduction. So it is necessary for the present series to follow up more. Precise staging must be done before radiotherapy to modify dose and to combine chemotherapy or not, for the improvement of therapeutic ratio.

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= 국문초록 =

후두와 선량 및 전중추신경계 치료방법을 중심으로 한 수아세포종의 방사선치료 성적

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1979년부터 1984년까지 서울대학교병원 치료방사선과에서 수아세포종으로 전중추신경계 방사선치료를 받은 25예의 치료성적을 분석하였다.

수술시 종양절제는 조직생검이 2예, 부분절제가 18예, 완전절제가 5예였다. 전중추신경계 방사선치료는 15예가 orthogonal법에 의하여 원발병소 및 후두와에 55 Gy, 전뇌에 40 Gy, 전척수에 30 Gy를 주로 조사받았으며, 10예는 AP:PA 법으로 원발병소 및 후두와에 50 Gy, 전뇌에 40~45 Gy, 전척수에 36 Gy를 주로 조사받았다.

치료직후 84%(21/25)의 완전관해 상태가 관찰되었으나 완전관해 21예중 10예가 재발하여 56%의 치료실패율을 얻었다. 치료실패 14예중 13예는 후두와에 종양잔존 또는 재발 소견이 있어 11예는 후두와의 단독 실패, 1예는 후두와 실패와 광범위의 뇌실벽 침윤, 다른 1예는 후두와 실패와 경부 임파절 전이 양상을 보였다. 척수강만에서의 재발이 1예에서 관찰되었다.

전체 25예의 3년 및 5년 생존율은 75%였으며, 무병생존율은 각각 58% 및 36%였다. 후두와 선량이 55 Gy인 예가 50 Gy인 예보다 5년 무병생존율이 월등하였고(62%:17%, $p<0.05$), orthogonal법으로 치료받은 예가 AP : PA 법으로 치료받은 예보다 양호하였으며(87%:12%, $p<0.05$), 종양이 완전절제된 예가 부분절제된 예보다 양호하였다(56%:30%, $p>0.05$). 재차 방사선치료의 성적은 불량하였다. 치료후 중증의 후유증은 관찰되지 않았다.

따라서 최대의 치료 결과를 얻기 위하여는, 수술적으로 종양을 가능한 완전히 절제한 후 orthogonal법으로 후두와에 55 Gy를 조사해야 할 것이다. 그러나 전뇌 및 전척수에 대한 방사선량을 30 Gy 이하로 감소시켜도 무방할 것인가는 단정할 수 없다. 이는 앞으로 관찰기간이 더 경과한 이후에 판단할 수 있겠고 또한 방사선치료전에 전지주막하의 종양범위를 명확히 확인할 것이 요구된다.