The Effect of Radiation Therapy on Oligodendrogliomas

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From April, 1983 through April, 1989, we have treated histologically proven 21 patients with oligodendroglioma using 6 MV linear accelerator at the Division of Radiation Therapy, Kangnam St. Mary's Hospital Catholic University Medical College. These are 8% of the irradiated 246 primary brain tumors during the same period.

To investigate influencing factors on the survival of irradiated 21 patients with oligodendroglioma, we analyzed the cerebral location of the involvements, initial symptoms, CT findings and survival rates, retrospectively. One case was lost to follow up and excluded from survival data.

Of the 21 patients, thirteen were male and 8 female. Ages ranged from 5 to 68 years with a median age of 38 years. Radiation doses varied from 3960 cGy to 6480 cGy and were given for 5 to 8 weeks. All but one were supratentorial. The involvement of the frontal and parietal lobes were 10 (48%) patients in each and temporal lobe in 8 (38.1%).

Histological diagnosis was made by stereotactic biopsy in 3 and postoperatively in 18. The type of surgery was divided into partial, subtotal and total resection in 7, 9 and 2 cases respectively. In 6 cases, chemotherapy was also tried during or after radiation therapy. Major presenting symptoms were headache, cerebral motor, nausea & vomiting and epilepsy in 18, 12, 7 and 5 respectively in decreasing order. In CT analysis, low density (62%), cystic mass (33%), calcification (66%) and positive contrast enhancement (42.8%) were observed as the highest frequency. Mean survival duration after radiation therapy was 38 months (K-M methods).

We could not achieve statistically significant factors influencing on the survival rate after radiation therapy for oligodendrogliomas by one or two tail test.

Key Words: Radiation therapy, Oligodendroglioma, Cerebral location, Symptom, CT, Survival Rate

INTRODUCTION

Oligodendrogliomas (OD) are slowly growing relatively benign tumors with a long pre and post-treatment history[1,3~7].

The primary aim of treatment is radical surgical removal as much as possible and recurrence may be reoperated upon several times[2,5,7]. Because they are usually highly invasive, they can rarely be completely excised[2,7]. On account of the slow growth and the relative rarity of the tumor, the value of additional postoperative radiation therapy (RT) is difficult to assess, but a number of retrospective studies have suggested a beneficial role of RT in OD not only incompletely resected at surgery but inoperable and/or recurrent ones[4~7].

There is still no general agreement as to nature of symptom and survival times related to the therapy, pattern of recurrence and best modalities of treatment of OD between authors[1,2].

The purpose of this paper is to analyze the cerebral location of the involvement, initial symptoms, CT findings, survival rate and prognostic factors retrospectively in 21 irradiated OD.

METHODS AND MATERIALS

From April 1983 through April 1989, 21 cases of histopathologically proven oligodendrogliomas (OD) were reviewed. These are 8% of the irradiated 246 primary brain tumors during the same period at the Division of Radiation Therapy, Kangnam St. Mary's Hospital usig 6 MV linear accelerator (NELAC-6).

Of the 21 patients treated, thirteen were male and 8 female. Ages ranged from 5 to 68 years with

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a median age of 38 years (Table 1).

·All patients had several series of brain CT for follow up scans to be analyzed(Table 2). Histopathologic diagnosis was made by stereotactic biopsy in 3 and postoperatively in 18 cases (Table 3). There were pure OD in 16 cases and mixed type in 5 (Table 1). The type of surgery was divided into partial, subtotal and total resection in 7, 9 and 2 cases respectively. In 6 cases, chemotherapy was also given during or after radiation therapy (Table 3). Radiation doses varied from 3960 cGy to 6480 cGy, and were given as 5 fractionation per week for 5 to 8 weeks. Total radiation doses and volumes were selected depending on the patients ages performance status and type of surgery, the volume of post-surgical residual tumor (Table 4). Most patients were 2 or 3 fields technique along with or without wedge pairs. Wide local fields were employed with SAD of 80 cm, except for a few cases which used whole brain fields followed by local small boost irradiation technique.

Results were analyzed using both Kaplan-Meyer method and one or two tail test. Follow-up was done from 8 months to 72 months (median 38 months) for. 20 cases.

Table 1. Patients Characteristics, Histology & Symptoms

Sex	Male	13
	Female	8
Age	range	5 – 62 years
	median	38 years
Histologic grades and subtypes. (n=21)		
	I II III	Total
pure	9 1 2 2 2	16
mixed	3 1 1	5
Symptoms at presentation (may be multiple ; %)		
headache		18 (85.7)
cerebral motor		12 (61.2)
nausea / vomiting		7 (33.3)
dizziness		6 (28.6)
seizure		5 (23.8)
cerebral sensory		5 (23.8)
cranial nerve		3 (14.3)

Table 2. Analysis of the CT Findings (%)

Density	
low	13 (62)
iso	2 (10)
high	3 (14.3)
mixed	3 (14.3)
Mass	
cystic	7 (33.3)
necrotic	1 (5)
hemorrhage	1 (5)
calcification	14 (66.7)
contrast enhancement (+/–)	9/12

RESULTS

All but one were supratentorial. The intracranial location of tumor was shown in Fig. 1. Involvement

Table 4. Relation between Radiation Doses & Type of Treatment (Tx). (n=21)

Type of Tx. \ dose (Gy)	40–50	50–60	60–
Biopsy		2/1*	
Partial		4/2*	0/1*
Subtotal	1/0	4/0	0/4*
Total	1/0	1/0	

. Survival number / dead number
* : Chemoradiation

Table 3. Treated Modalities of Oligodendroglioma of the Brain

	SURGERY				TOTAL (%)
	Biopsy	Partial	Subtotal	Total	
RT	2	5	6	2	15 (71.4)
RT + Chemo.	1	2	3		6 (28.6)
Total (%)	3 (14.3)	7 (33.3)	9 (42.9)	2 (10)	21 (100)

of the frontal and parietal lobe were 10 (48%) patients in each and temporal lobe in 8 (38.1%). The brain stem and cerebellum were also involved in each one.

Major presenting initial symptoms were headache in 18, cerebral motor in 12, nausea and vomiting in 7 and epilepsy in 5 respectively (Table 1).

CT analysis showed most tumors were composed of low density (62%) and cystic mass (33%) as shown in Table 3. Calcification within mass was observed in 14 (66%). The ratio of contrast enhancement (+/−) was 9 (42.8%) to 12 (57.2%) (Table 3).

The mean survival time after RT were 38 months by K-M method (Fig. 2).

No statistical significance could be achieved the survival with following relations: 1) total radiation dose (p=0.72), 2) histologic grades and subtypes (p=0.19), 3) chemoradiation (p=0.455) 4) whole brain irradiation following small boosts and wide fields technique (p=0.604) and 5) extent of surgery (p=0.164).

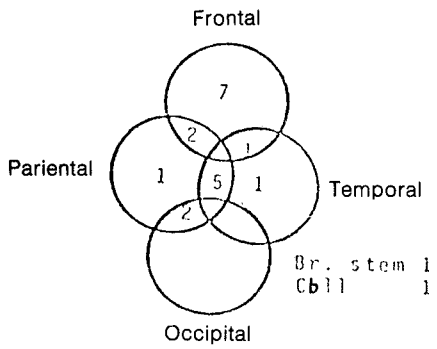

Fig. 1. Cerebral Lobes Involved (n=21).

DISCUSSION

OD is the third most common glioma following astrocytoma and glioblastoma[1]. It is known about 5% of all intracranial glioma[3,7,9] and 1~2.4% of brain tumors are OD[1]. In our series, it occupied 8% of all irradiated 246 primary brain tumors during the same periods.

This tumor is rare in children. It accounts for only 1~2% in pediatric series[1,7,8]. Authors treated 7 cases of children (M: F=3: 4, 4 alive, 2 dead, 1 lost). Generally, the sexes are affected equally and peak incidence is in the fourth and fifth decades. In our small series, ages ranged from 5 to 62 years with a median age of 38 years (Table 1). These tumors are usually located in the cerebral hemispheres but they can occur in the spinal cord and cerebellum[1,9]. Next to cerebral hemisphere, brain stem is the preferential site but we have experienced only 1 case (Fig. 1).

Most OD grow slowly and produce only focal symptoms such as epileptic seizures[1,2]. Patients usually present with a long duration of symptoms. The history of such attack may go back to many years (5 to 20 years)[9]. On the other hand, some in their rapid growth mimic glioblastomas[7,9]. OD involve the important vital structures predominantly frontoparietal region along the fissure of Sylvian

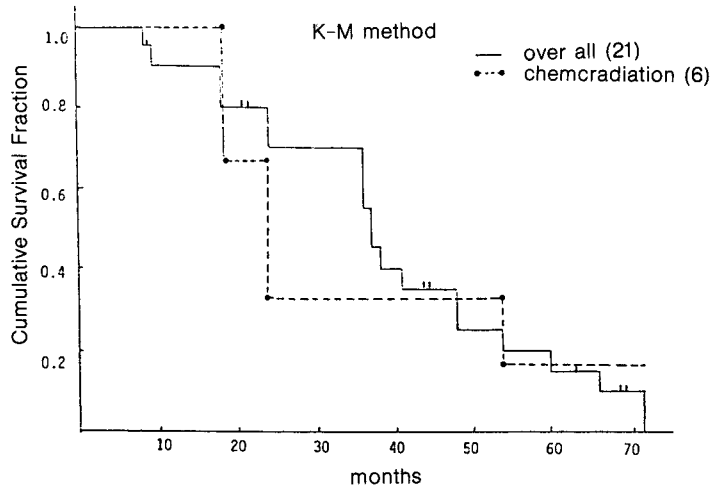

Fig. 2. Survival curves for 21 patients with oligodendroglioma.

and spreading upward anteriorly to the motor cortex of the frontal lobe and frequently calcify[2,7].

The remarkable clinical symptoms in OD are epilepsy (50~70%) with long standing seizure disorder and increased intracranial pressure (40~50%)[1,7,9]. Therefore, the kinds of clinical seizure presentation are characterized by primary site of the tumor[7]

Microscopic appearance can be quite variable and may exhibit anaplastic histologic characteristics. Most of OD are mixed tumors and usually have astrocytic components. A truly malignant variety of the oligodendroblastoma has also been described. There are often microcalcifications, mucoid degeneration and hemorrhage[7]. It is important to note that there is non correlation between the microscopic features of OD and its biologic behavior[7,9,14].

X-ray examination and CT scan can sometimes suggest an OD because of its tendency to calcify[2,9]. CT shows hypodense lesion on 26%, isodense ones in 5%, hyperdense ones in 14%, and mixed ones in 55%. Enhancement of contrast is seen in 46%. Focal edema is present in 38%[10]. Our data showed much more prevalent hypodense mass rather than mixed one and less calcification than abvove data (Table 2).

Many reports indicate that radical surgery for OD enhances survival but the tumor may be widely infiltrating and difficult to excise completely[1,2,6]. After surgery alone, patients may live free of symptoms for many years prior to tumor recurrence. OD have a tendency for local recurrence and for anaplastic transformation with occurance in 30~50% of the cases. When there is recurrence it can be managed with a second excision if the anatomy of the recurrence is suitable[2,6].

There is considerable controversy regarding the role of external beam radiotherapy in the treatement of these slow growing malignancies due to shortage of experiences[1,4,6]. Bochard and Sheline suggested the usefulness of postoperative treatment, meanwhile Shenkin recommended it only in the case of definite evidence of regrowth[1,2,11]. By their series the 24 patients who received postoperative RT survive more than 5 years. They received from 5300~7000 cGy during a period of 49~66 days using megavoltage machine. All the RT were given as soon as the surgical wound had completely healed[2,5]. A number of retrospective studies have suggested a beneficial role for radiotherapy in low grade astrocytoma incompletely resected at surgery but the role of RT in low grade OD is not clear[5,8,12]. Radiation may produce a tumor regrowth delay and increase 5 year survival[6].

According to some authors, postoperative survival time in children is 39~45 months and is not influenced by RT at all[13]. Müll et al found 42 months survival for low grade and 22 months for high grade OD[7]. Sheline[5] reported a 5 year survival rate of 85% in irradiated and only 31% in nonirradiated group of patients whereas Marsa[14] recorded a 5 year survival rate of 74%[7]. Many authors believe the irradiation proved to be quite effective for survival as well as for the quality of survival of patients[1,2,5,12]. In this report, twelve of 21 who received irradiation were alive and free of disease for 9~66 months after RT. At the time of this report, 8 patients died during the period of 8~72 months after RT. Our data did not show statistical significance to induce the prognostic factors because the numbers in each group were too small.

Recurrence after surgery is seen in about 50% with rather little tendency towards anaplasia and about 75% of recurrence showing similar histological features as primary tumor with multiple recurrence.

Packer et al.[8] suggested OD of posterior fossa in childhood frequently disseminate and leptomeningeal metastasis to be the site of first relapse in children treated with only local irradiation. Nakamura et al.[16] reported one anaplastic OD who had dissemination to bone marrow for postoperatlively chemoirradiated. They recommended postoperative myelograms and cytologic examination of CSF for all OD of the posterior fossa. No such instances were noted in this series.

Finally, followings are generally accepted for proper management OD through combined modalities[2];

1. Diagnosis of OD can be made as soon as possible because of radiologic examination and presymptomatic signs allow the early diagnosis.

2. Surgical extirpation can be done by way of meticulous surgical art, especially for relatively early stage of the disease.

3. Patients receive adequate postoperative irradiation to sterilize the residual microscopic disease.

4. Recently, MR scan has been introduced in the fields of not only diagnosis of disease but the RT planning[17]. The interface between abnormality (tumor plus edema) and normality was depicted much more clearly by MR than CT in most cases. Such superiority of depiction of the margin of abnormality is important for radiation therapy plan-

ning because the known tendency of OD to infiltrate to adjacent edema making potential tumor bearing tissues.

SUMMARY

The results of irradiated 21 patients with OD were reported at the Division of Radiation Therapy, Kangnam St. Mary's Hospital from April 1983 to April 1989.

We intended to analyze the cerebral location of the involvement, initial symptoms & CT findings, survival rate and prognostic factors, retrospectively. One case was lost to follow up for survival data.

Of the 21 patients, thirteen were male and 8 female. Ages ranged from 5 to 68 years with a median age of 38 years. Radiation doses varied from 3960 cGy to 6480 cGy and were given for 5 to 8 weeks. Histologic diagnosis was made by stereotactic biopsy in 3 and postoperatively in 18 cases. All but one were supratentorial. The involvement of the frontal and pariental lobes were 10(48%) patients in each and temporal lobe in 8(38.1%) patients. Major presenting symptoms wer headache in 18, cerebral motor in 12, nausea/vomiting in 7 and epilepsy in 5

In CT analysis, low density (62%), cystic mass (33%), calcification (67%) and positive contrast enhancement (42.8%) were observed with high frequency. Mean survival after RT were 38 months (K-M method).

We believe that radiacal surgery following postoperative radiation therapy is the standard treatment for OD to improve survivals and life quality.

We could not achieve any significant prognostic factors statistically influencing the results of RT for OD in this series.

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= 국문초록 =

희돌기교종의 방사선치료 효과

가톨릭의과대학 방사선과학교실 신경외과학교실*

윤세철 · 김성환 · 정수미 · 길학준 · 신경섭 · 박용휘 · 강준기* · 송진언*

가톨릭의대 방사선치료실에서는 1983년 4월부터 1989년 4월 사이 6년 동안에 희돌기교종환자 21예를 외부방사선 치료하였다. 전예에 대하여, 연령 및 발병부위별 빈도와 임상증상과 CT 소견 그리고 추적 가능하였던 20예의 생존율에 관한 후향적 분석을 하여 다음과 같은 성적을 얻었다.

1. 전예는 원발성 뇌종양으로 방사선치료 하였던 환자(246예)의 약 8%의 빈도를 보였으며, 연령분포는 5~62세(중앙값 38세)이고, 남녀의 비는 13 : 8이었다.

2. 임상 주 증상은 두통 18예(86%), 뇌운동신경마비 12예(57%), 오심구토 7예(33%), 경련 5예(24%)등 순을 보였다.

3. 발병부위는 전두엽 10예(48%), 두정엽 10예(48%), 측두엽 7예(33%), 후두엽 2예(10%)그리고 뇌간 및 소뇌가 각각 1예(5%)씩 이었다.

4. 조직학적 진단은 정위다방향 조직생검이 3예(14%), 종양의 수술적 제거(부분 전체제거)에 의함이 18예(86%)이었다. 전예에서 전뇌 및 소부위에 3960~6480 cGy/5~8주 외부방사선 치료를 하였고, 6예(29%)에서는 항암약물 치료도 병행하였다.

5. CT음영은 저, 고, 혼합 및 등가음영이 각각 13(62%), 3(14%), 3(14%), 2(10%), 예씩 이었고, 낭성종괴 7예(33%), 괴사 및 출혈성 종괴가 각각 1예(5%)씩 이었다. 석회와 음영은 14예(67%)에서 관찰되었으며, 조영증강 유무는 9 : 12로 나타났다.

6. 평균생존기간은 38개월이었다.