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Preliminary experiences with intraoperative radiation therapy (IORT) for the treatment of brain tumors

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Ten brain tumor patients underwent wide resection of the tumor followed by Intraoperative Radiation Therapy (IORT) at the first surgery or at the second salvage surgery after failure of conventional external beam irradiation. Two patients(1 meningioma, 1 glioblastoma multiforme) were treated at the first surgery and 8 patients(3 anaplastic astrocytoma, 3 glioblastoma multiforme, 1 meningioma, 1 gliosarcoma) were treated after salvage surgery. The IORT doses were ranged from 15—25 Gy depending on the tumor volume and previous radiation therapy. The neurological status(Karnofsky performance status) was improved in 4 cases, not changed in 6 cases after IORT. There were several complications after IORT; radiation necrosis, communicating hydrocephalus, wound infection, and abnormal CT findings such as diffuse low density area in and around operation site. The radiation necrosis was confirmed by operation in a recurrent meningioma patient 12 months after IORT. At follow-up, ranging from 1 to 16 months, there was no deaths. Based on our limited experiences, the IORT might be one of the adjuvant therapeutic modalities especially for the malignant brain tumors and unresectable huge meningioma.

Key Words : *Glioblastoma multiforme, Anaplastic astrocytomas, Meningioma, IORT*

INTRODUCTION

Malignant glioma such as anaplastic astrocytoma and glioblastoma multiforme has a high incidence of recurrence at the primary site after operation and external beam irradiation(Sakai et al., 1991).

There is evidence indicating that for most tumor types local tumor control increased with higher doses of radiation. The advantage of Intraoperative radiation therapy(IORT) is that by irradiating during the surgery, the physician is able to visualize directly the tumor volume as well as areas at risk, and able to exclude normal structures during the treatment from the radiation beam. It is also possible to shield tissues underneath the tumor volume or to adjust the electron energy to spare structures located beneath the tumor mass. For all these reasons it is possible to deliver a very high dose to the tumor while minimizing the dose to the normal tissue(Kinsella et al., 1987). To control advanced or recurrent malignancies, the use of surgical resection and IORT has become increasingly frequent(Abe et al., 1974; Tepper et al., 1986;

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Gunderson et al., 1988). Trials in the United States have confirmed the usefulness of IORT alone, in the palliation and survival of patients with unresectable pancreatic cancer(Goldson et al., 1981 ; Shipley et al., 1984). IORT has rarely been used for the treatment of recurrent malignant glioma(Matsutani et al., 1986 ; Sakai et al., 1989). Here, we discuss our experiences with IORT as part of primary or salvage treatment for various kinds of brain tumors.

MATERIALS AND METHODS

Ten patients who underwent wide tumor resection with IORT or salvage surgery followed by IORT at Korea University Hospital from December 1994 to April, 1995 were reviewed. The age of patients(7 males, 3 females) ranged from 25 to 61 years, with a median age of 35 years. To evalutate the patient's neurological status we evaluated the Karnofsky performance status before and after IORT. The Karnofsky performance status before operation ranged from 50 to 100 %. The tumor sites were identified by preoperative computed tomography(CT) scan, MRI, and surgical findings. There were 3 cases in the frontal lobe, 2 cases each in the parietal, the occipital lobe, 1 in the parasagittal area, and 3 in the temporal lobe. Eight patient had malignant gliomas, and two had meningiomas. All the tumors were recurrent cases except 2 patients who had a meningioma and GBM respectively(Table 1). Surgery was performed in the operating room in the Department of Radiation Oncology. After exploration, surgeon resected all gross tumor if possible. The radiation oncologist and surgeon then determine the feasibility of IORT, size and shape of electron beam cone, and the depth to be treated. The patient is transported to linear accelerator room and a sterile treatment cone is then placed into position and docked to the treatment head of the linear accelerator(Clinac 1800, Varian, U.S.A). In those patients in whom subtotal or total resections were performed, saline-saturated cotton balls were inserted into the surgical field as tissue-compensating material to maintain dose homogeneity. The appropriate IORT cone diameter was measured to give a 1-cm perimeter of normal brain tissue. The cone size was from 5 cm to 9 cm. The energy of the electron beam is chosen on the basis of thickness of tumor or tumor bed from 9 MeV to 20 MeV. The single IORT dose in all patients has been 10−25 Gy specified at the 80−90 % isodose.

External irradiation was given prior to IORT in all but 2 cases which included 1 meningioma and 1 glioblastoma multiforme. It was given in 1.2 or 1.8 Gy fraction with 6 MV photon beam from linear accelerator(Clinac 1800). Parallel-opposed external irradiation-(right and left laterals) were used to deliver 50.4 Gy over 51/2 weeks to the whole brain and then the tumor bed was again boosted by 5.5−21.6 Gy over

Table 1. Results of IORT for various types of brain tumors.

Tumor				IORT			Status	
Type Age/Sex	Pathology	Site	XRT(Gy)	Dose(Gy)	Field Size (cm)	Beam Energy (MeV)	KPS preop/postop	F/U(mo)
Primary								
1. M/33	Mening.	P-S	none	25	9	16	70/70	16
2. M/61	GBM	T	none	15	7	16	100/70	3
Secondary								
3. M/28	AA	O	55.8	15	5	9	50/90	15
3.*M/28	AA	O	55.8	15	5	9	90/90	2
4. F/27	AA	T	63	25	7	16	100/70	3
5. F/60	AA	T-P	59.4	25	5	16	70/70	14
6. M/30	GBM	F	72(bid)	15	6	12	100/100	7
7. F/61	Mening.	P	61.2	15	6	12	100/100	16
8. M/48	GBM	F	72(bid)	15	7	20	70/80	3
9. M/37	GBM	P	72(bid)	15	5	16	70/90	1
10. M/25	Gliosarc	F	72(bid)	20	7	16	100/100	1

Mening. : meningioma, GBM : glioblastoma multiforme, AA : anaplastic astrocytoma, Gliosarc : gliosarcoma,
P-S : parasagittal area, O : occipital lobe, F : frontal lobe, P : parietal lobe, T-P : temporoparietal lobe
* : second IORT case

1−2 weeks. Four patients received total dose of 72 Gy with hyperfractionated schedule(1.2 Gy/f bid, daily 2.4 Gy/2f). External irradiation was given in one glioblastoma multiforme patient but not for the meningioma after IORT. The IORT was given twice for a patient with the recurrent ananplastic astrocytoma located at right occipital region.

RESULTS

All cases were followed up for 1 to 16 month (median, 3 months) after IORT. The combined therapy(external irradiation and IORT) was employed for 10 cases of brain tumors. All the patients treated by IORT survived the follow-up duration for 1 to 16 months(Table 1). The neurologic performance status judged by Karnofsky scale was not changed or improved after IORT in all cases except one anaplastic astrocytoma patient who developed neurological deficit by vascular injury during operation. Two patients (1 recurrent anaplastic astrocytoma and 1 primary meningioma) receiving more than 25 Gy intraoperatively demonstrated mental dullness and a wide low-density area on CT scan taken 6 months and 9 months after IORT respectively. Based on operative and radiological findings, the radiological and clinical changes seemed to associate with the IORT. Even though there were no significant radiological changes on follow-up studies, some improvement noted clinically. There were three other IORT complications which included one wound infection, one communicating hydrocephalus, and one radiation necrosis. The radiation necrosis was confirmed by the operation and histological study in a recurrent parasagittal meningioma patient a year after IORT. There was no perioperative complications in a recurrent anaplastic astrocytoma patient treated twice with IORT. IORT was given two times for a recurrent anaplastic astrocytoma in the occipital lobe without any complications.

A case of huge parasagittal meningioma was too vascular to remove totally in the first operation. Nine months after IORT, second operation was done to remove tumor totally. Operative findings showed some gliosis and cyst around the remaining meningioma but the size of tumor was remarkably shrinked compared with that of previous operation. The huge meningioma was successfully removed without bleeding.

DISCUSSION

In the 1940s, Pack(Pack and Livingston, 1940) in the United States and Henschke(Henschke and Henschke, 1944) in Germany used IORT with a small portable Phillips contact therapy machine. Abe and his associates(Abe et al., 1975) in Japan played a major role in reviving the current international interest in this form of therapy.

This modality has been used to treat a host of malignant tumors including those arising in the pancreas, stomach, colorectum, cervix, bladder, brain, kidney, soft tissue, and head and neck. Although IORT may prove to be a useful radiotherapeutic modality, its use in inexperienced hands can result in unacceptable morbidity. Some of the complications attributable to IORT can be quite debilitating including bowel hemorrhage, vascular damage and occlusion, bone damage, and painful nerve injury.

Margin status was the single most important prognostic factor predicting both IORT in-field recurrence and survival. The application of IORT was beneficial even in patients with macroscopic(gross) residual disease after surgical resection. Pelton et al. showed that no effect of total dose per field or size of the field was noted on the in-field failure rate. Higher IORT doses, field size>7cm or multiple IORT fields did not improve local control(Pelton et al., 1993).

Several important problems developed in performing IORT for malignant gliomas. The irradiated field cannot be completely restricted to the residual tumor after surgery because an exact clinical determination of the extent of malignant glioma is almost impossible. The optimal tumoricidal radiation dose also remains unclear. Therefore, external whole brain irradiation is still necessary to control residual tumor cells. Higher radiation doses may not always achieve better results even if given to a limited area, since higher doses increase the deleterious effects, especially in the brainstem. In our IORT series, there were no serious induced complications such as fatal cerebral necrosis. However, two cases (1 recurrent anaplastic astrocytoma and 1 primary meningioma) receiving more than 25 Gy intraoperatively, demonstrated mental dullness and wide low-density area on CT scan taken 6 months and 9 months after IORT respectively. The radiological and clinical findings seemed to be associated with the IORT. There were no significant radiological changes on follow-up studies but clinically some improvement noted. Localized necrosis in the treat-

ment area developed in 32 % of patients.(Matsutani et al., 1986) IORT may be a favorable management method if the CT/MRI shows the malignant glioma locates near the brain surface and is not small. IORT is therefore a suitable treatment for management of residual malignant glioma following surgery. IORT should therefore be considered in those selective patients with locally advanced or recurrent cancer where an aggressive surgical approach is warranted. As we removed huge meningioma considered inoperable successfully 9 months after IORT, IORT can be used as a form of adjuvant therapy for a huge parasagittal meningioma which is too vascular to remove totally.

Although this retrospective study suggests the feasibility and clinical potential of IORT, any long-term benefits need to be studied in the context of prospective patient trials. However, a randomized study is necessary to prove the effectiveness of this therapy. Our study is a single-institution study with one group of surgeons and radiation oncologists. Multiinstitution and radomized prospective studies are necessary to confirm our findings. At this time, however, this procedure appears relatively safe and feasible if facilities are available.

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