CLINICAL ARTICLE

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Novalis Shaped Beam Radiation Treatment for Craniopharyngiomas

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Objective : To evaluate the effectiveness of Novalis shaped beam radiation treatment as an adjuvant treatment in patients with craniopharyngiomas.

Methods : We reviewed 8 patients with craniopharyngiomas who had recurring tumors during follow-up or had residual lesions after primary surgery. Three of 8 patients were found to have recurrence after gross total excision of the tumor and 5 patents had residual lesions after subtotal resection. All patients were treated with fractionated stereotactic radiation treatment(FSRT) using Novalis system. The mean age of patients was 28 years (range 16~52). The median irradiation dose per fraction was 1.7Gy (range 1.7~2.0). The median fraction number was 23 (range 15~25), and the median total dose was 39.1Gy (range 25.5~42.5). Follow-up included MR imaging, and ophthalmologic and endocrine examinations.

Results : The median follow-up period was 23 months (range 12~43). The local tumor control rate was 87.5%. One patient had a recurring tumor, in which cystic change developed 2 months after FSRT. Four patients showed a decrease in size of their tumor, while 3 patients remained stable. Seven out of 8 patients had hormonal dysfunction that remained unchanged after initial surgery. No further progression of visual impairment was observed.

Conclusion : FSRT using Novais system is effective and safe for the treatment of recurring or residual craniopharyngiomas without toxicity like optic neuropathy.

KEY WORDS : Craniopharyngioma · Shaped beam radiation treatment · Optic neuropathy.

Introduction

The craniopharyngioma is a slowly growing and histologically benign parasella tumor that thought to be derived from the squamous cell remnants of an incompletely involuted hypophyseal-pharyngeal duct[8]. They occur with a peak incidence between 5 to 15 years of age, but can be present at any age. Visual loss and impairment, headache, apathy, cognitive deficit, and endocrinologic deficits are typical symptoms. Although these tumors are usually well circumscribed and encapsulated, dissection of the tumors are often complicated by its propensity to cause an intense gliosis and its dense arachnoid adhesions to the surrounding brain parenchyma and neurovascular structures such as the hypothalamus, cavernous sinus, interpeduncular fossa and optic structures. Treatment options are total surgical excision or subtotal resection followed by radiation therapy. Despite advances in microneurosurgical techniques, the management of these tumors remains controversial. If it is possible, a total resection of the tumor offers the best chance of cure for the patients. However, because of the high rate of visual impairment and endocrine dysfunction, many authors recommended subtotal resection followed by radiation therapy. Recent advances in fractionated stereotactic radiosurgery/radiotherapy techniques, including dynamic arc therapy, have improved the conformality of FSRT and provided the ability to avoid damage of normal tissues[12]. We treated 8 patients who had recurring tumors or postsurgical residual craniopharyngimas with FSRTusing the Novalis system. In addition, we evaluated the effectiveness of FSRT in craniopharyngioma patients.

Materials and Methods

Between November 2000 and December 2004, 8 patients with craniopharyngiomas received fractionated stereotactic radiotherapy. Seven patients were male and one was

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Table 1. Patients treatment characteristics

Patient	Sex	Age	Vol (cc)	Dose (Gy)/ Fx	No. of Fx	Total dose (Gy)	No. of isocenter	Previous RT.
1	F	38	29.23	1.7	15	25.5	1	No
2	M	16	16.69	1.7	25	42.5	1	No
3	M	21	4.50 0.16	2	15	30.0	2	No
4	M	21	4.23	1.7	20	34	1	No
5	M	21	1.83	1.7	25	42.5	1	No
6	M	31	1.63	1.7	25	42.5	1	Yes (GK)
7	M	52	1.82	1.7	23	39.1	1	No
8	M	23	6.85	1.7	25	42.5	1	No

Fx : Fraction, No : Number, RT : Radiotherapy, GK : Gamma Knife

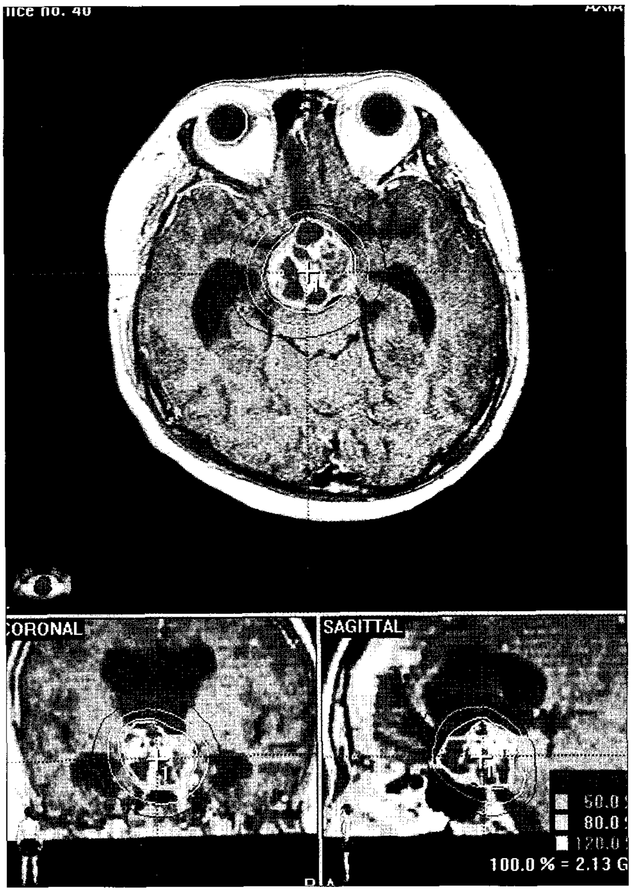

Fig. 1. Three dimensional dose distribution in a craniopharyngioma. Red line = target volume, Light green line = 80% isodose line.

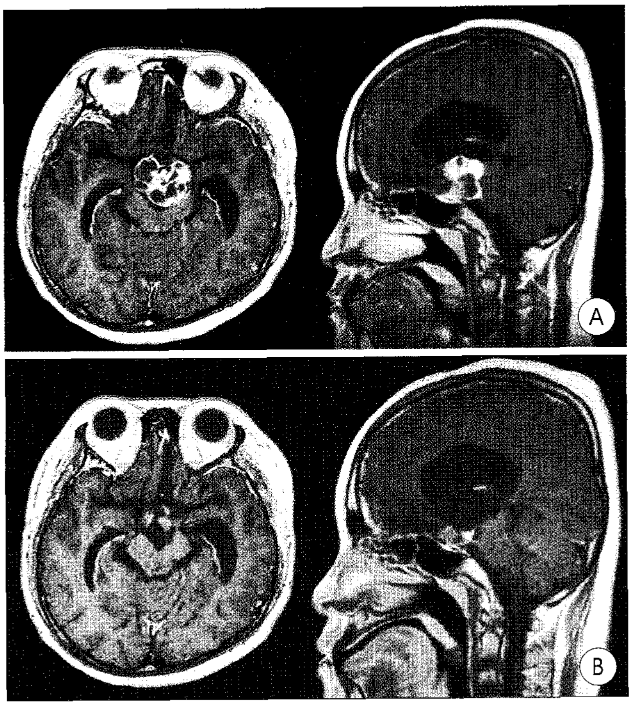

Fig. 2. 16-year old male, recurred craniopharyngioma. A : T1Wcontrast enhanced axial and sagittal magnetic resonance images show a large parasella tumor consist of multiple cysts with distortion of the visual pathway. B : Seven months after fractionated stereotactic radiation treatment using Novalis system (42.5Gy : 1.7Gy, 25fraction), contrast enhanced magnetic resonance images demonstrating remarkable tumor shrinkage.

female. All patients had undergone prior surgical intervention : total resection in 3 patients and subtotal resection in 5. Three patients that had total resection and were found to have recurrence of the tumor on MR imaging and 4 patients that had subtotal resection were treated with FSRT one month after surgery. One patient had had surgery and Gamma knife radiosurgery before FSRT. The main symptoms before FSRT were loss of visual acuity, disturbance of visual field, and hormonal deficiency. The mean age of the patients was 28 years (range 16~52). The median volume was 4.23cc (range 0.16~29.23). The median irradiation dose per fraction was 1.7Gy (range 1.7~2.0). The median fraction number was 23 (range 15~25), and the median total dose was 39.1Gy (range 25.5~42.5). The patients' characteristics are described in Table 1.

Treatment planning

Patients were immobilized with a relocatable thermoplastic face mask. Each tumor was localized using an MR image (1.5-tesla, Siemens) and CT scanning. The axial slice thickness of each MRI was 2mm. Fusion of the CT and MR imaging was performed, and three dimensional treatment planning was generated using a planning system (Brain LAB). The planning target volume(PTV) was defined as the gross tumor volume(GTV), with a margin of 2mm. The clinical target volume(CTV) was considered to be identical to the gross tumor volume. In all cases, field shaping was performed with a micromultileaf collimator to optimize dose distribution in nonspherical tumors. The collimator consists of 26 pairs of leaves varying in thickness from 3 to 5.5 mm. Treatment was delivered to a single isocenter in 7 cases, and two isocenters in one case, by a dedicated 6-MV Novalis LINAC (BrainLAB). Treatment was administered through six noncoplanar dynamic arcs. The planning target volume was encompassed by an 80% isodose line. The daily dose to the optic apparatus was kept strictly below 2Gy in fraction. Fig. 1. shows the dose distribution of the treatment plan.

Results

The mean time period of follow up was 22.8 months (range 12~43). Four patients showed a marked decrease in the size of tumor volume on follow-up MR imaging (Fig. 2), (Fig. 3). Three patients had no change or a slight decrease of tumor volume. One patient showed an almost complete resolution of the solid component of the tumor, but the cystic lesion was slightly increased. Surgery was recommended but she refused. We considered that this patient had failure to local tumor control. So, the overall local control of tumors

Fig. 3. 21-year old male, residual craniopharyngioma after surgery. A : T1W contrast enhanced axial and sagittal magnetic resonance images show a suprasella tumor. B : Fourteen months after fractionated stereotactic radiation treatment using Novalis system (30Gy : 2Gy, 15 fraction), contrast enhanced magnetic resonance images reveal remarkable decrease in tumor size.

Table 2. Visual acuities of patients

patient	VA (Before FSRS) (right / left)	VA (After FSRS) (right/left)	Result	Total dose (Gy)
1	FC/ HM	FC/0.2	Improved (L)	25.5
2	1.0/LP (-)	1.0/LP(-)	NC	42.5
3	LP(-)/HM	LP(-)/FC	NC	30
4	0.8/0.6	0.8/0.4	NC	34
5	HM/1.0	0.1/1.0	Improved (R)	42.5
6	0.15/0.9	0.8/0.6	Improved (R)	42.5
8	1.0/FC	0.1/0.6	Improved (L)	42.5

FC : finger count, LP : light perception, HM : hand motion, VA : visual acuity, NC : no change

was 87.5% and all patients survived. Seven out of eight patients were treated with hormonal replacement therapy for panhypopituitarism. The panhypopituitarism occurred as a result of the tumor itself or previous surgical resection and was present prior to FSRT. In seven of the eight patients, a visual acuity test was performed both before and after FSRT. All the patients showed a visual disturbance prior to FSRT and the follow up visual study showed either no changes or mild improvement (Table 2). Therefore, no complications directly related to FSRT have been encountered.

Discussion

Usually, total resection is recommended as the initial management of craniopharyngiomas. Although gross total resection in principle is an attempt at a cure, it has been very difficult to remove the tumor without neurological or endocrinologic dysfunction. Following a total resection, local relapses have been exhibited 0 to 60%, the majority being 25% or so[6,9]. In the case of subtotal resection, the relapse rate was increased to 60% and above[1]. Total resection of the tumor may be associated with high risk of morbidity, with panhypopituitarism in up to 95% of patients, and diabetes insipidus in about 80~93% of all patients[11,13]. In addition, impairment of vision is reported in about 20% of patients after total resection. Daniela et al reported preservation of normal hormone function in 6 of 19 patients treated with FSRT after subtotal resection[4]. Impairment of visual acuity is reported in less than 10% and up to 30% of all patients treated with partial or subtotal resection followed by RT[7,11]. Total resection of tumor can be obtained, with a long-term control rate that is between 50 and 80%; however, after subtotal resection, 50~100% of patients showed a local recurrence[5,13].

Therefore, in general, subtotal or partial resection of tumors can prevent surgical morbidity, but the procedure requires follow-up adjuvant radiation therapy. The best treatment strategy for craniopharyngiomas still remains a controversy, but the major goal of treatment is preservation of neurological function and a good quality of life. Radiation therapy modalities, including single stereotactic radiosurgery or fractionated radiotherapy, provide excellent tumor control and minimize the radiation-induced complications. Mokry treated 23 patients with radiosurgery combined with an intracystic instillation of Bleomycin in 10 patients with cystic tumors[10]. As a result, there was a volume reduction of the residual tumor in 74% of the patients. In 2001, Chang et al. reported the efficacy of GKS for craniopharyngiomas as an adjuvant treatment after microsurgical resection[2]. Chung et al. treated 31 patients using Gamma knife radiosurgery with a prescribed dose to the tumor margin, varying from 9.5 to 16Gy, with the visual pathway receiving 8Gy or less[3]. They achieved tumor control in 87% of patients and 84% had fair to excellent clinical outcome in the average follow-up period of 36 months. Although GKS in principle is useful in the treatment of craniopharyngioma, the tumor volume and its close attachment to critical structures like the optic apparatus are limiting factors that have limited its application. When tumors are large or located close to critical structures such as the optic pathway, it is necessary to either compromise the dose to the tumor or use dose fractionation. The recent advances in FSRT technique have improved the conformality and have provided the ability to avoid damaging normal tissue. Daniela et al. treated 26 patients with craniopharyngiomas using fractionated stereotactic radiotherapy[4]. They reported that the actuarial local control rate and the overall survival rate were 100% and 100% at 5-years, and 100% and 83% at 10-years, respectively. They delivered a median 52.2Gy (range 50.0~57.6) of target dose to the tumor and the target volume was encompassed by the 90% isodose line. They did not observe any visual impairment, radionecrosis, or secondary malignancies. FSRT using the Novalis system can reduce the safety margin to 2mm. Therefore, it is possible to get a much smaller target volume and it is safer for radiosensitive structures than conventional RT. Initially we irradiated safe dose of 1.7Gy/fraction to the target volume, but these days we try to escalate the dose/fraction and reduce the fraction size. In comparison to radiosurgery, FSRT fully exploits the radiobiologic advantages of fractionation and accuracy of stereotactic radiosurgery. In the case of subtotal resection or recurring tumors, FSRT can be considered an excellent treatment modality without any further progression of neurological and endocrinologic dysfunction in selected patients.

Conclusion

Regarding the complications related to FSRT using the Novalis system, we have not yet encountered any mortality or significant morbidity. Although our number of patients is too small and follow-up period is relatively short for drawing any definite conclusions at this time, our series shows that FSRT using Novalis system may be an excellent treatment method for recurring or residual tumors of craniopharyngioma.

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Commentary

The authors reviewed the clinical experiences of Novalis shaped-beam radiation treatment as an adjuvant treatment for 8 cases of recurred or residual craniopharyngiomas.

The craniopharyngiomas are histologically benign however, recurrence rates is relatively high if these are incompletely excised. Nevertheless, radical excision is harzardous and accompanied by high mortality and morbidity because these are very closed to critical neurovascular structures such as hypothalamus, optic apparatus, internal carotid arteries and brain stem. So, another treatment strategy is subtotal removal followed by fractionated radiation. Recently, stereotactic radiosurgery has been introduced to lessen late radiation adverse effect of surrounding organs. Kobayashi et al recently reported 98 cases craniopharyngiomas treated by Gamma Knife radiosurgery. The tumor control rate was 79.6%, actuarial 10-year survival rate was 91%, progression free survival at 10 years was 53.8%. Factors related to better responses to radiosurgery were advanced age, solid tumor, fewer previous treatments, and smaller tumors whereas factors associated with tumor progression after radiosurgery were youth, cystic or mixed tumor, several previous treatment, and larger tumors. Excellent clinical outcomes can be achieved with stereotactic radiosurgery without ophthalmologic and endoclinologic complications if we can apply this treatment strategy to relatively small, solid residual or recurrent craniopharyngiomas.

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