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Fractionated Gamma Knife surgery for giant pituitary adenomas

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ABSTRACT

Objective: To analyze the feasibility and effectiveness of fractionated Gamma Knife surgery (FGKS) for giant pituitary adenomas.
Methods: From June 2005 to May 2016, 14 patients with giant pituitary adenomas were treated with FGKS, and 10 patients (71%) completed follow-up evaluation. All patients had undergone surgical resection at least once prior to FGKS. The median-volume of the adenomas was 17.6 cm^3(range 4.9–61 cm^3).
Results: The median follow-up period was 31.5 months (range 6–58 months). The size of the tumors decreased in 6 patients and remained stable in 4 patients. The visual acuity improved in 1 patient. None of the patients suffered from vision deterioration caused by FGKS.
Conclusion: FGKS is an effective treatment modality for giant pituitary adenomas in selected patients.
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1. Introduction

Treatment of giant pituitary adenomas or maroadenomas is challenging, especially for those with infiltration of the adjacent sphenoid sinus, cavernous sinus, and diaphragm sellae, or that compress the optic nerve. Most of neurosurgeons choose resection primarily [2,3,9–11].

Unfortunately, the complete resection rates for giant pituitary adenomas are only 47.2% for endoscopic transnasal transsphenoidal surgery, 9.6% for open transcranial surgery, and 30.9% for transsphenoidal microscopic surgery [14,15]. Gamma Knife radiosurgery is also a therapeutic option for such tumors, and significant control has been achieved with this approach. The term "fractionated therapy" is use for general radiotherapy traditionally, and it is regarded as a conventional adjuvant to surgical treatment or as primary treatment for inoperable tumors. In the present study, we evaluated the outcomes of giant pituitary adenoma patients treated with fractionated gamma knife surgery (FGKS).

2. Materials and methods

2.1. Patient population

From June 2005 to May 2016, fourteen patients with giant pituitary adenomas underwent FGKS at the Gamma Knife Center, Department of Neurosurgery, the Second Hospital of Tianjin Medical University, Tianjin, China. Clinical, radiological, and endocrinological information were gathered for this research. Four patients were excluded due to a lack of follow-up data. Five male patients and five female patients were included in the study. The median age was 50.5 years (range 29–63 years). All patients had at least one surgical resection prior to FGKS. One patient had received conventional whole-brain radiotherapy. Four patients took endocrine medications regularly.

The functional/non-functional adenoma ratio was 1/1. With respect to hormone-producing pituitary adenomas, 3 patients had prolactinomas, 1 patient had a growth hormone-producing adenoma, and 1 patient had an adrenocorticotropic hormone (ACTH)-producing adenoma. Of the three patients with prolactinomas, 1 patient could not endure bromocriptine-induced gastrointestinal discomfort, while the other two patients suffered from visual field defects caused by compressed optic nerve. Moreover, one patient with a functional adenoma was diagnosed with an invasive pituitary giant adenoma. All patients underwent thorough endocrinological testing conducted by an endocrinologist prior to FGKS. Three patients diagnosed with pituitary insufficiency, and six patients experienced vision loss or visual field defects prior to FGKS.

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2.2. Radiosurgical treatment

Coronal T1-weighted contrast-enhanced magnetic resonance imaging was performed with a Leksell model G stereotactic head frame (Elekta AB) affixed to the head, and it was transferred to the workstation later. After carrying out the Leksell SurgiPlan, the patients usually kept the head frame on their head until 2 or 3times irradiation treatments were completed. Two patients could not tolerate standing for the night while wearing the head frame; thus, they had to restart this progress before each subsequent round of therapy. But the interval of two times GKS would not spend too long time. A female patient experienced a 3-days interval between her second and third rounds of therapy, and this was the longest interval of all time between treatments. As the technology had matured, we performed it once a daily.

FGKS adopted the method of Dose Fractionation. It means that FGKS had the same irradiated field with GKS, but the single irradiated dose was decreased. Moreover, the accumulated dose was invariable or increased slightly. In the therapy interval, the irradiated field kept unaltered as long as the head frame had not been dismantled, but the irradiated dose's slight adjustment could be done. In addition, the doctors needed to carry out the surgery plan again before the next irradiation once the patients had removed their head frame.

After several MRI sequences had been done, the Gammaplan 10.1.1 dose plan system worked out the residual tumor volume by them.

The median volume of the adenomas was 17.6 cm^3 (range 4.9–61 cm^3). Four patients underwent two sessions of FGKS continuously, and the other six patients received three treatments. The mean maximum dose was 14.5 Gy (range 10–18 Gy), and the mean margin dose was 7.2 Gy (range 5–8 Gy).The mean max dose to optic apparatus was 2.9 Gy (range 1.8–5.1 Gy).

2.3. Follow-up

Clinical evaluations were scheduled at 6-month intervals after FGKS during the first 2 years, and then annually thereafter. The follow-up examinations consisted of MRI, visual field tests, ophthalmological examination, and endocrinological testing. The hormones tested included follicle-stimulating hormone, luteinizing hormone, prolactin, growth hormone, cortisol, free triiodothyronine, and free thyroxine. Treatment effect was evaluated by comparing results from before and after the FGKS. Additionally, we defined adenoma control as a lack of changes or decrease in adenoma volume after FGKS.

3. Results

10 patients were incorporated the assessment of tumor control group. The median follow-up period was 31.5 months (range 6–58 months). Patient and disease characteristics are shown in Table 1.

3.1. Tumor size

According to tumor sizes on MR images at the last follow-up, tumor regression occurred in six patients, and the tumor size remained stable in the other four, No patient experienced tumor growth. Among the patients, whose tumors shrank, the median duration to tumor regression was 6.5 months (range 6–13 months) after FGKS.

3.2. Endocrine outcomes

Of the five patients with functional pituitary adenomas, four patients showed no obvious change in endocrine parameters after FGKS, and the one patient, with an ACTH-producing adenoma, achieved endocrine remission.

Table 1
Attributes for the giant pituitary adenoma and outcomes of therapy.

Variable	No. of patients
Patients included in the study	
total	10
male	5
female	5
age(yrs)	
median	50.5
range	29–63
treated tumor volume(cm^3)	
median	17.6
range	4.9–61
tumor category	
functional	5
nonfunctional	5
maximum dose(Gy)	
mean	14.5
range	10–18
No. of fractionated	
2	4
3	6
follow-up(months)	
median	31.5
range	6–58
tumor control	
shrink	6
stable	4

3.3. Radiation effects and complications

No patients experienced radiation-induced hypopituitarism. One patient with a non-functional adenoma underwent surgical resection follow by FGKS twice in 5 years. After the second resection surgery, this patient diagnosed with hypopituitarism via endocrine testing, but the pathogenesis could not be defined. No patients suffered from radiation-induced optic neuropathy after FGKS, or complications related to the other cranial nerves. Pituitary apoplexy and radiation-induced encephaledema did not occur among these patients either.

4. Illustrative case

A 29-year-old man, who had 3-year history of erectile dysfunction with hyperprolactinemia, he experienced one transcranial pituitary adenoma resection before FGKS. Brain MRI scans showed a giant pituitary adenoma (Fig. 1A–D). Later, FGKS was performed three times in three days. The tumor volume was 32.4 cm^3. The margin dose was 7 Gy with a 50% isodose line. The follow-up MRI examination 26 months later showed the tumor shrank obviously (Fig. 1E–H), and the erectile dysfunction improved as he informed.

5. Discussion

Surgery is generally accepted treatment for giant pituitary adenomas. But the residual or recurrent tumors can be treated by GKS, especially if infiltrating the adjacent sphenoid sinus, cavernous sinus, and diaphragm sellae, or compressing the optic nerve. Some aged patients with comorbidities cannot tolerate operation or anesthetic risk, and for these patients, GKS is an option consider. Jay et al. [1,7] demonstrated the admissive effect of combining two neurosurgical treatment modalities-microsurgical resection and GKS in the management of pituitary adenomas.

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