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Gamma Knife Surgery for the Pineal Region Tumors

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Objective : Gamma Knife Surgery(GKS) for the management of pineal region tumors is challengeable strategy as direct access to this area is not easy. The experiences of pineal region tumor patients treated with GKS were analyzed to evaluate the effectiveness.

Methods : Seven patients with tumors in the pineal region were treated with GKS between September 1998 and May 2005. The histological diagnosis were pineal parenchymal tumor (2 patients), low-grade astrocytoma (2 patients), immature teratoma (1 patient), and choriocarninoma (1 patient). One patient was diagnosed as metastatic brain tumor based on histological diagnosis for primary site and brain imaging study. The median marginal dose was 15Gy (range; 11~20) at the 50% isodose line. The median target volume was 2.5cm^3 (range; 0.8~12.5). The median clinical follow up period was 29 months (range; 13~93) and the median radiological follow up period was 18 months (range; 6~73).

Results : Tumor volume measured in follow-up images showed reduction in six patients, disappearance in one. No adverse effect due to GKS was found during the follow-up period . The performance status was preserved in all patients except one who died due to progression of primary cancer in spite of controlled metastatic brain lesion.

Conclusion : Gamma Knife Surgery can be applied to pineal region tumors irrespective of their histology whenever surgery is not indicated.

KEY WORDS : Gamma knife surgery · Radiosurgery · Pineal · Pineal parenchymal tumor.

Introduction

Various types of tumors can be found in the pineal region. Germ cell tumors(GCT) and pineal parenchymal tumors(PPT) such as pineocytoma and pineoblastoma are the most frequent tumors[11]. Other tumors include glial tumors, meningiomas, epidermoid tumors and so on. The pineal region tumors are relatively rare and are generally difficult to remove surgically. The necessity of a histopathological diagnosis, significance of tumor markers and cerebrospinal fluid cytology, controversy in the extent of resection, the use of stereotactic biopsy and neuroendoscopy, and the optimal adjuvant therapy protocols remain unsolved problems for tumors in this region. Gamma knife surgery(GKS) has also been advocated as an alternative to surgical removal of pineal tumors. To evaluate the role of GKS for the treatment of pineal region tumors, the authors analyzed the experience of seven pineal region tumor patients treated with GKS and reviewed the reported literatures.

Materials and Methods

Patient characteristics

Between September 1998 and May 2005, seven patients with the pineal region tumor were treated with GKS. There were three male and four female patients with a median age of 26 years (range 9~46 years). The most common symptoms were increased intracranial pressure with hydrocephalus. Histological diagnosis were confirmed after stereotactic biopsy in three, and craniotomy with tumor removal in two and endoscopic biopsy in one respectively. The diagnoses were astrocytoma in two, choriocarcinoma, immature teratoma, pineocytoma, and pineal parenchymal tumor of intermediate differentiation in one. One patient were clinically diagnosed as metastatic tumor from lung cancer, as histological diagnosis was made at the primary site.

Gamma Knife Surgery

Patients were treated using a Gamma knife GK-B or C model

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(Elekta Ltd.®, Stockholm, Sweden) with Leksell Gamma Plan (Elekta Ltd.®, Stockholm, Sweden, version 5). T1-weighted three-demensional multiplanar rapid-acquisition gradient echo magnetic resonance(MR) images were obtained before and after gadolinium enhancement to determine the target volume. Planning was performed on axial images supplemented by coronal and sagittal reconstructed by coronal and sagittal reconstructed images. The median marginal dose was 15Gy (range; 11~21) at the 50% isodose line. The median target volume was 2.5cm^3 (range; 0.4~12.5).

Follow-up

The tumor volumes were measured in follow-up MR images using volumetric program (Osiris® version 4.0; Unite d'Imagerie Numerique [Digital Imaging Unit] / Hopitaux Universitaires de Geneve [University Hospital of Geneva] (UIN / HIG), Geneva, Switzerland) as previously described elsewhere[8]. The tumor volume change and occurrence of adverse side effects were evaluated to the last follow-up from medical records and radiological studies. The median clinical follow up period was 29 months (range; 13~93). The median radiological follow up period was 18 months (range; 6~73).

Table 1. Summary of clinical outcome of 7 patients

Patient number	Sex/ Age (years)	Diagnosis	Radiosurgical protocol	Dose at 50% (Gy)	Initial volume (cm^3)	Follow-up volume (cm^3)	Image F/U period (months)	Clinical F/U period (months)
1	M / 9	Choriocarcinoma	Adjuvant therapy	20	2.9	1.5 (50%↓)	18	26
2	M / 12	Immature teratoma	Primary treatment for recurrent tumor	20	2.5	1.5 (40%↓)	11	13
3	F / 30	Pineocytoma	Primary treatment	11	5.4	1.8 (70%↓)	73	91
4	F / 46	Pineal parenchymal tumor	Primary treatment	13	12.5	0.2 (98%↓)	15	27
5	F / 33	Metastasis (Lung cancer)	Primary treatment	20	0.8	0 (100%↓)	13	93
6	F / 19	Astrocytoma	Primary treatment	15	1.4	0.3 (80%↓)	35	53
7	M / 26	Astrocytoma	Primary treatment	12.5	2.3	2.9 (23%↑)	23	29

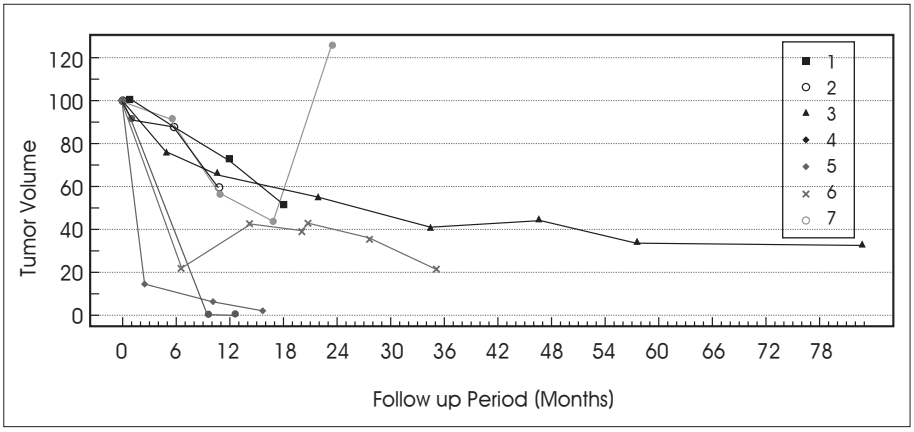

Fig. 1. Relationship between tumor volume changes and follow-up period after Gamma knife surgery.

Results

The treatment outcomes are summarized in Table 1. Tumor volume measured in follow-up images showed reduction in six patients, disappearance in one. Most of them showed rapid decrease in volume within a year. But, tumor volume was regrowthed 18 months after GKS in one. The relationship of tumor volume changes and follow-up period is visualized in Fig. 1. No adverse effect due to GKS was found to the last follow-up. The performance status was preserved in all patients except one patient of metastatic tumor who died due to progression of primary cancer.

Case 1 (patient number 2)

A 12-year-old boy presented with severe headache and vomiting. His brain MRI showed a pineal tumor with ventriculomegaly. Endoscopic third ventriculostomy with biopsy was done without complication. After third ventriculostomy, his headache was subsided. He was treated with chemotherapy using cisplantin, etoposide, vincristine, cyclophosphamide and carboplatin followed by craniotomy and near total resection of residual tumor. The histological diagnosis was immature teratoma. One year after craniotomy, follow up MR shows newly enhancing mass at pineal region. GKS was done for the recurrent mass. Marginal dose was 20 Gy at 50% isodose line. The target volume was 2.5cm^3. Gradual decrease of mass was observed in follow-up MR images to measured volume of 1.5cm^3 at 11 months after GKS (Fig. 2). His Karnofsky performance score(KPS) at the last follow-up (13 months after GKS) was 100.

Case 2 (patient number 4)

A 46-year-old female patient presented with mild headache. Her brain MRI showed a pineal tumor with inhomogeneous enhancement. Endoscopic biopsy was done for the mass and the histological diagnosis was pineal parenchymal tumor of intermediate differentiation. Marginal dose was 13Gy at 50% isodose line. The target volume was 12.5cm^3. Marked reduction of tumor volume was achi-

Table 2. Summary of reported studies about Gamma knife surgery for the pineal region tumor

	Number of cases	Dose at 50% (Gy)	Tumor control rate (%)	Follow-up (months)
Kobayashi et al.[7]				
GCT	25	15.3	52	21.7
PPT	5		80	25.0
Others	3		100	23
Hasegawa et al.[6]				
GCT (NGGCT)	4	14	75	25.2
Endo et al.[4]				
GCT (germinoma)	3	11.3	100	NA
Hasegawa et al.[5]				
PPT	16	15	100	52
Reyns et al.[10]				
PPT	13	15	100	34
Deshmukh et al.[3]				
PPT (pineocytoma)	5	14.8	100	36.0

NA : not available, GCT : germ cell tumor, PPT : pineal parenchymal tumor

eved at 16 months after GKS (Fig. 3). Her KPS at the last follow up (23 months after GKS) was 100.

Discussion

Gamma knife surgery for pineal region tumors is attractive treatment strategy. Firstly, tumors in the pineal region become symptomatic at an early stage of tumor development, because they often cause obstructive hydrocephalus or direct compression of brainstem to induce increased intracranial pr-essure signs or cranial nerve deficits. Therefore pineal region masses tended to be small when they were found. This is one of the good indicative factors for GKS. Secondly, it is true that surgery may be the first-line treatment for the local control of pineal tumors, but surgical approach to pineal region has relatively high risk of possible injury of the surrounding vital neurova-scular structures. Therefore GKS, as minimally invasive modality in its nature, can be a good alternative treatment strategy if local tumor control is guaranteed irrespective of the various histological diagnoses.

Published reports about GKS for pineal region tumors are summarized in Table 2. Non-germinomatous germ cell tumors(NGGCT) are rare and controversies are still exists in their management. Hasegawa et al. reported four cases of NGGCT treated by radiosurgery in conjunction with other treatments[6]. Three of four patients showed good local tumor control during the mean follow-up period was 25.2 months[6]. In conjunction with NGGCT cases shown in the present study, GKS can be one of the options for the treatment of NGGCT especially in pineal region as an additional therapy after surgical treatment, chemotherapy, and/or radiotherapy. Recent reports of pineal parenchymal

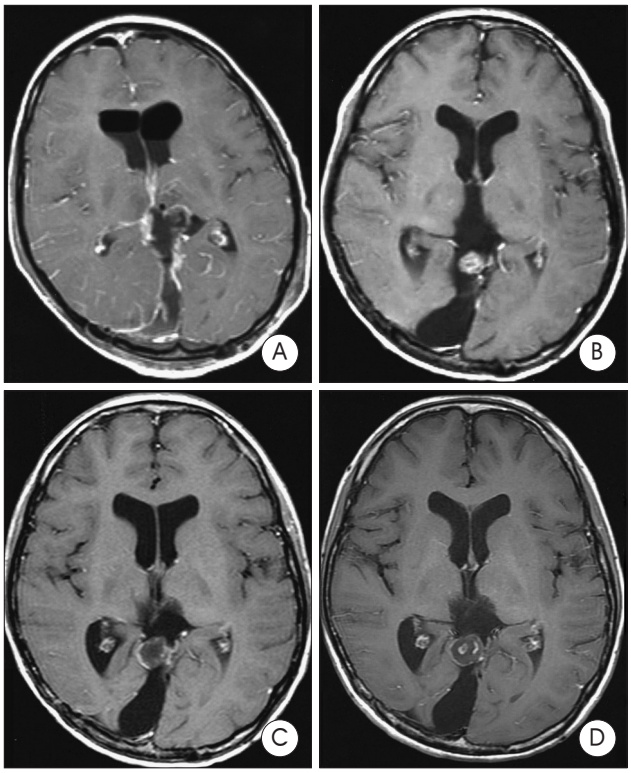

Fig. 2. Gamma knife surgery(GKS) for immature teratoma. A : After craniotomy and tumor removal, T1-weighted Gd-enhancement magnetic resonance(MR) image shows small enhancing remnant mass. B : T1-weighted Gd-enhancement MR image showing newly enhancing mass (volume 2.5cm^3). C : Six months after GKS, follow-up MR image shows slight decreased size of enhancing portion (volume 2.2cm^3). D : The last follow-up MR image take at 11 months after GKS. Marked decrease of enhancing mass is seen (volume 1.8cm^3).

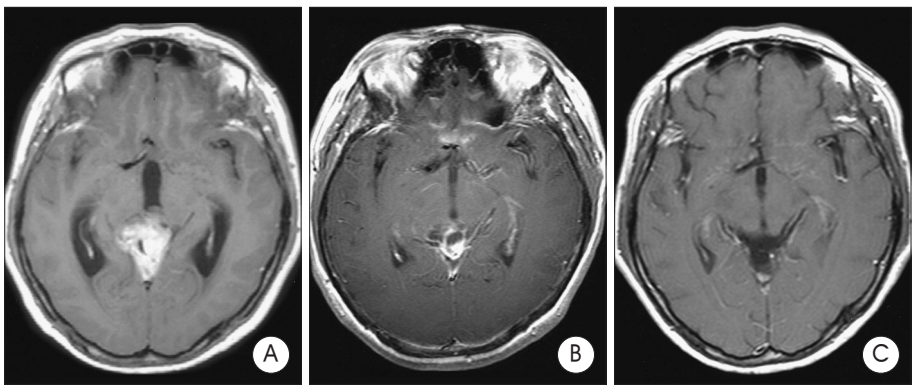

Fig. 3. Gamma knife surgery(GKS) for pineal parenchymal tumor. A : T1-weighted Gd-enhancement magnetic resonance(MR) image showing pineal region tumor (volume 12.5cm^3. B : Three months after GKS. Follow-up MR image shows marked decreased tumor size (volume 1.7cm^3). C : The last follow-up MR image take at 16 months after GKS. Only small residual mass is seen (volume 0.2cm^3).

tumors suggest that these tumors can be treated either by stereotactic radiosurgery or in combination with chemotherapy and radiation therapy[8]. Backlund et al. reported two pineocytoma cases of disappearance of tumor after GKS[1]. Subach et al. reported ten PPT cases treated by GKS[11]. Eight patients of ten were pineocytoma and showed tumor control in five patients among them[11]. And other two patients of pineoblastoma also showed disappearance or decrease of the tumor[11]. Hasegawa et al. reported 16 cases of PPT who undergone GKS[5]. Their radiological tumor control rate was 100%. However, five of sixteen patients, including four patients of pineoblastoma, died during follow-up. Deshmukh et al. reported seven cases of pineocytoma who underwent GKS after tumor resection[3]. All of them showed stable state[3]. The outcomes of the present study of two PPT cases shares the results of reported ones. Both cases, pineocytoma and pineal parencymal tumor of intermediate differentiation, showed favorable tumor control in follow-up images. Additionally, the present study shows good result in low grade glioma patients and even in metastatic tumor patient. These experiences may provide ground for treating patients with pineal region tumors with GKS regardless of their histological diagnosis.

Granted for limitations of case numbers and short follow-up periods, the present study showed favorable initial outcomes of GKS for pineal region tumors of diverse histology within a short period.

Conclusion

It is suggested that GKS can be applied to pineal region tumors irrespective of their histology whenever surgery is not indicated.

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Commentary

The authors precisely describe the experience of Gamma knife surgery in pineal tumors with very nice review of literature. The aim of this study was to document the possible role of Gamma Knife radiosurgery in the management of pineal region tumors. All tumors responded to treatment and disappeared or ceased growing. The response rate is 100%. However, tumor recurrence was found in 1 case of astrocytoma. Although number of cases is small and follow-up duration is relatively short, finally time to progression(TTP) and survival duarion must be obtained. This study shows that Gamma knife radiosurgery can be an effective and safe treatment modality for patients with pineal region tumors. It should have a role in multimodality therapy which includes microsurgical resection, fractionated radiotherapy and chemotherapy for the management of pineal region tumors.

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