Role of Gamma Knife Radiosurgery in Multimodality Management of Craniopharyngioma

M. Abid Saleem, A. Sattar M. Hashim, Azher Rashid, and Muhammed Ali

Abstract *Objective*: This retrospective study evaluated the efficacy and safety of the use of Gamma Knife Radiosurgery (GKS) along with other surgical procedures in the management of craniopharyngioma.

Methods: Thirty-five patients (17 children and 18 adults) with craniopharyngioma were treated with GKS between May 2008 and August 2011. The age of the patients ranged from 2 to 53 years (mean 20 years). There were 26 males and 9 females. Craniopharyngiomas were solid in 7 patients, cystic in 4, and mixed in 24. Tumor size ranged from 1 to 33.3 cm^3 (mean 12 cm^3). The prescription dose ranged from 8 to 14 Gy (mean 11.5 Gy). Maximum dose ranged from 16 to 28 Gy (mean 23 Gy). Before GKS 11 patients underwent subtotal resection of the neoplasm, 2 – neuroendocopic fenestration of the large cystic component, and 10 – stereotactic aspiration of the neoplastic cyst content.

Results: The length of follow-up period varied from 6 to 36 months (mean 22 months). The tumor response rate and control rate were 77.1 % and 88.5 %, respectively. Clinical outcome was considered excellent in 10 cases, good in 17, fair in 4, and poor in 4. No one patient with normal pituitary function before GKS developed hypopituitarism thereafter. Deterioration of the visual function after treatment was noted in one patient.

Conclusion: After GKS tumor control can be achieved in significant proportion of patients with craniopharyngioma. Treatment-related neurological morbidity in such cases is rare. Therefore, radiosurgery may be considered useful for management of these tumors.

M.A. Saleem (✉) and A.S.M. Hashim
Department of Neurosurgery,
Pakistan Gamma Knife and Stereotactic Radiosurgery Center,
NeuroSpinal and Medical Institute,
100/1 Mansfield Street, M.A. Jinnah Road,
Sadder, Karachi 74400, Pakistan
e-mail: m_abidsaleem@hotmail.com

A. Rashid and M. Ali
Department of Radiation Oncology,
Pakistan Gamma Knife and Stereotactic Radiosurgery Center,
NeuroSpinal and Medical Institute,
Karachi, Pakistan

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Introduction

Craniopharyngiomas are histologically benign tumors originating from embryonic epithelial cells deposited along the incompletely involuted hypophyseal-pharyngeal duct [24, 33]. Approximately 60 % of these lesions are primarily solitary cysts, 30 % have small neoplastic nodules with one or more cysts, and 10 % are solid [3]. Their management has been controversial. Attempted complete surgical resection can result in significant morbidity and mortality especially at facilities with a low case load. Alternatively, subtotal resection followed by conventional radiotherapy may lead to comparable outcomes while maintaining a good quality of life [25]. Particularly, the volume of cystic craniopharyngiomas can be easily reduced using various surgical techniques, including neuroendoscopic fenestration or stereotactic aspiration, with subsequent irradiation of the collapsed lesion [13, 22, 23, 26]. Nevertheless, still there are serious concerns considering possible posttreatment complications because of exposure of the peritumoral vital structures to irradiation.

Since the advent of radiosurgery, precise stereotactically guided radiation treatment has been applied to primary or residual intracranial tumors while sparing the surrounding tissues by a steep dose falloff outside the target volume [1–4, 31]. In the present study, we reviewed our experience with Gamma Knife radiosurgery (GKS) of craniopharyngiomas and analyzed the complementary role of this treatment modality along with other surgical methods in patients with these neoplasms.

Material and Methods

From May 2008 till August 2010, a total of 35 consecutive patients (17 children, 18 adults) with craniopharyngioma underwent GKS at the Pakistan Gamma Knife and Stereotactic

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Table 1 Characteristics of patients with craniophharyngioma treated with GKS at the Pakistan Gamma Knife and Stereotactic Radiosurgery Center

No. of patients	35
Children/adults	17/18
Age (years)	2–53 (mean 20)
Sex (male/female)	26/9
Surgical procedures before GKS	
Microsurgical tumor resection	11
Neuroendoscopic cyst fenestration	2
Stereotactic aspiration of the cyst content	10
Ventriculoperitoneal shunting	17
Ommaya reservoir placement	5
Fractionated radiotherapy before GKS	2
Tumor volume (cm^3) at the time of GKS	1–33.3 (mean 12)
Type of tumor (solid/cystic/mixed)	7/4/24
Prescription radiation dose (Gy)	8–14 (mean 11.5)
Maximum irradiation dose (Gy)	16–28 (mean 23)
Length of follow-up (months)	3–36 (mean 22)
Tumor response to GKS	
Complete response	10 (28.6 %)
Partial response	17 (48.6 %)
No change	4 (11.4 %)
Progression	4 (11.4 %)
Additional surgical procedures after GKS	
Stereotactic aspiration of the cyst content	4
Ventriculoperitoneal shunting	2
Ommaya reservoir placement	2

GKS Gamma Knife radiosurgery

Radiosurgery Center. These cases were analyzed retrospectively. The main clinical, treatment, and outcome characteristics of the series are presented in Table 1.

The age of the patients varied from 2 to 53 years (mean 20 years). There were 26 males (74 %) and 9 females (26 %). Craniopharyngiomas were solid in 7 patients, cystic in 4, and mixed in 24. The tumor size ranged from 1.0 to 33.3 cm^3 (mean 12 cm^3). Before GKS, subtotal resection of the neoplasm was performed in 11 patients, neuroendocopic fenestration of the large cystic component was undertaken in 2 patients, stereotactic aspiration of the neoplastic cyst content was performed in 10 patients, a ventriculoperitoneal shunt was placed because of associated hydrocephalus in 17 patients, and an Ommaya reservoir was implanted in 5 patients to reduce the cyst size. Two patients underwent previous conventional fractionated radiotherapy.

Radiosurgical Technique

The Leksell G stereotactic head frame was attached to the patient's head after application of a local anesthetic. Children less than 12 years of age received general anesthesia. Gadolinium-enhanced axial T1-weighted and T2-weighted magnetic resonance imaging (MRI) and computed tomography (CT) scans were acquired in 1-mm slices and imported into the Leksell GammaPlan (Elekta Instruments AB, Stockholm, Sweden).

Radiosurgery was carried out using the Leksell Gamma Knife Model 4C (Elekta Instruments AB). Prescribed doses were calculated on the basis of the tumor volume, location, previous fractionated radiotherapy, and isodose line used. A progressively smaller dose was chosen for larger neoplasms and in cases with previous irradiation to reduce the possible risk of complications. The prescription and maximum radiation doses varied from 8 to 14 Gy (mean 11.5 Gy) and 16 to 28 Gy (mean 23 Gy), respectively. The maximum dose to the optic pathways was kept below 8–10 Gy in all patients who had not received prior radiotherapy. If it was deemed necessary, selected beam channels within each collimator were plugged to shift the peripheral isodose curves away from the optic nerve, chiasm, or optic tract.

Follow-Up

The follow-up period varied from 6 to 36 months (mean 22 months). After treatment, the patients were evaluated every 6 months with MRI or CT. Any changes in neuroendocrinological status and the presence of side effects were also assessed. Neuroimaging findings were classified into four groups to assess the tumor response, as described by Chung et al. [5]: complete response (CR)—residual tumor volume was <20 %; partial response (PR)—residual tumor volume was 20–50 %; no change (NC)—residual tumor volume was 50–80 %; progression (PG)—tumor volume increased or was >80 % of the initial volume. The clinical outcome was assessed by direct inquiry or clinical records and classified according to Kobayashi et al. [18] as excellent, good, fair, and poor.

Results

The tumor response rate and control rate after GKS were 77.1 % and 88.5 %, respectively. The overall responses of craniopharyngiomas evaluated on the latest postradiosurgery MRI scans were CR in 10 patients, PR in 17, NC in 4, and PG in 4. Solid and monocystic neoplasms after initial size reduction obtained with various surgical procedures had a

better control rate after radiosurgery than did the mixed-type craniopharyngiomas with multicystic components.

In the present series, five patients had long-standing complete visual loss before referral to our center. Among 14 other patients with visual impairment, visual acuity improved after GKS in 7 patients, whereas 6 others had maintained their original visual status at the latest follow-up. One patient with mixed-type multicystic craniopharyngioma complained of deteriorated vision after initial improvement despite a significantly reduced tumor volume. None of the patients in this series developed additional endocrinological impairment or neurological deterioration that could be attributed to radiosurgical treatment.

Increased neoplastic cyst volume at various time periods after GKS necessitated stereotactic aspiration of their contents in four patients and implantation of an Ommaya reservoir in two of them. Ventriculoperitoneal shunting was performed in two patients to relieve hydrocephalus.

Overall, the clinical outcome was considered excellent in 10 patients, good in 15, fair in 6, and poor in 4. Patients with mixed-type craniopharyngiomas harboring multicystic components had worse clinical outcomes than did those with single-component tumors.

Illustrative Cases

Case 1

A 7-year-old boy presented with headache and vomiting. A large cystic craniopharyngioma with associated obstructive hydrocephalus was diagnosed on neuroimaging. Neuroendoscopic fenestration of the cystic lesion was undertaken and a ventriculoperitoneal shunt was placed, which led to immediate relief of symptoms. GKS was performed subsequently. It was noted that prominent reduction of the cyst size permitted clear identification and delineation of the optic pathways and other adjacent anatomical structures, significantly facilitating treatment planning (Fig. 1a, b). The volume of the residual cystic lesion was 5.2 cm^3. A marginal dose of 12 Gy was applied to the 50 % isodose line with 98 % conformity. Multiple isocenters with 8- and 4-mm collimators were used in automatic positioning system (APS) mode. Follow-up CT scan after 1 year showed only a calcified spot (Fig. 1c). At 36 months after treatment, the child remains asymptomatic and is doing fine in school. The radiological findings are stable.

Case 2

A 32-year-old man was admitted after subtotal resection of a solid craniopharyngioma. He had reduced vision, which was more significant in the left eye, and experienced a single episode of generalized tonic-clonic seizure. The volume of the residual tumor was 7.2 cm^3. GKS was performed with a 12 Gy marginal dose applied to the 50 % isodose line with 98 % conformity (Fig. 2a). In all, 22 isocenters with 8- and 4-mm collimators were used in APS mode. At 6 months after treatment, the tumor size was reduced and central hypodensity had appeared, accompanied by markedly improved visual functions. At 12 months after GKS, the patient had no complaints and no neurological deficit. MRI demonstrated complete response of the tumor (Fig. 2b). At the 2-year follow-up, the patient had normal vision, and his clinical condition and MRI findings were stable (Fig. 2c).

Case 3

A 33-month-old child presented with headache and vomiting and was diagnosed with a craniopharyngioma. The tumor had a mixed structure and compressed the visual pathways. Parents refused the proposed surgical treatment but agreed to radiosurgery. At the time of GKS, the tumor volume was 3.0 cm^3. The marginal radiation dose of 10.5 Gy was applied to the 50 % isodose line with 89 % conformity (Fig. 3a). Three isocenters with an 8-mm collimator and 14 isocenters with a 4-mm collimator were used. At 3 months after treatment, 80 % reduction of the lesion volume was noted (Fig. 3b). Follow-up MRI at 1 year demonstrated a further reduction in the size of the neoplasm (Fig. 3c). At the last follow-up, the child is clinically asymptomatic.

Discussion

Craniopharyngiomas have haunted the most experienced investigators since the time of Cushing, who declared them to be neurosurgeons' most baffling problem [6]. Radical excision is the primary intervention [8, 21, 36] but is difficult to achieve without significant morbidity and mortality, despite the advances in microsurgery, neuroradiology, and neuroendocrinology [6, 7, 11, 12, 14, 15, 17, 23, 26, 28]. On the other hand, incomplete tumor resection has led to high rate of recurrences, which are even more difficult to treat [16, 17, 27, 29, 30, 32, 34].

During the 1960s, Kramer was seemingly the first to mention that craniopharyngiomas "are eminently suitable for radiation therapy and that combined treatment by surgery and irradiation offers these patients their best chance" [19]. This view was supported by various later studies [9–11, 14, 20, 27, 35]. As these tumors proved to be radiosensitive [5, 9, 18], stereotactic radiosurgery has been effective in their

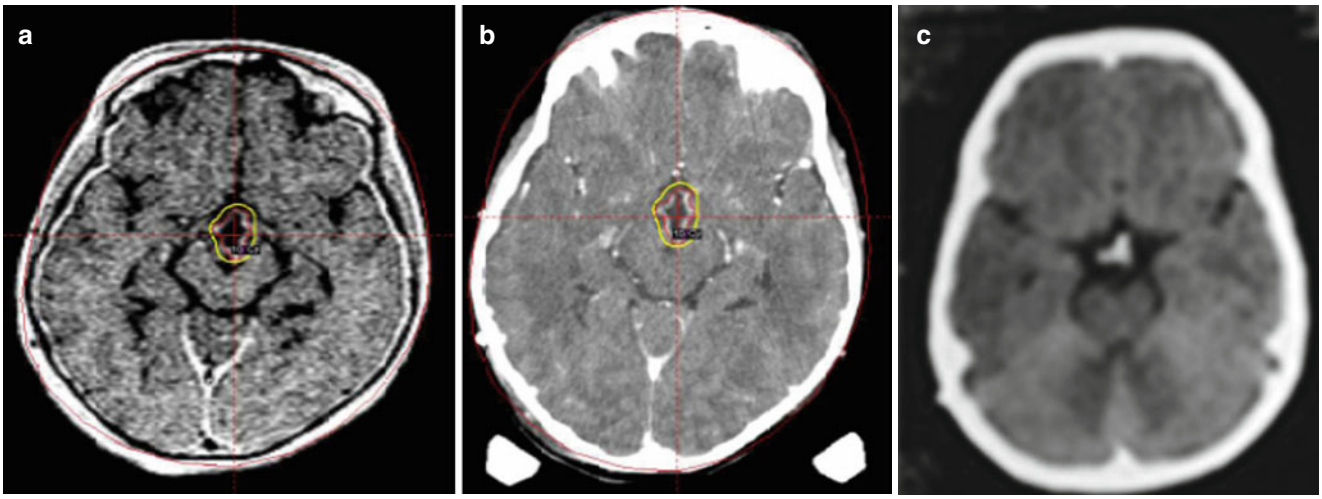

Fig. 1 Neuroimaging findings in a 7-year-old boy with a predominantly cystic craniopharyngioma treated with neurooendoscopic cyst fenestration, placement of a ventriculoperitoneal shunt, and GKS. Contrast-enhanced T1-weighted magnetic resonance imaging (MRI) (**a**) and computed tomography (CT) (**b**) performed at the time of radiosurgery demonstrated residual neoplastic cyst with a volume of 5.2 cm^3, and 12 Gy marginal dose was applied to the 50 % isodose line (*yellow circle*). CT at 12 months after treatment showed only a calcified spot (**c**)

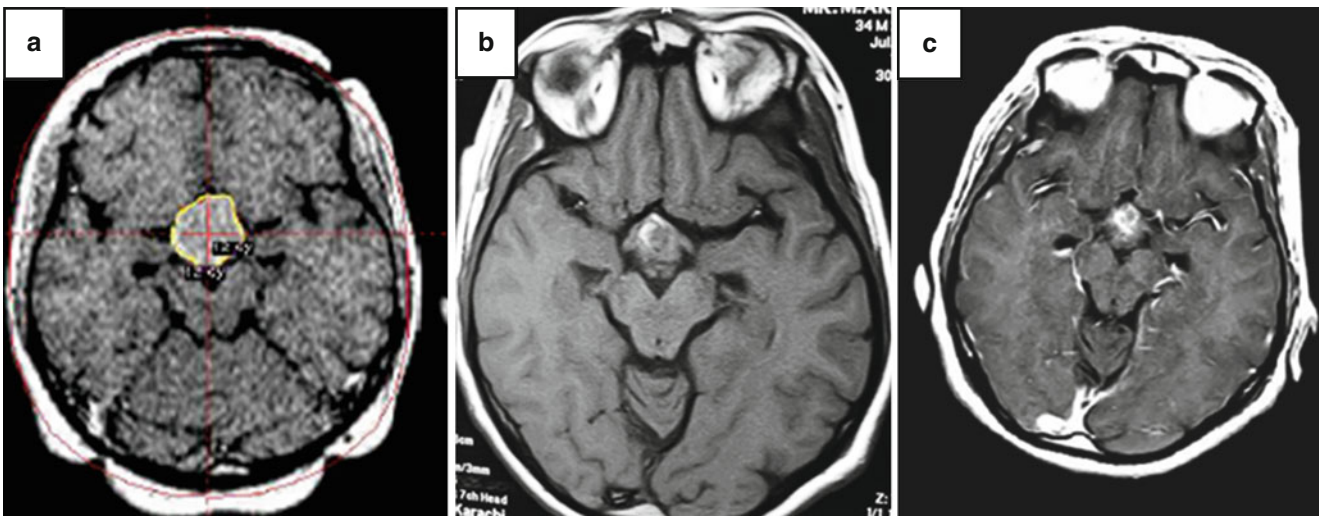

Fig. 2 Contrast-enhanced T1-weighted MRI of a 32-year-old man with a solid craniopharyngioma treated with subtotal resection and subsequent GKS. (**a**) At the time of radiosurgery, the volume of the residual tumor was 7.2 cm^3 and 12 Gy marginal dose was applied to the 50 % isodose line (*yellow circle*). (**b**) At 12 months after treatment, the tumor showed complete response, accompanied by significantly improved vision. (**c**) At 24 months after treatment, the tumor was stable, and visual functions of the patient were normal

management, particularly if combined with subtotal resection and/or other treatment modalities. The majority of lesions in our series were either purely cystic or had a significant cystic component. Their management was effective after initial application of subtotal microsurgical resection, neuroendoscopic cyst fenestration, stereotactic cyst aspiration, ventriculoperitoneal shunting, and/or Ommaya reservoir placement. Reduction of the lesion size, particularly of its cystic component, may significantly facilitate radiosurgical treatment planning. It not only reduces the target volume but permits clear identification and delineation of the adjacent anatomical structures. Nevertheless, our illustrative case 3 clearly demonstrates that GKS also can be used as a primary treatment modality in some patients with craniopharyngiomas. Thus, management can be individualized to the patient.

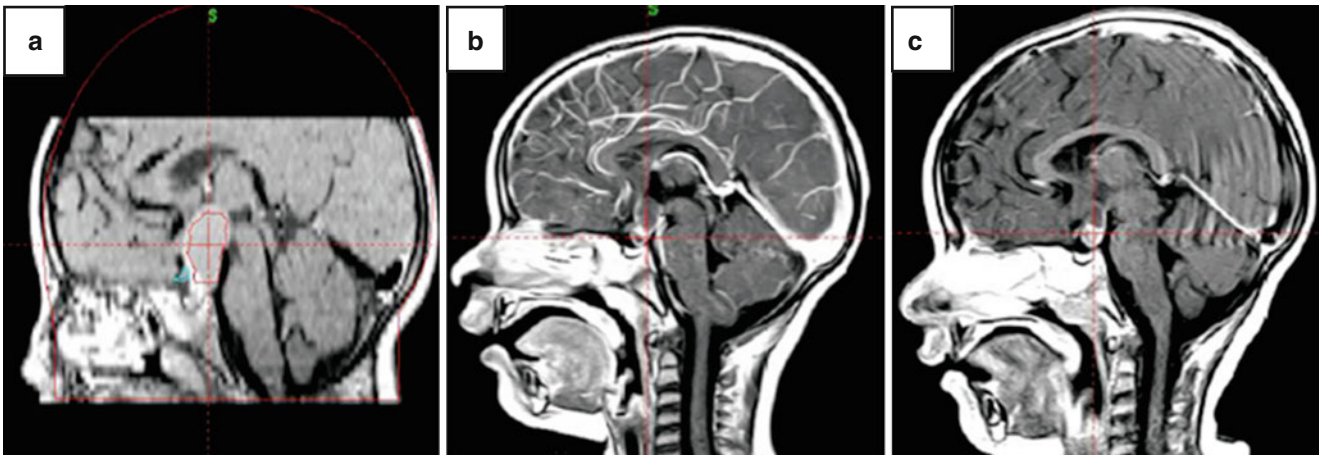

Fig. 3 Contrast-enhanced sagittal T1-weighted MRI in a 33-month-old child with a mixed-type craniopharyngioma treated solely with GKS. (**a**) At the time of radiosurgery, the volume of the tumor was 3.0 cm^3. At 3 months (**b**) and 1 year (**c**) after treatment, there was prominent reduction of the lesion size.

The optimal marginal doses usually recommended for GKS of craniopharyngioma vary from 6 to 12 Gy [5, 18, 31, 37]. In our series, marked regression of the tumor was frequently observed at doses of approximately 10 Gy. Such low doses allow preservation of the adjacent functionally important radiosensitive anatomical structures with or without use of the beam-plugging technique, even if the lesion is in direct contact with, for example, the visual pathways.

It was noted previously that cystic craniopharyngiomas may be resistant to radiosurgery [37]. In fact, in four our patients with mixed tumors, despite significant reduction of the solid component, prominent enlargement of the multicystic part of the neoplasm was observed after GKS. It necessitated stereotactic aspiration of the cyst content and implantation of an Ommaya reservoir in two of them. On the other hand, in many cases small monocystic craniopharyngiomas responded to radiosurgical treatment and showed excellent clinical outcomes within the limited follow-up period.

Conclusion

Gamma Knife radiosurgery may provide good tumor control and improve the quality of life of adult and pediatric patients with a craniopharyngioma. It may play a significant role in the management of such tumors as a single modality or in combination with other treatment options, such as microsurgery, neuroendoscopy, and stereotaxy.

Conflict of Interest The authors declare that they have no conflict of interests.

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