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46.1 Introduction

Cavernous sinus hemangiomas are an extremely rare benign tumor that have been reported to account for less than 3% of all benign tumors occurring in the cavernous sinus and 2% of all tumors, both benign and malignant [1–3]. Cavernous sinus hemangiomas may present with a variety of neurological features, for example, headache, seizure, hemorrhage, or neurological deficits. The incidence is higher in females in the fifth and sixth decade of their lives. Cavernous sinus hemangiomas can be diagnosed by their characteristic imaging appearance. The optimum treatment strategy is still controversial. Current treatment modalities for symptomatic cavernous sinus hemangiomas include microsurgical resection, embolization, fractionated radiation therapy, and stereotactic radiosurgery. Complete resection of cavernous sinus hemangioma is potentially curative but may be complicated by severe intraoperative hemorrhage and the complicated neurovascular structures. The reported incidences of postoperative complications have varied from 8 to 80%, whereas complete excision can be accomplished in only 30–60% of cases [4–15]. Thus, treatment of these lesions remains a therapeutic challenge. Because of the high possibility

of profuse bleeding during surgical intervention combined with potential for long-term cranial nerve deficits, some practitioners have focused on radiotherapy and stereotactic radiosurgery for treatment of these lesions. Patients with cavernous sinus hemangiomas often respond well to treatment involving ionizing radiation [16–19]. In 1999, Iwai et al. reported the first cavernous sinus hemangioma case treated with Gamma Knife radiosurgery. The tumor had previously been partially removed, but removal was complicated by severe bleeding. Radiosurgery was performed as adjuvant therapy and dramatically decreased tumor size [20]. Since then, more reports have been published, all showing good response. In most reports, radiosurgery is used as adjuvant therapy after partial tumor removal. Radiosurgery has also been used as the primary treatment modality with good results for patients who had small- to medium-sized CSHs [21–32].

However, the lesion size and location make single-fraction radiosurgery for large CS hemangiomas very challenging. Although the targeting accuracy and dose fall-off of radiosurgery are excellent, single-fraction radiosurgery may not be ideal for large or giant tumors adjacent to optic pathways [33, 34]. As the target lesion size increases, so does the area of normal brain and other critical anatomic structures, such as optical nerves, that is irradiated, thereby increasing the risk of radiation complications [35].

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Recently, multisession CyberKnife radiosurgery has been shown to be effective, even in control of large tumors, with excellent functional preservation [36–38]. The CyberKnife system (Accuray, Sunnyvale, CA) allows convenient dose fractionation with a frameless delivery that can comfortably treat patients on consecutive days in the outpatient setting without reacquisition of imaging or reapplication of rigid head frame fixation. To achieve favorable local control while maintaining low optic pathway toxicity for large CSHs, we started protocol-based multisession stereotactic radiosurgery with the CyberKnife system for large CSHs in 2007 [36]. This article addresses the safety and efficacy of Gamma Knife radiosurgery and multi-session CyberKnife radiosurgery for CSHs.

46.2 Presentations

Cavernous sinus hemangiomas have an overwhelming predilection for women. In our center, of the 186 cases, 42 (22.5%) have occurred in men, and 144 (77.5%) have occurred in women. Mean age at diagnosis was 50 years (range, 22–80 years). Clinical signs and symptoms and clinical tumor course cannot distinguish cavernous sinus hemangiomas from other cavernous sinus neoplasms. The most common symptoms in these patients were cranial neuropathy including diplopia, blurred vision, facial numbness, and abducens palsy. The second most common symptoms were headache and dizziness. Less frequent signs or symptoms include endocrinopathy, exophthalmos, trigeminal neuralgia, and nausea, vomiting, and gait instability when the tumor was giant. About 5% of cases were an asymptomatic incidental MRI examination finding. Duration of symptoms was from 1 week to 10 years.

46.3 Radiographic Appearance

Cavernous sinus hemangiomas characteristically are not calcified and demonstrate bony erosion or remodeling rather than hyperostosis. The MR images obtained in these patients showed well

demarcated, low- to iso-signal mass on T1-weighted images, extremely high signal on T2-weighted images (as bright as cerebrospinal fluid signal), high signal on FLAIR-weighted (fluid attenuated inversion recovery) images, and strong homogeneous or heterogeneous enhancement after Gd-DTPA injection. When the CSHs were small to medium-sized tumors, they usually showed sharply delineated and intensely enhanced sellar masses without “dural tail sign.” But when the CSHs were large or giant in size, some tumors showed heterogeneous enhancement and delayed homogeneous enhancement [40–44]. We found the CSHs have no metabolism on 18F- FDG PET CT. That means the SUV value was lower (very low) compared with normal brain tissue. The radiological characteristics of a representative case of CSH are shown in Fig. 46.1.

For patients with atypical manifestations, digital subtraction angiography (DSA) was performed to differentiate CSH from meningioma, neurilemmoma, and other cavernous sinus tumors. In patients with CSH, there is no tumor staining on the cerebral angiography with internal carotid artery DSA. But there is little flecked tumor enhancement on external carotid artery DSA. No intracavernous carotid artery stenosis was ever seen despite the complete involvement of the cavernous sinus in these patients (Fig. 46.2).

46.4 Therapeutic Option

Treatment options include the wait-and-see approach with serial images, microsurgery, single-fraction SRS and multisession SRS. If patients have asymptomatic small-sized tumors, a wait-and-see approach with serial images may be a reasonable treatment option, because CSHs are generally slow-growing tumors. Microsurgery was a common treatment before the advent of SRS. Complete resection is an ideal treatment, but it is not so easily achievable without any complications. Although recently skull base surgery has contributed to an increased rate of complete resection, there is no doubt that this is one of the most invasive treatments. SRS is a less invasive

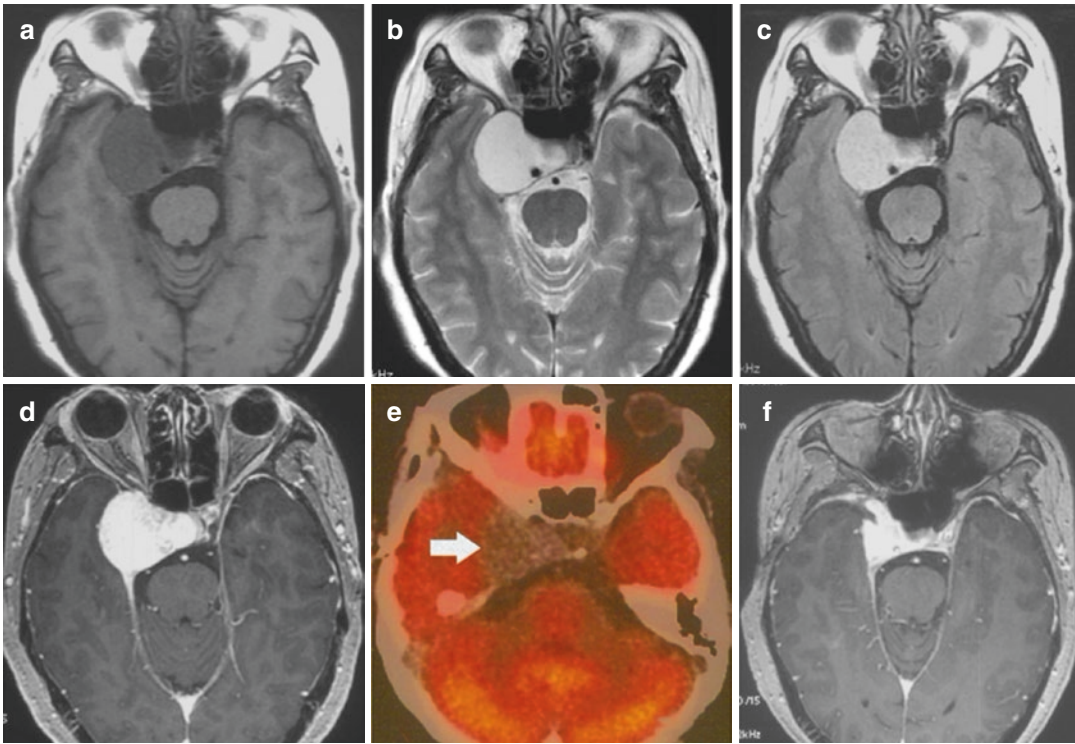


Fig. 46.1 MR images of a representative case showing radiological characteristics of CSH. A 50-year-old male patient suffered from slight headache and went for an MR scan, which showed a sharply delineated iso- or hypo-signal mass lesion on T1-weighted images (a), extremely high signal on T2-weighted images (b) and FLAIR sequence images (c), and intensely enhanced sellar mass

(d). He had an operation for the cavernous sinus hemangioma and CSH was confirmed by histopathology. 18-F FDG PET-CT showed that CSH had no metabolism with lower SUV (e). During the operation only a small piece of tumor was removed because of bleeding. Then the patient was treated with CyberKnife radiosurgery. The CSH reduced in volume at 6 months post CyberKnife (f)

treatment option for small- to medium-sized CSHs, and multisession CyberKnife radiosurgery is a treatment option for large or giant CSHs, with good tumor control as well as improving neurological deficits.

46.5 Clinical Outcomes

Contemporary series of Gamma Knife radiosurgery and multisession CyberKnife radiosurgery for CSHs are shown in Table 46.1.

Our colleague Dr. Wang published a systematic review and meta-analysis of 59 cases of CSHs treated with Gamma Knife radiosurgery (GKR) [46]. The results suggest that GKR not only achieves good tumor control and symptom improvement but also avoids the complications

associated with embolization, biopsy, and attempted microsurgical resection. However, most of the patients underwent GKR as an adjuvant treatment after open surgery, and the number of cases using GKR as a primary treatment was limited.

At the author's institution, 53 patients harboring CSHs were treated using Leksell Gamma Knife radiosurgery. Of the 53 patients, 15 with definitive histopathologic diagnoses after surgery, 38 were diagnosed based on their MR imaging findings. There were 15 male and 38 female patients with a mean age of 52 (range 25–76) years old. The mean volume of the tumors was $13.2 \pm 8.2 \text{ cm}^3$ (range 1–41 cm^3). A mean marginal dose of 13.3 Gy (range 8–15 Gy) was directed to the 49–64% isodose line (mean 53%). The mean radiological and clinical follow-up

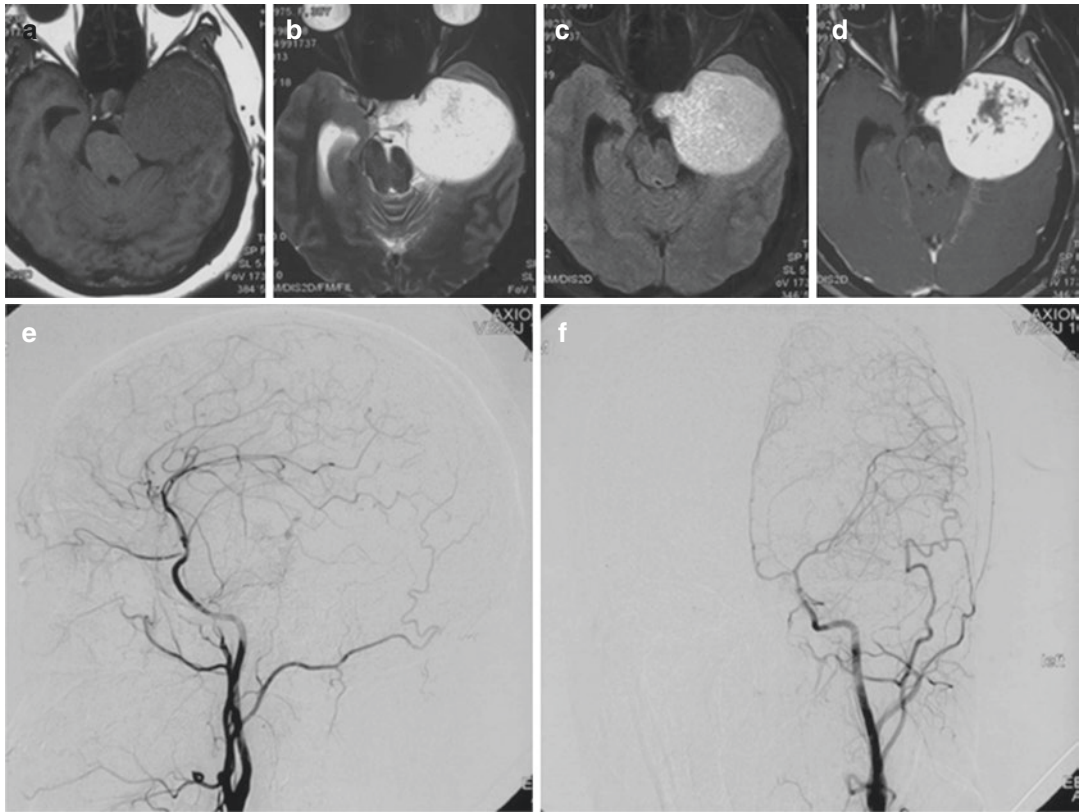


Fig. 46.2 A 32-year-old female had headache and vomiting and MRI examination was performed. The MRI showed low- to iso-signal giant mass on T1-weighted images (a), extremely high signal on T2-weighted images (as bright as cerebrospinal fluid signal) (b), high signal on FLAIR-weighted (fluid attenuated inversion recovery) images (c) and strong homogeneous or heterogeneous

enhancement after Gd-DTPA injection (d). The DSA demonstrates elevation of the left middle cerebral artery and medial deviation of the left internal carotid artery (e). No tumor staining was seen on artery phase angiography although the CSH is a hypervascular lesion by nature (f). The patient had an operation and CSH was confirmed by histopathology

Table 46.1 Stereotactic radiosurgery series of cavernous sinus hemangioma

Authors	No. of patients	Methods	Tumor volume [Range] (cm ³)	Marginal dose [Range] (Gy)	Follow-up (months)	Tumor control rate (%)	Improvement of clinical symptoms/signs (%)	New or worsening symptoms (%), no.
Huang [37]	12	CK	24.3 [11–96]	19.5–30	16.3	100	100	No
Wang [38]	31	CK	64.4 [40–145.3]	18–22	30	100	100	1 (3%)
Wang [48]	32	GK	30.5 [2.5–78.6]	14.2 [11–16]	30.2	97	97	No
Lee et al [32]	31	GK	9.3 [1.5–42.1]	12.6 [12–19]	54	100	97	1 (3%)
Xu [45]	7	GK	12.5 [5.3–33.2]	14 [10–15]	20	100	100	No
Park [39]	13	GK	2.7 [1.3–8.0]	12.9 [12–14]	90	100	100	No
Tang [46]	53	GK	13.2 [1–41]	13.3 [8–15]	34	100	94	3 (5.6%)

Table 46.1 (continued)

Authors	No. of patients	Methods	Tumor volume [Range] (cm ³)	Marginal dose [Range] (Gy)	Follow-up (months)	Tumor control rate (%)	Improvement of clinical symptoms/signs (%)	New or worsening symptoms (%), no.
Anqi [47]	15	GK	29.3 [8.5–138]	13.4 [10–16]	13	100	100	No
Song [31]	19	GK	6.1	14.5 [11.5–16]	37	100	100	No
Li [30]	16	GK	30.4 [1.5–61.5]	13.3 [11–14]	21.5	100	100	No
Chou [28]	7	GK	7.6 [2.9–23.1]	12.5	22	100	100	No
Yamamoto [29]	30	GK	11.5 [1.5–51.4]	13.8	53	100	97	1 (3%)

time of this study was 24 (range 2–67 months) and 34 months (range 2–73 months), respectively. The tumor control rate was 100%. The mean tumor volume reduction was 79.5% (range 16.5–100%) compared with the pre-GKR volume. A typical case of CSH is shown in Fig. 46.3. Neurologically, only two of these patients showed clinical deterioration, and the other 51 patients demonstrated an obvious improvement in symptoms.

Similarly, Lee and colleagues reported the results of GKR in 31 patients with CSHs. The median radiosurgery target volume was 9.3 cm³ and the median marginal dose was 12.6 Gy. At a mean follow-up period of 54 months (range 6–200 months), the tumor control rate was 100%. The average tumor reduction at 12 months was 64%; at 24 months, 73%; at 36 months, 79%; at 48 months, 82%; and at 60 months, 84%. No recurrence was found.

46.6 Multi-session CyberKnife Radiosurgery

We first reported the effectiveness and safety of multisession CyberKnife radiosurgery for controlling large CSHs. A Phase II study to substantiate the role of CyberKnife radiosurgery was conducted in our department in which we evaluated patients with a large CSH that had a clear “geographic” separation between the tumor and the optic apparatus on MRI. We found that a multi-fraction SRS dose of 21 Gy delivered in three fractions was effective in reducing the

tumor volume without causing any new neurological deficits [36].

46.7 Rationale for Multisession CyberKnife Radiosurgery

Our dose not only was based on our and others’ previous experience with SRS and radiotherapy, but also previous studies concerning the dose tolerance of the optic apparatus and brainstem. Although the exact α/β ratio that corresponds to CSHs has not been established, we assumed a value of 3 Gy and used the linear-quadratic model to estimate the biologically equivalent dose to a single-dose SRS of 10–13 Gy (a dose that yields remarkable tumor shrinkage for CSHs after radiosurgery) for a 3- or 4-fraction course of CyberKnife SRS (listed in Table 46.2). The dose prescription was based on intent to cover the entire tumor with a higher dose while ensuring dose limitation to the visual pathways and brainstem. General guidelines for dose limitations to normal structures included the following. The maximum permissible point dose to the optic nerves and chiasm was 14.1 Gy in 3 fractions (4.7 Gy per fraction) or 15.6 Gy in 4 fractions (3.9 Gy per fraction), similar to a single-fraction SRS of 9 Gy. The maximum permissible point dose to the brainstem was 21 Gy in 3 fractions (7 Gy per fraction) or 23.6 Gy in 4 fractions (5.9 Gy per fraction), similar to a single-session SRS dose of 13 Gy.

Thirty-one patients harboring giant CSHs were treated with multisession CyberKnife radio-

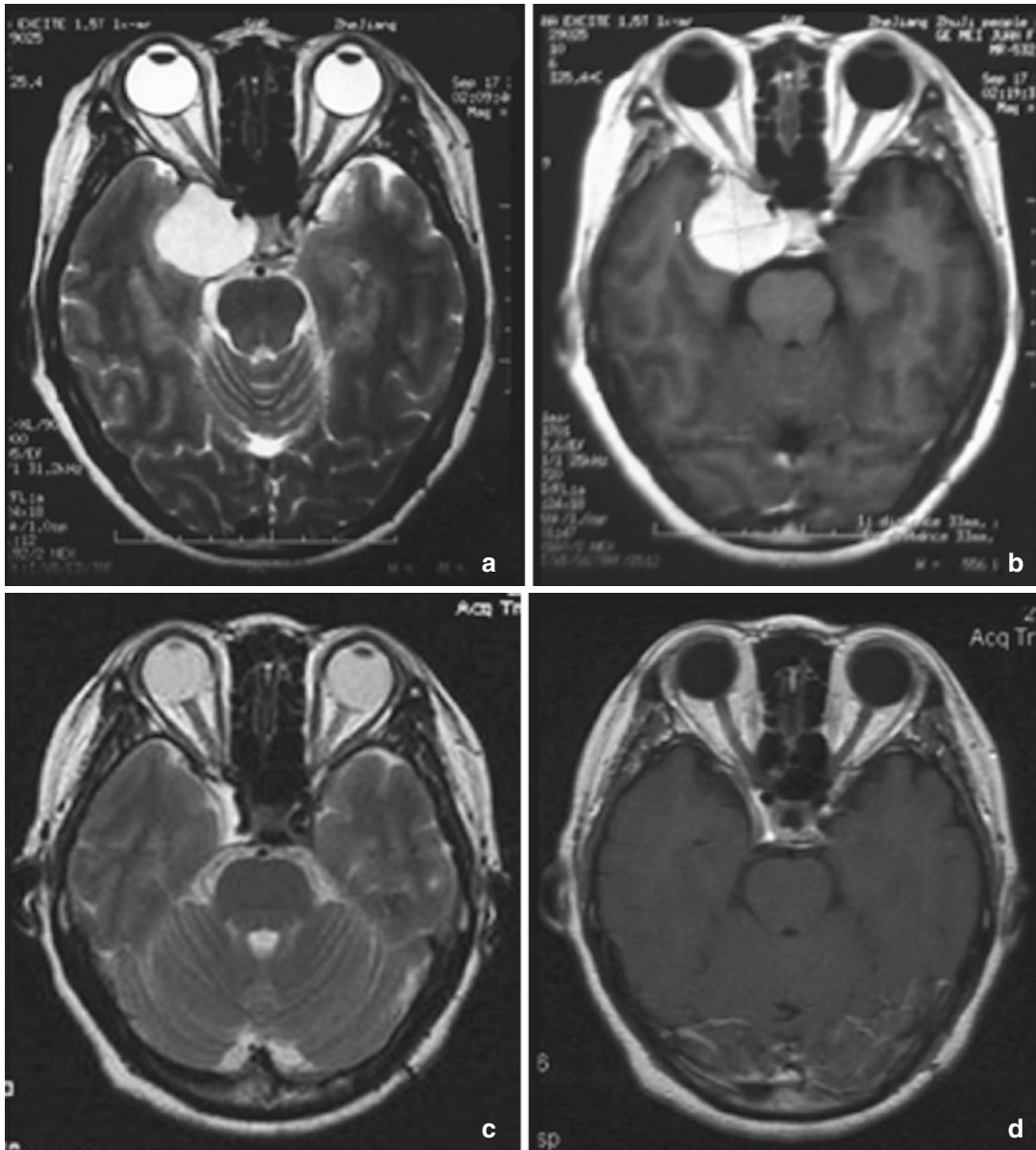


Fig. 46.3 A 47-year-old female patient underwent GKR primarily (maximal dose of 23.3 Gy and a margin dose of 14 Gy) (a, b). Her diplopia and blurred vision disappeared

1 month after GKR and the tumor exhibited evidence of shrinkage 45 months after treatment (c, d)

surgery at the author's institution, among whom 27 underwent multisection CyberKnife radiosurgery as the initial treatment. Four patients had a histological diagnosis at the time of a prior resection. In those four patients, three underwent a biopsy and one underwent partial resection. There were 8 male and 23 female patients with a

mean age of 54 (range 22–80) years old. The median CSH volume was 64.4 cm³ (range 40.9–145.3 cm³). Three or four sessions of CyberKnife radiosurgery were used with a prescription dose based on the intent to cover the entire tumor with a higher dose while ensuring dose limitation to the visual pathways and brainstem. The median

marginal dose to the tumor was 21 Gy (range 19.5–21 Gy) in 3 fractions for 11 patients and 22 Gy (range 18–22 Gy) in 4 fractions for 20 patients. During a median follow-up of 30 months (range 6–78 months), all patients achieved good

tumor control. Follow-up MRI scans revealed a median tumor volume reduction of 88.1% (62.3–99.4%) at last examination compared with the pretreatment volume. Ten patients developed new or aggravated temporary headache, and 5 experienced vomiting during the treatment. These acute symptoms were relieved completely after steroid administration. Among the 30 patients with symptoms observed before treatment, 19 achieved complete symptomatic remission, and 11 had partial remission. One patient reported seizures, which were controlled after antiepileptic drug administration. No radiation-induced neurological deficits or delayed complications were reported during the follow-up period [38]. A typical case of giant CSH is shown in Fig. 46.4.

Huang and colleagues documented 12 patients with high volume cavernous sinus hemangioma-

Table 46.2 Summary of dosing schedules, biologically equivalent doses, and single-dose equivalents

Total dose (Gy)	No. of fractions	Biologically equivalent dose ($\alpha/\beta = 3$)	Single-dose equivalent (Gy)	No. of patients (%)
<i>Prescribed dose</i>				
18	4	45.00	10.22	5
20	4	53.33	11.23	2
20.8	4	56.9	11.65	2
22	4	62.33	12.25	11
19.5	3	61.75	12.20	1
20.4	3	66.60	12.71	1
21	3	70	13	9

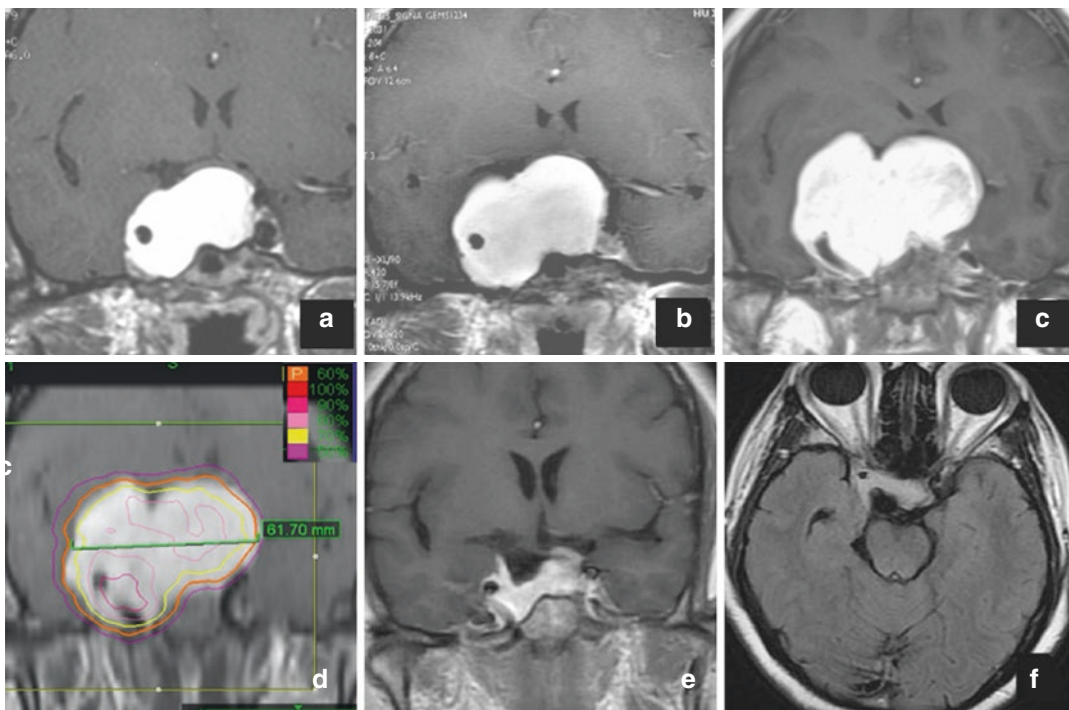


Fig. 46.4 A 43-year old woman had a visual field defect, blurred vision, and ipsilateral abducens nerve palsy. MRI found a cavernous sinus hemangioma on the right side in 1998 (a). The patient underwent resection and experienced severe intraoperative bleeding. Only a piece of tumor was removed during the operation. The tumor pro-

gressed slowly (b) and in 2011 the tumor became a giant tumor (c). The pretreatment tumor volume was 76.5 cm³ (d). Three and half years post multisection CyberKnife radiosurgery (21 Gy in 3 fractions), the tumor shrank to 2 cm³ (e, f). Clinical symptoms also improved

was treated with hypofractionated stereotactic CyberKnife [37]. Initial tumor volumes ranged from 11.8 to 96.6 cm³ with a median of 24.3 cm³. Irradiation doses were 19.5 Gy with 3 fractions in 2 patients, 21 Gy with 3 fractions in 8 patients, 25 Gy with 5 fractions in 1 patient, and 30 Gy with 3 fractions in 1 patient. Follow-up ranged from 3 to 54 months, with a mean follow-up of 16.3 months. All tumor volumes decreased (28.6–94.1%) and symptoms improved (including blurred vision, visual field defects, diplopia, headaches, and facial numbness) after therapy. A patient experienced radiotherapy-related cerebral edema, which resolved after 5 days of mannitol and dexamethasone.

46.8 Summary

Gamma Knife radiosurgery is a safe and effective treatment for patients with small- to medium-sized cavernous sinus hemangiomas. When the tumor is relatively large (e.g., compressing the optic nerves or chiasm), multisession CyberKnife radiosurgery would be an alternative treatment option. Multisession CyberKnife radiosurgery delivery of 18–22 Gy in 3–4 fractions is effective in reducing tumor volume and improving neurological symptoms without causing any new complications. Until now microsurgery has been a common treatment option for cavernous sinus tumors, but, even with recent refinement of microsurgical techniques, it is unable to avoid the risk of complications such as cranial nerve injury and avoid partial resection of the tumors. Accordingly, single-fraction or multisession stereotactic radiosurgery can be a reasonable alternative to surgical resection not only as adjuvant treatment but also as the initial treatment, with respect to preservation of cranial nerve function.

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