Intracranial cavernous hemangiomas are hamartomatous vascular lesions that occur in approximately 0.1 to 4.0% of the general population. Neuronavigator-guided excision is used for superficial lesions or deep brain lesions, but radiosurgery may be preferred for diencephalic or brainstem cavernous hemangiomas. There have been few long-term studies concerning the natural history of cavernous hemangiomas. There have also been difficulties in determining the exact size of lesions on MR images, which meant accurate volume–dose criteria were hard to determine, and GKS was performed as a supportive treatment. In recent years, with refined MR imaging techniques, the detection rate of cavernous hemangiomas has increased. Most occult vascular malformations are reported as cavernous hemangioma. We describe the results of GKS for cavernous hemangiomas.

Clinical Material and Methods

Between October 1994 and December 2002, GKS was performed in 65 patients with cavernous hemangiomas. Forty-two cases underwent follow-up MR imaging. Gamma knife surgery was conducted after injection of a local anesthetizing. Stereotactic MR imaging involved T1-weighted spin echo, T2-weighted, and gradient echo axial imaging sequences. Dose planning was performed using the KULA planning system (Elekta Instruments AB, Stockholm, Sweden) until August 1997, and using the Leksell GammaPlan (Elekta Instruments AB) since September 1998. The gamma knife model B was used. All patients were discharged the morning after treatment. Follow-up MR imaging findings were evaluated every 6 months.

Patient Demographics

The mean patient age was 37.6 years (range 7–60 years). There were 23 males and 19 females. The mean MR imaging follow-up duration was 29.6 months (range 5–93 months).

Clinical Symptoms

The presenting symptoms were seizures in 12 (28.6%), bleeding in 11 (26.2%), and focal neurological deficits.
sis, headache and dizziness) in 45.2%. Two patients sustained more than two hemorrhages. Surgery was performed before GKS in one case involving a lesion in the basal ganglia that hemorrhaged.

Location of the Tumor

The locations of the cavernous hemangiomas were frontal in 12, parietal in five, pons–midbrain in six, basal ganglia in five, cerebellum in three, temporal in three, occipital lobe in one, and multiple locations in seven.

Combined Anomalies

Combined anomalies included three venous malformations (7.1%), one falx meningioma, one vestibular schwannoma, and one distal anterior cerebral artery aneurysm.

Dose Planning

The mean dose delivered to the margin of the malformations was 14.55 Gy (range 10–25 Gy), and the mean maximum dose was 26.78 Gy (range 20–55 Gy). In 11 cases (26.2%), there was a new or increased perilesional signal demonstrated on the follow-up T2-weighted MR images. In three cases these changes were associated with symptoms. In an 18-year-old male patient cystic enlargement of a left frontal cavernous hemangioma developed 93 months after GKS. It was removed at craniotomy.

The group in which a high signal change was documented on the follow-up MR images had received a mean marginal dose of 18.33 Gy (range 12–32 Gy) as shown in Table 1.

### Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>Range</th>
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<tbody>
<tr>
<td>max dose (Gy)</td>
<td>26.78</td>
<td>20–55</td>
</tr>
<tr>
<td>margin dose (Gy)</td>
<td>14.55</td>
<td>10–25</td>
</tr>
<tr>
<td>margin dose (Gy)*</td>
<td>18.33</td>
<td>12–32</td>
</tr>
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</table>

* On T2-weighted MR imaging.

### Table 2

<table>
<thead>
<tr>
<th>Initial Symptom (no. of patients)</th>
<th>Change of Size</th>
<th>Seizure (12)</th>
<th>Hemorrhage (11)</th>
<th>Others (19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>increase</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>stationary</td>
<td>0</td>
<td>7 (edema 1)</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>decrease</td>
<td>12 (edema 6)</td>
<td>4</td>
<td>13 (edema 5)</td>
</tr>
</tbody>
</table>

Imaging Changes

In the 12 seizure cases, all exhibited a decrease in lesion size, and in six of these the high perilesional signal change was observed on T2-weighted images. They gradually improved. In the 11 patients with bleeding, seven lesions remained unchanged and four decreased. In the remaining 19 cases, lesion size decreased in 13 cases, was unchanged in five, and progressed in one (Table 2).

Seizure Control

In nine of the 12 patients with seizures the seizures were controlled without anticonvulsant medication (Engel Grade 1) after a mean latency of 31.3 months (range 12–80 months). In three patients intermittent persistent seizures occurred despite anticonvulsant medication during a mean follow-up period of 86 months (range 76–93 months) (Table 3).

Hemorrhage Rate After Radiosurgery

One 7-year-old boy who harbored a pontine cavernous hemangioma developed rebleeding 13 months after GKS. Follow-up MR imaging revealed a decrease in size, and symptoms improved.

Other Symptoms

Of 19 patients with other symptoms, the lesion decreased in size in 13 and remained unchanged in five. Five cases showed edema on the follow-up T2-weighted MR image,
but symptoms have gradually improved, and the lesion size has decreased. Three cases showed increased neurological aggravation compared with the status prior to GKS.

One 36-year-old woman had a pituitary microadenoma with a left frontal cavernous hemangioma. Both were treated with GKS. The pituitary microadenoma received 13 Gy to the margin and the cavernous hemangioma received 18 Gy to the margin. Ten months later, a right hemiparesis developed. The patient received rehabilitation treatment and the hemiparesis improved.

Discussion

Cerebral vascular malformations occur in approximately 0.1 to 4.0% of the general population.1 The most common symptoms are seizures (38%), neurological deficits (25%), no symptoms (21%), hemorrhage (13%), and headache (6%). Additional rare manifestations are hydrocephalus, cranial neuropathy, papilledema, and hypothalamic disturbance.1 Supratentorial lesions were more likely to cause seizures, whereas infratentorial lesions were more likely to give rise to focal neurological deficits.18 Seventy-three percent of patients younger than the age of 40 years experienced seizures, whereas 69% of patients older than 40 years of age initially complained of focal neurological deficits. Robinson and Awad17 found that males are more likely to experience seizures (62%) and females were more likely to present with focal deficits (66%). Fifty percent of the patients who were asymptomatic at the time of initial diagnosis later developed symptoms after a mean follow up of 26 months.9

There are three important pathophysiological phenomena to consider in cases of cavernous hemangioma. 1) Blood oozes slowly into the surrounding brain, causing a “surrounding ring” of hemosiderin and gliosis. In cortical regions, notably in the area adjacent to limbic structures or central gyri, there is significant association with poorly controlled epilepsy, presumably related to chronic irritation from blood breakdown products and iron deposits. 2) Lesions frequently exhibit sudden thrombosis in one or more of the venous caverns, with an increase in size or turgor within one or more compartments and occasionally resulting in acute cavernous expansion into the surrounding brain. 3) Gross hemorrhage into the surrounding brain is usually rare and often self-contained due to the low-pressure and low-flow dynamics within the lesion.17

Three rare variants of cavernous hemangiomas have been described: 1) A cystic cavernous hemangioma is characterized by a cyst with surrounding edema and a tendency for continuous growth with progressive neurological deficits due to recurrent hemorrhaging.11 Cystic malformations are more common in the posterior fossa.11 2) A dural-based malformation is characterized as cavernous hemangiomas histologically composed of dilated cavernous channels lacking mural smooth muscle, which usually arises from the middle cranial fossa near the midline or parasellar regions involving the cavernous sinus.11 3) The so-called hemangioma calcificans11 are commonly reported to be located in the temporal lobe and are associated with bone metaplasia and abnormal vascular channels.

In one study, in 8 to 10% of patients with cavernous hemangiomas plain skull radiographs showed abnormal fine granular or coarse calcifications.7 In 30 to 33% of cavernous hemangiomas, angiography has revealed a capillary blush and early filling of veins without enlarged feeding arteries.13 On contrast-enhanced computerized tomography

<table>
<thead>
<tr>
<th>Age (yrs), Sex</th>
<th>Location</th>
<th>GKS Day</th>
<th>Max Dose (Gy)</th>
<th>Margin Dose (Gy)</th>
<th>MRI Follow Up (mos)</th>
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</thead>
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<tr>
<td>18, M</td>
<td>lt frontal</td>
<td>10/27/1994</td>
<td>30</td>
<td>18</td>
<td>decreased size cyst</td>
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<tr>
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<td>18</td>
<td>disappeared</td>
</tr>
<tr>
<td>42, F</td>
<td>multiple</td>
<td>02/20/1997</td>
<td>40</td>
<td>20</td>
<td>decreased size</td>
</tr>
</tbody>
</table>

FIG. 2. This 62-year-old woman was treated with a margin dose of 10 Gy for a hemorrhaged pontine cavernoma. Six months later, MR imaging demonstrated decreased size of the cavernoma.
scans cavernous hemangiomas appear with a punctate increased attenuation coefficient (probably related to calcifications), and the lesions are seen in approximately 14% of the cases. The high sensitivity of MR imaging makes it the choice in the evaluation of cavernous hemangioma. The typical appearance is peripheral hypointense rim with a heterogeneous central signal. Positron emission tomography scanning has demonstrated normal or decreased uptake of $^{11}$C-methionine and $^{11}$C-glucose. In one study, the majority (61%) of the patients were between 20 and 40 years of age. The sex ratio was shown to be equal in a review of the literature. In one series, a female predominance occurred in 6 to 18.7%. Supratentorial lesions comprised 90% of the total. The most common location of infratentorial lesions was in the pons.

Kondziolka, et al., treated 47 hemorrhaged cavernous hemangiomas with GKS. They reported a brainstem location with a prior hemorrhage and a subsequent annual hemorrhage rate of over 50%, with a prospective annual hemorrhage rate of 2.4% in the brainstem location, 2.9% in the basal ganglia thalamus location, 2.7% in the hemisphere location and 0.6% in patients in whom hemorrhage had not previously occurred.

In a mean follow-up period of 3.6 years, the annual hemorrhage risk during the first 2 years was 8.8%. In contrast, the hemorrhage risk rate dropped to 1.1% 2 to 6 years after treatment. Neurosurgical changes were observed in 12 cases (26%) and associated with parenchymal imaging changes. Eight cases showed temporary symptoms with full recovery, but craniotomy was performed in two cases. In cases of brainstem cavernous hemangiomas, the temporary morbidity rate was 8.8%.

Kida, et al., reported an annual bleeding rate of 31.8% during the first 5 years after diagnosis of a cavernous hemangioma and 5.2% during patients’ life span. The annual bleeding rate was 6.3% during the 1st year, 8.3% during the 2nd year, 5.2% during the 3rd year, and 7.3% of the mean hemorrhagic rate after GKS. They reported no hemorrhagic difference after GKS.

In a review of the literature of hemorrhage risk after GKS, Amin-Hanjani, et al., reported 10.4% and Chang, et al., reported 9.4% during the first 3 years and 1.6% after 3 years. Among our 42 cases, one (2.3%) presenting with a hemorrhagic cavernous hemangioma suffered rehemorrhage 13 months after GKS.

In seizure patients, electroencephalography should be performed and excision performed in accessible regions with the assistance of a neuronavigator.

Bertalanffy, et al., performed surgery in 18 cases in which progressive neurological deficits were present (severe deficits in eight cases). The complications were characterized by distinct pathogenetic mechanisms that included: 1) recurrent hemorrhage from residual angioma, 2) manipulation-induced damage to the internal capsule, 3) injury to the lenticulostriate arteries, 4) damage to venous drainage, 5) air embolism and resulting cortical infarction. These complications seemed to be related more to lesions located deep within the cerebral hemisphere than to those within the brainstem.

Fortuna, et al., undertook surgery in 50 cavernous hemangioma patients. Total excision was accomplished in 87.2%, and the perioperative mortality rate was 4.6%. Sixty-five percent of the seizure patients were seizure free while not receiving medication, and the remaining 35% experienced reduced frequency in combination with anticonvulsant therapy. Scott, et al., reported on pediatric cavernous hemangioma in patients who underwent surgery to relieve symptoms related to mass effect, hemorrhage, and/or seizures, if the cavernous hemangioma was safety accessible.

Zimmerman, et al., performed surgery to test 22 infratentorial cavernous hemangiomas. Their operative indications included: 1) progressive symptomatology, 2) superficial location of the lesion within the brainstem, and 3) an operative approach that could spare eloquent brain tissue. Complete resection was achieved in 86% of cases. The median follow-up period was 27 months. Permanent minor morbidity related to surgery was 23%. Complications related to surgery were transient hemiparesis in 23%, transient diplopia in 18%, sixth and seventh cranial nerve neuropathies in 18%, hydrocephalus in 14%, dysmetria with intranuclear ophthalmoplegia in 9%, and meningitis in 9%.

The obliteration of true arteriovenous malformation after radiosurgery is well documented. We speculate that the vessels of a cavernous hemangioma may respond similarly to high-dose single-session radiation. This response might consist of endothelial cell proliferation, vessel wall hyalinization and thickening, and eventual luminal closure.
latency interval of 2 to 3 years may be necessary to achieve these results.\textsuperscript{14} Kondziolka, et al.\textsuperscript{14} have proposed dose-reduced GKS for cavernous hemangiomas. Despite the dose reduction, they could not decrease the incidence of complications; however, the severity of complications was reduced. In the dose reduction treatment group, most new symptoms consisted of transient cranial neuropathy or mild ataxia, whereas, in the initially treated group, larger regions of altered long-TR signal changes on MR images were associated with hemiparesis, hemisensory deficits, and cranial neuropathies. Another group concluded that GKS was effective for treating brainstem or diencephalic cavernous hemangiomas.\textsuperscript{1} Kida, et al.\textsuperscript{11} treated 100 cavernous hemangiomas in a mean follow-up period of 26.5 months during which the neurological status improved in 38 cases, remained the same in 33 cases, and deteriorated in nine. In the hemorrhage group, symptoms improved in 57.5%. In six patients with neurological deficit, symptoms improved. Of 14 patients with seizures, nine (64,3%) improved but their clinical condition was aggravated by rebleeding or radiation-induced brain injury. Amin-Hanjani, et al.\textsuperscript{1} reported a decrease in seizure frequency despite unchanged cavernoma size because the focus of epilepsy existed in the hemosiderin ring after GKS and was not related to volume.

The results of our study are in keeping with the findings of the aforementioned reports with respect to hemorrhage control, neurological improvement, and seizure control. There was one unusual case: a 22-year-old man developed a cyst 93 months after GKS despite a decrease in the size of his cavernous hemangioma. A craniotomy and cyst removal were performed.

The incidence of post-GKS cerebral edema has been reported to be 10.5%,\textsuperscript{2} 6.5%,\textsuperscript{1} 26%,\textsuperscript{14} and was 26% in this study. The edema was primarily controlled with steroid and glycerine medication. Permanent neurological deficits sometimes persisted. Kida, et al.\textsuperscript{12} reported an increased frequency of postradioablation edema if the margin dose exceeded 17 Gy. The findings in this study are in keeping with findings reported by Kida, et al.\textsuperscript{13} Of the 11 lesions (26.2%) that showed a high signal on follow-up T2-weighted MR images, the mean margin dose was 18.3 Gy (range 12–32 Gy) compared with the mean margin dose of 14.6 Gy (range 12–25 Gy) for the group as a whole.

Conclusions

Excision of cavernous hemangiomas in noneloquent and surgical accessible area of the brain in patients with intratable seizure is an effective treatment. Gamma knife surgery is effective for cavernous hemangiomas in eloquent regions. The maximal therapeutic effect with minimal complications is achieved when the margin dose is below 15 Gy.

References


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