Tumors of the orbit are rare diseases in ophthalmic pathology. The orbit is a pyramidal space that contains the eyeball, extraocular muscles, vessels, and nerves. All anatomical structures of the orbit can give rise to a neoplasm; in this region a heterogeneous array of lesions poses numerous challenges to diagnosis, imaging, and management. The Gamma Knife has been widely used to treat a variety of intracranial tumors and vascular malformations, many of which have pathological characteristics similar to orbital lesions. The present study was devoted to evaluating the safety and effectiveness of GKS as a primary or adjuvant treatment for orbital tumors.

Methods

Patient Selection

We sought to identify all patients with presumed or pathologically proven orbital tumors who were evaluated at the Gamma Knife Center of Tianjin Medical University Second Hospital between 1995 and 2008. Detailed records regarding treatment were available for all patients. All patient information was obtained from a retrospective review of medical records.

Object. The authors evaluated the results they obtained using Gamma Knife surgery (GKS) in patients with orbital tumors.

Methods. This is a retrospective clinical evaluation of 202 patients with orbital tumors who were treated with GKS between September 1995 and October 2008. The series included 84 men and 118 women with a mean age of 39.5 ± 14.6 years (range 5–85 years). The diagnoses were determined based on pathological analyses in 113 patients and presumed based on characteristic clinical and imaging findings in 89 patients. There were 84 meningiomas, 38 epithelial tumors of the lacrimal gland, 23 schwannomas, 18 malignant choroidal melanomas, 12 optic nerve gliomas, 11 orbital metastases, 10 pseudotumors of the orbit, 3 retinoblastomas, and 3 cases of fibromatosis. The median target volume was 5.4 cm³ (range 0.04–35.6 cm³). The tumor margin dose ranged from 10 to 40 Gy.

Results. At a median follow-up period of 34.5 ± 14.7 months (range 12–114 months), tumor shrinkage was observed in 118 patients (58.4%) and stable tumor size in 71 patients (35.1%). Regularly scheduled neuroimaging studies demonstrated evidence of tumor progression in only 13 patients (6.4%): 9 of these patients underwent repeated GKS and 4 received surgical treatment. Visual acuity was preserved in 129 patients. Seventy-two patients experienced some degree of improvement in vision. Severe deterioration of visual acuity was found in 18 of 147 patients who had useful vision before treatment. Nineteen patients (9.4%) experienced transient conjunctival edema; no other serious acute side effect was observed.

Conclusions. Gamma Knife surgery provides an effective management strategy in patients with orbital tumors; it achieves excellent preservation of neurological function and is associated with few treatment-related complications.

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Gamma Knife surgery for orbital tumors

The diagnoses were determined based on pathological analyses in 113 patients and were presumed based on characteristic clinical and neuroimaging findings in 89 patients (Table 1).

The patients’ clinical symptoms and signs are shown in Table 2. The most common clinical symptoms were proptosis and visual loss. The most common lesion was meningioma. Other benign lesions encountered in our case series were schwannoma, fibromatosis, and pseudotumor of the orbit. Malignant neoplasms were found in 77 patients. Malignant orbital tumors included squamous cell carcinoma, adenoid cystic carcinoma, hemangiopericytoma, malignant choroidal melanoma, optic nerve glioma, retinoblastoma, and metastatic orbital tumors from lung cancer.

Baseline evaluation of visual acuity and field testing were performed using the Standard Logarithmic Visual Acuity chart and dynamic perimetry in all patients. One hundred seventeen patients (57.9%) had visual loss that had lasted, on average, 11 months (median 9 months) before GKS. One hundred twenty-four patients (61.4%) had proptosis in the affected eye, and 7 patients had enophthalmos due to prior resection. All patients underwent MR imaging and/or CT scan before treatment. Ninety-two patients harbored a space-occupying mass in the orbit only and 64 had tumors that extended into the optic canal. Tumors producing cranioorbital communication were found in 46 cases.

**Gamma Knife Surgery**

Stereotactic radiosurgery was performed using the Leksell Gamma Knife model B before February 2005 and model C (Elekta Instruments AB, Stockholm, Sweden) thereafter. After a local anesthetic agent (a mixture of xylocaine and normal saline) had been applied to the patient’s head, a head frame was attached. General anesthesia was induced in children younger than 10 years of age before they underwent GKS. Stereotactic MR images were obtained, and the digitized images were transferred to the Leksell GammaPlan workstation for use in dose planning. The prescribed peripheral radiation dose varied from 10 to 40 Gy (Table 1). One hundred eighty-seven patients were treated in a single session. Fifteen patients were treated in 2 sessions, separated by a 24-hour interval, because their tumors enveloped the optic apparatus and their visual acuity was 0.5 or better. The dose plans were created with high conformality and selectivity, especially at the margin of the optic nerve or retina. During the 2-session GKS, we used a dose-planning method similar to that used in the single-session procedure, except for the prescribed dose, which was adjusted depending on tumor growth control and the tolerance of the optic apparatus. In each session, we tried not to deliver more than 10 Gy of radiation to any portion of the anterior visual pathway. The median volume of the lesion pre-GKS was 5.4 cm³ (range 0.04–35.6 cm³). A median of 10 isocenters (range 5–16) were used for treating these lesions. One hundred twelve patients with preoperative visual function received a single 40- to 80-mg dose of methylprednisolone intravenously 1 hour before GKS and a 40-mg dose every 12 hours intravenously for the next 3 days.

**Follow-Up and Statistical Analysis**

Patients underwent follow-up examinations by the

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**TABLE 1: Clinicopathological summary of 202 cases treated with GKS**

<table>
<thead>
<tr>
<th>Pathological Condition</th>
<th>No. of Cases (%)</th>
<th>Dose in Grays (median)</th>
<th>Vol in cm³ (mean)</th>
<th>No. of Cases w/ Tumor Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Shrinkage</td>
</tr>
<tr>
<td>meningioma</td>
<td>84 (41.6)</td>
<td>10–15 (13)</td>
<td>1.4–35.6 (5.1)</td>
<td>45</td>
</tr>
<tr>
<td>tumors of the lacrimal gland</td>
<td>38 (18.8)</td>
<td>15–22 (18)</td>
<td>1.2–22.4 (9.3)</td>
<td>19</td>
</tr>
<tr>
<td>schwannoma</td>
<td>23 (11.4)</td>
<td>12–17 (14)</td>
<td>1.9–11.7 (5.3)</td>
<td>16</td>
</tr>
<tr>
<td>malignant choroidal melanoma</td>
<td>18 (8.9)</td>
<td>40</td>
<td>0.04–1.0 (0.5)</td>
<td>10</td>
</tr>
<tr>
<td>optic nerve glioma</td>
<td>12 (5.9)</td>
<td>14–20 (16)</td>
<td>2.3–7.8 (4.4)</td>
<td>8</td>
</tr>
<tr>
<td>orbital metastasis</td>
<td>11 (5.4)</td>
<td>16–20 (18)</td>
<td>0.3–5.4 (2.8)</td>
<td>8</td>
</tr>
<tr>
<td>pseudotumor of the orbit</td>
<td>10 (5.0)</td>
<td>15–16 (16)</td>
<td>2.2–11.4 (6.6)</td>
<td>9</td>
</tr>
<tr>
<td>retinoblastoma</td>
<td>3 (1.5)</td>
<td>18–20 (18)</td>
<td>0.03–2.7 (1.1)</td>
<td>1</td>
</tr>
<tr>
<td>fibromatosis</td>
<td>3 (1.5)</td>
<td>13–18 (14)</td>
<td>3.4–7.8 (5.5)</td>
<td>2</td>
</tr>
</tbody>
</table>

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**TABLE 2: Clinical characteristics of patients**

<table>
<thead>
<tr>
<th>Symptoms &amp; Signs</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>proptosis</td>
<td>124</td>
</tr>
<tr>
<td>loss of visual acuity</td>
<td>117</td>
</tr>
<tr>
<td>visual acuity</td>
<td></td>
</tr>
<tr>
<td>1.0 or better</td>
<td>31</td>
</tr>
<tr>
<td>0.4–1.0</td>
<td>57</td>
</tr>
<tr>
<td>0.1–0.4</td>
<td>59</td>
</tr>
<tr>
<td>CF–0.1</td>
<td>39</td>
</tr>
<tr>
<td>blind</td>
<td>16</td>
</tr>
<tr>
<td>headache or orbit pain</td>
<td>59</td>
</tr>
<tr>
<td>diplopia</td>
<td>36</td>
</tr>
<tr>
<td>conjunctival chemosis &amp; injection</td>
<td>41</td>
</tr>
<tr>
<td>lid retraction</td>
<td>21</td>
</tr>
<tr>
<td>enophthalmos</td>
<td>7</td>
</tr>
</tbody>
</table>

* CF = count fingers.
neurosurgeon and by an ophthalmologist who did not assist in the GKS. These examinations were scheduled at 6-month intervals for the first 2 years after GKS and at 2-year intervals thereafter. The median follow-up period was 34.5 ± 14.7 months (range 12–114 months). Results of the most recent follow-up examination were compared with the patient’s baseline results for assessment. A clinically significant change in visual acuity was defined as more than a 2-line improvement in the Standard Logarithmic Visual Acuity chart. A significant change in tumor size was described as at least 2 mm of enlargement or regression on follow-up MR images.

Local control probabilities were calculated using the Kaplan-Meier method. Statistical analysis was performed using commercially available statistical software (SPSS, version 10.0; SPSS Inc.).

Results

Clinical Outcome

With respect to initial presenting symptoms, improvement was observed in 102 patients (50.5%), stabilization in 79 (39.1%), and continued progression in 21 (10.4%). In our series, following GKS, visual acuity was preserved in 129 patients. Seventy-two patients experienced some degree of improvement in their vision. Severe deterioration in visual acuity—a decline in visual acuity from normal to count fingers or light perception—was found in 18 of 147 patients who had had useful vision before treatment. Nineteen patients (9.4%) experienced transient conjunctival edema, but no other serious acute side effect was observed. Thirteen patients experienced improvements in visual fields, color discrimination, and contrast sensitivity. Fourteen (78%) of the 18 patients exhibiting exophthalmos before GKS had diminished exophthalmos after the procedure.

Tumor Control

Tumor shrinkage was observed in 118 patients (58.4%) and stable tumor size in 71 (35.1%) (Fig. 1). Regularly scheduled neuroimaging studies demonstrated evidence of tumor progression in only 13 patients (6.4%): 9 of these underwent repeated GKS and 4 were referred for surgical treatment. Tumor sizes remained stable throughout the next 2 years of follow-up. No further enlargement of tumor was identified from 4 to 9 years after GKS. In patients we observed for 12, 24, 48, and 60 months, the tumor control rates were 98.5%, 94.3%, 92.8%, and 100%, respectively. The overall 5-year tumor control rate in all patients was 93.5% (Fig. 2).

Discussion

Although the diagnosis of and treatment strategy for orbital tumors is generally considered to fall within the domain of the ophthalmologist, many orbital tumor processes, such as orbital apex tumors, require the involvement of other specialties. The evolution in management of orbital tumors has been facilitated by the multidisciplinary involvement of specialists from neurosurgical, ophthalmological, and craniofacial disciplines. Current treatment strategies for orbital tumors include observation, surgical treatment, and radiotherapy.1–6 Despite great advances in microsurgery, surgery-related morbidity remains an issue after total or partial excision of orbital tumors. Symptoms rarely improve after resection; thus, many patients now prefer options involving minimal risk.8,18 For many patients with intraorbital or cranioorbital tumors, radiosurgery is an effective alternative.
Gamma Knife surgery for orbital tumors

Radiation Dose Selection

In practice, the radiation dose is determined by what is considered curative or palliative. A wide spectrum of doses is considered, depending on the type of tumor and the condition of the eye and orbit. For example, benign and radiation-sensitive tumors are usually treated with low doses (10–18 Gy), while malignant or radiation-resistant tumors are treated by relatively high doses (18–40 Gy). The same is true for normal tissues. Whereas the natural lens, optic nerve, and retina are particularly radiation sensitive, the sclera and orbital bone will tolerate a very high dose.13–16 Another important consideration for dose selection is the dose-volume effect, according to which there is an inverse correlation between the size of the tumor and the amount of radiation that is needed.7

Tumor Control

The goal of GKS is permanent control of tumor growth as well as preservation of neurofunctional function. Follow-up MR imaging is needed to fully assess the effectiveness of tumor control. The results of GKS can be evaluated by measuring the maximum tumor diameter on follow-up MR or CT images. When no enlargement in tumor volume is seen, we conclude that the lesion’s growth has been arrested by GKS; otherwise, growth will continue due to the natural course of tumors.9,11,12 Kim et al.10 reported on a series of 15 consecutive patients who underwent GKS for orbital tumors; control of tumor growth was confirmed in 12 of the 15 patients within the 6- to 50-month follow-up period. Three patients with malignant lesions had to undergo resection during open surgery due to tumor progression. Thompson et al.19 reported on 4 patients harboring hemangiomas of the cavernous sinus and orbit. These patients presented with ocular symptoms or signs, and all were treated using GKS. Follow-up examinations revealed a reduction in tumor volume in 3 patients and no tumor progression in the 4th. All patients experienced improvement in their symptoms, but one had persistent diplopia.

In this study, we found that GKS provided a high rate of tumor growth control. We administered 8–40 Gy to various orbital tumor margins and achieved a total tumor control rate of 93.5%. Tumor shrinkage usually occurred slowly, beginning approximately 6–12 months after GKS but continuing even years later. Delayed (> 5 years) regression in tumor volume was not associated with symptoms.

The Optic Apparatus’ Radiation Tolerance

Intraorbital and cranioorbital tumors are contiguous with the optic nerve and chiasm; thus, it is important to consider control of tumor growth as well as avoidance of optical pathway neuropathy.15–17 Many articles have been published on the tolerance of the optic apparatus. Tishler et al.20 evaluated 62 patients with cavernous sinus lesions. At a median follow-up of 19 months, 4 (24%) of 17 patients whose optic apparatus received a dose greater than 8 Gy developed optic neuropathy, compared with 0 of 35 patients whose optic apparatus received less than this dose. On the basis of their findings, these investigators concluded that the dose to the optic nerve and chiasm during radiosurgery should be limited to less than 8 Gy. Leber et al.13 retrospectively analyzed optic nerve toxicity after GKS in 50 patients with various types of tumors. These authors reported the actuarial incidence of optic neuropathy to be 0, 26.7%, and 77.8%, in patients who underwent GKS during which the optic pathways received < 10 Gy, 10–15 Gy, and > 15 Gy, respectively. On the basis of these findings, it is safe to say that the dose administered to the optic nerve and chiasm should be below 10 Gy. At a median follow-up of 35 months, Morita et al.15 reviewed the cases of 88 patients with skull base meningiomas who underwent GKS with a median dose to the optic apparatus of 10 Gy (range 1–16 Gy). None of their patients developed optic neuropathy, and thus, the investigators believe the optic apparatus can tolerate doses greater than 10 Gy. More recently, Stafford et al.16 found an incidence of optic neuropathy of 1.9% in a series of 215 patients with a median follow-up of 48 months after stereotactic radiosurgery for benign tumors of the sellar or parasellar region. For 212 patients who underwent a single stereotactic radiosurgical procedure, the rates of optic neuropathy were 1.7% when the dose was less than 8 Gy, 1.7% when it was between 8 and 10 Gy, and 6.9% when the dose was in excess of 12 Gy.

In our series the optic pathways received doses ranging from 6 to 16 Gy, and only 23 patients suffered additional impairment in visual acuity after GKS. We believe that the point dose is not a sufficient parameter to predict the risk of radiation-induced injury to the optic nerve. Instead, dose-volume histograms must be considered. We suspect that the portion of the optic nerve that lies within the orbit may be able to endure a higher radiation dose than the cranial portion.

Complications

Complications related to GKS can be acute, intermediate, or chronic. Acute reactions are rapid in onset and typically reversible; they generally happen within 24 hours after GKS. Examples of these complications are orbital pain and nausea sometimes accompanied with vomiting. Intermediate complications such as radiation blepharocconjunctivitis may be seen after GKS, as are impaired visual acuity and eyelid edema, which may occur within 3 months after treatment and can be treated with a regimen of hormones and mannitol. Chronic changes are delayed in onset and may not improve. The permanent side effects most often reported are related to a loss of visual acuity, which generally occurs 6 months after treatment. In our series, 23 patients suffered from impairment of visual acuity.

Conclusions

Gamma knife surgery provides an effective management strategy in patients with orbital tumors; it preserves excellent neurological function and is associated with few treatment-related complications.

Disclosure

The authors report no conflict of interest concerning the mate-
rial or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following: Conception and design: D Liu, Xu, Y Zhang, Zheng, Song. Acquisition of data: Xu, Z Zhang, Analysis and interpretation of data: Xu, Z Zhang, Li. Drafting the article: D Liu, Xu. Critically revising the article: D Liu, Jia. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: D Liu, Xu, X Liu. Study supervision: D Liu.

References

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