Evaluation of a new concept for the management of skull base chordomas and chondrosarcomas

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Objective. Chordomas and chondrosarcomas of the skull base are rare locally invasive tumors associated with high recurrence rates. The aim of this study was to evaluate the concept of microsurgical tumor volume reduction followed by early gamma knife surgery (GKS).

Methods. Thirteen patients with 15 tumors were treated between October 2000 and June 2003. There were three patients (23.1%) with chordomas and 10 (76.9%) with chondrosarcomas. There were nine men and four women who ranged in age between 19 and 69 years. All patients first underwent maximal tumor resection. Within 2 to 10 months after surgery they were treated with GKS. The mean postoperative tumor volume treated with GKS was 9.7 cm³ (range 1.4–20.3 cm³). Follow-up computerized tomography and magnetic resonance imaging examinations with volumetric tumor analysis were performed every 6 months after GKS.

The mean treatment dose was 17 Gy and the mean isodose was 52%. The mean follow-up duration was 17 months during which there was only one tumor recurrence at the margin of the radiation field. The mean volume reduction was 35.4%.

Conclusions. Results of this treatment strategy are encouraging but the efficacy of this multimodal treatment combining surgery and early GKS requires a longer follow up.

Key Words: chordoma • chondrosarcoma • skull base tumor • gamma knife surgery • volumetry
Clinical Material and Methods

Patient Population

In this retrospective study data obtained in 13 patients, treated between October 2000 and July 2003, were analyzed. There were nine men and four women who ranged in age between 19 and 69 years. Three patients (23.1%) harbored chordomas and 10 patients (76.9%) harbored chondrosarcomas. The sex predilection in chordoma and chondrosarcoma patients was 2:1 for males. Two patients (15.4%), one with a chordoma and one with a chondrosarcoma underwent multiple surgical treatments before being treated at our institution. No patient underwent any type of radiotherapy before the GKS. Initial symptoms and neurological deficits were defined as those apparent on admission. The outcome used for statistical analysis was based on the neurological findings at the last follow-up examination.

Tumor Visualization and Location

Before surgery all patients underwent thorough imaging examination: T1-weighted MR imaging with and without a contrast medium, T2-weighted MR imaging, and computerized tomography scanning with a bone window mode for optimal visualization of any bone destruction. The purpose of the imaging was not to distinguish between chordomas and chondrosarcomas but to define the exact location and extent of the tumor so as to demarcate it from the surrounding structures. The images obtained in all 13 patients demonstrated a total of 15 tumors (Table 2). Two tumors (13.3%) were located in the petrous bone, two (13.3%) in the clivus, nine (60%) in the petroclival region, one (6.7%) at the jugular foramen, and one (6.7%) at the CCJ (Table 3).

Treatment and Follow Up

The treatment concept in all cases was the maximum microsurgical tumor resection with the emphasis consistent with the preservation of all vascular and nervous structures followed by early GKS, which was performed 2 to 10 months after surgery. A Leksell Gamma Knife model C with an APS was used for all radiosurgery procedures. Gamma knife surgery was performed with multiple isocenters, using the APS when applicable, to reach a high conformity between the prescription dose and the target and a steep dose gradient with respect to surrounding eloquent structures. Follow-up examinations were performed every 6 months after GKS for the first 2 years and annually thereafter. Patients underwent neurological examination during each follow-up visit, and disability assessment was performed using the KPS. Because of the short interval between surgery and GKS, disability was evaluated only before surgery and then again before GKS. Successful treatment was defined as the lack of tumor recurrence within the field of tumor resection and GKS. Treatment failure was defined as local tumor recurrence in the surgical and GKS field. Follow-up imaging included T1-weighted with contrast-enhanced MR imaging and computerized tomography scanning. Volumetric tumor analysis was performed with the GammaPlan 5.3 software (Elekta Instrument AB, Stockholm, Sweden) and only volume changes of more than 10%, either growth or shrinkage, were considered to be significant.

Data Management and Statistical Analysis

All patient data and digital imaging data were managed using MeDiGSI Archive V1.1, a medical multimedia database. GammaPlan 5.3 was used for dose planning and tu-
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TABLE 4
Functional outcome

<table>
<thead>
<tr>
<th>Cranial Nerve Deficits</th>
<th>II</th>
<th>III–VI</th>
<th>V</th>
<th>VII</th>
<th>VIII</th>
<th>IX–XI</th>
<th>XII</th>
</tr>
</thead>
<tbody>
<tr>
<td>preop</td>
<td>91</td>
<td>8 (61.5)</td>
<td>5 (38.5)</td>
<td>1</td>
<td>8</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>after op/before GKS</td>
<td>94</td>
<td>8 (61.5)</td>
<td>0</td>
<td>1</td>
<td>8</td>
<td>3*</td>
<td>1</td>
</tr>
<tr>
<td>after GKS</td>
<td>96</td>
<td>4 (30.8)</td>
<td>3 (23.1)*</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

* Transient symptom.

TABLE 5
Tumor volumes after GKS

<table>
<thead>
<tr>
<th>Tumor Vol Change</th>
<th>Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>overall tumor control rate</td>
<td>93.3</td>
</tr>
<tr>
<td>no. smaller</td>
<td>9 (60)</td>
</tr>
<tr>
<td>no. unchanged</td>
<td>5 (33.3)</td>
</tr>
<tr>
<td>no. grown</td>
<td>1 (7.7)</td>
</tr>
<tr>
<td>tumor vol reduction</td>
<td></td>
</tr>
<tr>
<td>mean</td>
<td>35.4</td>
</tr>
<tr>
<td>range</td>
<td>19.7–69.8</td>
</tr>
</tbody>
</table>

The CONVIS DICOM viewer and GammaPlan were used during each follow-up examination for volume analysis. Commercially available software (SPSS V11.0) was used to perform all statistical analyses.

Results

Surgery-Related Data

The mean patient age was 41.5 ± 14.3 years (range 19–69 years). The mean tumor volume before GKS (Table 2) was 9.7 ± 5.2 cm³ (range 1.4–20.3 cm³). Histopathological analysis was necessary for the definitive diagnosis in all cases as these tumors could not be distinguished from each other on the basis of neuroimages alone.16 Pathological findings (Table 2) showed four low-grade chordomas (26.7%) and 11 low-grade chondrosarcomas (73.3%). Analysis showed a male sex predilection of chordomas as well as chondrosarcomas of 2:1. The most common presenting symptoms were double vision in eight patients (61.5%), headaches in five (38.5%), hoarseness in four (30.8%), dizziness in four (30.8%), and swallowing difficulties in one (7.7%). The first treatment for all patients was a maximal microsurgical tumor resection including extensive bone drilling. Two patients (15.4%) required a second operation via a different approach to achieve the maximal tumor volume reduction prior to GKS. There were no complications, neither in the peri- nor postoperative period. In all patients the goal of sufficient microsurgical tumor volume reduction was achieved. With one exception, there were no new permanent neurological deficits after surgery (Table 4). The preservation of vascular and neural structures during the tumor resection was considered the highest priority to achieve a good overall outcome. After surgery temporary trigeminal dyesthesias were observed in three patients (23.1%), and one patient (7.7%) developed hoarseness. The mean preoperative KPS score was 91 and this improved to a mean KPS score of 94 after surgery (Table 4). In the second treatment step all patients underwent early GKS, which was performed a mean latency of 5.3 months following surgery.

Gamma Knife Surgery Treatment

The mean tumor volume at GKS was 9.7 cm³ (range 1.4–20.3 cm³) (Table 2). The mean prescription dose was 17 Gy (range 14–18 Gy), and the mean margin isodose was 52%. A mean number of 21 isocenters (range 12–36) were used. The mean follow-up period after GKS was 17 months (range 6–36 months). Two patients (15.4%), both with chordomas, exhibited tumor recurrences outside the treated area; however, one recurrence was so close to the treated region it is counted as a local recurrence. Thus, the local tumor control rate has so far been 93.3%. One patient (7.7%) who harbored a chordoma at the CCJ suffered a tumor recurrence 13 months after GKS. Strictly speaking, the new tumor was just outside the treated area. Nonetheless, it was counted as a local recurrence because the borders of the treated area and the recurrent tumor were within 1 cm of each other. A second patient with a petroclival chordoma had undergone two operations before being treated at our clinic. In this case the tumor recurred contralateral to the surgically and GKS-treated side. The treated side remained tumor free. The mean tumor-free survival period for the series was 17 months. The volume of four tumors (33.3%) remained unchanged after GKS, whereas nine tumors (60%) showed volume reduction after GKS (Table 5). The mean GKS-induced tumor shrinkage (Figs. 1–3) was 35.4% (range 19.7–69.8%). The mean time to tumor shrinkage was 11 months. The mean KPS score after radiosurgery increased from 94 to 96. Cranial nerve function after GKS (Table 4) improved in seven patients (53.8%). Because of the early postoperative application of GKS, this outcome might not solely be credited to the effect of GKS.

FIG. 1. Preoperative MR images obtained in a 53-year-old man with a chondrosarcoma in the petroclival region. The preoperative tumor volume was 35.9 ml.
Discussion

Because chordomas and chondrosarcomas of the skull base are rare tumors, only a few large series have been published, and most include both tumor types.6,14,18, 26,32,33,39–41,44,45 In our series we included both types of tumors because their neuroradiological appearance and differential diagnosis are similar, and our proposed treatment strategy for both entities is identical. There has not yet been a general consensus on treatment guidelines. The spectrum of proposed management choices includes clinical and neuroradiological observation, biopsy sampling followed by observation, biopsy sampling followed by radiotherapy, tumor resection, and surgery followed by radiotherapy or implantation of iodine-125 seeds.28 Neurological symptoms on admission (Table 4) did not differ from those reported in other series, and the male predilection for both chordomas and chondrosarcomas was also in keeping with those described in the literature.9,31,12,27,10,23,35

Surgical Treatment

The authors of most series have emphasized the extent of tumor resection and rate of recurrences without providing a detailed evaluation of surgery-induced morbidity. It has been reported that maximal tumor resection improved the recurrence-free survival in cases of chordomas and chondrosarcomas.4,8,14,41 Postoperative KPS scores in these studies, however, showed that patients had to pay a high price, suffering new and permanent neurological deficits after surgery either because structures were sacrificed during surgery or because of severe radical excision-related complications.

Surgery and GKS

During the last decade there has been a trend toward multimodal treatment strategies including surgery and irradiation because this strategy showed a better overall outcome than either treatment alone.16,24,13,44 Treating patients with surgery and irradiation, however, means that there may be a higher overall morbidity rate due to exposure to the side effects of both procedures. Nevertheless, if everything is done to reduce the risks in each treatment step a lower overall morbidity rate could be achieved. The treatment concept presented in this paper is based on a multimodal treatment principle in which surgery is followed by early GKS. This concept is not new in terms of its combination of modalities16,24,31 but rather in the surgical approach and in the timing of GKS. The philosophy underlying our management concept was to achieve maximal tumor-free survival without increasing the overall morbidity rate. The highest priority during the surgical stage of our treatment was the preservation of vessel and neural structures. Maximal tumor resection was a secondary priority and was not undertaken if it involved damage to important nerves and vessels. Extensive bone drilling of tumor-infiltrated bone was performed only in areas where it was considered safe. Minimizing the surgical trauma and avoiding ischemic tissue damage was essential for a good overall outcome. Only with these considerations was it possible to avoid both intra- and postoperative complications as reported in other studies.51,14,41 The good results of this surgical strategy are also reflected in the high mean postoperative KPS score of 94 compared with other studies and the excellent postoperative functional outcomes (Table 4) with only temporary trigeminal dysesthesias in three patients (23.1%) and accentuated hoarseness in one (7.7%). Because we included only two patients (15.4%) who had undergone previous operations, these results cannot as yet be applied to patients in whom tumor recurs with any certainty as the number is too small. Further investigations are necessary to answer this question. Nonetheless, our strategy for patients with recurrences is at present the same as for patients after initial tumor diagnosis.

Gamma Knife Surgery Treatment

Chordomas and chondrosarcomas have been considered radioresistant tumors by some authors.22 It has been shown, however, that irradiation affects the tumor control rate of these tumors,24,29,41 and it is possible that the dose was too low in cases in which tumor control was not achieved.14 It has been demonstrated before that GKS has potential advantages over conventional radiotherapy.24 In this study GKS was also chosen over conventional fractionated radiotherapy because a much higher dose can be delivered to the tumor with stereotactic accuracy and in a single session,24 which is less stressful for the patient. Furthermore, because of its high accuracy GKS has a lower treatment-induced morbidity rate than other forms of irradiation. The new model C Gamma Knife with the APS permits an even better radiation dose–tumor conformity than has been possible in the past. Gamma knife surgery has the disadvantage of functioning better with smaller volumes, which is only a problem if the method were used alone; however, with our current concept it is used after safe surgical tumor volume reduction, permitting treatment of lesions of a size suitable for Gamma Knife surgery.
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for the method. Although proton-beam irradiation has been recommended by some authors19,33,38,42 as one of the currently best available options for patients with chordomas and chondrosarcomas, there are too few centers worldwide for this treatment option to be available for most patients. Chordomas and chondrosarcomas are considered slow-growing lesions,3,18 but tumor-free survival after surgery can be less than 6 months. Because of this fact we recommended GKs as early as 2 to 3 months after surgery, as soon as the perioperative artifacts in neuroradiological imaging allow good tumor delineation for stereotactic radiosurgery. As the results of this study show, GKs plays not only a role in the control of local tumor growth but has also a significant volume-reducing effect that has not been previously evaluated for chordomas and chondrosarcomas in this detail. Results of the overall morbidity of this proposed treatment concept are encouraging. Evaluation of the GKs-related and the functional outcome before and after radiosurgery showed excellent results (Table 4) with no GKs-induced neurological deficits. Overall the local tumor control rate of 93.3% was encouraging, and the mean tumor-free survival period was 17 months. Compared with other studies a low overall morbidity rate is reflected in the mean overall KPS score of 96.

Conclusions

A multimodality management of chordomas and chondrosarcomas is proposed in which surgery is followed by early GKs. The top priority at operation is preservation of vital structures and functions, even at the expense of radical tumor removal if necessary. In this series GKs contributed to the reduction of tumor volume. Based on these results, the role of GKs in the treatment of these lesions should be redefined. We also recommend using the same treatment strategy for patients with tumor recurrences.

References


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