Skull Base Chordomas: Management and Results

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Abstract

Growth patterns of skull base chordomas are related to important neurovascular structures. Local invasiveness results in “clinically malignant” behavior. A high rate of transient neurological deficits occurs following radical surgery. At our institution, the principle of radical removal is not followed at any price. This study compared the results of our management with recent series. Eleven patients, five females and six males aged 24–65 years (mean 41 years), underwent removal of skull base chordoma with size one < 3 cm, five 3–5 cm, and five > 5 cm. Mostly, standard operative approaches were chosen. All patients underwent postoperative radiotherapy. Resection was subtotal/partial in seven patients and total in four with no mortality. Neurological deterioration occurred due to transient cranial nerve deficits in six patients. Temporary surgical morbidity (including cranial nerve deficits) was observed in seven patients. Median Karnofsky performance status score improved compared to preoperative (80), early postoperative (70), and latest assessment (90) (median 36 months). Five patients underwent reoperation due to tumor recurrence after 4–48 months (mean 24 months). Most patients undergoing removal of skull base chordomas suffer from transient neurological deficits which are mainly nonsignificant as the patients return to preoperative functional status. The apparently high rate of incomplete tumor resection (64%) reflects the infiltrative behavior and relationship with neurovascular structures. The operative strategy should not be excessively aggressive at any price, but rather take into account the options of radiotherapy and observation of residual tumor.

Key words: skull base chordoma, microsurgery, operative approach, extent of resection, irradiation

Introduction

Chordomas originate from embryonic remnants of the primitive notochord, a primitive cell line around which the vertebral column and the skull base develop. Chordomas account for 1% of intracranial and 4% of primary bone tumors and rarely metastasize. The peak prevalence is in the 4th decade of life with a 2:1 male predilection. Chordomas of the skull base constitute one third of all chordomas, are usually located in the vicinity of the sphenoparietal bones, and show infiltrative growth pattern. Management of these lesions remains a challenge despite the introduction of microsurgical techniques as they develop in close relationship to neurovascular and bony structures and have a high recurrence rate. Thus, the behavior can be described as “clinically malignant.” The combination of aggressive surgical removal and postoperative proton beam therapy seems to be the most efficacious treatment for chordomas with acceptable morbidity and mortality.

The present study retrospectively analyzed a single institution series of skull base chordoma for comparison with other reported microsurgical series.

Patients and Methods

Eleven patients, five females and six males aged 24–65 years (mean 41 years), underwent microsurgical removal of skull base chordoma (Table 1). The decision to use one or a combined surgical approach was based on presurgical conferences among staff members of the neurosurgical and frequently the otolaryngological department. Basically, the standard axial (transnasal-transsphenoidal, subfrontoal) and extraaxial/combined extraaxial (e.g. transcondylar, frontotemporal, subtemporal/presigmoidal, and pre-/retrosigmoidal) approaches were chosen. Figures 1–3 illustrate the respective policies with regard to individual pathoanatomical conditions.
### Table 1 Characteristics of the 11 patients with skull base chordomas

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Tumor location</th>
<th>Tumor size (cm)</th>
<th>Approach</th>
<th>Extent of resection</th>
<th>Early deficit</th>
<th>Late deficit</th>
<th>Radiotherapy</th>
<th>Outcome (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64, F</td>
<td>upper clivus, sella turcica, cavernous sinus</td>
<td>2.5</td>
<td>TS</td>
<td>subtotal</td>
<td>no</td>
<td>no</td>
<td>PBRT</td>
<td>AWR (36)</td>
</tr>
<tr>
<td>2</td>
<td>65, F</td>
<td>clivus, orbit, ethmoid, sphenoid, cavernous sinus, sella turcica, infratemporal</td>
<td>10</td>
<td>SF</td>
<td>subtotal</td>
<td>no</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>3</td>
<td>43, M</td>
<td>upper clivus, midclivus, ethmoid, sella turcica, cavernous sinus, sphenoid</td>
<td>8</td>
<td>TS</td>
<td>subtotal</td>
<td>no</td>
<td>no</td>
<td>SSCI</td>
<td>AWR (48)</td>
</tr>
<tr>
<td>4</td>
<td>46, M</td>
<td>upper clivus, midclivus, sphenoid, sella turcica, cavernous sinus, ethmoid</td>
<td>3.2</td>
<td>TS</td>
<td>partial</td>
<td>hypopituitarism</td>
<td>hypopituitarism</td>
<td>CI</td>
<td>AWR (24)</td>
</tr>
<tr>
<td>5</td>
<td>48, F</td>
<td>petroclival, lower clivus, posterior fossa, sphenoid</td>
<td>4</td>
<td>ST/PS (RS)</td>
<td>total</td>
<td>lower CN paresis, DVT, meningitis</td>
<td>no</td>
<td>SCI/Ph</td>
<td>AWLC (32)</td>
</tr>
<tr>
<td>6</td>
<td>24, M</td>
<td>lower clivus, sphenoid, petrous bone, condyle-C-1, foramen magnum</td>
<td>6</td>
<td>TC</td>
<td>total</td>
<td>CN VI paresis, gait disturbance, tracheostomy</td>
<td>no</td>
<td>PBRT</td>
<td>AWLC (48)</td>
</tr>
<tr>
<td>7</td>
<td>26, F</td>
<td>midclivus, lower clivus, sphenoid, petrous bone, foramen magnum</td>
<td>5</td>
<td>TC</td>
<td>total</td>
<td>lower CN paresis, unilateral hearing loss</td>
<td>as early deficit</td>
<td>CI</td>
<td>AWLC (156)</td>
</tr>
<tr>
<td>8</td>
<td>25, M</td>
<td>clivus, posterior fossa, petrous bone, infratemporal</td>
<td>3.5</td>
<td>ST/PS</td>
<td>total</td>
<td>CN III paresis, lower CN paresis</td>
<td>no</td>
<td>GK</td>
<td>NED (67)</td>
</tr>
<tr>
<td>9</td>
<td>38, M</td>
<td>midclivus, cavernous sinus, sella turcica, sphenoid</td>
<td>4</td>
<td>TS</td>
<td>subtotal</td>
<td>no</td>
<td>no</td>
<td>CI</td>
<td>AWLC (23)</td>
</tr>
<tr>
<td>10</td>
<td>36, M</td>
<td>clivus, cavernous sinus, petrous bone, sphenoid, brainstem, basangialgia</td>
<td>10</td>
<td>1. FT 2. TS</td>
<td>subtotal</td>
<td>CN III paresis, hypopituitarism, meningitis</td>
<td>no</td>
<td>CI</td>
<td>AWLC (12)</td>
</tr>
<tr>
<td>11</td>
<td>32, F</td>
<td>posterior fossa, midclivus, lower clivus, petrous bone</td>
<td>6</td>
<td>ST/PS</td>
<td>partial</td>
<td>CN VI paresis, lower CN paresis, tracheostomy</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>


The principal goal for surgical resection was to achieve as complete removal as possible without putting important neural and neurovascular structures at risk. Degree of resection was either microscopically total, that is leaving no visible remnants except small questionable areas of tumor in situ, subtotal (removal >90%), or partial (removal <90% with clear presence of residual tumor). Extent of resection was assessed by computed tomography in the immediate postoperative course and by magnetic resonance (MR) imaging after 3 months. All surgical specimens were analyzed by board certified neuropathologists.

The patients were followed up. First postoperative outpatient examination took place 1–4 months after surgery. All patients were sent for postoperative consultation at a radiotherapy center (i.e. proton beam therapy, heavy/carbon ion irradiation, or...
gamma knife surgery). Afterwards, patients were seen on a yearly follow-up basis at our institution and rated according to the Karnofsky performance status scale. Control MR imaging was performed yearly for screening for recurrent disease. Management of recurrent tumors and the indication to reoperate or not was discussed as prior to first surgery.

Results

Clinical manifestation of the tumors is listed in Table 2 and compared to previously reported results. Diplopia, sixth cranial nerve paresis, and headaches were the most common signs, followed by middle and lower cranial nerve deficits, hypopituitarism, and visual deficits. An overview of the extension of the tumors in the present series is provided in Table 1. According to the classification system by Al-Mefty and Borba,2) 10 tumors of our series were grade II chordomas, localized in two or more compartments of the bony skull base. One tumor was a grade III chordoma which had to be removed in two operative procedures.

The surgical approaches (see also Figs. 1–3) were tailored according to individual pathoanatomy and...
are listed in Table 1. Most approaches were standard, whereas combined infra-/supratentorial approaches were used in three of the 11 patients. Operative planning was related to the growth pattern of the tumors. In general, the least extensive approach was selected to avoid the risk for additional surgical morbidity. Thus, four tumors with para-/suprasellar localization and upper clival extension were treated by the transnasal-transphenoidal approach, whereas one tumor with fronto-clivobasal extension was approached via a subfrontal approach. A giant grade III chordoma with destruction of the dura, infiltration of the basal ganglia, and compression of the brainstem was approached in two operative procedures: frontotemporally in the first and transsphenoidally in the second step. Petro-/retroclivally located tumors and tumors extending into the posterior fossa and/or the foramen magnum were treated via subtemporal/presigmoidal (n = 2), pre-/retrosigmoidal (n = 1), and transcondylar (n = 2) approaches. Occipito-cervical fusion was performed in one case due to condyle-C-1 instability partially caused by the tumor and partially by the approach. Ventriloculoperitoneal cerebrospinal fluid (CSF) shunt was placed prior to surgery in one patient initially presenting with hydrocephalus.

Intraoperative monitoring (auditory evoked potentials, facial nerve monitoring) was performed in two cases, with one patient showing intraoperative loss of potentials after mobilizing the internal auditory artery. This patient developed a hearing loss postoperatively.

Degree of tumor removal was as follows: microscopically total or near total in four patients, subtotal in five, and partial in two.

Temporary surgical morbidity was observed in seven of the 11 patients, consisting of meningitis and hydrocephalus with consequent CSF shunt placement, pituitary dysfunction, gait ataxia, and cranial nerve deficits. Two patients with lower cranial nerve paresis required postoperative temporary tracheostomy, and additional esophageotraheal plastic operation in one. The median Karnofsky performance status score of the study group deteriorated from 80 (preoperative) to 70 at early postoperative assessment. Non-significant neurological deficits were observed in two patients: pituitary dysfunction and sixth cranial nerve paresis in one, and third, fifth, sixth, and eighth cranial nerve pareses in another. A significant permanent deficit (unilateral hearing loss) was seen in one patient. There was no mortality at a median follow up of 36 months in nine patients. Two patients were lost to follow up after the initial examination at 3 months.

Median Karnofsky performance status score recovered to preoperative levels at late reassessment (90; normal range 10–100). All patients were routinely referred for postoperative radiotherapy. According to postoperative tumor size, proton beam therapy was performed in two patients, carbon ion radiation (60 GyE) in four, combined stereotactic carbon ion/photon radiotherapy (70.2 GyE), gamma knife radiosurgery (17.5 GyE), and single dose stereotactic conventional irradiation (8 GyE) in one patient each. During follow up five patients underwent reoperation due to tumor recurrence after 4–48 months (median 24 months). At median follow up of 36 months (range 23–156 months), MR imaging confirmed local control in five patients, recurrence-free survival in one, and disease with recurrence in three (Table 1).

**Table 2 Synopsis of clinical findings in the present and previous series**

<table>
<thead>
<tr>
<th>Signs and symptoms</th>
<th>Present series (n = 11)</th>
<th>Previous series*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diplopia</td>
<td>5</td>
<td>45%</td>
</tr>
<tr>
<td>CN VI paresis</td>
<td>4</td>
<td>36%</td>
</tr>
<tr>
<td>Headache</td>
<td>4</td>
<td>36%</td>
</tr>
<tr>
<td>CN III paresis</td>
<td>4</td>
<td>36%</td>
</tr>
<tr>
<td>Decreased vision</td>
<td>4</td>
<td>36%</td>
</tr>
<tr>
<td>Hypopituitarism</td>
<td>4</td>
<td>36%</td>
</tr>
<tr>
<td>Facial pain/dyesthesia</td>
<td>3</td>
<td>27%</td>
</tr>
<tr>
<td>CN IV paresis</td>
<td>3</td>
<td>27%</td>
</tr>
<tr>
<td>Visual field deficit</td>
<td>3</td>
<td>27%</td>
</tr>
<tr>
<td>Lower CN paresis</td>
<td>3</td>
<td>27%</td>
</tr>
<tr>
<td>Gait disturbance</td>
<td>1</td>
<td>9%</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>1</td>
<td>9%</td>
</tr>
<tr>
<td>Vertigo, difficulty swallowing</td>
<td>1</td>
<td>9%</td>
</tr>
</tbody>
</table>

*From references 2, 13, 14, 23). CN: cranial nerve, NA: not available.

Despite the small number of reported surgical series of skull base chordomas, the role of radical surgical removal in the management is well established. In recent studies, the extent of removal was microscopically total in 43.5% and 42.3%, subtotal in 47.8% and 27.0%, and partial in 8.7% and 30.0%. In our study, total or near total removal was achieved in four patients (36%), subtotal resection in five (45%), and partial removal in two (18%) despite the less aggressive strategy. Recurrence was observed in five patients at 4 to 48 months (mean 24 months). The shortest interval to recurrence was 4 months in one patient after partial

**Discussion**

Despite the small number of reported surgical series of skull base chordomas, the role of radical surgical removal in the management is well established. In recent studies, the extent of removal was microscopically total in 43.5% and 42.3%, subtotal in 47.8% and 27.0%, and partial in 8.7% and 30.0%. In our study, total or near total removal was achieved in four patients (36%), subtotal resection in five (45%), and partial removal in two (18%) despite the less aggressive strategy. Recurrence was observed in five patients at 4 to 48 months (mean 24 months). The shortest interval to recurrence was 4 months in one patient after partial
transsphenoidal removal of the tumor localized in the upper clivus, sella turcica, and cavernous sinus. This case of early recurrence due to an aggressive histomorphological growth pattern corresponds to a few cases described elsewhere.2,5) Due to the high propensity of chordomas for local recurrence, second surgery was performed in all five patients, third in four, and fourth in one. Surgical seeding4) was not seen in any of the recurrences treated in our institution. After these operations for tumor recurrence, MR imaging confirmed local tumor control in two and local recurrence in three patients at a median follow up of 32 months.

The transient morbidity of patients harboring chordomas in published series in the first half of the 1990s (including some patients operated prior to the microsurgical era) ranges from 14% to 67% as related to follow-up time.14,15) This is higher than the recently reported rates of 0.1–23% and may be due to refinement of skull base surgical techniques.1,2,9,11,20,24,32) Early postoperative neurological deterioration, mainly cranial nerve deficits, occurred in 27–80% of cases in recent series.2,15,27) Fortunately, postoperative neurological deterioration is transient in most cases, and most patients show functional recovery to the premorbid level at follow up.15) In our series, complications included CSF leakage with consequent meningitis and hydrocephalus. Our rates for transient surgical morbidity (63% including temporary cranial nerve deficits) are similar to recent reports, and median Karnofsky performance status scores at late reassessment (median follow up 36 months) exceeded those prior to surgery.80).

All tumors in our series were grade II chordomas (tumor extending to two or more contiguous areas of the skull base), except one grade III tumor, according to the chordoma classification of Al-Mefty and Borba.21) Most chordomas are midline tumors displacing the neuraxis dorsally/dorsolaterally, so anterior midline approaches are generally preferred.9,11,13,20,32) Thus, chordomas localized at the upper clivus, sellar region, and sphenoid were resected via the transsphenoidal approach. This “classic” standard approach allows exposure of these areas with limitation to the lateral cavernous sinus, the petrous apex, and inferior skull base regions. One tumor of our series, a \(7 \times 7 \times 6\) cm size fronto-clivo-basal mass, was resected via the subfrontal approach without extending to the basicranial bones.

Orbitofrontal osteotomy to further improve exposure of the tumor is not a prerequisite for anterior skull base lesions.29,30) The transcondylar approach was used in two of our patients for lesions located at the inferior clivus with lateral extension to the craniocervical junction and upper cervical vertebrae (condyle-C-1). The transcondylar approach has the advantage of a short and wide surgical field, so has a broad spectrum of indications, but is limited superiorly by the jugular bulb.3,4,6) Chordomas infiltrating the infratemporal fossa, petrous apex, midclivus, and posterior fossa in two of our patients were treated by a combined subtetralral/presigmoidal approach and with retrosigmoidal extension in one. This combined approach allows for slight brain retraction and provides a short route to the petrous bone, midclivus, and posterior fossa, and control of the ventral and lateral aspects of the brainstem. Moreover, the cochlea and the bony labyrinth as well as the transverse and sigmoid sinuses are preserved.1) Subtotal removal of the grade III chordoma infiltrating both cavernous sinuses, sphenoid, petrous bone, clivus, brainstem, and basal ganglia was achieved through a two-stage operative procedure: a standard frontotemporal approach in the first and transsphenoidal approach in the second. Despite the many different approaches tailored to the lesion location and refinement of skull base surgical techniques, highly aggressive surgical treatment continues to be associated with higher mortality and morbidity and must be questioned with respect to equal functional outcome.2)

Histologically confirmed complete resection is rare despite microsurgical techniques for radical tumor removal.22) Chemotherapy has proved ineffectice, so management of skull base chordomas indicates postoperative radiotherapy.17,18,31,34) The proximity of chordomas to vital structures such as the brainstem, optic nerves, and spinal cord limits the use of conventional radiation, resulting in high rates of local recurrence and poor outcome. In general, postoperative conventional standard dose irradiation has no significant effect on the survival rate of patients.14) Furthermore, stereotactic gamma knife radiosurgery providing dose escalation is limited to small tumor volumes due to its increasing single dose toxicity.25)

Compared to conventional radiotherapy, fractionated stereotactic irradiation with photons yields better results.12) In the early 1970s, radiation doses greater than 70 Gy were proposed.28) Thus, proton beam therapy has been employed, delivering fractionated high doses of radiation to the skull base while sparing surrounding normal tissue. Even in patients with poor prognostic factors (large tumor size, abutment of crucial normal structures), local tumor control rates of 50% and 5-year survival rates of 80% have been reported.17,19,22,26,34) Similar results
were reported with the use of heavy ions other than protons.\(^7\) Within this group carbon ions may have greater biologic effectiveness compared to protons.\(^3\) Over a short follow up of 2 years, local control rates of 90%, mild toxicity, and absence of local recurrence are promising after therapy with 60\,GyE.

In our series, proton beam therapy was performed in two patients, carbon ion radiation (60\,GyE) in four, combined stereotactic carbon ion/photon radiotherapy (70.2\,GyE), gamma knife radiosurgery (17.5\,GyE), and single dose stereotactic conventional irradiation (8\,GyE) in one patient each. At a median follow up of 36 months, MR imaging confirmed local control in five patients, recurrence-free survival in one, and disease with recurrence in three. Thus, the overall outcome of our patients seems comparable to that reported in major series.

Microsurgery including standard approaches to skull base chordomas in conjunction with postoperative skull base irradiation can yield acceptable results with respect to surgical and functional outcome and overall survival. Surgical aggressiveness for “total removal” must be weighed against the probability of neurological impairment.

References


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Commentary

The authors present a series of 11 cases of skull base chordomas with surgical excision at the reasonable level and with complementary radiotherapy. Different surgical approaches were used, and the authors were able to achieve subtotal/partial resection of the tumor in seven cases and “total” in four cases. There was no surgical mortality. Seven patients had temporary surgical morbidity. In five cases, they had re-operate after 4 to 48 months. The authors are advocating: not excessively aggressive resection of the tumor in combination with radiotherapy and observation of the residual lesion.

There is no doubt that the surgical resection of a chordoma is a difficult task, however, it can never be complete due to its location and spread. Cranial nerve deficit as presented in this series is rather high. Re-operations in five out of eleven patients, though at different time periods after initial surgery, are not surprising.

If one considers that the total resection of skull base chordoma is impossible, then it is only necessary to match this fact to the experience of the surgeon as to how far it is wise to go with the resection in order to go far enough and not to go too far. To go far enough, it is again possible to judge from the neuroradiological aspect, and that is to remove the extradural tumor to such an extent that there is no compression of the pituitary gland, visual apparatus, brain stem, and possibly also no compression of the cranial nerves traversing the skull base through the tumor. At the same time, sufficient space could be achieved between the aforementioned neural structures and the rest of the tumor, to be able to hit the rest of the tumor with PBRT as the most successful treatment of these lesions at the time being. And what means not to go too far? Not to create a canal through which, if the dura is also opened, the CSF can escape into the splanchnocranium and throughout.

There is no doubt that the authors should be commended for a nicely presented clinical picture prior to surgery, the surgical approaches, and the amount of the resection of the tumor, as well as the postoperative clinical pictures. However, important questions do remain to be answered. Where could and should the most complex skull base chordomas be dealt with: in the hospital where they are diagnosed or in special centers where qualified and adequate team approach is possible regarding surgical and complementary treatment?

No doubt, this is the most important question to be answered in the future, since skull base chordoma can easily be operated by any neurosurgeon with some or no skull base experience. The fact is that the tumor is soft and is “pulling” the neurosurgeon into it. But the quantity, and even more important, the quality of the tumor’s resection (preservation of the cranial nerves) is what matters. It should be understood that the role of surgery is not just to perform biopsy and to provide the material for pathohistological study, but on the contrary, is to be qualified as part of the complex treatment and that is to provide preconditions for successful radiosurgery.
In the future, it is very probable that special centers where, through a large enough volume of patients, the best and adequate surgical resection of the tumor will be possible without negative side effects, and where the optimum complementary treatment will also be possible.

This would be ideal but cannot be set up overnight for many reasons. However, what is possible to be started soon is a generally accepted protocol with which nobody would be offended and everybody could profit. With a cooperative study, by using the generally accepted protocol, a large enough number of tumors could be collected and the best treatment conducted by including the anatomical and biological parameters.

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Chordomas are pathologically benign but clinically malignant, and might not be cured even by recent techniques of skull base surgery. Such patients must undergo multiple operations for tumor recurrence in the central skull base. Modern adjuvant radiosurgery using proton beam or carbon ion irradiation is expected to provide better results and decrease the biological activity.

This paper summarizes the results of 11 cases of clival chordomas. The surgical methods are fairly usual for typical epidural lesions, and the number of cases is not so great. However, the series includes advanced radiation treatments, using proton beam and carbon ion irradiation. The better surgical outcome could result from combination with these advanced radiation protocols.

We are continuing clinical trials of the combined treatment of surgery and carbon ion irradiation for 4 years as well. Only one patient died of tumor recurrence after the combined treatment. However, such radiotherapy is not indicated for tumors attached to the brain stem or optic nerve. The surgeon’s role is to remove the tumor affecting the brain stem via the epidural space as far as possible without aiming for radical dissection.

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The authors have presented 11 cases of clival chordomas that were treated with microsurgical excision using a variety of surgical approaches and radiation therapy. The surgical approaches used were the transsphenoidal approach (4 patients) or transcranial approaches in the rest. In 4 patients they were able to accomplish a total or near total resection and subtotal in 5 patients (>90% resection). The complications, which were low, are the usual ones reported in other major series including cranial nerve impairments, cerebrospinal fluid fistulae, hydrocephalus, meningitis, etc. Despite an immediate postoperative drop in the Karnofsky performance status score, the patients ultimately improved to 90 over the length of follow up (higher than the baseline). In an average 36 month follow up they had disease control in 5 patients, recurrence free survival in 1 patient, and recurrent disease in 3 patients. The authors have advocated repeated operations for recurrent disease.

The results that the authors have published are in keeping with other series in the literature. The relatively short follow up prevents any conclusion to be drawn regarding the patients’ ultimate survival from their treatment algorithm.

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