A multidisciplinary team approach to skull base chondrosarcomas


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Object. The authors review their experience with treating skull base chondrosarcomas, which are much rarer than skull base chordomas and differ from them in prognosis and treatment.

Methods. Seventeen patients (12 male and five female patients) with histologically verified chondrosarcomas were followed up prospectively over a 12-year period. The mean age at presentation was 35.9 years. Most patients presented with cranial nerve palsies. Seven had undergone surgery prior to referral to the authors' unit. All underwent maximum surgical cytoreduction by the most direct surgical approach; only the two patients harboring the mesenchymal variant underwent radiotherapy.

Conclusions. One patient died of a pulmonary embolus; the patients harboring mesenchymal chondrosarcomas died at 20 and 36 months, respectively, after treatment. Of the remaining patients, 93% were alive 5 years postsurgery and had a projected 10-year survival rate of 84% (mean survival time 9.3 years). These data emphasize the very slow progression of this tumor compared with skull base chordoma.

Key Words • chondrosarcoma • skull base tumor • cranial nerve palsy

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Abbreviations used in this paper: CT = computerized tomography; MR = magnetic resonance.
Skull base chondrosarcoma

**TABLE 1**

*Characteristics of 17 patients with skull base chondrosarcomas*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Location of Tumor</th>
<th>Presentation†</th>
<th>Previous Radiotherapy</th>
<th>Surgical Approach</th>
<th>Extent of Resection</th>
<th>Pathological Diagnosis</th>
<th>Outcome‡</th>
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<td>R</td>
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<td>R</td>
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<td>R</td>
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</table>

* A = alive; B = biopsy; C = clivus; ChT = chemotherapy; CN = cranial nerve; D = dead; FM = foramen magnum; LGC = low-grade chondrosarcoma; MC = mesenchymal chondrosarcoma; MF = middle fossa; ODM = open-door maxillotomy; P = partial; PA = petrous apex; PF = posterior fossa; Pt = pterional; R = radical; TF = transfrontal; T Pet = total petrosectomy.
† Cranial nerve deficits are listed by nerve in Roman numerals.
‡ Timing from first diagnosis is given in parentheses.

Only those tumors that fulfilled strict histological and immunohistochemical criteria were included. The diagnosis of chondrosarcoma was confirmed by a review of original histological material, which was supplemented when necessary by additional 5-μm paraffin sections stained with hematoxylin and cosin and as well as alcin blue. In all cases immunohistochemical staining techniques for S-100 protein, cytokeratin, and epithelial membrane antigen were performed on one or more sections. Diagnosis of chondrosarcoma was made in tumors demonstrating morphological features of chondroid differentiation, in which immunohistochemical findings proved to be positive for S-100 protein, but negative for the epithelial markers cytokeratin and epithelial membrane antigen, which are positive in samples of chordoma. Examples of mesenchymal chondrosarcoma exhibited biphasic differentiation with areas of apparently well-differentiated cartilage accompanied by poorly differentiated tumor composed of sheets of small spindle cells with pleomorphic, hyperchromatic nuclei. Immunohistochemical staining for S-100 protein was positive in well-differentiated chondrocytes.13

**Pathological Diagnosis**

As with chordomas, the aim of surgery was maximum safe cytoreduction achieved using the most direct surgical route. Preoperative and postoperative tumor volumes were assessed. The extent of surgery was defined as being complete when there was no evidence of remaining tumor, radical if up to 90% of the tumor was removed, partial if between 50% and 90% of the tumor was removed and a biopsy sample if less than 50% of the tumor was removed during surgery. The surgical approaches are listed in Table 1. In general terms, because these tumors usually arose from structures lateral to the midline, a lateral approach, rather than a ventral transoral approach, was used in most cases. If there was any question of breaching the dura, a lumbar drain was inserted at the time of anesthesia induction and cerebrospinal fluid was allowed to drain at a rate of 10 to 15 ml/hour for the first 2 or 3 days if the dura had been breached. If the dura had been breached, a careful multilayer closure was performed.

The removal of many of the tumors required sequential procedures and these were staged between 3 weeks and 3 months apart. In cases in which tumors were located around the cranovertebral junction, the possibility of craniovertebral instability had to be considered. Stabilization was usually performed subsequent to the surgery for cytoreduction. The number of operations mentioned here pertains to one treatment episode and, thus, if a patient underwent two operations for cytoreduction spaced 3 weeks apart, it would be regarded as one “operation episode” for the purposes of this review. The time to presentation was taken as the length of time

**Tumor Volume**

Tumor volumes were calculated by examining adjacent MR imaging slices by using an imaging software program available in the open domain (Image [version 1.61]; National Institutes of Health, Bethesda, MD).9 The first measurements were obtained from 3-month postoperative images to minimize postoperative artifacts. In cases in which staged procedures were performed, the postoperative measurements were obtained from images obtained 3 months after the last procedure (see further discussion).
the patient exhibited symptoms or signs prior to receiving the first histological diagnosis. Survival time was taken to be the length of survival from the time of the first tissue diagnosis, whether surgery was performed in our unit or elsewhere.

Case Management Protocol

As is the case with our chordoma patients, a team composed of an oncologist and pathologists and surgeons reviewed all cases. Based on our previous experience and findings provided by other publications, it is not our practice to irradiate low-grade chondrosarcomas of the skull, but instead to review them and be prepared for further surgery. Patients with mesenchymal chondrosarcomas, however, are treated aggressively by maximum cyto-reduction and skull base radiotherapy in the same way as patients with chordomas. Details of the radiation protocol are given elsewhere.6,19

Surgical Approaches

The aim of surgery was to achieve maximum reduction in tumor volume and the types of procedure selected for that goal are summarized in Table 1. Only four patients underwent midline open-door maxillotomies.15 In six patients we performed a low pterional approach, which usually involved the temporary disconnection of the lateral orbital wall and zygoma. A transfrontal approach was used in two patients and extensions based on a radical petrosectomy in three patients. Some transdural surgery had to be performed in one patient to allow a supra- and infratentorial approach, in another patient with Ollier disease for excision of tumor from the cavernous sinus,3,4 and in the posterior fossa of a third patient who at presentation was already found to harbor a tumor that had breached the dura. Occipitocervical fixation with bone grafts was used to effect stability.

Results

In the 17 patients, 12 tumors arose in the area of the petrous apex, two of which were considered to have originated in the maxilla and spread through the orbit and into the anterior and middle cranial fossa. There were two midline clivus chondrosarcomas; both patients harbored chondrosarcomas in other bones and one of the patients suffered from Ollier disease.1 The two patients with mesenchymal chondrosarcomas presented with extensive masses, one of which was located in the maxilla and the other was considered to have arisen in the area around the occipital condyle. This latter patient harbored an extensive tumor in the soft tissues of the neck.

Presentation and Duration of Symptoms

Fifteen of the 17 patients presented with cranial nerve deficits, the most common being a sixth nerve palsy (11 of 15 patients). Six patients experienced trigeminal pain; the lower cranial nerves were less often involved than was the case in our chordoma series. The two patients with mesenchymal chondrosarcomas presented with a facial mass or a neck mass and facial or neck pain.

The time from onset of symptoms to pathological diagnosis ranged from 1 month to 8 years, with the mean duration of symptoms in these patients being 14 months.

Previous Surgery and Radiotherapy

Seven of the 17 patients had undergone surgery before their referral to our unit. Three had undergone a single procedure, two had undergone two previous operations, and two had undergone three previous operations before being referred to our unit because of an additional recurrence. Two patients had undergone conventional radiotherapy prior to their presentation. One patient had undergone a needle biopsy followed by chemotherapy.

Neuroimaging Findings

A nonenhanced CT scan generally revealed a lytic lesion originating in the medial petrous area with variable extension into the middle and posterior fossa (Fig. 1). Contrast enhancement was variable. There was no significant difference between chondrosarcomas and chordomas with respect to density and signal characteristics on CT scans, although in the former there was slightly more calcification.

On MR imaging, the lesions exhibited predominantly

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**Fig. 1.** Example of a low-grade chondrosarcoma. **Upper Left:** Axial CT scan (bone window) obtained in February 1992, demonstrating erosion of the left petrous apex and sphenoid. **Upper Right:** Preoperative gadolinium-enhanced axial MR image revealing an enhancing mass arising from the left medial petrous region. Extension into the clivus, posterior fossa, and retropharynx is seen. **Lower Left:** Postoperative gadolinium-enhanced axial MR image obtained after transcoclear and transpetrous resection of the low-grade chondrosarcoma, demonstrating no visible tumor. **Lower Right:** Axial T1-weighted MR image obtained 3 years after transcoclear resection. The dermal fat graft is seen at the site of the mastoid resection.
low density on T1-weighted images. On T2-weighted and proton-density images, the lesions generally displayed a high signal. The tumors enhanced uniformly, although in some cases there was a variegated heterogeneous appearance.

**Tumor Volumes and Tumor Volume–Doubling Times**

As was the case with chordomas, there was a wide range of tumor volumes at the time patients presented to our unit. The patient with the smallest tumor (2 cm³) presented with an isolated sixth cranial nerve palsy; the largest tumors were the two mesenchymal chondrosarcomas (168 and 240 cm³). The mode volume was 40 to 50 cm³.

The fastest tumor volume–doubling times were exhibited by the mesenchymal chondrosarcomas at 3 months and 6 months, respectively. The slowest tumor volume–doubling time was found in one patient in whom there has been no perceived progression for longer than 14 years. Excluding the mesenchymal variants, the average volume–doubling time was 51 months.

**Cytoreductive Surgery**

In no patient could we totally excise the lesion but in 14 of the 17 cases there was a radical clearance. In the other cases there was partial removal. One patient, in whom there was encasement of the brainstem and basilar artery by a solid calcified tumor and scar tissue, had undergone previous surgery and conventional radiotherapy. The tumor mass could not be significantly reduced in size in this case; despite only partial tumor removal the patient survived 6 years.

The two patients with mesenchymal chondrosarcomas underwent two additional operations (Fig. 2), one at 10 months and the other at 14 months after surgery performed in our unit. Despite this, these patients died at 20 months and 36 months, respectively, after their first presentation.

**Extent of Surgery**

Despite our best efforts there was always residual tumor (Table 1). In two patients the material was found to be very calcified or fibrous, or surrounding virtual structures and, therefore, very little of the tumor could be removed. In the two mesenchymal variants, the tumor was soft and friable and a huge cavity remained following resection.

**Outcomes of Surgery**

One postoperative death occurred within the first 28 days in a 44-year-old man who harbored a massive petrous apex chondrosarcoma that was treated using a combined transtemporal–extradural middle fossa approach; the patient had a pulmonary embolus.

There were two cerebrospinal fluid leaks through mastoidectomies, which were difficult to control and required several procedures including lumbar drains. There were no instances of meningitis.

New cranial nerve deficits developed in four patients as a result of the surgery.

One patient who had undergone previous surgery and radiotherapy suffered a wound breakdown that required a secondary closure.

One patient with a recurrent mesenchymal chondrosarcoma, in whom a large cavity remained after tumor debulking in the neck and skull base, experienced an abscess in the cavity area. This lesion responded to drainage and curettage.

**Radiation Therapy**

The two patients with mesenchymal chondrosarcomas and two other patients in whom asymptomatic regrowths appeared on MR images were treated with a combination of conventional radiotherapy and stereotactic multiple arc radiosurgery.

**Patient Outcomes**

Excluding the patient who died of pulmonary embolus, the shortest follow-up period was in a patient with mesenchymal chondrosarcoma who died 20 months after her presentation. The longest survival duration after primary diagnosis has been 23 years. If mesenchymal chondrosarcomas are excluded, the mean survival time for this group is 9.3 years. Using life-table analysis (with the exclusion of patients with mesenchymal chondrosarcomas), the...
5-year survival rate for skull base chondrosarcoma in this group was 93% and the 10-year projected survival rate is 84%.

Discussion

Skull base chondrosarcomas tend to present a decade or more earlier than skull base chordomas (although the range is large in both groups). The 2.4:1 male predominance has been reported by other authors.10,20 The challenge these tumors present after their diagnosis is their management. Apart from mesenchymal chondrosarcomas, most of these tumors grow extraordinarily slowly. Thus, one has to weigh the benefits of a surgical cytoreduction against the possibilities of complications such as additional cranial palsies. Authors of previous reports do not support the routine use of conventionally fractionated radiotherapy because this tumor seems to be extremely radioresistant. It should be noted that three very different management protocols (Table 2) have produced the same 5-year survival rate. Modern stereotactically mapped, focal radiation techniques may have a highly selected future role for treating incompletely resected disease. This relatively new technology allows the deposition of obliteratively high dose single-fraction radiation therapy onto discrete targets and is associated with anecdotal evidence of regression (Fig. 3). Particularly in cases in which adjacent healthy nervous system tissue permits such therapy (or can be displaced away from the target, as we have described for clival chordoma2), there may be a highly selected place for postoperative radiosurgery in this disease or at the time of focal recurrence.

Mesenchymal chondrosarcoma was first described by Lichtenstein and Bernstein.17 This tumor consists of islands of cartilage and sheets of undifferentiated small stromal cells with hyperchromatic nuclei. Occasionally, these tumors arise in an extraosseous region and may have been previously misdiagnosed as a meningioma.11 Patients with the tumor have a highly variable prognosis and some present with widespread metastasis before the original diagnosis is made (Unni21 published survival rates of 54% for 5 years and 27% for 10 years for trunk and extremity lesions). There have been so few cases of cranial chondrosarcomas reported that it is impossible to make valid comparisons; however, one of our patients who had undergone three operations, radiotherapy, and chemotherapy prior to presentation to our unit, and who subsequently died 36 months after presentation (and two additional procedures), in fact lived 9 years from the time of the initial diagnosis. Another patient died within 5 years. These very aggressive tumors should be treated more like chordomas with a preparedness for multiple surgery or, as for aggressive chondrosarcomas located outside the cranium in young patients, with aggressive chemo-(radio-)therapy protocols. To date there is no consensus on the optimal therapy.

In comparison with chordomas, which we believe to be an entirely different management problem, low-grade chondrosarcomas should, in our opinion, be treated by radical surgical cytoreduction by using modern surgical access with the aim of minimizing side effects in a patient who otherwise has the potential to live a long time.

References


### Table 2

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<th>Authors &amp; Year</th>
<th>No. of Cases</th>
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* All patients in each series had their diagnosis confirmed by histological and/or immunological findings, and surgery details were given in each case.
† Combined series of chordomas and chondrosarcomas.
‡ Excludes the two mesenchymal chondrosarcomas in the series (see text).

![Fig. 3. Sagittal T₁-weighted MR images of a skull base chondrosarcoma (arrow) that has recurred in the region of the dorsum sellae after previous surgery. Images were obtained before (left) and 1 year after (right) the patient underwent stereotactic radiosurgery.](image-url)
Skull base chondrosarcoma

17. Lichtenstein L, Bernstein D: Unusual benign and malignant chondroid tumors of bone. A survey of some mesenchymal cartilage tumors and malignant chondroblastic tumors, including a few multicentric ones, as well as many atypical benign chondroblastomas and chondromyxoid fibromas. Cancer 12:1142–1157, 1959

Manuscript received August 9, 2000.
Accepted in final form February 5, 2001.
Timothy Steel, M.B.B.S.(Syd), F.R.A.C.S., was a Visiting International Spine Fellow and was supported by St. Vincent’s Hospital, Sydney, Australia during the period of this study.

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