Journal of Clinical Neuroscience 22 (2015) 1792–1796

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Clinical Study

Predictors of recurrence following resection of intracranial chordomas

Winward Choy [a], Sergei Terterov [a], Tania B. Kaprealian [b], Andy Trang [a], Nolan Ung [a], Antonio DeSalles [a], Lawrance K. Chung [a], Neil Martin [a], Michael Selch [b], Marvin Bergsneider [a], Harry V. Vinters [c], William H. Yong [c], Isaac Yang [a,d,*]

[a] Department of Neurosurgery, University of California, 300 Stein Plaza, Suite 562, Fifth Floor, Wasserman Building, Los Angeles, CA 90095-6901, USA
[b] Department of Radiation Oncology, University of California, Los Angeles, CA, USA
[c] Department of Pathology and Laboratory Medicine, University of California, Los Angeles, CA, USA
[d] Jonsson Comprehensive Cancer Center, University of California, Los Angeles, CA, USA

ARTICLE INFO

Article history:
Received 21 May 2015
Accepted 30 May 2015

Keywords:
Chordoma
Prognostic factors
Radiation therapy
Radiosurgery
Surgery

ABSTRACT

Management of intracranial chordomas remains challenging, despite improvements in microsurgical techniques and radiotherapy. Here, we analyzed the prognostic factors associated with improved rates of tumor control in patients with intracranial chordomas, who received either gross (GTR) or subtotal resections (STR). A retrospective review was performed to identify all patients who were undergoing resection of their intracranial chordomas at the Ronald Reagan University of California Los Angeles Medical Center from 1990 to 2011. In total, 57 patients undergoing 81 resections were included. There were 24 females and 33 males with a mean age of 44.6 years, and the mean tumor diameter was 3.36 cm. The extent of resection was not associated with recurrence. For all 81 operations, the 1 and 5 year progression free survival (PFS) was 87.5 and 40.4%, and 88.0 and 33.6% for STR and GTR, respectively ($p = 0.90$). Adjuvant radiotherapy was associated with improved rates of PFS (hazard ratio [HR] 0.20; $p = 0.009$). Additionally, age >45 years (HR 5.88; $p = 0.01$) and the presence of visual deficits (HR 7.59; $p = 0.03$) were associated with worse rates of tumor control. Tumor size, sex, tumor histology, and recurrent tumors were not predictors of recurrence. Younger age, lack of visual symptoms on presentation and adjuvant radiotherapy were associated with improved rates of tumor control following surgery. However, GTR and STR produced comparable rates of tumor control. The surgical management of intracranial chordomas should take a conservative approach, with the aim of maximal but safe cytoreductive resection with adjuvant radiation therapy, and a major focus on quality of life.

1. Introduction

Chordomas are rare and locally aggressive tumors that originate from fetal notochord remnants. Intracranial chordomas often present along the midline sagittal axis and comprise up to 0.2% of all primary intracranial tumors [1–4]. Skull base tumors comprise 32% of all chordomas, the majority of which involve the clivus [5–7]. Chordomas are associated with a poor prognosis due to local progression and mass effect, rather than metastatic spread. The management of intracranial chordomas remains challenging, despite improvements in microsurgical techniques and radiotherapy (RT) [8,9].

Given the deep location and involvement with adjacent neurovascular structures, gross total resection (GTR) may not be a viable option without significant morbidity and mortality. Additionally, management of these locally aggressive tumors is limited by the high risk for tumor recurrence following the initial resection. The current literature is heterogenous, comprising mostly small patient series with variable lengths of follow-up, treatment algorithms, and clinical end points. Elucidating prognostic factors which impact recurrence following resection is critical to optimize the role of surgical resection in the treatment of intracranial chordomas.

We report our institutional experience in the treatment of intracranial chordomas, to identify the prognostic factors that are associated with recurrence following either a GTR or subtotal resection (STR).

2. Methods and materials

2.1. Patient selection

A retrospective review was conducted at the Ronald Reagan University of California Los Angeles (UCLA) Medical Center, of all

* Corresponding author. 650 Charles E. Young Dr. UCLA Wasserman Bldg, Rm 562, Los Angeles, CA 90095, USA. Tel.: +1 310 267 2621; fax: +1 310 825 9385.
E-mail address: iyang@mednet.ucla.edu (I. Yang).

http://dx.doi.org/10.1016/j.jocn.2015.05.024
0967-5868/

patients who were evaluated and treated for intracranial chordoma from January 1990 to December 2011. This study was approved by the Office of the Human Research Protection Program and Institutional Review Board at UCLA. Only patients with histologically confirmed chordomas were included. All patients underwent a surgical resection. Any patients who were lacking an adequate preoperative evaluation and postoperative follow-up, or were diagnosed with any other tumors, were excluded. A total of 81 operations were performed on 57 patients who met the study criteria (Table 1).

2.2. Treatment

Prior to surgery, all patients underwent MRI using a T1-weighted sequence, with and without gadolinium contrast, and T2-weighted sequences. Additionally, CT scans or catheter angiography were performed if the tumor was in close proximity to major intracranial vessels. The aim of surgery was to safely and maximally resect the tumor and decompress the adjacent neural structures. Of the total 81 surgeries, 57 (70.4%) were primary resections and 24 (29.6%) were repeat operations for recurrent tumors. Of the 81 resections, 40 were followed by adjuvant RT, either adjuvant stereotactic RT (n = 34) and/or stereotactic radiosurgery (n = 8).

2.3. Data collection and statistical analyses

The extent of surgical resection was determined by the neurosurgeon at the end of the procedure and later confirmed by postoperative MRI. The tumor diameter was defined by the largest radiographically measured diameter in any of the three dimensions (anteroposterior × transverse × cranio-caudal). For reporting the presenting symptoms, visual impairment included decreased visual acuity and any other visual deficits that do not include diplopia. Univariate Kaplan–Meier log-rank analyses and multivariable Cox regression was used to analyze all rates of progression free survival (PFS). The Fisher's exact test was utilized to evaluate the categorical data based on prognostic factors. The differences in means were evaluated with *t*-tests. All tests for significance were two-sided, with a two-tailed *p* value of 0.05 or smaller considered statistically significant.

Table 1
Summary of intracranial chordoma patient demographics and treatment

Feature	Value
Sex, n	
Female	24
Male	33
Age, mean years (range)	44.6 (3–74)
Tumor diameter, mean cm	3.36
Follow-up, mean months	57.8
Histology, n (%)	
Chrondroid	18 (31.6)
Classic	39 (68.4)
All operations	81
GTR only	20
STR only	21
GTR + RT	5
STR + RT	35
Primary operations*, n (%)	57
GTR	22 (38.6)
STR	35 (61.4)
Additional operations*, n (%)	24
1	15 (26.3)
2	7 (12.2)
3	2 (3.5)

* Both surgery and surgery + adjuvant RT.
GTR = gross total resection, RT = radiotherapy, STR = subtotal resection.

3. Results

3.1. Patient demographics

The demographic features are summarized in Table 1. There were 24 females and 33 males, with a female to male ratio of 1:1.38. The mean age was 44.6 years, and the mean follow-up was 57.8 months (range: 1–269). The differences in age, sex and length of follow-up from first surgery were not statistically significant between the STR and GTR groups. Nearly all patients presented with some cranial nerve involvement or other neurological symptoms; and only three patients had incidental diagnoses (Table 2).

3.2. Tumor characteristics

Classic and chondriod histologies were present in 68.4 and 31.6% of patients, respectively. The mean tumor diameter was 3.2 cm (standard deviation 1.4; range: 1–8) for all patients. The mean tumor diameter was 2.6 cm for GTR and 3.6 for STR ($p = 0.015$). There were no significant differences in age, histological subtype or location between the STR and GTR groups. Most of the tumors were clival, comprising 79.2%. Petroclival, petrous, and sellar chordomas were present in 9.7, 5.6, and 1.4% of patients, respectively. Additionally, one tumor involved the basion, and another involved the sphenoid sinus.

3.3. Treatment and outcomes

In total, 57 patients underwent a total of 81 tumor resections, of which 40 were followed by RT. The rate of tumor recurrence at the last clinical follow-up for all patients who underwent an initial surgical resection, with or without RT, was 42%. The mean time to recurrence was 38.1 months (range: 2.4–103). The overall rates of PFS were 88.8 and 41.0% at 1 and 5 years, respectively.

Following the first resection for primary tumors, the mean time to the first recurrence was 43.3 months (range: 5.9–159). Fifteen patients, of whom four received GTR and 11 STR, underwent a second surgery for recurrence. The mean time to recurrence was 31.5 months, and the mean time between the first and second surgery was 38.3 months. GTR and STR were achieved in two and 13 patients, respectively. Following the second resection, the rate of a second recurrence was 12 out of 15 (80%), which was significantly higher than the recurrence rate following the initial resection (42%; $p = 0.0182$). Table 1 summarizes the treatments and the number of repeat surgeries for recurrences. Overall, the PFS at 1 and 5 years for all recurrent tumors was 91.7 and 27.3%, respectively. The rate of GTR was lower in recurrent, compared to primary, tumors (12.5 *versus* 38.6%; $p = 0.020$).

Table 2
Summary of presenting symptoms of patients with intracranial chordoma

Symptoms	n (%)
Diplopia	26 (47.3)
Visual impairment	10 (18.2)
Hypacusis	4 (7.3)
Headache	4 (7.3)
Trigeminal signs	4 (7.3)
Dysphonia	4 (7.3)
Incidental	3 (5.5)
Anosmia	3 (5.5)
Oculomotor nerve palsy	3 (5.5)
Dysphagia	3 (5.5)
Neck pain	2 (3.63)
Tinnitus	2 (3.63)
Dizziness	2 (3.63)