Journal of Clinical Neuroscience xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

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

Clinical Study

Outcomes and patterns of care in adult skull base chondrosarcomas from the SEER database

Pamela S. Jones [a], Manish K. Aghi [b], Alona Muzikansky [c], Helen A. Shih [d], Fred G. Barker II [a], William T. Curry Jr. [a,*]

[a] Department of Neurosurgery, Stephen E. and Catherine Pappas Center for Neuro-Oncology, Massachusetts General Hospital, 55 Fruit Street, Yawkey 9E-9026, Boston, MA 02114, USA
[b] Department of Neurosurgery, University of California, San Francisco, San Francisco, CA, USA
[c] Biostatistics Center, Massachusetts General Hospital, Boston, MA, USA
[d] Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA

ARTICLE INFO

Article history:
Received 3 February 2014
Accepted 11 February 2014
Available online xxxx

Keywords:
Chondrosarcoma
Population study
Radiation therapy
Skull base tumors

ABSTRACT

This study aims to demonstrate survival rates and treatment patterns among patients with chondrosarcomas of the skull base using a large population database. Patients with skull base chondrosarcomas between 1973 and 2009 were identified from the USA Surveillance, Epidemiology, and End Results (SEER) database. Kaplan–Meier survival analysis was used to examine the effect of surgery and radiation on overall survival. We identified 226 patients with skull base chondrosarcomas. Median follow-up was 5.4 years. Median overall survival was 22 years, and 10 year survival was 68.2%. Most patients underwent surgery (92.5%). Few received radiation after diagnosis (38.1%). Ten year survival for all patients treated with surgery was significantly increased compared to those without surgery (69.3% *versus* 53.9%, $p = 0.02$). There was a significant difference in survival amongst treatment groups ($p = 0.02$), with median overall survival not yet reached for patients who received surgery and radiation (median follow-up 5.3 years), compared to 22 years for non-irradiated surgical patients. Surgery predicted better overall survival by univariate analysis (hazard ratio [HR] 0.420, $p = 0.03$). Female sex (HR 0.470, $p = 0.011$), younger age at diagnosis (HR 1.046, $p < 0.0001$), and later year of diagnosis (HR 0.949, $p = 0.0006$) were prognostic of improved survival in a multivariate model. In subgroup analysis of patients with documented tumor size, smaller tumor size (HR 1.054, $p = 0.0003$) and younger age (HR 1.021, $p = 0.0067$) predicted improved survival. This population based study further reaffirms the role of surgery as an effective treatment for skull base chondrosarcoma as previously reported in small case series. Adjuvant radiation may also confer survival benefit. Optimal treatment strategy has yet to be defined in the literature.

1. Introduction

Chondrosarcomas are rare tumors, and account for only 6% of all tumors occurring in the skull base [1]. They often arise from the lateral aspects of the skull base that house cartilage, including the temporo-occipital synchondrosis, the spheno-occiput, and the sphenoethmoid complex [2]. Because of this, they typically involve the cavernous sinus, the petrous bone, the sphenoid bone, and the clivus [3].

While *en bloc* or gross total resection of chondrosarcomas remains the therapeutic ideal, the proximity of skull base tumors to critical neurovascular structures and possible bony invasion often limits extent of safe surgical resection [4]. Therefore, treatment may also include the use of adjuvant radiation for patients with unresectable, subtotally resected, or even gross totally resected tumors to limit tumor growth and recurrence. While the use of adjuvant postoperative radiotherapy, particularly proton beam radiotherapy, has been shown in single institution retrospective series to prolong the survival of patients with skull base chondrosarcomas, there have been no prospective or large population studies analyzing the outcomes of adjuvant radiotherapy specifically for these tumors to our knowledge [5,6].

Given the overall low incidence of this disease, single institution series are often subject to selection biases associated with referral and treatment patterns and contain too few patients to provide definitive understanding of the prognoses and role of radiotherapy in treating these diseases. To clarify the epidemiologic patterns, treatment, and prognosis of skull base chondrosarcoma in the general USA population, we evaluated patients reported to the

* Corresponding author. Tel.: +1 617 726 3779; fax: +1 617 726 3365.
E-mail address: wcurry@mgh.harvard.edu (W.T. Curry Jr.).

http://dx.doi.org/10.1016/j.jocn.2014.02.005
0967-5868/

population based registries within the Surveillance, Epidemiology, and End Results (SEER) program between 1973 and 2009. We paid particular attention to outcomes and trends in radiation utilization.

2. Methods

2.1. The SEER program

The SEER registry, a database maintained by the USA National Cancer Institute, collects incidence and survival data from population based cancer registries. Data on chondrosarcoma patients diagnosed between 1973 and 2009 were available from 18 population based cancer registries across the USA that together represent approximately 25% of the USA population. The 18 registries included nine entire states and nine metropolitan regions. These registry populations are comparable to the overall USA population on a variety of socioeconomic indices, including poverty indices, high school graduation rate, percentage in rural areas, and percentage foreign-born. The database contains information on patient demographics, primary cancer site, histology, methods of diagnostic confirmation, treatment regimens including surgery and radiation therapy, and year of death. Institutional Review Board approval was not required for this study, as the SEER database is free of any sensitive patient information or identifiers. An overview of the SEER database is available at http://seer.cancer.gov/about/.

2.2. Chondrosarcoma definition

We compiled chondrosarcoma patients diagnosed between 1973 and 2009. Patients were identified through the World Health Organization's International Classification of Diseases for Oncology, Version 3 (ICD-O-3) morphology code for chondrosarcoma (9220–9239). Primary sites of disease presentation were compiled according to ICD-O-3 topography codes and were limited to skull and face bones (410); meninges (700); any structure in the brain (710–9, 751, 753); connective and soft tissue of head, face and neck (490); or any head structure (760). We restricted our analysis to patients with histologic confirmation of chondrosarcoma.

2.3. Treatment

Treatment types were limited to surgery and radiation. The SEER surgery code of 0 was used to indicate that surgery was performed. For the purpose of our analysis, all surgical cases were considered to include some type of tumor resection. All other codes were considered cases where only a diagnostic biopsy had been performed. Adequate information on extent of resection was not available from the database. The SEER radiation codes 0, 6, 7, 8, 9 represented no radiation treatment. We sub-categorized registries according to number of skull base patients in order to assess for potential volume-outcome effect. This is an effect whereby better outcomes are observed at treatment centers with higher volume. We looked at numbers of both skull base chordomas (ICD-O-3 code 9370–9373) and chondrosarcomas treated by each registry to assess for volume of skull base cases from 1973 to 2009. A registry was considered to contain a high-volume treatment center if it contained 40 or more histologically-confirmed skull base chordomas and chondrosarcomas over the study period.

2.4. Statistical analysis

The primary outcome of interest was overall survival. Survival analysis was performed using Kaplan–Meier product limit estimators and Cox univariate and multivariate proportional hazards models. Predictors of overall survival in univariate analysis ($p < 0.05$) were included in the multivariate model. Treatment strategies were compared using chi-squared analysis. Calculations were performed using SAS version 9.3 (SAS Institute, Cary, NC, USA).

3. Results

3.1. Demographics

Between 1973 and 2009, 226 patients were diagnosed with skull base chondrosarcoma. The median age at diagnosis was 43 years, with age range of 1 to 82, and a fairly equivalent sex distribution (50.9% female). A slightly greater proportion of patients (123 patients, 54.4%) were diagnosed before the median diagnosis year of 2002. Cases occurred across 16 registries, of which nine were considered low-volume (66 patients) and seven were considered high-volume (160 patients). The results are summarized in Table 1.

3.2. Tumor characteristics

Information regarding tumor size was available in 111 of 226 patients. The mean diameter was 3.7 cm (range 1.0 to 10.7 cm). Information regarding histologic subtype of chondrosarcoma was not available.

3.3. Treatment

Most patients (209 of 226, 92.5%) underwent some type of surgical resection beyond biopsy. The SEER data only specified whether surgery was performed, and did not reliably specify extent of skull base tumor resection. Ultimately, 128 patients were treated with surgery alone (56.6%), 81 patients were treated with surgery and radiation (35.8%), and five patients treated with radiation alone (2.2%). Twelve patients received no treatment (5.3%). Radiation utilization did not increase over time (chi-squared analysis, $p = 0.9$), and there were no significant differences in the rates of radiation use among small and large registries ($p = 0.23$).

Table 1
Characteristics of 226 patients with chondrosarcoma tumors of the skull base registered in the SEER database (1973–2009)

Patient characteristics	
Patients, n	226
Mean age, years (± SD)	44.3 (± 17.7)
Median age, years	43
Females	115 (50.9)
Race	
White	192 (85.0)
African American	15 (6.6)
Asian	16 (7.1)
Unknown	3 (1.3)
Registry	
Low volume (<40 skull base cases)	66 (29.2)
High volume (⩾40 skull base cases)	160 (70.8)
Year of diagnosis	2002 median year (1999 mean)
⩽2002	123 (54.4)
>2002	103 (45.6)
Surgical data available	
No resection	17 (7.5)
Resection	209 (92.5)
Radiation therapy	86 (38.1)
Median survival, years (months)	22 (264)
5 year survival,%	86.9
10 year survival,%	68.2

Data presented as number of patients (%) unless otherwise indicated.

Please cite this article in press as: Jones PS et al. Outcomes and patterns of care in adult skull base chondrosarcomas from the SEER database. J Clin Neurosci (2014), http://dx.doi.org/10.1016/j.jocn.2014.02.005