Patterns of Care for Craniopharyngioma: Survey of Members of the American Association of Neurological Surgeons

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Key Words

Craniopharyngioma · Resection · Radiation therapy · Neurosurgeon

Abstract

Background: Initial therapy for craniopharyngioma remains controversial. Population-based datasets indicate that traditional algorithms [gross total resection (GTR) vs. subtotal resection (STR) +/- radiation therapy (XRT)] are often not employed. We investigated neurosurgical practice patterns. **Methods:** A ten-question survey was electronically distributed to members of the American Association of Neurological Surgeons. Responses were analyzed using standard statistical techniques. **Results:** 102 responses were collected, with a median of 25 craniopharyngiomas managed per respondent. 36% estimated that their practice included $\geq 75\%$ pediatric patients and 61% had an academic practice. 36% would recommend observation or XRT for a suspected craniopharyngioma in the absence of a tissue diagnosis, with 46% of these indicating this recommendation in $\geq 10\%$ of the cases. Following STR, 35% always recommend XRT and 59%

recommend it in over half of the cases. However, following STR or biopsy alone, 18 and 11% never recommend XRT. There was no association between the type of practice (i.e. academic or $\geq 75\%$ pediatric patients) and practice patterns. **Conclusions:** This survey verifies that a deviation from established algorithms is common, underscoring the clinical complexity of these patients and recent secondary data analyses. This should influence clinical researchers to investigate outcomes for patients treated using alternative methods. It will lend insight into appropriate treatment options and contribute to quality of life outcomes studies for craniopharyngioma.

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Introduction

Initial therapy for both adult and pediatric patients with craniopharyngioma has been the subject of considerable controversy. While the most commonly described algorithm centers around the choice between gross total resection (GTR) and subtotal resection (STR) augmented

by external beam radiation (XRT), multiple groups promote an individually tailored treatment approach [1–6]. Two recent analyses of the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) datasets indicate that a significant portion of patients in the United States are not initially treated with GTR or STR + radiation therapy [7, 8]. While alternative therapeutic regimens, such as intracystic therapy or progression contingent XRT are well established, these data prompted us to further explore the initial practice patterns of neurosurgeons using a brief survey. We intended to survey as broad a population of practicing neurosurgeons as possible, with the knowledge that this would predispose the instrument to a low response rate. We hypothesized that neurosurgeons commonly elect initial treatment strategies other than surgical GTR or STR followed by XRT. Clarification of initial practice patterns not only offers the potential to detail the application of less commonly described approaches, but also contributes to efforts to design clinical outcomes studies for patients with craniopharyngioma.

Methods

A ten-question survey was designed and then reviewed by the leadership of the Joint Sections of the American Association of Neurological Surgeons (AANS) and the Congress of Neurological Surgeons on Tumors and Pediatric Neurosurgery. The survey was electronically distributed through 2 electronic AANS Special Announcements to 2,974 AANS members in June and July 2012 (see Appendix 1). Results were collected through Zoomerang (SurveyMonkey, Palo Alto, Calif., USA). Statistical analysis was performed using SAS® 9.3 (SAS® Institute, Cary, N.C., USA). Frequencies, proportions, and measures of the central tendency were used to describe study results, and χ^2 analysis was used to evaluate bivariable associations. Statistical significance was set at a value of $p < 0.05$.

Results

Characteristics of Respondents

Responses to 102 surveys (3.4%) were received. The estimated number of patients with craniopharyngioma that each respondent had assessed during her/his career ranged from 1 to 250 (median = 25), amounting to an estimated total of 2,550 cases. 37 (36.3%) respondents reported their practice to include $\geq 75\%$ pediatric patients and 62 (60.8%) described their practice as academic. 32 respondents (31.4%) completed neurosurgical training between 1977 and 1989, 37 (36.3%) between 1990 and 1999, and 33 (32.4%) between 2000 and 2008.

Respondents who described their practices as academic were more likely to report evaluating more than 25 patients with craniopharyngioma compared to those in private practice (54.8 vs. 22.5%, $p = 0.001$).

Initial Treatment

In response to the question 'Have you ever recommended observation or treatment without a tissue diagnosis for a patient presenting with a newly diagnosed lesion considered likely to be a craniopharyngioma?' 37 (36.3%) respondents responded in the affirmative. They reported this recommendation in 0.2–80% of the cases (median = 5%), with 17 (16.8% of the total sample) respondents reporting this recommendation in at least 10% of the cases. Questions 7–9 (see Appendix 1) queried how often respondents recommend XRT immediately following surgery [GTR, STR, and biopsy, respectively]. 100 respondents (99.0%) do not recommend XRT in the majority of the cases, in which GTR is achieved. Following STR, 18% never recommend XRT, 41% recommend it in half or fewer of the cases, and 35% always recommend XRT. Following biopsy alone, 56% always recommend postoperative XRT and 71% recommend it in $\geq 90\%$ of the cases. Following biopsy alone, 11/99 (11.1%) never recommend XRT.

There were no statistically significant differences in the initial treatment patterns of respondents based on the demographic parameters assessed: experience (based on date of training or number of craniopharyngiomas evaluated), practice type, and proportion of practice that is composed of pediatric patients (tables 1, 2). Regarding the recommendation for treatment or observation without tissue biopsy, 66.1% of those in academic practice have never done so and 60.0% of those in private practice have never done so ($p = 0.53$).

Discussion

Craniopharyngioma is a tumor that is well known for the options that exist regarding initial surgical management. While considerable literature compares the merits and limitations of initial GTR versus STR and external beam radiation therapy as the mainstays of initial therapy [5, 9–19], alternative algorithms including intracystic therapies [20–26], progression-contingent XRT [27], and stereotactic radiosurgery [28–31] have also been well described through both primary and secondary data analyses [7, 8, 32, 33]. This survey intended to expand on recent secondary data analyses by assessing how commonly al-

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* 1. Does your surgical practice consist of $\geq 75\%$ pediatric (≤ 18 yo) patients?

- ☐ Yes
☐ No

* 2. What year did you complete neurosurgical training?

* 3. Do you work in an academic or private practice setting?

- ☐ Academic
☐ Private Practice

* 4. Approximately how many patients with craniopharyngioma have you evaluated in your career?

* 5. Have you ever recommended observation or treatment without a tissue diagnosis for a patient presenting with a newly diagnosed lesion considered likely to be a craniopharyngioma?

- ☐ Yes
☐ No

6. If yes for question 5, in what percentage of craniopharyngioma patients have you made this recommendation?

* 7. Following a gross total resection of craniopharyngioma, in what percent of cases would you recommend immediate post-operative radiation?

* 8. Following a sub-total resection of craniopharyngioma, if further surgery is not an option, in what percent of cases would you recommend immediate post-operative radiation?

* 9. Following tissue biopsy of craniopharyngioma, if further surgery is not an option, in what percent of cases would you recommend immediate post-operative radiation?

10. If you would like to clarify your answer to any question(s), please do so here.

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Appendix 1.

Table 1. Reported likelihood of recommending XRT following STR (n = 100)

	Patients		p value
	≤50%	>50%	
<i>Practice experience</i>			
Year of training completion			
1977–1989	13	19	0.12
1990–1999	19	17	
2000–2008	9	23	
Number craniopharyngiomas evaluated			
0–25	27	31	0.19
30–250	14	28	
<i>Practice character</i>			
Proportion of pediatric patients			
≥75%	11	25	0.11
<75%	30	34	
Practice setting			
Academic	22	40	0.15
Private	19	19	

ternative algorithms are employed by contemporary neurosurgeons. We found that many patients are managed with algorithms that differ from the pattern of GTR or STR + XRT. While not statistically significant, there was a trend of neurosurgeons who completed training between 2000 and 2008 to employ XRT following STR or biopsy at greater rates than their more senior colleagues (tables 1, 2). This may reflect a practice trend towards greater use of XRT, but further studies are required to more clearly address this question. We were surprised to find that 18 and 11% of respondents never recommend XRT immediately following STR or tumor biopsy, respectively. Additionally, 36.3% (37/102) of respondents indicated that they had treated or observed a patient with a presumptive craniopharyngioma without a biopsy. Although not a direct comparison, this is consistent with the rates of 12.7–20.8% of patients identified from the SEER datasets as receiving neither surgery nor XRT at the time of diagnosis with craniopharyngioma [7, 8]. However, such practice patterns are in distinction to reports from multiple high volume centers, in which all reported patients were treated with surgery, with or without postoperative XRT [5, 14, 16, 19]. Furthermore, recent systematic reviews [10, 11], while they provide excellent insight regarding comparative outcomes, focus on patients who were treated operatively, thereby excluding what may be a substantial subset of patients.

Table 2. Reported likelihood of recommending XRT following biopsy (n = 99)

	Patients		p value
	≤50%	>50%	
<i>Practice experience</i>			
Year of training completion			
1977–1989	6	26	0.31
1990–1999	10	26	
2000–2008	4	27	
Number craniopharyngiomas evaluated			
0–25	14	43	0.21
30–250	6	36	
<i>Practice character</i>			
Proportion of pediatric patients			
≥75%	6	30	0.51
<75%	14	49	
Practice setting			
Academic	12	50	0.79
Private	8	29	

These results are significant because they reinforce the concept that therapy for patients with craniopharyngioma is often individually tailored [2–6]. Furthermore, variability in initial treatment algorithms must be incorporated into the design and interpretation of high-quality clinical outcomes studies for patients with craniopharyngioma. While recent analyses of large retrospective datasets have associated posttreatment morbidity/mortality with factors such as surgical experience [34], the extent of resection [34], the age at presentation [18], tumor size [19], and hydrocephalus [18, 19], these conclusions are limited by the bias associated with their data sources, which include data collected over a wide time range [18], pooled data [34], and a study design focused on the difference in outcomes between primary and recurrent craniopharyngioma treatment [19].

While randomized clinical trials for craniopharyngioma are logistically challenging [35], pragmatically designed multicenter registries offer the opportunity for both retrospective data analysis using consistent definitions and prospective data collection. The trinational KRANIOPHARYNGEOM 2000 study collected observational data from 46 centers [36]. Among their findings, the authors identified low 3-year event-free survival rates in both the completely (EFS 0.64) and incompletely (EFS 0.31) resected populations. The subsequent study, KRANIOPHARYNGEOM 2007, includes ran-

domization of a subset of patients in an effort to ascertain the optimal timing of XRT, following incomplete surgical resection in children over 5 years of age [37]. Currently, there is no equivalent multicenter study ongoing in North America.

Despite the limited scope of this survey instrument and recognition that our highly diverse surveyed population would likely yield a low response rate, the response rate of 3.4% was suboptimal. As a result, response bias may lead to conclusions that are not generalizable. This point is demonstrated by a bias in the respondents towards both academic (60.8%) and pediatric (36.3%) practices. Nevertheless, the data represent the practice patterns of over 100 neurosurgeons and represent a large range of experience based on the years in practice and number of craniopharyngiomas assessed. Additionally, with nearly 40% of the respondents practicing outside an academic environment, we feel that these data do represent both the academic and private practice environments. A larger sample would be unlikely to refute the conclusion that a variety of approaches are used in the initial treatment of patients with craniopharyngioma. A second limitation of this work resulted from our effort to simplify the questionnaire as much as possible. This presented challenges to the respondents by limiting their capacity to answer with the optimal level of detail. Specific concerns resulted from our choices to exclude questions regarding the use of intracavitary therapy and to not rigidly define a time frame for 'immediate postoperative' XRT. The latter decision was made to allow respondents the freedom to express their intent regarding

the timing of therapeutic recommendations. Future clinical outcomes studies will allow for more detailed responses.

Conclusions

Using a streamlined survey instrument that gathered data from members of the AANS, we verified recent study results indicating that many patients with craniopharyngioma receive initial treatment that is tailored to the clinical situation, often deviating from the most common algorithm: GTR versus STR and XRT [7, 8]. This finding verifies that a deviation from this algorithm is common and should influence clinical researchers to investigate and document the outcomes of patients who are treated using alternative methods. This will not only lend insight into appropriate treatment options, but will contribute to the design of the prospective quality of life outcomes studies for patients with craniopharyngioma. Given the rarity of this tumor, pragmatic trial designs that accommodate less restrictive treatment algorithms will be necessary in order to complete such studies.

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