Recurrence and Outcome in Skull Base Meningiomas: Do They Differ from Other Intracranial Meningiomas?

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ABSTRACT

Background and Objectives: Meningiomas have diverse presentations and the skull base harbors the most difficult of them to operate upon. The objective of this study was to learn whether the recurrence and outcome of these tumors may differ based on their location. **Design:** Consecutive admissions with intracranial meningiomas between 1999 and 2004 were considered according to their location, WHO grade, recurrence, and outcome following treatment. **Results:** There were 83 skull base meningiomas and 86 at other locations. In 22 cases of skull base tumors there was recurrence (26.5%), while 15% (13) of the other group showed recurrence. There was no statistically significant difference in the outcome between the two groups; though skull base lesions had a better outcome based upon a raw count. Only 5.1% of skull base meningiomas in comparison to 10.6% of non-skull base meningiomas had death or significant morbidity. Increasing age was associated with poor outcome ($p < 0.001$) while recurrence was a function of skull base location ($p < 0.03$) on logistic regression analysis. **Conclusion:** Skull base meningiomas can be operated upon with good outcome, which is comparable to the convexity meningiomas. Except for the increasing age, skull base location does not contribute to increased mortality or morbidity.

KEYWORDS: Convexity, meningioma, outcome, recurrence, skull base

Intracranial meningiomas constitute 15 to 20% of primary brain tumors.¹ Of these intracranial meningiomas, 20 to 30% are in the skull base.² Meningiomas located on the convexity are usually accessible, circumscribed, and well demarcated from the neural and vascular structures. In

contrast, skull base meningiomas are extensive, invasive, and intimately associated with cranial nerves, vessels, and brainstem. Taking into account these anatomical differences, the aim of surgery is complete resection in the case of convexity meningiomas and maximal possible resection with

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Received: September 6, 2007. Accepted: November 5, 2007. Published online: December 31, 2007.

DOI 10.1055/s-2007-1016956. ISSN 1531-5010.

minimal neurological disability in the case of skull base meningiomas.

Meningiomas have diverse presentations and the skull base harbors the most difficult to operate upon. Recurrence and outcome of these tumors may differ based on their location. Skull base meningiomas are often believed to have a higher rate of recurrence and worse prognosis compared with other intracranial meningiomas. However, the literature does not clearly and objectively support this opinion. The natural history of meningiomas has shown that tumor doubling times are much shorter in younger patients and annual growth rates tend to be higher.³ The biologic behavior of meningiomas varies considerably and the histology is not strongly predictive of behavior, especially in those categorized as WHO I meningiomas, since 21% of these tumors recur over 5 years.⁴ On the other hand, studies are available on tumor markers and labeling indices for proliferation/growth potential of meningiomas to predict recurrences and outcome.^{5,6}

MATERIAL AND METHODS

This was a retrospective study to compare skull base meningiomas with other intracranial meningiomas regarding the recurrence of tumor and outcome following operative treatment. Consecutive admissions with intracranial meningiomas between 1999 and 2004 were considered according to tumor location, WHO grade, recurrence, and outcome (Glasgow Outcome Scale [GOS] score) following microsurgical gross total removal (GTR) apart from gender and age. Only tumors that had GTR (intraoperatively confirmed under microscope and as on postoperative scans) were considered for inclusion. After Institutional Review Board permission was obtained for accessing the medical records and other information for this study, case records and all the pre- and postoperative computed tomography/magnetic resonance imaging scans were collected and reviewed.

All of the data were coded for both groups and entered into a statistical worksheet for analysis using Sigma Stat (version 3.01, 2004 Systat Software, Inc., San Jose, CA). Both groups were evaluated together as well as separately for differences and intervariable relationships using univariate and multivariate analysis. Logistic regression model was applied for detection of significant variables influencing recurrence in each group and also the complete dataset. Outcome was also compared and analyzed as a dependent variable in the combined dataset. Statistical significance was assumed at a *p* value of 0.05.

RESULTS

In all, there were 83 skull base meningiomas and 86 at other locations. The mean age for skull base tumor group was 55 (standard deviation, 12; range, 32 to 85) years and the other group had a mean age of 54 (standard deviation, 14; range, 13 to 89) years. Interestingly, 80.7% of patients with skull base tumors were females while only 69.8% were female patients in the non-skull base meningiomas group. However, statistically age and gender distribution turned out to be nonsignificant and symmetrical.

All meningiomas in non-skull base locations belonged to WHO grade 1, while three of the skull base tumors were grade 2, which provided no statistical significance. All meningiomas underwent microsurgical gross total excision. The follow-up period reached 3 to 5 years in some patients (range, between 3 months and 5 years).

In 22 cases of skull base tumors there was recurrence (26.5%), while 15% of the other group showed recurrence as well.⁷ Though this difference between the two groups was not statistically significant (*p* = 0.07, univariate analysis), on multivariate analysis, with recurrence as the dependent variable, skull base meningioma exhibited significant correlation (*p* = 0.03). However, the occurrence of recurrence had no relationship with outcome.

Figure 1 Outcome (Glasgow Outcome Scale) differences between the two groups show that good outcome was seen in skull base meningiomas, comparable to the other group (marginally better but not statistically significant).

Notably, there was no statistically significant difference in the outcome between the two groups; however, skull base lesions had a better outcome on raw count (Fig. 1). Only 5.1% of skull base meningiomas in comparison with 10.6% of non-skull base meningiomas had death or significant morbidity. Mortality for skull base tumors was 1.26% and for the other group, 2.35% (not significantly different), with a median of 1 person for both groups. Fig. 1 depicts the outcome between the two groups, wherein the good outcome was proportionately better among skull base meningiomas (not statistically significant). The statistical significance in the comparison between variables of skull base and those of non-skull base meningiomas can be seen in Table 1 (univariate analysis). There was no significant difference between the two groups, especially when comparing age, recurrence, and outcome.

The statistical analysis of variables of non-skull base meningiomas results showed that an

increasing age had significant association with poor outcome (GOS) ($p < 0.03$). However, gender, histopathology, and recurrence had no relationship with outcome whatsoever.

In the statistical analysis of skull base meningiomas' variables, outcome did not correlate significantly with gender, histopathology, and recurrence. Also, recurrence was not influenced by any of the other variables. Only gender had an equivocal or marginal relationship with recurrence in skull base lesions ($p = 0.08$).

When looking at the complete dataset of all meningiomas, we found that increasing age was associated with poor outcome ($p < 0.001$) (Fig. 2), and recurrence was a function of skull base location ($p < 0.03$).

Illustrative cases shown in Figs. 3, 4, 5, and 6 show that postoperative course of these lesions could be a function of parameters other than location alone (Figs. 3 to 6).

Table 1 Statistical Significance* in the Comparison between Variables of Skull Base and Those of Non-Skull Base Meningiomas

Variable	p Value
Age	0.5
Gender	0.1
Pathology	0.07
Recurrence	0.07
Glasgow Outcome Scale score	0.2

*Statistical significance assumed at $p < 0.05$; t -test.

DISCUSSION

Meningiomas are common central nervous system tumors that originate from meningeal coverings of the brain and spinal cord. They account for nearly 25% of all primary intracranial tumors with an estimated annual incidence of 6 per 100,000 people.⁸ Although considered benign, the biological behavior

of meningiomas varies considerably. The molecular mechanisms underlying their development and progression remain poorly understood. The histological features are not always reliable indicators of the aggressive behavior of these tumors, and the extent of tumor resection has often been used as a predictor of recurrence. In incompletely resected tumors, the tumor cell proliferation rate becomes particularly significant since small fragments of tumor tissue may remain attached to important structures like the brainstem and blood vessels even after microscopically complete excision.⁹⁻¹¹ The 5-year recurrence rate for patients with benign meningiomas is 21%, and for atypical and anaplastic meningiomas, 38% and 78%, respectively.⁴

The location of the meningioma influences the extent of resection, which, in turn, influences the rate of recurrence. In 1957, Simpson observed that the recurrence of meningiomas correlated well

Figure 2 Linear regression model showing the relationship between age and outcome (Glasgow Outcome Scale). Age and Glasgow Outcome Scale had a significant relationship ($p < 0.01$).

Figure 3 Convexity meningiomas tend to have less postoperative edema and good outcomes. However, swelling in the parietal region is relatively common.

with the extent of tumor removal (Simpson's grade).¹² The recurrence rates were 8% for grade I, 16% for grade II, 29% for grade III, and 42% for grade IV. Since Simpson's study, various others have confirmed that the extent of surgical resection has strong prognostic influence on local recurrence.^{13–15} Jääskeläinen and colleagues reported an overall recurrence rate of 19% over 20 years.¹⁶ For histologically benign tumors the recurrence rate was 3% at 5 years and 21% at 25 years. Mahmood and associates reported recurrence-free rates of 98% at 5 and 10 years in patients having complete resections of benign meningiomas, as compared with 54% and 36% in those with incomplete removals at the same intervals.¹⁷ Mathiesen et al published their results of patients with skull base meningiomas treated exclusively with surgery between 1947 and 1982.¹⁸ They documented a 5-year recurrence rate of 4% for patients undergoing radical surgery (grade 1 and grade 2) and 25 to 45% for patients undergoing grade 3 or 4 operations. No patients who underwent grade 4 or 5 operations were free from symptomatic progression after 20 years.

De Jesus and colleagues reported that the 5-year local control rate was 81% after complete resection compared with 62% after subtotal resection in cavernous sinus meningiomas.¹⁹ Couldwell and others published a 32% morbidity rate with 69% gross total removal rate for 109 petroclival meningiomas treated by single-stage microsurgery.²⁰ Recurrence or progression of disease occurred in 13% over a 6.1-year mean follow-up period. DeMonte et al reported the results of 41 patients who underwent resection for cavernous sinus meningiomas between 1982 and 1992.²¹ Complete resection was achieved in 76%. After complete resection, local control was obtained in 89%. Kinjo and coworkers studied the results of grade 0 removal of supratentorial meningiomas.²² In their series, none had tumor recurrence. Out of the 37 patients, only 19 had follow-up more than 5 years. Kajiwar et al also reported no recurrence in 20 patients.²³ In other series the recurrence rate of convexity meningiomas is estimated to be between 5% and 15%.^{7,16,24}

Various studies have been undertaken to look into the factors influencing the recurrence in skull base meningiomas. Ayerbe and associates studied the factors predicting recurrence of meningiomas following operation.²⁵ In their paper, tumors located at petroclival regions and in the parasagittal (middle third) area are associated with a high rate of recurrence. Tao et al studied the factors responsible for recurrence.²⁶ With multivariate analysis four factors showed significant danger of recurrence of meningiomas: pathological grade, extent of resection, tumor shape, and contrast enhancement. Lefkowitz and colleagues studied the prognostic variables in surgery for skull base meningiomas.² The results of this study suggest that prognostic factors for skull base meningioma recurrence may be unique in part due to their location and propensity to invade the muscle, bone, nerve, and the carotid artery.

Even though various authors have reported the recurrence rates for skull base meningiomas and convexity meningiomas in separate reports, a comparative study measuring difference in tumor

Figure 4 (A) A standard cerebellopontine angle meningioma with good operative technique can be excised completely (B) with a good postoperative outcome and no recurrence.

Figure 5 (A) Convexity meningiomas, especially large tumors encroaching on the parietal lobe, can have a bad postoperative course due to (B) edema and midline shifts.

recurrences and the patient outcomes is distinctly lacking in the literature. Ours is the first study to compare the recurrence and outcome between the two groups operated at a single institute.

In the present report, we observed a recurrence rate of 26.5% in the skull base group and 15% in the non-skull base group. These results are in agreement with the published literature. Furthermore, this difference in recurrence was not statistically significant ($p = 0.07$). With technical advances in microsurgical approaches, total excision of skull base lesions is feasible. Even though total excision of skull base meningiomas is possible, it may not be a

more radical removal equivalent to Simpson's grade I or grade 0 excisions in skull base meningiomas when compared with convexity meningiomas. In our study, there was no statistically significant difference between the recurrences for skull base location or non-skull base location.

Several authors have reported on the reliability of proliferative indices in predicting recurrence-free survivals following apparent complete removal of meningiomas.²⁷⁻²⁹ In the majority of instances, an elevated proliferative index correlated with aggressive histology and/or biologic behavior. Al-Mefty and others reported increasing MIB-1

Figure 6 Large skull base tumors close to vascular structures can be technically demanding and result in postoperative deterioration, especially when near the sylvian fissure.

LI in recurrent meningiomas showing progression to malignant changes.¹¹ Our unpublished data on Ki-67, in a moderate number of patients, showed no relationship between this marker and the location of the tumor.²⁹ Other studies also emphasized the utility of molecular genetic markers, in prediction of recurrence and their relationship with pathological grade to tumor and other variables.^{5,6,30} It might be necessary for us to examine the etiology for recurrences in meningiomas apart from the extent of surgical excision, especially when pathological grades were also not significantly different from others. It is also equally important to observe that skull base location per se does not

significantly increase the recurrence rate (univariate analysis, comparison between the two groups; see Table 1; $p = 0.07$) and had no statistically significant increase in the occurrence of proliferation indices as shown in our previous study on Ki-67.³¹ However, the overall relationship between recurrence and skull base location observed in our complete dataset requires further analysis, with respect to the pathological grade of meningiomas²⁶ and the female gender.³² Both gender and pathology in our data had some association with skull base meningiomas, though not statistically significant. The floating tissue fragments and the residual dural attachment in the skull base²

might also play some role in the recurrence pattern.

Additionally, we did not find any statistically significant difference between the outcomes (GOS) of the two groups. Contrary to expectations, outcome was better in patients operated on for skull base meningiomas compared with the other group (though not statistically significant, Fig. 1). In the entire group of patients the only factor that was associated with poor outcome was increasing age (Fig. 2).

CONCLUSIONS

Contrary to popular belief, skull base meningiomas can be operated upon with good outcome comparable to the convexity meningiomas. Except for increasing age, skull base location per se does not contribute to increased mortality or morbidity for intracranial meningiomas.

ACKNOWLEDGMENTS

The authors would like to thank Dr. Vijayakumar Javalkar and Mrs. Dena Pruett.

This material was presented as an oral presentation at the 2005 North American Skull Base Society Annual Meeting, Toronto, Canada.

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