Editorial

Dural detachment and long-term tumor control in unresectable meningiomas

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This issue of the Journal of Neurosurgery includes a very nice paper by Fukushima and colleagues from the University of Tokyo, analyzing the influence on recurrence of detaching the residual tumor from its dural origin in meningiomas that cannot be completely removed surgically.1 The authors were very careful to analyze a very specific group of patients. They retrospectively studied all cases of Simpson Grade IV resection for WHO Grade I meningiomas operated on at their institution from 1995 to 2010. From this group they excluded patients who were lost to follow-up, patients who had a history of radiation treatment before or soon after surgery, patients who underwent operations for recurrent meningioma, and patients with neurofibromatosis Type 2. This process left them with a relatively homogeneous group of 38 patients with benign meningiomas who had as their first and only treatment an incomplete resection of their tumor. These patients were monitored with MRI every 6 months and the mean follow-up period was 6.1 years. They defined recurrence as retreatment by either radiosurgery or surgery, and the indications for retreatment were either growth of the tumor or progressive symptomatology. They then set out to identify factors that may have influenced the duration of the recurrence-free period. On univariate analysis, they found that postresection tumor volume of 4 cm³ or more, age younger than 50 years, no dural detachment of the residual tumor at the time of surgery, and skull base location were associated with a shorter recurrence-free survival. On multivariate analysis, only skull base location and no dural detachment remained as significant factors associated with a shorter time to retreatment.

I believe that the findings of this careful study are important; however, as with almost any study, there are some limitations, which the authors discuss nicely. The most important ones, of course, are the relatively small number of patients and the retrospective nature of the study. Also, the authors define “recurrence” as retreatment and not necessarily regrowth, which is the more generally accepted modern definition of recurrence when it involves residual tumors. However, all but 2 of the tumors that demonstrated growth by MRI were re-treated and the 2 that were not had only minimal asymptomatic growth, which in the judgment of the authors did not require retreatment. It appears that the assessment of whether the tumor was completely detached from the dura or not was made retrospectively, and the accuracy of this assessment could be questioned. However, the authors assure us that this assessment was made from a careful study of the operative notes, operative videos, and postoperative MR images; therefore, I suspect that it is relatively accurate, with the caveat that it is not always easy on a postoperative MR image to ascertain whether the residual tumor has been completely separated from its dural attachment or not.

There are some counterintuitive findings in this study and there are also some findings that contradict existing literature. Why was the volume of the residual tumor not an independent risk factor for a shorter recurrence-free interval? Although this does appear to be counterintuitive, whether it makes sense or not would depend on how recurrence is defined. Clearly, if recurrence were defined by progression of symptomatology, as it was in the original Simpson article, then it should follow that progressive symptomatology should develop faster in those patients who had a large volume of tumor left.6 In the article by Fukushima et al., recurrence was defined by retreatment, and the indication for retreatment was most commonly tumor growth rather than progressive symptomatology. It is, therefore, not surprising that a small remnant of tumor could show evidence of growth just as quickly as a larger residual tumor. In other words, whether a residual tumor grows or not has more to do with the intrinsic biological properties of that tumor than with its size. In a previous publication by the group at the University of Tokyo,5 for which I was privileged to write an editorial comment,1 it was nicely demonstrated that in benign meningiomas a high MIB-1 labeling index was highly correlated with a shorter time to recurrence, and yet in this article the MIB-1 labeling index was not a significant factor. I suspect that the authors are correct in explaining that the reason for this discrepancy may be that in this particular series there were only 2 meningiomas that had an MIB-1 labeling index of 3% or higher, which was the threshold for a significantly shorter time to recurrence in their previous paper. More difficult to explain is the fact that in this series, skull base location was independently associated with a shorter recurrence-free time. This is surprising because other recent larger patient series have shown that skull base meningiomas tend to grow at a slower pace than...
those in other locations. The only explanation I can find for this discrepancy is that in this relatively small series there were only 7 patients with tumors in locations other than the skull base, and therefore the statistical analysis under these circumstances is not robust.

Finally, what may be the clinical significance of this article? First of all, we should not interpret the fact that residual volume was not an independent risk factor for a shorter time to recurrence as meaning that there is no value in trying to remove as much tumor as can be done safely in cases in which all of the tumor cannot be removed. Larger tumor residuals may not grow any faster than smaller residuals, but the clinical significance of growth when there is a large residual tumor is likely to be very different than when a small residual tumor grows. Frequently, patients with meningiomas are elderly, and if there is only a small residual tumor that shows some asymptomatic growth, it may be perfectly reasonable to continue to observe this tumor and not treat it. On the other hand, with the same rate of growth, a larger residual volume of tumor is more likely to result in progressive symptomatology requiring treatment. Therefore, it continues to be most reasonable to remove all of the tumor that can be removed safely, even if it becomes clear during surgery that not all of the tumor can be removed.

Clearly, the most significant finding from this study, which obviously makes sense but has not been specifically analyzed before, is that even when the preoperative studies indicate that a meningioma could not be removed completely or when the surgeon determines this at surgery, an effort at detaching the tumor from its dural origin and therefore from its predominant blood supply appears to be worthwhile. As the authors discussed, the value of this maneuver must be clearly related to devascularization of the tumor, and they appropriately refer to a recent study from the University of California at San Francisco that showed that preoperative embolization, which results in relative devascularization of the tumor, appears to be correlated with a prolongation of the time to recurrence of meningiomas. The caveat here is that the detachment of the tumor from its dural attachment in many cases in which the tumor cannot be removed completely is either not possible or not safe. One has to suspect that the reason that the current authors did not detach the tumor from the dura in many of these cases was that they believed it was either unsafe or impossible. Obviously, the clinical value of the paper would have been much greater if, under similar circumstances, the authors had decided in some cases to separate the tumor from its dural attachment and not to do so in other cases. Nevertheless, in spite of this caveat, this article emphasizes the fact that efforts at detaching residual tumor from its dural origin, provided that this is safe, are worthwhile. This alone is a very valuable contribution.

We are grateful to our colleagues from the University of Tokyo for another excellent analysis of their experience with meningiomas.

Disclosure

The author reports no conflict of interest.

References


Response

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We greatly appreciate the expert comments from Dr. Heros on our study. Although it is true that some meningiomas cannot be resected completely, even with the best efforts to do so, recent advancements in skull base surgery have resulted in improved rates of meningioma resection with good neurological outcomes. This higher rate of resection combined with timely stereotactic radiosurgery is associated with excellent long-term tumor control, even for meningiomas that are not amenable to gross-total resection.

In an important report from the University of California, San Francisco, the rate of meningioma recurrence treated using Simpson Grade IV resection was almost equivalent to that of meningiomas after Simpson Grade I, II, and III resections. In contrast, our previous study highlighted the persistent difficulty faced by surgeons in the management of meningiomas after Simpson Grade IV resection. Some minor methodological differences between these studies, such as the inclusion criteria regarding cavernous sinus meningiomas and the precise definition of Simpson Grade IV resection, may have influenced the results. Although this discrepancy may re-
sult from the differences in the present study design, we aimed to investigate this disparity in long-term surgical outcomes associated with Simpson Grade IV resection. We rigorously reanalyzed our data on Simpson Grade IV resections to identify any surgical nuances other than resection rate that could be altered to improve the treatment outcome associated with Simpson Grade IV resection. In the study mentioned above, the authors performed preoperative embolization for approximately 30% of the meningioma cases, a much higher percentage than in our series. We were initially skeptical about the effect of preoperative embolization on long-term tumor control because we expected new feeding arteries to develop rapidly in the affected dura, which would attenuate the long-term effect of embolization. However, considering this fundamental difference in the treatment strategy, we came to believe that their aggressive embolization technique might be responsible for the prolonged time of recurrence.

The long-term outcomes among our patients demonstrated the benefits of detaching meningiomas from the dura. The operative records in our department contained not only text but also intraoperative drawings to explain the surgical procedure in a stepwise manner. These resources facilitated our investigation of the relationship between the size of the residual mass and the nature of dural attachment. We agree with Dr. Heros that the process of tumor detachment can carry significant risks. Therefore, the risks associated with aggressive detachment must be weighed carefully during each surgery. However, in our perspective, our result provides collateral evidence to what neurosurgeons have already known on an empirical basis and what they have done instinctively. For example, it is probably not very rare that small, isolated masses of tissue remaining after the resection of benign meningiomas and schwannomas will adhere to the brain stem with no regrowth for years.

This study also has certain limitations. Other than those related to the small sample size and the retrospective nature of our analysis, we did not assess the actual condition of feeding arteries after surgery. However, unfortunately we currently do not have any established method to quantify the remaining vascular supply to tumors. The main outcome measured here was retreatment-free survival (RFS), rather than recurrence-free survival. This decision was made due to the conviction that Simpson Grade IV resection aims primarily to maximize RFS with good functional status. Our use of RFS to evaluate the surgical outcome of Simpson Grade IV meningioma resection may explain the discrepancies raised by Dr. Heros. Although recent reports revealed that skull base meningiomas tend to grow more slowly and exhibit a lower MIB-1 labeling index than those arising at non–skull base locations,1,3,4 the RFS rate among our study population was significantly shorter for skull base as opposed to non–skull base meningiomas. This difference indicates that an increase in the size of the residual mass is not the only factor in determining the timing of further treatment. We cannot deny that we possibly were inclined to intervene more aggressively for skull base meningiomas, because they usually carry higher risks for regrowth after surgery than non–skull base meningiomas, despite retreatment.

A possible alternative view for the shift in focus to functional preservation as well as significant advancements in the field of radiosurgery is that the efforts to maximize the resection rate may have reached a saturation point. However, we believe that the continued analysis of seemingly minor surgical nuances in the Simpson grading system will lead to improved outcomes after meningioma resection.

References

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