Factors affecting post-operative recurrence or growth of meningiomas, other than histological grade and extent of resection

Ayesha Quddusi, Qurat-ul-Ain Virani, Muhammad Shahzad Shamim

Abstract

Meningiomas are one of the commonest primary brain tumours, treated primarily with surgery. These are extra-axial tumours and their post-operative recurrence rates have been extensively studied. The most established predictor of meningioma recurrence is the WHO grade (based on histological features) and the Simpson grade, based on the extent of resection. In this review article, we look into the risk factors other than histological grade and Simpson grade that have been associated with recurrence of meningioma after resection.

Keywords: Meningioma, recurrence, brain tumour, radiotherapy.

Introduction

Meningiomas account for up to 20-30% of all primary brain tumours and are generally considered benign diseases with excellent prognosis if resected completely.[1] Surgery remains the mainstay of treatment although despite complete resection, they still carry a risk of recurrence.[1] The various risk factors influencing recurrence have been extensively studied. Donald Simpson in his landmark 1957 paper published a grading system that used extent of resection as a possible predictor of recurrence. His five grades have been validated through several papers and Simpson grading is now a standard operative observation for neurosurgical teams.[2,3] Herein, we review factors other than histological grade and extent of resection that may influence recurrence or growth of meningiomas after surgery.

Review of Evidence

Ros-Sanjuan et al., looked at atypical meningiomas and reported histological features such as necrosis or high Ki67 index as common features in patients with recurrence.[5] Sumkovski et al., supported this finding and showed that mitotic count is an independent predictor of meningioma recurrence, and tumours with malignant transformation have a worse prognosis compared to de novo highgrade tumours.[6] Kamamoto et al., also showed that CD133 and nestin expression was negatively associated with progression free survival and relapse of tumour.[7] Nakkad et al., investigated clinicopathological characteristics and whether receptor tyrosine kinases (RTKs) are associated with meningioma recurrence. They concluded that Simpson grade IV/V resection, a larger tumour size, location of tumour, a high VEGFR-2 expression level, WHO grade II/III, a high Ki-67 expression level, and the non-expression of progesterone receptor were all identified as significant factors affecting recurrence. Here once again we would like to point out that Nakkad et al., have oversimplified matters by including patients with residual tumours in their analysis of recurrence. However, their data also showed that patients with VEGFR-2 expression had a shorter progression free survival, that lead them to conclude that VEGFR-2 inhibitors might have a potential for molecular target therapy against recurrent meningiomas.[8] Pessina et al., in their study concluded that recurrence rates are influenced by grade, extent of surgical resection, and use of adjuvant RT in case of residual tumours, regardless of meningioma grade.[9]

Barresi et al., reported that high p-mTOR Ser2448 (phosphorylated form of mammalian target of rapamycin) immune-expression is significantly associated with recurrences and with lower disease free survival in patients with atypical meningiomas. Their study suggested that the evaluation of the immunohistochemical expression of p-mTOR Ser2448 should be carried out to identify cases with high risk of recurrence so that they could benefit from adjuvant treatment and low-risk patients are spared from the adverse effects of those treatments.[10]

San-Miguel et al., histopathologically analyzed low grade meningiomas and epigenetic changes that underlie their aggressiveness. The number of hypermethylated tumour suppressor genes per case was significantly higher in recurrences than in primary tumours. Moreover, hypermethylation in RASSF1A, MLH1, and CDKN2B was an independent prognostic factor associated with the time to recurrence of these benign tumours that were biologically aggressive. Furthermore, their study suggests that the occurrence of epigenetic changes in at least one tumour suppressor gene is an early event in meningioma

Department of Surgery, Aga Khan University Hospital, Karachi.
Correspondence: Muhammad Shahzad Shamim.
Email: shahzad.shamim@aku.edu

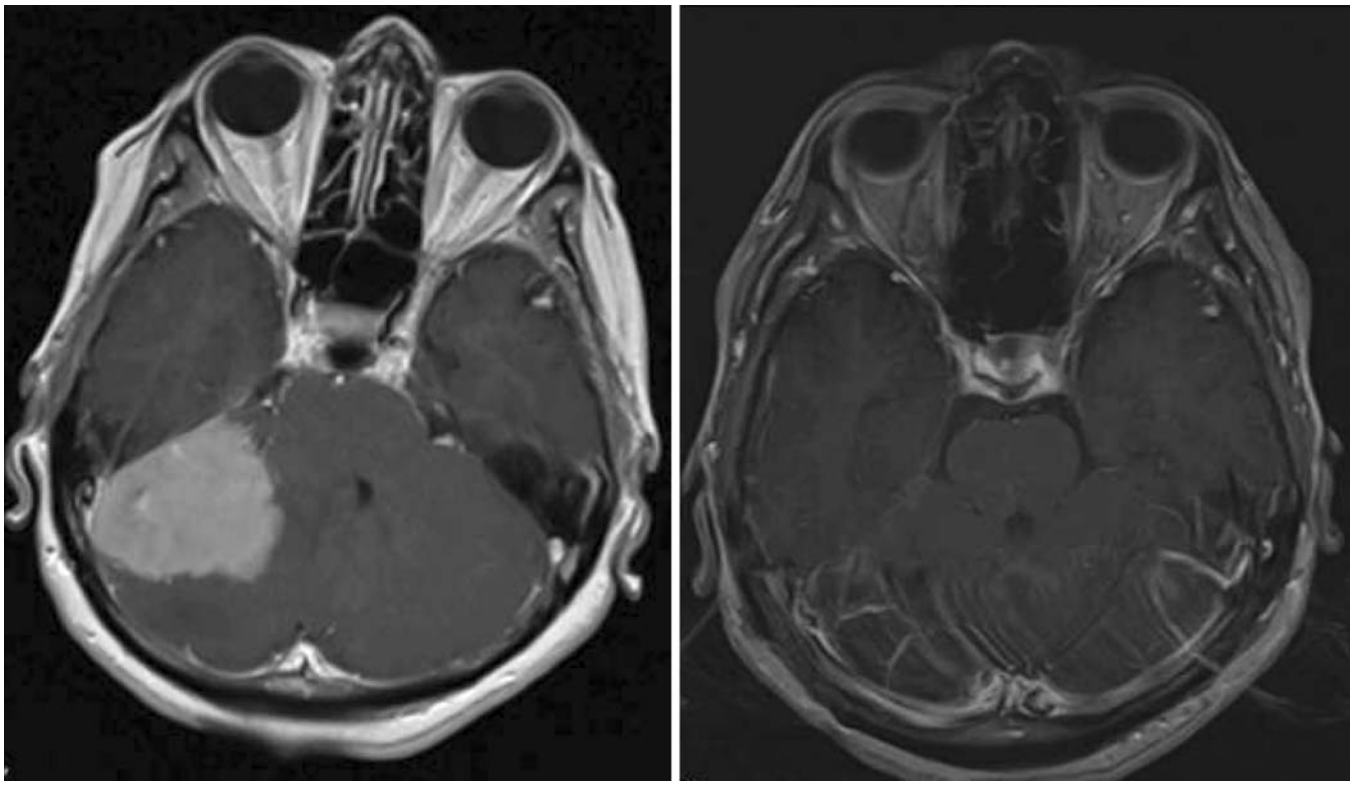

Figure: MRI brain axial post-contrast T1 weighted pre and post-operative images showing complete resection of a grade 1 meningioma arising from the tentorium cerebelli.

tumourigenesis. This suggests the potential clinical value of detecting accumulated epigenetic damage to predict tumour recurrences.[11]

Conclusion

We conclude that in addition to extent of resection and tumour grading, histopathological characteristics particularly molecular and genetic markers are of relevance with association of meningioma recurrence post resection. We believe that these factors may be incorporated in algorithms based on machine learning models and may be used for prognostication, as well as for counseling patients..

References

1. Quddusi A, Shamim MS. Simpson grading as predictor of meningioma recurrence. J Pak Med Assoc 2018; 68:819-821.
2. Simpson D. The recurrence of intracranial meningiomas after surgical treatment. J Neurol Neurosurg Psychiatry.1957; 20:22.
3. Perry A, Stafford SL, Scheithauer BW, et al. Meningioma grading: an analysis of histological parameters. Am J Surgical Pathology. 1997; 21:1455-1466.
4. Jiang Y, Lv L, Li J, Ma W, Chen C, Zhou P, et al. Clinical features, radiological findings, and treatment outcomes of high-grade lateral ventricular meningiomas: a report of 26 cases. Neurosurg Rev. 2019; https://doi.org/10.1007/s10143-019-01078-4.
5. Ros-Sanjuan A, Iglesias-Moroño S, Carrasco-Brenes A, Bautista-Ojeda D, Arraez-Sanchez MA. Atypical Meningiomas: Histologic and Clinical Factors Associated With Recurrence. World Neurosurg. 2019; 1: 56
6. Sumkovski R, Micunovic M, Kocevski I, Ilievski B, Petrov I. Surgical treatment of meningiomas - outcome associated with type of resection, recurrence, Karnofskyperformance score, mitotic count. Open access Maced J Med Sci. 2019; 7:56-64.
7. Kamamoto D, Saga I, Ohara K, Yoshida K, Sasaki H. Association Between CD133, CD44, and Nestin Expression and Prognostic Factors in High-Grade Meningioma. World Neurosurg. 2018; doi: 10.1016/j.wneu.2018.12.067.
8. Nakada S, Sasagawa Y, Tachibana O, Iizuka H, Kurose N, Shioya A, et al. The clinicopathological analysis of receptor tyrosine kinases in meningiomas: the expression of VEGFR-2 in meningioma was associated with a higher WHO grade and shorter progression-free survival.Brain Pathol. 2019; 36:7-13.
9. Pessina F, Navarria P, Clerici E, Soffietti R, Nibali MC, Ruda R, et al. Intracranial meningiomas: a systematic analysis of prognostic factors for recurrence in a large single institution surgical series. World Neurosurg. 2019; 123:e273-e9.
10. Barresi V, Lionti S, La Rocca L, Caliri S, Caffo M. High p-mTOR expression is associated with recurrence and shorter disease-free survival in atypical meningiomas. Neuropathol. 2019; 39:22-9.
11. San-Miguel T, Navarro L, Megias J, Munoz-Hidalgo L, Gil-Benso R, Roldan P, et al. Epigenetic changes underlie the aggressiveness of histologically benign meningiomas that recur. Human Pathol. 2019; 84:105-14.