Acta Neurochirurgica (2019) 161:2551–2552
https://doi.org/10.1007/s00701-019-04102-0

EDITORIAL (BY INVITATION) - TUMOR - MENINGIOMA

'Meningiomics'—an integration of data on the patient, tumour, extent of resection and molecular pathology to optimise the management and follow-up for meningiomas

Michael D. Jenkinson [1,2]

Received: 3 October 2019 / Accepted: 4 October 2019 / Published online: 28 October 2019

Champeaux and colleagues report on the outcomes from a single-institution study of 505 patients with WHO grade I cranial meningiomas who underwent treatment between 2003 and 2017. During the median follow-up period of 6.2 years (IQR, 2.8–9.5), 74 patients had meningioma recurrence or a meningioma-related death, whilst 84 patients died from other causes. The median age at death was 71.7 years (IQR, 59.6–78.6), and eight patients died within 1 month of surgery, and 29 within a year. Twenty-five patients had early recurrence requiring re-operating at a median 1.3 years (IQR, 0.2–2.6) after the first surgery. Eleven patients had progression to grade II or III meningioma. The authors performed a competing risk analysis, which takes into consideration that when death occurs due to other causes (e.g. myocardial infarction), it prevents the observation of the events of interest—namely meningioma recurrence or meningioma-related death. Based on analysis of their data, the absolute risk of WHO grade I meningioma recurrence or death is 16.2% at 5 years and 24.4% at 10 years. As expected, the factors for meningioma-related death or progression were venous sinus invasion, subtotal resection (defined as Simpson grade 4 or 5), and growth of residual tumour. The authors comment that this data can be used to rationalise follow-up and propose that when gross total resection (Simpson grades 1–3) is achieved, imaging surveillance for 3 years for convexity meningioma and 6 years for all other locations is required. When a subtotal resection is performed, then 8 years of imaging follow-up is sufficient if there is no evidence of meningioma progression.

This study highlights several important points when considering the management for patients with grade I meningioma. Firstly, not all grade I meningioma behave in a 'benign' manner and early occurrence and progression can occur. These so-called clinical aggressive meningiomas (CAMs) cannot be readily identified using the current WHO classification; however, DNA methylation [9] and molecular profiling [10] may help to identify them in the future and allow us to predict recurrence risk [6]. This would ensure patients are considered for adjuvant radiotherapy to reduce the risk of recurrence, but until these molecular features are validated in external data sets and become embedded in routine practice, follow-up imaging is still required to monitor for early recurrence.

Secondly, the optimum frequency and duration of imaging follow-up required for meningioma is not defined. The patterns of recurrence in meningioma tend to fall into three categories: early within 2 years of surgery, intermediate between 3 and 10 years, and late 10 years after surgery. Many recent studies report follow-up of approximately 5 years [2] and authors choose a time period to reflect 'modern' neurosurgery. This suggests that studies including patients operated in the 1990s lack validity and this is not the case—after all microneurosurgery was developed in the 1960s and has been in widespread use for meningioma surgery over the last 40 years [4]. Data from studies with 25 years of follow-up show that late meningioma recurrence can occur, especially in patients with subtotal resection [7]. The proposal by Champeaux et al., to discontinue follow-up in subtotal resection of meningioma even when there is no evidence of growth of the residual by 8 years, is not fully supported by their data. In addition, there is limited published literature on the natural history and growth rates of residual meningioma. Recent guidelines from the European Association for Neuro-Oncology advise

This article is part of the Topical Collection on *Tumor - Meningioma*

✉ Michael D. Jenkinson
michael.jenkinson@liverpool.ac.uk

[1] Institute of Translational Medicine, University of Liverpool, L9 7LJ, Liverpool, UK

[2] Department of Neurosurgery, The Walton Centre NHS Foundation Trust, L9 7LJ, Liverpool, UK

continued long-term follow-up with no recommendation to discontinue surveillance due to the late risk of recurrence for all meningiomas [3]. Nevertheless, it should be possible to optimise the frequency of follow-up and annual surveillance MRI is not necessarily required for all meningiomas and all patients. Neurosurgeons should take into consideration the patient's age and comorbidities as these may be competing risks for meningioma recurrence and the need for further treatment, which may make long-term MRI surveillance follow-up futile. Data from the English National Cancer Registry on surgically treated meningioma shows that only 66% of patients aged 70–79 years survive for 5 years, which falls to 49% in patients aged > 80 years [1], and this is particularly relevant since meningiomas are more common with advancing age.

Thirdly, the use of a competing risk analysis is appropriate in meningioma when there is a high risk that the event of interest (meningioma recurrence or meningioma-related death) will not be observed due to the high prevalence of over events, that is, death due to other causes. Indeed, this is the rationale behind current phase III atypical meningioma trials excluding patients with co-existing solid cancers [5] since the event of interest is recurrence.

The current management of meningioma relies on practicing evidence-based medicine, which integrates the best available evidence with individual clinician expertise [8]. Only by improving the evidence-base can we improve outcomes for more patients. The future of meningioma management will include a more personalised approach to treatment and follow-up that integrates data about patient comorbidities, meningioma location and extent of resection, WHO grade and molecular pathology. This so-called meningiomics approach is essential to improve the short-, medium- and long-term outcomes for patients with cranial meningioma.

References

1. Brodbelt AR, Barclay ME, Greenberg D, Williams M, Jenkinson MD, Karabatsou K (2019) The outcome of patients with surgically treated meningioma in England: 1999-2013. A cancer registry data analysis. Br J Neurosurg:1–7. https://doi.org/10.1080/02688697.2019.1661965
2. Gallagher MJ, Jenkinson MD, Brodbelt AR, Mills SJ, Chavredakis E (2016) WHO grade 1 meningioma recurrence: are location and Simpson grade still relevant? Clin Neurol Neurosurg 141:117–121. https://doi.org/10.1016/j.clineuro.2016.01.006
3. Goldbrunner R, Minniti G, Preusser M, Jenkinson MD, Sallabanda K, Houdart E, von Deimling A, Stavrinou P, Lefranc F, Lund-Johansen M, Moyal EC, Brandsma D, Henriksson R, Soffietti R, Weller M (2016) EANO guidelines for the diagnosis and treatment of meningiomas. Lancet Oncol 17:e383–e391. https://doi.org/10.1016/S1470-2045(16)30321-7
4. Hernesniemi J, Niemela M, Dashti R, Karatas A, Kivipelto L, Ishii K, Rinne J, Ronkainen A, Pelaez JG, Koivisto T, Kivisaari R, Shen H, Lehecka M, Frosen J, Piippo A, Avci E, Jaaskelainen JE (2006) Principles of microneurosurgery for safe and fast surgery. Surg Technol Int 15:305–310
5. Jenkinson MD, Javadpour M, Haylock BJ, Young B, Gillard H, Vinten J, Bulbeck H, Das K, Farrell M, Looby S, Hickey H, Preusser M, Mallucci CL, Hughes D, Gamble C, Weber DC (2015) The ROAM/EORTC-1308 trial: radiation versus observation following surgical resection of atypical meningioma: study protocol for a randomised controlled trial. Trials 16:519. https://doi.org/10.1186/s13063-015-1040-3
6. Nassiri F, Mamatjan Y, Suppiah S, Badhiwala JH, Mansouri S, Karimi S, Saarela O, Poisson L, Gepfner-Tuma I, Schittenhelm J, Ng HK, Noushmehr H, Harter P, Baumgarten P, Weller M, Preusser M, Herold-Mende C, Tatagiba M, Tabatabai G, Sahm F, von Deimling A, Zadeh G, Aldape KD, International Consortium on M (2019) DNA methylation profiling to predict recurrence risk in meningioma: development and validation of a nomogram to optimize clinical management. Neuro-oncology. https://doi.org/10.1093/neuonc/noz061
7. Pettersson-Segerlind J, Orrego A, Lonn S, Mathiesen T (2011) Long-term 25-year follow-up of surgically treated parasagittal meningiomas. World Neurosurg 76:564–571. https://doi.org/10.1016/j.wneu.2011.05.015
8. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS (1996) Evidence based medicine: what it is and what it isn't. BMJ 312:71–72. https://doi.org/10.1136/bmj.312.7023.71
9. Sahm F, Schrimpf D, Stichel D, Jones DTW, Hielscher T, Schefzyk S, Okonechnikov K, Koelsche C, Reuss DE, Capper D, Sturm D, Wirsching HG, Berghoff AS, Baumgarten P, Kratz A, Huang K, Wefers AK, Hovestadt V, Sill M, Ellis HP, Kurian KM, Okuducu AF, Jungk C, Drueschler K, Schick M, Bewerunge-Hudler M, Mawrin C, Seiz-Rosenhagen M, Ketter R, Simon M, Westphal M, Lamszus K, Becker A, Koch A, Schittenhelm J, Rushing EJ, Collins VP, Brehmer S, Chavez L, Platten M, Hanggi D, Unterberg A, Paulus W, Wick W, Pfister SM, Mittelbronn M, Preusser M, Herold-Mende C, Weller M, von Deimling A (2017) DNA methylation-based classification and grading system for meningioma: a multicentre, retrospective analysis. Lancet Oncol 18:682–694. https://doi.org/10.1016/S1470-2045(17)30155-9
10. Vasudevan HN, Braunstein SE, Phillips JJ, Pekmezci M, Tomlin BA, Wu A, Reis GF, Magill ST, Zhang J, Feng FY, Nicholaides T, Chang SM, Sneed PK, McDermott MW, Berger MS, Perry A, Raleigh DR (2018) Comprehensive molecular profiling identifies FOXM1 as a key transcription factor for meningioma proliferation. Cell Rep 22:3672–3683. https://doi.org/10.1016/j.celrep.2018.03.013