World Health Organization grade 1 meningioma

Up to 20% of World Health Organization grade 1 meningioma tumors reoccur and currently predictive cancer stem cells (CSCs) markers for aggressive and drug resistant meningiomas are scarce.

Meningioma tissues and primary cell lines were investigated using whole transcriptome microarray analysis, immunofluorescence staining of CSCs markers (including CD133, Sox2, Nestin, and Frizzled 9), and drug treatment with cisplatin or etoposide. RESULTS: Unsupervised hierarchical clustering of six meningioma samples separated tissues into two groups. Analysis identified stem cells related pathways to be differential between the two groups and indicated the de-regulation of the stem cell associated genes Reelin (RELN), Calbindin 1 (CALB1) and Anterior Gradient 2 Homolog (AGR2). Immunofluorescence staining for four tissues confirmed stemness variation in situ. Biological characterization of fifteen meningioma primary cell lines concordantly separated cells into two functionally distinct sub-groups. Pleomorphic cell lines (NG type) grew significantly faster than monomorphic cell lines (G type), had a higher number of cells that express Ki67, and were able to migrate aggressively in vitro. In addition, NG type cell lines had a lower expression of nuclear Caspase-3, and had a significantly higher number of CSCs co-positive for CD133+ Sox2+ or AGR2+ BMI1+. Importantly, these cells were more tolerant to cisplatin and etoposide treatment, showed a lower level of nuclear Caspase-3 in treated cells and harbored drug resistant CSCs.

Collectively, analyses of tissues and primary cell lines revealed stem cell associated genes as potential targets for aggressive and drug resistant meningiomas [1)].

Types

Meningothelial meningioma

Fibrous meningioma (fibroblastic) meningioma

Transitional meningioma (mixed) meningioma

Psammomatous meningioma

Angiomatous meningioma

Microcystic meningioma

Secretory meningioma

Lymphoplasmacyte rich meningioma

Metaplastic meningioma

Case series

2023

Patients diagnosed with World Health Organization grade 1 meningiomas and treated with surgical resection with subsequent recurrence were reviewed. Patient demographics, clinical outcomes, and radiographic characteristics were collected. Radiological images were analyzed to determine the location of recurrence relative to the initial tumor. Ong et al. characterized meningioma recurrence as type A (within the surgical bed), type B (outside of the surgical bed, within 1 cm from the site), and type C (distal ≥ 1 cm of the resection site).

Forty-two cases met the inclusion criteria. Twelve patients (29%) were male, and 30 (71%) were female. Median age at first treatment was 47 years, with 5.2 ± 3.4 years until recurrence. Recurrence rate was 54.7% at 5 years and 90.4% at 10 years. Twenty-eight patients (66.7%) had a type A recurrence, 11 (26.1%) had a type B recurrence, and 3 (7.1%) had a type C recurrence.

The series demonstrates that while lesions often recur within the original lesion site, a significant portion recurs beyond the surgical bed. This highlights the substantial possibility of recurrence outside the resection cavity for fully excised benign meningiomas, which may aid in understanding disease progression and in guiding adjuvant therapy [2)].

2016

A study aims to assess if the recurrence rates and recurrence-free survivals (RFS) are different after Simpson grading system I, II, and III resections in World Health Organization (WHO) grade I meningiomas

Otero-Rodriguez et al., retrospectively reviewed the data of patients who underwent surgical treatment of WHO grade I convexity meningiomas (group 1), falx meningioma/parasagittal meningioma(group 2), skull base, and tentorial meningioma (group 3) between June 1991 and December 2011. They compared the recurrence rates and RFSs between Simpson grades I, II, and III resections both overall cases and tumour subsets according to their localization.

224 meningiomas were included in this study. There were not significant differences in recurrence rates and RFSs between Simpson grades I, II, and III. In each of the location groups, no significant differences were noted between the different degrees of Simpson.

They have shown that complete resection of WHO grade I meningiomas achieves an excellent tumour control, regardless of Simpson grades. More aggressive attempts of tumour resection (i.e. Simpson grade I) must be balanced against the risks of removing dura or damaging critical neurovascular structures [3)]

Nanda et al., reviewed their experience in resecting WHO Grade I meningiomas and assessed the association between extent of resection, as evaluated using the Simpson classification, and recurrence-free survival (RFS) of patients after meningioma surgery.

Clinical and radiological information for patients with WHO Grade I meningiomas who had undergone resective surgery over the past 20 years was retrospectively reviewed. Simpson and Shinshu grading

scales were used to evaluate the extent of resection.

Statistical analysis was conducted using Kaplan-Meier curves and Cox proportional-hazards regression.

Four hundred fifty-eight patients were eligible for analysis. Overall tumor recurrence rates for Simpson resection Grades I, II, III, and IV were 5%, 22%, 31%, and 35%, respectively. After Cox regression analysis, Simpson Grade I (extensive resection) was revealed as a significant predictor of RFS ($p = 0.003$). Patients undergoing Simpson Grade I and II resections showed significant improvement in RFS compared with patients undergoing Grade III and IV resections ($p = 0.005$). Extent of resection had a significant effect on recurrence rates for both skull base ($p = 0.047$) and convexity ($p = 0.012$) meningiomas. Female sex and a Karnofsky Performance Scale score > 70 were also identified as independent predictors of RFS after resection of WHO Grade I meningioma.

In this patient cohort, a significant association was noted between extent of resection and rates of tumor recurrence. In the authors' experience the Simpson grading system maintains its relevance and prognostic value and can serve an important role for patient education. Even though complete tumor resection is the goal, surgery should be tailored to each patient according to the risks and surgical morbidity [4].

2012

A total of 240 patients harboring 248 benign meningiomas were included in this study. Simpson Grade IV resection was associated with a significantly shorter RFS than Simpson Grade I, II, or III resection ($p<0.001$), while no statistically significant difference was noted in RFS between Simpson Grades I, II, and III. Among meningiomas treated by Simpson Grade II and III resections, however, multivariate analysis revealed that an MIB-1 index of 3% or higher was associated with a significantly shorter time to recurrence.

The clinical significance of the different management strategies related to Simpson Grade I-III resection may have been diluted in the modern surgical era. The MIB-1 index can differentiate tumors with a high risk of recurrence, which could be beneficial for planning tailored optimal follow-up strategies. The results of this study appear to provide a significant backing for the recent shift in meningioma surgery from attempting aggressive resection to valuing the quality of the patient's life [5].

2010

Sughrue et al., evaluated all patients undergoing craniotomy for resection of a histologically proven WHO Grade I meningioma as their initial therapy. Clinical information was retrospectively reconstructed using patient medical records and radiological data. Recurrence analysis was performed using the Kaplan-Meier method.

The 5-year recurrence/progression-free survival for all patients receiving a Simpson Grade I, II, III, or IV resection was 95, 85, 88, and 81%, respectively (p = not significant, log-rank test). Kaplan-Meier analysis revealed no significant difference in recurrence-free survival between patients receiving a Simpson Grade I, II, III, or IV resection. Analysis limited to meningiomas arising from the skull base (excluding the cavernous sinus) similarly found no significant benefit to Simpson Grade I or II resection, and the survival curves were nearly superimposed.

In this study of a cohort of patients undergoing surgery for WHO Grade I meningiomas, the authors demonstrate that the benefit of more aggressive attempts to resect the tumor with dura and underlying bone was negligible compared with simply removing the entire tumor, or even leaving small amounts of tumor attached to critical structures. The authors believe that these data reflect an evolution in the nature of meningioma surgery over the past 2 decades, and bring into question the relevance of using Simpson's grading system as the sole predictor of recurrence [6].

1)

Khan I, Baeesa S, Bangash M, Schulten HJ, Alghamdi F, Qashqari H, Madkhali N, Carracedo A, Saka M, Jamal A, Al-Maghrabi J, AlQahtani M, Al-Karim S, Damanhouri G, Saini K, Chaudhary A, Abuzenadah A, Hussein D. Pleomorphism and drug resistant cancer stem cells are characteristic of aggressive primary meningioma cell lines. Cancer Cell Int. 2017 Jul 21;17:72. doi: 10.1186/s12935-017-0441-7. eCollection 2017. PubMed PMID: 28736504; PubMed Central PMCID: PMC5521079.

2)

Ong K, Rizzuto M, Makarenko S. Location pattern of recurrence of fully resected grade 1 meningiomas. Acta Neurochir (Wien). 2023 Aug 24. doi: 10.1007/s00701-023-05758-5. Epub ahead of print. PMID: 37620597.

3)

Otero-Rodriguez A, Tabernero MD, Munoz-Martin MC, Sousa P, Orfao A, Pascual-Argente D, Gonzalez-Tablas M, Ruiz-Martin L. Re-evaluating Simpson grades I, II, and III resections in neurosurgical treatment of World Health Organization grade I meningiomas. World Neurosurg. 2016 Sep 13. pii: S1878-8750(16)30820-8. doi: 10.1016/j.wneu.2016.09.007. [Epub ahead of print] PubMed PMID: 27637164.

4)

Nanda A, Bir SC, Maiti TK, Konar SK, Missios S, Guthikonda B. Relevance of Simpson grading system and recurrence-free survival after surgery for World Health Organization Grade I meningioma. J Neurosurg. 2016 Apr 8:1-11. [Epub ahead of print] PubMed PMID: 27058201.

5)

Oya S, Kawai K, Nakatomi H, Saito N. Significance of Simpson grading system in modern meningioma surgery: integration of the grade with MIB-1 labeling index as a key to predict the recurrence of WHO Grade I meningiomas. J Neurosurg. 2012 Jul;117(1):121-8. doi: 10.3171/2012.3.JNS111945. Epub 2012 May 4. Erratum in: J Neurosurg. 2012 Oct;117(4):806. PubMed PMID: 22559847.

6)

Sughrue ME, Kane AJ, Shangari G, Rutkowski MJ, McDermott MW, Berger MS, Parsa AT. The relevance of Simpson Grade I and II resection in modern neurosurgical treatment of World Health Organization Grade I meningiomas. J Neurosurg. 2010 Nov;113(5):1029-35. doi: 10.3171/2010.3.JNS091971. Epub 2010 Apr 9. PubMed PMID: 20380529.