D J Med Sci 2026;12(2):91-97
doi: 10.5606/fng.btd.2026.241

Original Article

Evaluation of matrix metalloproteinase-1 expression in meningiomas and its relationship with Ki-67 proliferation index and recurrence

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ABSTRACT

Objectives: This study aimed to evaluate the relationship between matrix metalloproteinase-1 (MMP-1) expression and histopathological features, Ki-67 proliferation index, and recurrence in meningiomas.

Materials and methods: This retrospective study included 49 patients who underwent surgery for meningioma between January 2003 and December 2006. Archived pathological specimens were re-evaluated for histopathological subtype, World Health Organization (WHO) grade, Ki-67 staining level, and MMP-1 staining characteristics. Age, sex, extent of resection, and recurrence data were obtained from clinical records. Statistical analyses were performed using Student's t-test, chi-square test, Mann-Whitney U test, and Spearman correlation analysis, as appropriate.

Results: Forty-nine meningioma cases (16 males, 33 females; mean age: 59.02 ± 13.96 years; range: 11 to 82 years) met the inclusion criteria. Recurrence was observed in nine of 49 cases (18.4%). Patients with recurrence were significantly younger than those without recurrence (49.67 ± 6.45 *vs.* 61.17 ± 11.68 years, $p = 0.024$). Recurrence was significantly more frequent in WHO Grade 2 tumors than in Grade 1 tumors ($p = 0.026$). Subtotal resection was associated with a significantly higher recurrence rate compared with total resection ($p = 0.002$). Ki-67 level was significantly higher in recurrent cases than in non-recurrent cases (11.05 ± 12.94 *vs.* 3.75 ± 5.31, $p = 0.010$). However, no significant relationship was found between recurrence and MMP-1 staining extent, staining intensity, or staining level. There was also no significant correlation between MMP-1 staining level and Ki-67 proliferation index (rho = −0.166, $p = 0.261$).

Conclusion: In this series, MMP-1 expression was not associated with recurrence or proliferative activity in meningiomas. In contrast, Ki-67 level, histological grade, and extent of resection were more meaningful predictors of recurrence. Matrix metalloproteinase-1 alone does not appear to be a reliable biomarker for predicting the biological behavior of meningiomas.

Keywords: Immunohistochemistry, Ki-67, matrix metalloproteinase-1, meningioma, MMP-1.

Meningiomas are among the most common primary central nervous system tumors in adults. Although most meningiomas show benign biological behavior, a subset demonstrates unexpectedly aggressive behavior and recurrence.[1] In recent years, prognostic evaluation of meningiomas has increasingly incorporated molecular features in addition to conventional histopathology.[2-5] Nevertheless, histological grade, extent of resection, and proliferation markers remain central in routine clinical practice.[6-12]

Ki-67 is one of the most widely used markers of proliferative activity in meningiomas, and both classical and recent studies continue to support its association with recurrence risk.[6-9,13-15] In addition, the tumor microenvironment, extracellular matrix remodeling, and invasion-related mechanisms have attracted growing interest in meningioma biology. Matrix metalloproteinases (MMPs) are proteolytic enzymes involved in extracellular matrix

Received: May 23, 2026
Accepted: July 16, 2026
Published online: August 25, 2026

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Cite this article as:
Bölükbaşı FH, Sarı R, Ayan E, Uyar Bozkurt S, Elmaci İ. Evaluation of matrix metalloproteinase-1 expression in meningiomas and its relationship with Ki-67 proliferation index and recurrence. D J Med Sci 2026;12(2):91-97. doi: 10.5606/fng.btd.2026.241.

degradation and remodeling and have been associated with invasion, angiogenesis, and tumor progression in several neoplasms.[16-21]

Among MMPs, MMP-1 (interstitial collagenase, or collagenase-1) is a secreted zinc-dependent endopeptidase that cleaves fibrillar collagens types I, II, and III at a specific site within the triple-helical domain.[18] This enzymatic activity initiates the breakdown of the interstitial collagen network, a rate-limiting step in extracellular matrix remodeling.[16] In several solid tumors, MMP-1 overexpression has been associated with stromal degradation, local invasion, and unfavorable prognosis.[17,19] Although other MMP family members, including MMP-2, MMP-3, and MMP-9, have been investigated in meningiomas with variable results,[20-24] direct evidence regarding MMP-1 expression in meningiomas and its relationship to recurrence or proliferative activity remains scarce.

The role of MMP-1 in meningioma biology, however, remains unclear. Although studies have addressed invasion biology and members of the MMP family, consistent evidence supporting the independent prognostic value of MMP-1 in meningiomas is limited.[17-21] Therefore, this study aimed to evaluate the relationship between MMP-1 expression and histopathological features, Ki-67 proliferation index, and recurrence in meningiomas.

MATERIALS AND METHODS

Study design and patient population

This retrospective study was conducted at Göztepe Training and Research Hospital, Department of Neurosurgery between January 2003 and December 2006. Formal ethics committee approval was not obtained because the study was conducted using retrospective archival data collected during routine clinical practice, and no additional patient contact or data collection was performed for this study. The study was conducted in accordance with the principles of the Declaration of Helsinki. Archived pathological specimens were re-evaluated for histopathological subtype, World Health Organization (WHO) grade, Ki-67 staining level, and MMP-1 expression characteristics. Age, sex, extent of resection, and recurrence data were obtained from clinical records.

Histopathological and immunohistochemical evaluation

All cases were reviewed histopathologically. Tumors were classified according to histopathological subtype and WHO grade. Immunohistochemical staining for MMP-1 and Ki-67 was evaluated. For MMP-1, staining extent and staining intensity were assessed. The Ki-67 proliferation index was recorded as a percentage of staining.

The MMP-1 immunohistochemical expression was evaluated semi-quantitatively according to staining intensity and staining extent. Staining intensity was classified as weak (1+), moderate (2+), or strong (3+) based on the chromogen signal observed in tumor cells. Staining extent was categorized as < 30%, 30-60%, or > 60% according to the percentage of positively stained tumor cells. In addition, the percentage of MMP-1-positive tumor cells (staining level) was recorded for statistical analyses. The Ki-67 proliferation index was determined as the percentage of positively stained tumor cell nuclei in representative high-power fields. All immunohistochemical evaluations were performed by an experienced neuropathologist.

Statistical analysis

Statistical analyses were performed using NCSS (Number Cruncher Statistical System) 2007 and PASS 2008 Statistical Software (NCSS, LLC, Kaysville, UT, USA). Student's t-test, chi-square test, Mann-Whitney U test, and Spearman correlation analysis were used, as appropriate. A p-value < 0.05 was considered statistically significant.

Time-to-event analyses such as Kaplan-Meier estimation and Cox proportional hazards regression were not performed in the present study. The limited number of recurrence events (n = 9) precluded reliable multivariable survival modeling, as stable parameter estimation generally requires a minimum of approximately 10 events per variable. Given these constraints, the present analysis was restricted to univariate comparisons between recurrence groups. Future studies with larger cohorts and sufficient event counts would be needed to evaluate independent prognostic

contributions through multivariable time-to-event models.

RESULTS

A total of 49 meningioma cases (16 males, 33 females; mean age: 59.02 ± 13.96 years; range: 11 to 82 years) were included in the study. Recurrence was observed in nine patients (18.4%), whereas 40 patients (81.6%) had no recurrence. The mean age was significantly lower in the recurrence group than in the non-recurrence group (49.67 ± 6.45 *vs.* 61.17 ± 11.68 years, $p = 0.024$). No significant association was found between sex and recurrence ($p = 0.105$). WHO grade was significantly associated with recurrence, with Grade 2 tumors showing a higher recurrence rate than Grade 1 tumors ($p = 0.026$). Extent of resection was also significantly associated with recurrence, and subtotal resection was associated with a higher recurrence rate than total resection ($p = 0.002$). The baseline clinicopathological characteristics of the study population are summarized in Table 1.

Recurrence-related variables are shown in Table 2. Grade 2 tumors and subtotal resections were more frequent in the recurrence group. No statistically significant difference was found between recurrence groups with respect to MMP-1 staining extent or intensity.

No statistically significant difference was found in MMP-1 staining level between recurrent

Table 1. Baseline clinicopathological characteristics of the study population (n = 49)

Variables	n	%	Mean ± SD	*p*
Recurrence	9	18.4		
No recurrence	40	81.6		
Age in no recurrence group (year)			61.17 ± 11.68	
Age in recurrence group (year)			49.67 ± 6.45	
Sex-recurrence association				0.105
WHO grade-recurrence association				0.026
Extent of resection-recurrence association				0.002

SD, standard deviation; WHO, World Health Organization.

Table 2. Comparison of recurrence-related variables

	No recurrence			Recurrence			
Variables	n	%	Mean ± SD	n	%	Mean ± SD	*p*
Age (years)			61.17 ± 11.68			49.67 ± 6.45	0.024
WHO Grade 1	39	97.5		7	77.8		0.026
WHO Grade 2	1	2.5		2	22.2		
Total resection	39	97.5		6	66.7		0.002
Subtotal resection	1	2.5		3	33.3		
MMP-1 extent: weak	11	28.2		3	33.3		0.649
MMP-1 extent: moderate	13	33.3		4	44.4		
MMP-1 extent: strong	15	38.5		2	22.2		
MMP-1 intensity: < 30%	11	28.2		1	11.1		0.418
MMP-1 intensity: 30-60%	18	46.2		4	44.4		
MMP-1 intensity: > 60%	10	25.6		4	44.4		

SD, standard deviation; WHO, World Health Organization; MMP-1, matrix metalloproteinase-1.

Table 3. Relationship between MMP-1 staining level and Ki-67 proliferation index

Parameters	Mean ± SD	Median	*p*
MMP-1 staining level in no recurrence group (%)	47.7 ± 21.7	50	
MMP-1 staining level in recurrence group (%)	44.4 ± 22.8	50	
MMP-1 staining level			0.697
Ki-67 level in no recurrence group (%)	3.75 ± 5.31	2.45	
Ki-67 level in recurrence group (%)	11.05 ± 12.94	5.5	
Ki-67			0.010
Spearman rho for MMP-1 *vs.* Ki-67			–0.166
Correlation			0.261

MMP-1, matrix metalloproteinase-1; SD, standard deviation.

and non-recurrent tumors (p = 0.697). In contrast, Ki-67 staining level was significantly higher in recurrent cases than in non-recurrent cases (11.05 ± 12.94 *vs.* 3.75 ± 5.31, p = 0.010). Moreover, no significant correlation was found between MMP-1 staining level and Ki-67 proliferation index (rho = –0.166, p = 0.261). These findings are summarized in Table 3.

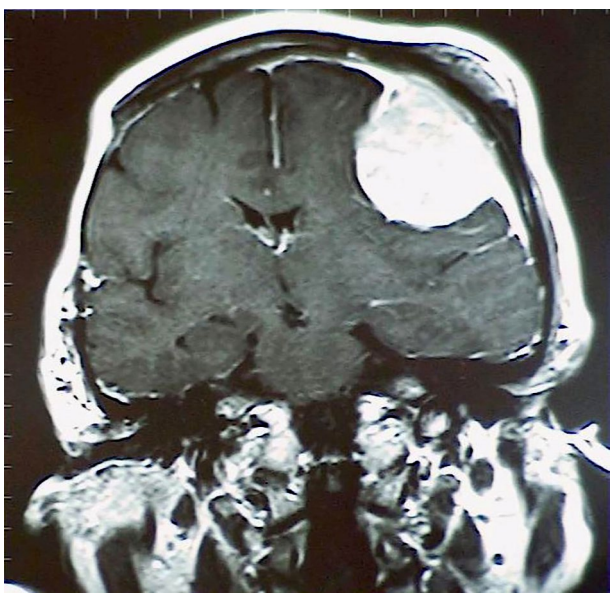

Figure 1. Preoperative magnetic resonance imaging findings of a representative transitional meningioma case. Axial and coronal contrast-enhanced T1-weighted magnetic resonance images obtained from a 61-year-old female patient demonstrating a well-circumscribed extra-axial mass compatible with transitional meningioma. The lesion shows homogeneous contrast enhancement and dural attachment. Surgical resection was subsequently performed, and histopathological examination confirmed the diagnosis of transitional meningioma.

Representative radiological and histopathological findings from a 61-year-old female patient with transitional meningioma are shown in Figures 1-3.

DISCUSSION

In the present study, MMP-1 expression was not significantly associated with recurrence or proliferative activity in meningiomas. Neither MMP-1 staining extent, nor staining intensity, nor staining level differed significantly between recurrent and non-recurrent tumors. In contrast, recurrence was more closely associated with higher histological grade, subtotal resection, and higher Ki-67 levels. These findings suggest that,

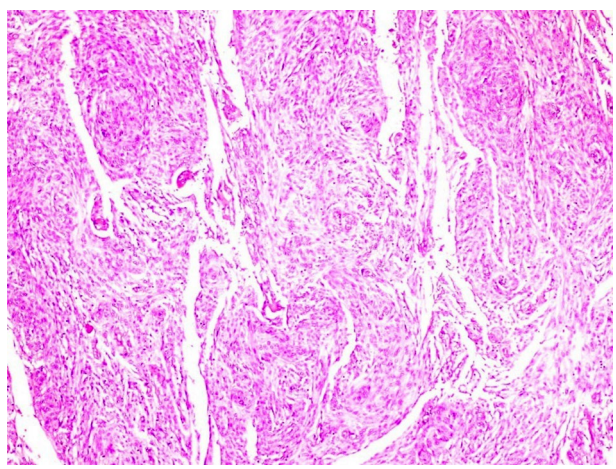

Figure 2. Histopathological features of transitional meningioma. Hematoxylin and eosin staining demonstrating characteristic histological findings of transitional meningioma, including meningothelial whorls and fascicular spindle-cell areas (H&E, ×100).

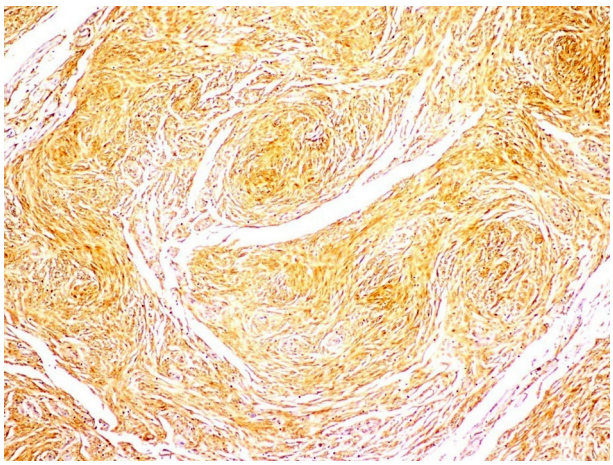

Figure 3. Immunohistochemical staining (IHC) for MMP-1 and Ki-67 in transitional meningioma. Representative immunohistochemical staining demonstrating MMP-1 expression within tumor cells and assessment of Ki-67 proliferative activity. MMP-1 staining intensity and distribution were evaluated semi-quantitatively. The Ki-67 labeling index was calculated as the percentage of positively stained tumor nuclei (IHC, ×200).
MMP-1, matrix metalloproteinase-1.

in this series, clinically established prognostic indicators remained more informative than MMP-1.

From a biological standpoint, MMP-1 contributes to extracellular matrix turnover through cleavage of fibrillar collagens, a process implicated in stromal remodeling, dural invasion, and tumor progression in various neoplasms.[16-18] In meningiomas, dural invasion involves degradation of the collagen-rich dural matrix, and MMPs have been proposed as mediators of this process.[21] However, whether MMP-1 specifically participates in meningioma invasion, independent of other collagenases and gelatinases, has not been convincingly demonstrated. The absence of a significant association between MMP-1 expression and recurrence in the present cohort raises the possibility that MMP-1 does not play a dominant role in meningioma progression, or that its contribution is masked by the stronger effects of histological grade and extent of resection.

Recent meningioma literature has shifted toward integrated prognostic assessment combining histopathology with molecular risk parameters. The 2021 WHO classification emphasized the growing role of molecular data, and subsequent updates further clarified the importance of alterations such as telomerase reverse transcriptase (TERT) promoter mutation and CDKN2A/B homozygous deletion in meningioma grading and risk stratification.[2-4] Earlier molecular work had already suggested that biological behavior in meningiomas cannot be fully explained by conventional morphology alone.[5]

The evolving molecular landscape of meningiomas now encompasses DNA methylation-based classification, which has demonstrated prognostic value independent of WHO grade.[25] Methylation profiling can stratify meningiomas into biologically distinct subgroups with differing recurrence risks, and the integration of molecular markers such as TERT promoter mutation, CDKN2A/B homozygous deletion, and methylation class is increasingly recommended for comprehensive risk assessment.[3,4,25] The present study, which relied exclusively on conventional histopathology and immunohistochemistry, did not incorporate these molecular parameters. While this reflects the clinical reality of many pathology laboratories where advanced molecular testing is not routinely available, the absence of molecular data limits the ability to contextualize MMP-1 expression within the current molecular classification framework.

Among conventional biomarkers, Ki-67 still retains substantial practical value. Classical studies showed that Ki-67/MIB-1 labeling indices are associated with proliferative potential and recurrence in meningiomas.[6-9] Likewise, recurrence after meningioma surgery has long been linked to the extent of resection, beginning with Simpson's original description and later recurrence analyses.[10-12] More recent studies also support the continued value of Ki-67, particularly when interpreted together with WHO grade and extent of resection rather than as an isolated variable.[13-15]

Our data are consistent with this line of evidence. In the present series, recurrent tumors had significantly higher Ki-67 indices, supporting the continued usefulness of Ki-67 as a marker of proliferative potential. Likewise, the strong association between subtotal

resection and recurrence is fully compatible with both classical and current meningioma literature.[10-12,13-15]

The negative findings for MMP-1 in the present study can be considered in the context of prior investigations of other MMP family members in meningiomas. The MMP-2 and MMP-9, both gelatinases, have been more extensively studied, and some reports have associated their expression with higher tumor grade, brain invasion, or recurrence.[22,23] The MMP-3 (stromelysin-1) expression was reported to correlate with aggressive histological features by Perret et al.[20] In contrast, MMP-1, as a fibrillar collagenase, acts on a different substrate spectrum and may not share the same prognostic associations. The discrepancy between MMP-1 and other MMP family members in meningioma may reflect differences in substrate specificity, cellular sources of expression (tumor cells versus stromal or inflammatory cells), or the relative contribution of each enzyme to the invasion cascade in the meningeal microenvironment.

Several limitations of this study should be acknowledged. First, the retrospective, single-center design limits generalizability and introduces potential selection bias. Second, the sample size (n = 49) and the number of recurrence events (n = 9) are relatively small, which reduces statistical power and precludes reliable multivariable modeling. The low event count also prevented the use of time-to-event analyses such as Kaplan-Meier estimation or Cox regression. Third, molecular markers that are now recognized as important prognostic determinants in meningiomas, including TERT promoter mutation status, CDKN2A/B deletion, and DNA methylation class, were not assessed. Their absence limits the interpretation of MMP-1 findings within the current molecular classification framework. Fourth, immunohistochemical evaluation was performed by a single pathologist, and formal interobserver reliability testing was not conducted. Finally, detailed clinical information such as symptom duration, preoperative embolization status, and adjuvant radiotherapy use was not systematically available, which may have influenced recurrence patterns.

Detailed follow-up duration data were not uniformly available in the archival records; therefore, median and range follow-up times could not be reliably calculated, and time-to-event analyses were not feasible.

In conclusion, despite this limitation, the present study demonstrated significant associations between recurrence and age, extent of resection, WHO grade, and Ki-67 expression, whereas MMP-1 expression was not significantly associated with recurrence or Ki-67 expression.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: F.H.B., İ.E.: Conceptualization; F.H.B., S.U.B., İ.E.: Methodology; F.H.B., R.S., E.A.: Investigation; S.U.B.: Pathological and immunohistochemical evaluation; F.H.B., R.S., E.A.: Data curation; F.H.B.: Formal analysis, writing-original draft preparation; R.S., E.A., S.U.B., İ.E.: Writing-review and editing; İ.E.: Supervision and project oversight. All authors have read and approved the final version of the manuscript.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

AI Disclosure: The authors declare that artificial intelligence (AI) tools were not used, or were used solely for language editing, and had no role in data analysis, interpretation, or the formulation of conclusions. All scientific content, data interpretation, and conclusions are the sole responsibility of the authors. The authors further confirm that AI tools were not used to generate, fabricate, or 'hallucinate' references, and that all references have been carefully verified for accuracy.

REFERENCES

1. Wang JZ, Landry AP, Raleigh DR, Sahm F, Walsh KM, Goldbrunner R, et al. Meningioma: International Consortium on Meningiomas consensus review on scientific advances and treatment paradigms for clinicians, researchers, and patients. Neuro Oncol 2024;26:1742-80. doi: 10.1093/neuonc/noae082.
2. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, et al. The 2021 WHO Classification of Tumors of the Central Nervous

System: A summary. Neuro Oncol 2021;23:1231-51. doi: 10.1093/neuonc/noab106.
3. Sahm F, Aldape KD, Brastianos PK, Brat DJ, Dahiya S, von Deimling A, et al. cIMPACT-NOW update 8: Clarifications on molecular risk parameters and recommendations for WHO grading of meningiomas. Neuro Oncol 2025;27:319-30. doi: 10.1093/neuonc/noae170.
4. Dwianingsih EK, Krisnugraha YP, Bawono RG, Malueka RG. Molecular biomarkers in meningioma (Review). Biomed Rep 2025;22:56. doi: 10.3892/br.2025.1934.
5. Perry A, Gutmann DH, Reifenberger G. Molecular pathogenesis of meningiomas. J Neurooncol 2004;70:183-202. doi: 10.1007/s11060-004-2749-0.
6. Roggendorf W, Schuster T, Peiffer J. Proliferative potential of meningiomas determined with the monoclonal antibody Ki-67. Acta Neuropathol 1987;73:361-4. doi: 10.1007/BF00688260.
7. Ohta M, Iwaki T, Kitamoto T, Takeshita I, Tateishi J, Fukui M. MIB1 staining index and scoring of histologic features in meningioma. Indicators for the prediction of biologic potential and postoperative management. Cancer 1994;74:3176-89. doi: 10.1002/1097-0142(19941215)74:12<3176::aid-cncr2820741217>3.0.co;2-n.
8. Matsuno A, Fujimaki T, Sasaki T, Nagashima T, Ide T, Asai A, et al. Clinical and histopathological analysis of proliferative potentials of recurrent and non-recurrent meningiomas. Acta Neuropathol 1996;91:504-10. doi: 10.1007/s004010050458.
9. Nakasu S, Li DH, Okabe H, Nakajima M, Matsuda M. Significance of MIB-1 staining indices in meningiomas: Comparison of two counting methods. Am J Surg Pathol 2001;25:472-8. doi: 10.1097/00000478-200104000-00006.
10. Simpson D. The recurrence of intracranial meningiomas after surgical treatment. J Neurol Neurosurg Psychiatry 1957;20:22-39. doi: 10.1136/jnnp.20.1.22.
11. Christensen D, Laursen H, Klinken L. Prediction of recurrence in meningiomas after surgical treatment. A quantitative approach. Acta Neuropathol 1983;61:130-4. doi: 10.1007/BF00697392.
12. Jääskeläinen J. Seemingly complete removal of histologically benign intracranial meningioma: Late recurrence rate and factors predicting recurrence in 657 patients. A multivariate analysis. Surg Neurol 1986;26:461-9. doi: 10.1016/0090-3019(86)90259-4.
13. Thirunavu V, Drumm M, McCord M, Steffens A, Youngblood MW, Nandoliya KR, et al. Optimizing the use of Ki-67 proliferative index as a prognostic biomarker in meningiomas using digital analysis. J Neurosurg 2024;141:1644-54. doi: 10.3171/2024.4.JNS232857.
14. Mizrachi M, Hartley B, Saleem S, Hintz E, Ziemba Y, Li J, et al. Ki-67 index as a predictive marker of meningioma recurrence following surgical resection. J Clin Neurosci 2024;124:15-19. doi: 10.1016/j.jocn.2024.04.015.
15. Mirian C, Jensen LR, Juratli TA, Maier AD, Broechner A, Torp SH, et al. The Ki-67 proliferation index and recurrence risk of intracranial meningioma: A multicenter, retrospective cohort study of 5,050 patients. Acta Neurochir (Wien) 2026;168:124. doi: 10.1007/s00701-026-06846-y.
16. Egeblad M, Werb Z. New functions for the matrix metalloproteinases in cancer progression. Nat Rev Cancer 2002;2:161-74. doi: 10.1038/nrc745.
17. Vihinen P, Kähäri VM. Matrix metalloproteinases in cancer: Prognostic markers and therapeutic targets. Int J Cancer 2002;99:157-66. doi: 10.1002/ijc.10329.
18. Goldberg GI, Wilhelm SM, Kronberger A, Bauer EA, Grant GA, Eisen AZ. Human fibroblast collagenase. Complete primary structure and homology to an oncogene transformation-induced rat protein. J Biol Chem 1986;261:6600-5.
19. Zhu Y, Spitz MR, Lei L, Mills GB, Wu X. A single nucleotide polymorphism in the matrix metalloproteinase-1 promoter enhances lung cancer susceptibility. Cancer Res 2001;61:7825-9.
20. Perret AG, Duthel R, Fotso MJ, Brunon J, Mosnier JF. Stromelysin-3 is expressed by aggressive meningiomas. Cancer 2002;94:765-72. doi: 10.1002/cncr.10270.
21. Wang JZ, Landry AP, Raleigh DR, Sahm F, Walsh KM, Goldbrunner R, et al. Meningioma: International Consortium on Meningiomas consensus review on scientific advances and treatment paradigms for clinicians, researchers, and patients. Neuro Oncol 2024;26:1742-80. doi: 10.1093/neuonc/noae082.
22. Okada M, Miyake K, Matsumoto Y, Kawai N, Kunishio K, Nagao S. Matrix metalloproteinase-2 and matrix metalloproteinase-9 expressions correlate with the recurrence of intracranial meningiomas. J Neurooncol 2004;66:29-37. doi: 10.1023/b:neon.0000013474.01161.58.
23. Panagopoulos AT, Lancellotti CL, Veiga JC, de Aguiar PH, Colquhoun A. Expression of cell adhesion proteins and proteins related to angiogenesis and fatty acid metabolism in benign, atypical, and anaplastic meningiomas. J Neurooncol 2008;89:73-87. doi: 10.1007/s11060-008-9588-3.
24. Okeda R. Pathological changes in the cerebral medullary arteries of five autopsy cases of malignant nephrosclerosis: Observation by morphometry and reconstruction of serial sections. Neuropathology 2003;23:153-60. doi: 10.1046/j.1440-1789.2003.00492.x.
25. Sahm F, Schrimpf D, Stichel D, Jones DTW, Hielscher T, Schefzyk S, et al. DNA methylation-based classification and grading system for meningioma: A multicentre, retrospective analysis. Lancet Oncol 2017;18:682-94. doi: 10.1016/S1470-2045(17)30155-9.