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Retrospective Analysis of Meningioma and Alternative Method of Grading

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ABSTRACT

Objective: The current classification of meningioma is based on the mitotic count, brain invasion and atypical histological changes. We re-evaluated the cases of meningioma to make accurate grading and to investigate the effects of morphological parameters and their relationship with each other. We discussed the counting method of mitotic activity. We tried to develop a novel method to determine the most accurate grade.

Materials and Methods: In this study, three hundred nine cases of meningioma were re-evaluated. The number of mitosis in 10 consecutive high-power fields, as well as the total number of mitosis in 1 cm^2 area, was found for all cases. Receiver Operating Characteristics curve analysis was performed on the mitotic counts of 304 cases (grade I and II) in both 10 consecutive high-power fields and 1 cm^2 for predicting the grade.

Results: In Receiver Operating Characteristics curve analysis, the number of mitoses determining grade II with 99% specificity and 84.4% sensitivity in 1 cm2 was 7 or more. Receiver Operating Characteristics curve analysis for the mitotic count in 10 consecutive high-power fields when the number of mitosis 4 or more, the sensitivity was 84.4%, and it was 100% specific for grade II.

Conclusion: The major cause of the grade change was the number of mitotic activities. We recommend that the mitotic activity count in a large area. Especially, if there is 7 or more mitosis in 1 cm^2, the case is to be high-grade. On the other hand, the presence of 1 or more mitosis in 42 high-power fields supports that this case is more likely to be grade II.

Keywords: Meningioma, retrospective analysis, mitosis, grade, ROC curve analysis

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INTRODUCTION

Meningiomas are the most common neoplasms of the central nervous system composed of cells resembling normal meningothelial cell morphologically, immunohistochemically and ultrastracturally. In 1831, the histologic similarity between meningioma cells and arachnoid villi cells was described by Bright (1). Subsequently, it was supported by Cleland and Schmidt's (2) study.

The median age of the patients with meningioma is 65 and its incidence increases with age (3). Women are at greater risk than men. The vast majority of meningiomas locate in intracranial, intraspinal and orbital region. Cerebral convexities, parasagittal areas, olfactory groove, sphenoid wings, para/suprasellar regions, optic nevre sheath, tentorium and posterior fossa are the most common intracranial localizations (4, 5). Malignant progression in meningiomas is low. Lungs (60%), pleura (9%), mediastinum (5%), liver, lymph nodes and bones are the most frequent site for distant metastasis (6).

Different criteria have been used for the classification of meningioma. Anaplastic meningioma, a subtype of meningioma with aggressive and poor prognosis, was defined by World Health Organization (WHO) in 1979. Atypical meningioma which was an intermediate group tumor with a significant recurrence risk was described in 1993. In 2000, five histopathological criteria which were significant for recurrence risk and prognosis were determined for meningioma grading, which increased cellularity, small cell formation (high nuclear to cytoplasmic ratio), prominent nucleoli, sheet-like growth, and necrosis (foci of "spontaneous" or geographic). For definition of Grade II meningioma three of the five criteria were required. In 2007, WHO defined that any type of meningioma with a high proliferation index or brain invasion as aggressive tumor with a high recurrence risk. However, in the 2016 WHO classification, brain invasion in meningioma were defined as grade II directly (7).

In 2016, WHO classified meningiomas in three degrees according to their morphological, immunohistochemical and ultrastructural characteristics. The current classification is primarily based on the number of mitotic activities, brain invasion and atypical histological changes.

Thanks to advances in imaging techniques and their widespread use, brain tumors are diagnosed more frequently

Table 1. Histomorphological parameters and their distribution according to the grade

Histomorphological parameters	Total cases n=309	Low grade cases*		High-grade cases**		p†
		n	%	n	%	
Hypercellularity	34	16	47.1	18	52.9	<0.001
Small cell formation	54	26	48.1	28	51.9	<0.001
Macronucleoli	7	4	57.1	3	42.9	0.387
Sheet-like growth	30	10	33.3	20	66.7	<0.001
Necrosis***	32	7	21.9	25	77.1	<0.001
Lymphocyte	195	147	75.4	48	24.6	0.317
Hyalinized vessel	93	70	75.3	23	24.7	0.740
Psammoma body	174	135	77.6	39	22.4	0.062
Nuclear groove	120	88	73.3	32	26.7	0.963
Intranuclear inclusion	144	109	75.79	35	24.3	0.407
Cellular atypia	60	33	55.0	27	45.0	<0.001
Bone invasion	16	12	75.0	4	25.0	1.000

*: Grade I cases; **: Grade II and III cases; ***: Foci of spontaneous or geographic necrosis; †: p-values for relationship between histological parameters and high grade

today. Grading of meningiomas is important due to its high incidence. The aim of meningioma grading is to assist predicting aggressivity of tumor, recurrence risk, overall survival, and to guide the management of treatment. The more accurate classification of meningioma is the more accurate identification of patients who will receive additional treatment.

In meningiomas, WHO grade of tumor and extent of surgical resection is the best indicator of progression-free survival (8). Thus, the grade should be stated in pathology report for each patient. In some studies, it has been reported that recurrence is seen in approximately 20% of grade I meningiomas (9,10), which shows that the WHO classification system may be inadequate to determine the progression of some meningiomas.

Here, we re-evaluated the cases of meningioma in our pathology archive to make accurate grading and to investigate the effects of morphological parameters and their relationship with each other. Then, we discussed the counting method of mitotic activity, which is the most effective and single quantitative criteria in grading. We also discussed the difficulties of mitotic activity counting in consecutive 10 High-power fields (HPFs) and interobserver variability. In addition, we tried to develop a novel method to help determine the most accurate grade and to minimize interobserver variability.

MATERIALS and METHODS

In this study, three hundred and nine meningioma cases that were retrieved from our archive of department between 2008 and 2016 were re-evaluated by two neuropathologists. In meningioma grading, important morphological parameters, including mitosis count, brain invasion, hypercellularity, small cell formation, macronucleoli, necrosis and sheet-like growth architecture, were determined. Some other parameters, such as lymphocyte, hyalinizing vessel, psammoma body, nuclear pseudoinclusion, nuclear groove, nuclear atypia and bone invasion, were also determined. Mitosis was counted in 10 consecutive HPFs according to WHO parameters (11). Hypercellularity was defined by light microscopy as ≥53 nuclei/HPF diameter (12). Small cell formation was defined by light microscopy as clusters of lymphocyte-like tumor cells with high nuclear to cytoplasmic ratio (13). The presence of easily observed nucleoli with a 10x objective ratio was considered macronucleoli (13). Sheet-like growth architecture was a loss of whorled or fascicular growth patterns (13).

Tumor diameter and localization were obtained from magnetic resonance (MR) reports on the system of the data processing center. In addition, the number of mitosis in 10 consecutive HPFs, as well as the total number of mitosis in 1 cm^2 area (counted by using a transparent millimetric grid), were found for all cases. Thus, we could see where the mitotic figures were located densely. Then, grading of the cases was determined according to the count of the mitotic figure in 10 consecutive HPFs.

Statistical Analysis

SPSS 23.0 statistical package program was used for the analysis of the data. The descriptive statistics of the evaluation results were expressed as numbers and percentages for categorical variables and as mean, standard deviation, minimum, and maximum for the continuous variables. Chi-square test was used to analyze the differences between the observed and expected values of categorical variables.

Receiver Operating Characteristics (ROC) curve analysis was performed on the mitotic counts of 304 cases (grade I and II) in both 10 consecutive HPFs and 1 cm^2 for predicting the grade. The areas under the curve were represented with a 95% confidence interval (CI). When an optimal cut off value was observed, the sensitivity and specificity values were presented. A p-value of less than 0.05 was considered to show a statistically significant result.

RESULTS

Two hundred and twenty-eight of the 309 cases were female and 28 were male. The age distribution was between 13-89 years and the mean age was 54 years. After re-evaluation of the cases, 227 of them were grade I (69 transitional, 64 fibroblastic, 54 meningothelial, 14 psammomatous, 15 angiomatous, five secretory, four microcystic, two metaplastic), 77 were grade II (atypical), five were grade III (anaplastic). One of the anaplastic meningiomas was papillary and rhabdoid. In addition, in focal areas, there was xanthomatous metaplasia in three cases, adipocytic metaplasia in three cases, osteoid metaplasia in 11 cases. Two hundred and thirty-four of the cases were located in supratentorial, 75 were in infratentorial (35 were in the posterior fossa, 31 were in the spinal cord, nine were in the olfactory groove).

According to our study, findings, such as age, sex distribution, localization and types of meningiomas, are similar to the current data of literature.

All histological parameters of the cases and their grades obtained by retrospective analysis are given in Table 1. The histological pa-

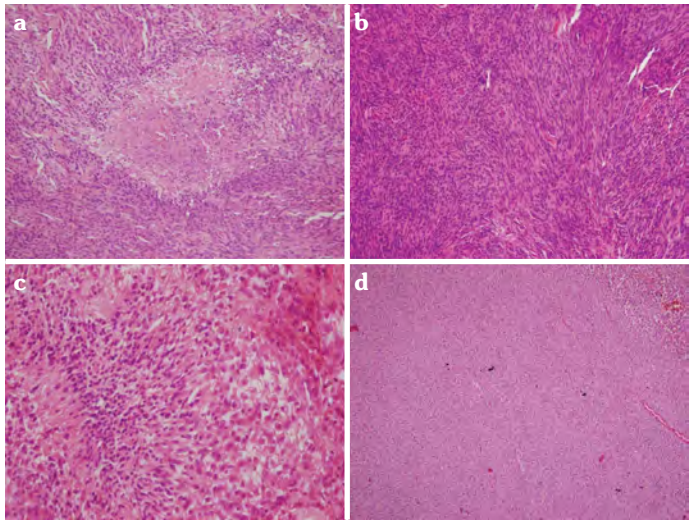

Figure 1. (a) HEx400: Foci of spontaneous necrosis. (b) HEx400: Hypercellularity. (c) HEx400: Small cell formation. (d) HEx100: Sheet-like growth

HE: Hematoxylin and eosin

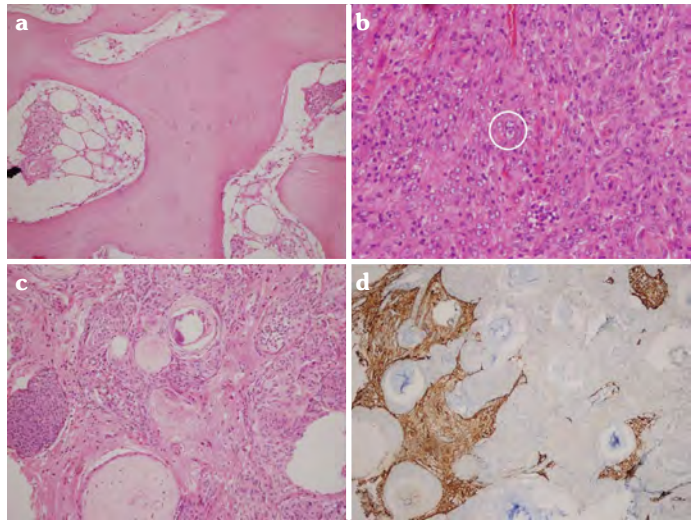

Figure 2. (e) HEx200: Bone invasion. (f) HEx400: Macronucleoli. (g) HEx200: Brain invasion. (h) GFAPx200: Brain invasion

HE: Hematoxylin and eosin; GFAP: Glial fibrillary acidic protein

Table 2. Grades of the cases first and after re-evaluation

	Histological grade	Results of the re-evaluation									Total
		Grade I			Grade II			Grade III			
		n	%*	%**	n	%*	%**	n	%*	%**	n
Results of the first evaluation	Grade I	227	81.7	100.0	51	18.3	66.2	0	0.0	0.0	278
	Grade II	0	0.0	0.0	26	92.9	33.8	2	7.1	40.0	28
	Grade III	0	0.0	0.0	0	0.0	0.0	3	100.0	60.0	3
Total n		227			77			5			309

*: Row %; **: Column %

rameters of the cases are shown in Figure 1 and 2. The relationship between histological parameters (hypercellularity, small cell formation, sheet-like growth pattern, cellular atypia) and the high grade was found to be statistically significant ($p<0.001$).

The grades of the cases before and after re-evaluation and the cases in which grades changed after re-evaluation was demonstrated in Table 2. Grade II-III cases were defined as high grade, grade I was defined as low grade. The number of high-grade cases was 31 in the first evaluation and 82 in the re-evaluation. The grade of 53 cases increased after re-evaluation.

The distribution of the cases according to the factors that increase the grade after re-evaluation was given in Table 3. Sixty of all cases were high grade due to mitotic activity only. One case was defined as high grade due to morphological features. After re-evaluation, the distribution of the cases according to factors affecting the grade change was also given in Table 3.

Brain invasion was seen in 12 cases (3.9%). The relationship between brain invasion and other morphological parameters was given in Table 4. The relationship between brain invasion and histological parameters (small cell formation, sheet-like growth pattern, necrosis) was found to be statistically significant (p-values found as 0.009, 0.003, and 0.004, respectively). There was no statistically significant relationship between brain invasion and other histological parameters (macronucleoli, hypercellularity, cellular atypia) (p-values found as 1.000, 0.134 and 1.000, respectively).

Eleven of the 309 cases relapsed. Three of the recurrent cases (27%), which called grade I in the first evaluation, were defined as grade II after re-evaluation. Although one recurrent case was grade II, it was grade III after re-evaluation. One case also showed recurrence although it was grade I.

The mean tumor diameter was 3.5 cm in low grade (grade I) tumors and it was 4.2 cm in high grade (grade II and III) tumors. The mean tumor diameter was 5.5 cm in the cases with brain invasion and in those without was 3.6 cm.

In 147 cases, no mitotic activity was observed according to mitosis count in 1 cm^2. The mean number of mitotic activities in 1 cm^2 was 1 in grade I cases. However, it was 21 in grade II cases. Mitotic activities in different areas were shown in Figure 3. ROC curve analysis and comparative results applied to both mitotic count data (in 1 cm^2 and in 10 consecutive HPFs after re-evaluation) are given in Table 5. In ROC curve analysis, according to the number of

Table 3. Distribution of the high-grade cases according to factors affecting the grade

The factors affecting the grade	Cases with high grade		Cases with grade changes	
	n	%	n	%
Mitosis	60	73.1	48	90.5
Brain invasion	7	8.5	–	–
Three of the five criteria	3	3.7	2	3.8
Mitosis and three of the five criteria	6	7.5	2	3.8
Morphology	1	1.2	–	–
Mitosis and brain invasion	1	1.2	–	–
Brain invasion and three of the five criteria	2	2.4	1	1.9
Mitosis, brain invasion and three of the five criteria	2	2.4	–	–
Total	82	100.0	53	100.0

Table 4. The relationship between brain invasion and morphological parameters

	Brain invasion				Total	p
	Absent		Present			
	n	(%)**	n	(%)**		
Morphological parameters						
Small cell formation						
Absent	249	97.6	6	2.4	255	0.009
Present	48	88.9	6	11.1	54	
Macronucleoli						
Absent	290	96.0	12	4.0	302	1.000
Present	7	100.0	0	0.0	7	
Hypercellularity						
Absent	266	96.7	9	3.3	275	0.134
Present	31	91.2	3	8.8	34	
Sheet-like growth						
Absent	272	97.5	7	2.5	279	0.003
Present	25	83.3	5	16.7	30	
Necrosis*						
Absent	270	97.5	7	2.5	277	0.004
Present	27	84.4	5	15.6	32	
Cellular atypia						
Absent	239	96.0	10	4.0	249	1.000
Present	58	96.7	2	3.3	60	

*: Foci of spontaneous or geographic necrosis; **: Row %

mitosis in consecutive 10 HPFs, statistical data determining grade II the most accurately were as follow: p<0.001, 84.4% sensitivity and 100% specificity. Moreover, according to this findings, the mitotic count which was 7 or more in 1 cm^2 was also statistically significant in determining grade II (p<0.001 for 99% sensitivity and 84.4% specificity) and the area under the curve was found as 0.949 (95% CI: 0.912–985).

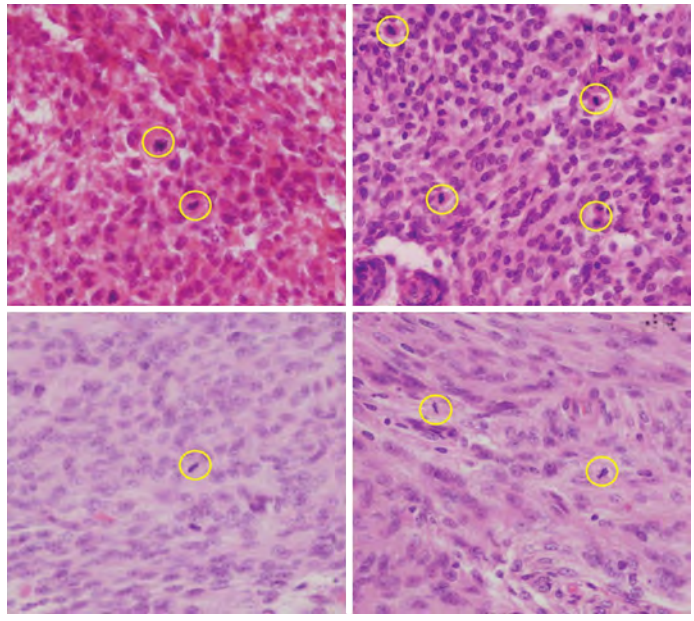

Figure 3. HEx400: Mitotic activities in different areas
HE: Hematoxylin and eosin

DISCUSSION

WHO grading and the extent of surgical resection are the most important prognostic indicators for meningiomas. Clinicians determine the treatment option according to these parameters. Nevertheless, grading does not always provide reliable information about tumor recurrence and aggressive behavior (14). In the study of Loewenstern et al. (15), they said that high-grade meningiomas may recur even after gross total resection. They also found that a high mitotic index was associated with recurrence and mortality. Some grade I meningiomas also show recurrence and malignant transformation even if they are totally removed. According to the Simpson Grading System, the amount of resection closely correlated with progression-free survival (8). Sumkovski et al. (16) said that the surgical resection and the patient's survival have a significant relation to the mitotic count of the meningiomas. Rao et al. (17) pointed out that some grade I cases are biologically aggressive, and Ki 67 and P53 are useful for identifying them.

Table 5. Receiver Operating Characteristics (ROC) curve analysis of mitosis count in 1 cm^2 and in 10 consecutive High-power fields (HPFs)

Mitosis in 1 cm2 Areas under the curve: 0.949 (95% CI: 0.912–985)			Mitosis in 10 HPFs Areas under the curve: 0.942 (95% CI: 0.903–980)		
Cut-off value	**Sensitivity**	**1 - Specificity**	**Cut-off value**	**Sensitivity**	**1 - Specificity**
-1.00	1.000	1.000	-1.00	1.000	1.000
0.50	0.948	0.370	0.50	0.948	0.366
1.50	0.948	0.326	1.50	0.844	0.075
2.50	0.935	0.181	2.50	0.844	0.018
3.50	0.870	0.128	**3.50**	**0.844**	**0.000**
4.50	0.857	0.084	4.50	0.584	0.000
5.50	0.844	0.031	5.50	0.325	0.000
6.50	**0.844**	**0.009**	6.50	0.117	0.000
7.50	0.818	0.000	7.50	0.078	0.000
8.50	0.792	0.000	8.50	0.052	0.000

CI: Confidence interval

In our study we realised that, the criteria used for grading of meningioma were insufficient in some cases. In addition, some morphological parameters may be interpreted differently from person to person.

Among five atypical histological changes that affect grading, hypercellularity, small cell formation, sheet-like growth and necrosis, as well as cellular atypia, were found to be statistically significant in determining high-grade meningiomas. Macronucleol, which is one of the five atypical histological changes, is ineffective in showing high-grade meningiomas in our study. In addition, some morphological parameters, such as intratumoral lymphocyte, hyalinized vessel, psammoma body, nuclear groove, intranuclear inclusion and bone invasion, were not associated with high-grade meningioma.

In our study, tumor diameter was associated with high tumor grade and brain invasion. Therefore, it can be said that the probability of recurrence may increase in cases with high diameter. In the study of Ildan et al. (18), tumor volume was reported to be an independent marker of meningioma recurrence. Magill et al. (3) also showed that there was a significant relationship between tumor size and grade II meningiomas.

According to the first and re-evaluation results in our study, it was striking that the most important parameter affecting the grade is mitotic activity. After re-evaluation, the grades of the majority of the cases changed. The major cause of the grade change was the number of mitotic activities. As in our other study, it is clear that the difference in the number of mitotic figures in 10 consecutive HPFs among observers is the cause of grade discordance. Reasons for failing to accurate determining the number of mitosis in 10 consecutive HPFs; the presence of cases which have low mitotic figures, the variability of the mitotic count from field to field, lack of knowledge of the number of mitosis in the entire slide, and difficulty fitting 4 or more mitotic activities into 10 consecutive HPFs (Fig. 4).

Olympus Bx51 microscope that the field diameter of HPF is 0.55 mm and the area of one HPF is 0.238 mm^2 was used in our study. The area we scanned on slides is 1 cm^2. There are approximately

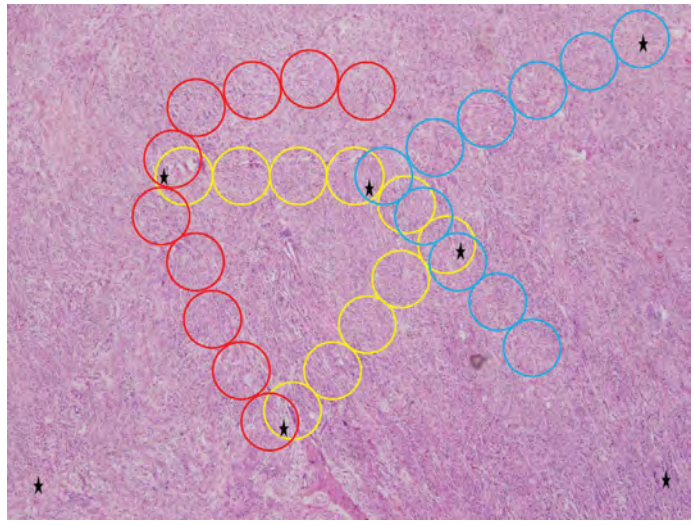

Figure 4. Demonstration of counting mitosis in consecutive 10 HPF: Stars demonstrates the mitotic figures. Each of the rings demonstrates 1 HPF. There are two mitosis in consecutive 10 HPF indicated by the red rings, three mitosis in blue rings, four mitosis in yellow rings

HE: Hematoxylin and eosin; HPFs: High-power fields

420 HPFs in an area of 1 cm^2. In meningioma grading, the number of mitosis in 10 consecutive HPFs is evaluated. How many different 10 consecutive HPFs are there in these 420 HPFs within 1 cm^2? The number is quite high. In this case, the probability of finding the right consecutive 10 HPFs, which include sufficient mitosis, appears to be quite difficult. It is obvious that this possibility becomes more difficult as the number of mitotic figures decreases in 1 cm^2 area (Fig. 4).

These calculations show that how difficult our job is to determine the correct number of mitosis in 10 consecutive HPFs. Should we determine the grade by counting the mitotic figures in a larger area? Thus, we decided to perform the ROC curve analysis of the total number of mitosis in cm^2. According to ROC curve analysis,

the number of mitosis determining grade II with 99% specificity and 84.4% sensitivity in 1 cm^2 was 7 or more. According to the results of the ROC curve analysis for mitotic count in 10 consecutive HPFs, when the number of mitosis 4 or more, the sensitivity was 84.4%, and it was 100% specific for grade II. In other words, both methods are highly specific. Their sensitivities are very close to each other. The number of high-grade cases was 31 in the first evaluation and 82 in the re-evaluation. The cases with a high grade that could not be determined in the first evaluation could be determined by mitosis counting method in 1 cm^2.

Inter-observer variability is common in mitosis counting. In the cases with low mitotic figures, it is more difficult to find the 10 consecutive HPF, including four or more mitosis. Although counting mitosis in 1 cm^2 takes some time, it can reduce the differences among observers. In addition, high-grade cases will not being overlooked. Instead of seeking seven or more mitosis in 1 cm^2 (420 HPFs), a grade II tumor may be present in the presence of 1 or more mitosis (0.8 was accepted as 1) in 10 mm^2 (42 HPFs). In this case, we should be more carefully. In daily routine practice, if there is one or more mitosis in 42 HPFs, seven or more mitosis can be sought in 1 cm^2 by scanning the entire slide. If there is one or more mitosis in 42 HPFs, we can also count the mitotic figures in 10 consecutive HPFs by marking the mitotic figures found.

It is more difficult to find accurate 10 consecutive HPFs (containing four or more mitosis) in numerous possibilities than to find seven or more mitosis at 1 cm^2. After re-evaluation, it turned out that, although recurrent cases were grade II, three of them were called as grade I. Therefore, these cases had no additional treatment after surgery. One case also showed recurrence despite low grade. At this point, to determine the high-grade meningiomas or recurrence potential of meningiomas only with morphological parameters can be misleading. Therefore, as reported in Aizer et al.'s study (19), it is clear that molecular methods are needed to predict recurrence or to determine the patients who will receive treatment.

CONCLUSION

The grading of meningiomas is significant for guiding the treatment. Mitotic activity is the most crucial factor in the grading of meningiomas. Due to the difficulty of counting of mitotic activities in 10 consecutive HPFs and interobserver variability, we recommend that the mitotic activity count in a large area (1 cm^2). Especially if there are seven or more mitosis in 1 cm^2, the case is highly likely to be high-grade, and it can be accepted as grade 2. On the other hand, according to our experience, the presence of one or more mitosis in 42 HPFs (10 mm^2) supports that this case is more likely to be grade 2.

Ethics Committee Approval: The Karadeniz Technical University Scientific Research Ethics Committee granted approval for this study (date: 08.11.2019, number: 24237859-780).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – IS; Design – IS; Supervision – IS, EC; Data Collection and/or Processing – IS, EC; Analysis and/or Interpretation – IS, EC; Literature Search – IS, EC; Writing – IS; Critical Reviews – IS, EC.

Conflict of Interest: The authors have no conflict of interest to declare.

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REFERENCES

1. Albayrak SB, Black PM. The Origin of Meningiomas. In: Pamir MN, McL Black P, Fahlbusch R, editors. Meningiomas: a comprehensive text. Philadelphia, PA. Saunders/Elsevier, 2010.p.53–60. [CrossRef]
2. Yamashima T. On arachnoid villi and meningiomas: functional impli-cation of ultrastructure, cell adhesion mechanisms, and extracellular matrix composition. Pathol Oncol Res 1996; 2(3): 144–9. [CrossRef]
3. Magill ST, Young JS, Chae R, Aghi MK, Theodosopoulos PV, McDermott MW. Relationship between tumor location, size, and WHO grade in meningioma. Neurosurg Focus 2018; 44(4): E4. [CrossRef]
4. Levy WJ Jr, Bay J, Dohn D. Spinal cord meningioma. J Neurosurg 1982; 57(6): 804–12. [CrossRef]
5. Shrilakshmi S. Meningiomas: A Clinicopathological study. Int J Med Res Health Sci 2015;4(4): 827–31. [CrossRef]
6. Mutnuru PC, Ahmed SF, Uppin SG, Lachi PK. Pulmonary metastases from intracranial meningioma. Lung India 2015; 32(6): 661–3. [CrossRef]
7. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK. WHO Classification of Tumours of the Central Nervous System. Revised 4th edition, Vol 1st. Lyon: IARC; 2016.p.232–45.
8. Gousias K, Schramm J, Simon M. The Simpson grading revisited: aggressive surgery and its place in modern meningioma management. J Neurosurg 2016; 125(3): 551–60. [CrossRef]
9. Gallagher MJ, Jenkinson MD, Brodbelt AR, Mills SJ, Chavredakis E. WHO grade 1 meningioma recurrence: Are location and Simpson grade still relevant?. Clin Neurol Neurosurg 2016; 141: 117–21.
10. van Alkemade H, de Leau M, Dieleman EM, Kardaun JW, van Os R, Vandertop WP, et al. Impaired survival and long-term neurological problems in benign meningioma. Neuro Oncol 2012; 14(5): 658–66.
11. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol 2016; 131(6): 803–20. [CrossRef]
12. Perry A, Stafford SL, Scheithauer BW, Suman VJ, Lohse CM. Meningioma grading: an analysis of histologic parameters. Am J Surg Pathol 1997; 21(12): 1455–65. [CrossRef]
13. Perry A, Daniel JB. Meningiomas. Practical surgical neuropathology: A Diagnostic Approch. Philadelphia, PA, USA: Churchill Livingstone Elsevier; 2010.p.185–215. [CrossRef]
14. Proctor DT, Ramachandran S, Lama S, Sutherland GR. Towards Molecular Classification of Meningioma: Evolving Treatment and Diagnostic Paradigms. World Neurosurg 2018; 119: 366–73. [CrossRef]
15. Loewenstern J, Shuman W, Rutland JW, Kessler RA, Kohli KM, Umphlett M,et al. Preoperative and Histological Predictors of Recurrence and Survival in Atypical Meningioma After Initial Gross Total Resection. World Neurosurg 2019; 128: e148–56. [CrossRef]
16. Sumkovski R, Micunovic M, Kocevski I, Ilievski B, Petrov I. Surgical Treatment of Meningiomas - Outcome Associated With Type of Resection, Recurrence, Karnofsky Performance Score, Mitotic Count. Open Access Maced J Med Sci 2019; 7(1): 56–64. [CrossRef]
17. Rao S, Sadiya N, Doraiswami S, Prathiba D. Characterization of morphologically benign biologically aggressive meningiomas. Neurol India 2009; 57(6): 744–8.
18. Ildan F, Erman T, Göçer AI, Tuna M, Bağdatoğlu H, Cetinalp E, et al. Predicting the probability of meningioma recurrence in the preoperative and early postoperative period: a multivariate analysis in the midterm follow-up. Skull Base 2007; 17(3): 157–71. [CrossRef]
19. Aizer AA, Abedalthagafi M, Bi WL, Horvath MC, Arvold ND, Al-Mefty O, et al. A prognostic cytogenetic scoring system to guide the adjuvant management of patients with atypical meningioma. Neuro Oncol 2016; 18(2): 269–74. [CrossRef]