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Classic, atypical, and anaplastic meningioma: three histopathological subtypes of clinical relevance

HANS MAIER, M.D., DIETMAR ÖFNER, M.D., ANTON HITTMAIR, M.D., KLAUS KITZ, M.D., AND HERBERT BUDKA, M.D.

Neurological Institute and Neurosurgical Clinic, University of Vienna, Vienna, and Institute of Pathology and Department of Surgery I, University of Innsbruck, Innsbruck, Austria

✓ This study correlates the histopathological classification of meningiomas with clinicopathological features of biological activity. A retrospective evaluation of 1799 surgical specimens of meningiomas from 1582 patients was made. The classic histopathological type, atypical meningiomas defined by increased cellularity and at least five mitotic figures in 10 high-power fields, anaplastic (malignant) meningiomas, and hemangiopericytic or papillary meningiomas were seen in 87.6%, 7.2%, 2.4%, and 2.8% of operations, respectively. The rates of recurrence in surgically treated patients with classic, atypical, anaplastic, and hemangiopericytic or papillary meningiomas were 6.96%, 34.6%, 72.7%, and 68.2%, respectively. The extent of surgery and the tumor size and site were studied in detail in 252 tumors of all histopathological types. Recurrences were rare in classic meningiomas after complete resection, whereas atypical and anaplastic tumors recurred after complete resection much more frequently. Classic meningiomas, hemangiopericytomas, and papillary meningiomas were smaller at surgery than atypical and malignant meningiomas. Atypical and malignant tumors were operated on more often in falcine and lateral convexity regions than were classic meningiomas.

To support the authors' subjective categorization by a quantitative parameter related to proliferation, 112 meningiomas comprising all histopathological subtypes were investigated for staining of argyrophilic nucleolar organizer region proteins (Ag-NOR's). The Ag-NOR counts showed significant differences between classic, atypical, and anaplastic tumors but no significant differences between primary and recurrent tumors. Hemangiopericytomas and papillary meningiomas had lower Ag-NOR values than anaplastic meningiomas.

A correlation of Ag-NOR numbers with the authors' histopathological scale of malignancy supports the introduction of atypical meningiomas with intermediate biological behavior on the classification scale between classic and anaplastic meningiomas. Overlapping of Ag-NOR numbers among all groups of malignancy may restrict the prognostic value of Ag-NOR counting in the individual case.

KEY WORDS • **meningioma** • **malignant tumor** • **tumor recurrence** • **argyrophilic nucleolar organizer region protein**

MENINGIOMAS are the most frequently encountered nonglial primary intracranial brain tumors, with an incidence of between 13% and 19% in large series of primary intracranial tumors;[23] they are diagnosed in about 12% of tumors arising in the spinal canal.[50] The characteristic morphology of these usually benign tumors and of malignant variants has been exhaustively described.[23] However, the existence of an intermediate group of meningiomas exhibiting less favorable behavior than classic tumors but a better course than definitive malignant meningiomas has been postulated.[19,51] The histopathological definition of this group remains to be established, and its clinical relevance has to be confirmed by correlation with behavior.

In a previous study on paraffin-embedded tissue samples of human brain tumors,[31,32] we found no correlations between counts of silver-stained nucleolar organizer region proteins (Ag-NOR's) and proliferation indices or malignancy, except in a small number of meningiomas. This result contrasted with that of other authors who had investigated brain-tumor smear preparations.[43,44] The Ag-NOR's can be visualized by a silver staining method that was introduced into histopathology by Ploton, *et al.*,[45] and by Crocker and Nar.[7] Electron microscopic studies have demonstrated that nucleolar organizer regions are more numerous and smaller in cells of malignant tumors than in normal or benign neoplastic cells.[9–11,29] However, after promising results in lymphomas,[6,7] the evaluation of mean num-

TABLE 1

*Histological subtype and operations in 1582 meningioma patients with or without recurrence**

Type of Meningioma	No. of Operations	No. of Cases		
		Total	With Recurrence	Without Recurrence
classic	1576 (87.6%)	1423	99 (7%)	1324
atypical	129 (7.2%)	104	36 (34.6%)	68
anaplastic	43 (2.4%)	33	24 (72.7%)	9
hemangiopericytic & papillary	51 (2.8%)	22	15 (68.2%)	7
all types	1799	1582	174 (11%)	1408

* Values in parentheses reflect percentage of total of all types.

TABLE 2

*Extent of operation in 252 meningiomas**

Meningioma Subgroup	No. of Cases	Extent of Operation			
		Complete	Subtotal	Partial	Undetermined
classic					
all cases	163	119 (73)†	32 (19.6)†	7 (4.3)†	5
prim without reop	128 (78.5)	107 (89.9)	16	5	0
prim with reop	13 (8)	3 (2.5)	5	1	4
recurrences	22 (13.5)	9 (7.6)	11	1	1
atypical					
all cases	35	22 (62.9)†	6 (17.1)†	3 (8.6)†	4
prim without reop	16 (45.7)	12 (54.5)	1	1	2
prim with reop	6 (17.1)	4 (18.2)	1	0	1
recurrences	13 (37.2)	6 (27.3)	4	2	1
anaplastic					
all cases	40	24 (60)†	9 (22.5)†	4 (10)†	3
prim without reop	8 (20)	4 (16.7)	1	2	1
prim with reop	7 (17.5)	6 (25)	0	1	0
recurrences	25 (62.5)	14 (58.3)	8	1	2
hem/pap					
all cases	14	9 (64.3)†	3 (21.4)†	0	2
prim without reop	5 (35.7)	3 (33.3)	0	0	2
prim with reop	3 (21.4)	1 (11.1)	2	0	0
recurrences	6 (42.9)	5 (55.6)	1	0	0
all tumors					
all cases	252	174 (69)†	50 (19.8)†	14 (5.6)†	14
prim without reop	157 (62.3)	126 (72.4)	18	8	5
prim with reop	29 (11.5)	14 (8.1)	8	2	5
recurrences	66 (26.2)	34 (19.5)	24	4	4

* Extent of operation in 252 primary (prim) meningiomas with or without reoperation (reop) and recurrent tumors in subgroups of classic, atypical, and malignant meningiomas, and hemangiopericytomas and papillary meningiomas (hem/pap). Numbers in parentheses reflect percentages of cases within tumor subtype category.

† Numbers in parentheses reflect percentages of cases in "No. of Cases" column.

bers of Ag-NOR's on paraffin-embedded samples of other tumors led to controversial results in attempts at correlation with malignancy in several studies.[12–14,16,26,38,39,48,53,54,56] Other authors have demonstrated that the Ag-NOR counts reflect proliferative activity[6,12,15,54] and cell duplication rate,[55] and rise with increasing malignancy, with differences between borderline lesions and definite neoplasia.[28,41]

The aims of this study were: 1) to investigate the recurrence rate, tumor size, and site, and extent of surgery of meningioma subtypes with defined histopathology; and 2) to examine whether this histopathological categorization can be supported by quantitative criteria related to proliferative activity, such as Ag-NOR counts.

Materials and Methods

Between January, 1964, and May, 1990, 1799 surgical specimens received by the Neurological Institute were diagnosed as meningioma (Table 1). Surgically treated recurrences were registered during the same observation period.

In this retrospective series, a uniform procedure for histological tissue sampling cannot be claimed. However, as much available tissue from as many fragments as possible was usually placed into an embedding capsule covering an area of 8 sq cm. Large specimens and nonclassic tumors were often embedded in several capsules; atypia and anaplasia were present in every large (capsule-sized) section sampled from different areas, but not always in small tumor fragments.

Histopathological Classification

The meningiomas were divided into four categories: 1) classic meningiomas with typical histological pattern,[23] without prominent mitotic activity or cellularity; 2) atypical tumors with signs of rapid growth (focally increased cellularity and raised mitotic rate: at least five mitotic figures per 10 high-power fields (HPF's) at × 400 magnification) in the most active area; 3) anaplastic meningiomas with high cellular density, high mitotic rate with pathological mitoses, cytological anaplasia, and necrosis (in contrast to sarcomas, however, the meningiomatous character is still apparent); and 4) hemangiopericytomas (of meninges) and papillary meningiomas with characteristic histology.[23,30,42]

Clinical Data

To identify factors other than histological subtype that might contribute to recurrence, a set of clinical data including tumor site and size (largest diameter) at surgery and apparent degree of surgical extirpation were analyzed in 252 tumors (14% of the large series) (Tables 2–4). There was no special mode of selection other than histological diagnosis. Care was also taken that a significant number of cases were studied from rarer histological variants.

Silver Staining of Nucleolar Organizer Region Proteins

Among the 252 tumors summarized in Table 2, we investigated 112 meningeal tumors, including 23 classic

TABLE 3
*Tumor size in meningioma subgroups**

Meningioma Subgroup	No. of Cases	Tumor Size (cm)	
		Median	Range
classic			
all cases	163	4	1–12
prim without reop	128	4	1–12
prim with reop	13	4	2–8
recurrences	22	4	2–6
atypical			
all cases	35	5	2–15
prim without reop	16	5	2–15
prim with reop	6	5	3–7
recurrences	13	5	2–10
anaplastic			
all cases	40	5	2–12
prim without reop	8	5	3–10
prim with reop	7	7	5–10
recurrences	25	5	2–12
hem/pap			
all cases	14	4	2–8
prim without reop	5	4	3–5
prim with reop	3	4	2–8
recurrences	6	3	2–5

* Median and range of tumor size (largest diameter) in histopathological subgroups of 252 meningiomas: primary (prim) tumors with and without reoperation (reop) and recurrent tumors. Hem/pap = hemangiopericytoma/papillary.

meningiomas (17 primary tumors and six recurrent tumors), 35 atypical meningiomas (22 primary tumors and 13 recurrent tumors), 40 anaplastic meningiomas (15 primary tumors and 25 recurrences), and 14 hemangiopericytomas or papillary meningiomas (eight primary tumors and six recurrences).

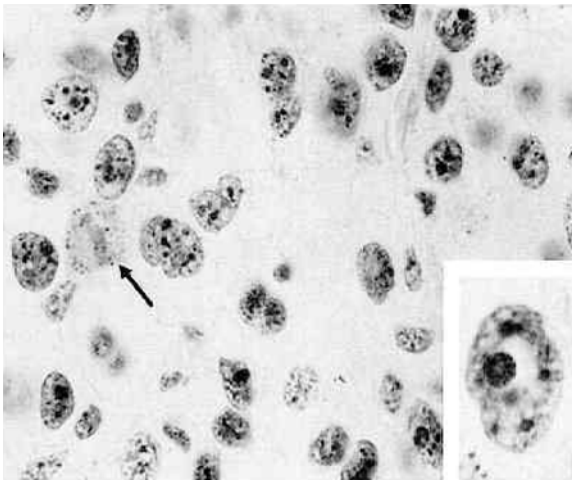

FIG. 1. Photomicrograph showing silver-stained nucleolar organizer region proteins (Ag-NOR's), distinguishable as *black dots* outside and within the nucleolus *(inset)*, as seen in this case of anaplastic meningioma. Even cells in mitosis *(arrow)* display finely dispersed Ag-NOR's. Silver stain for Ag-NORs, no counterstain, × 730; *inset* × 1150.

Tissue samples were fixed in neutrally buffered 3.5% formaldehyde, cut into slices 4 μm thick, embedded in paraffin, dewaxed in xylene, and rehydrated through an alcohol series to deionized water. The staining procedure followed the modified protocol of Hittmair, *et al.* (unpublished data). Sections were incubated at 37°C in a solution containing (vol/vol) one part 2% gelatin in 1% formic acid and two parts 20% aqueous silver nitrate. Preceding tests confirmed that the best staining results were achieved with an incubation time of 12 minutes. Sections were washed in deionized water, fixed with a few drops of 5% sodium thiosulfate for 5 minutes, and dehydrated through ethanols. Finally, sections were cleared in xylene and mounted with Entellan. No counterstain was applied.

Counting of Ag-NOR's

Silver-stained nucleolar organizer region proteins were counted in 200 cells of each specimen under oil immersion at × 1000 magnification in at least four HPF's. In heterogeneous tumors, as in some atypical meningiomas, counting was performed in those tumor areas that showed the highest degree of atypia, although counts from less atypical areas did not significantly differ when two tumors were examined in this respect. In all cases, counting was performed independently by two of the authors (H.M. and A.H.). Interobserver variation was less than 4.5%. Counts by one of us (H.M.) were entered into statistical analysis.

Statistical Analysis

All data were entered into a computer.* Statistical analysis was performed by a nonparametric multivariant analysis (Kruskal-Wallis test[27]), and comparison between groups was carried out using Nemenyi's test.[37]

Results

Histological Subtypes and Tumor Recurrences

Table 1 summarizes the occurrence of histopathological subtypes of meningiomas and surgically treated recurrences in 1582 patients. The recurrence rates are significantly different between each of the three groups of classic, atypical, and combined anaplastic/hemangiopericytic/papillary tumors (chi-squared test 284.9; 3 df; $p = 0.0001$).

Histological Subtypes and Extent of Surgery

Complete tumor resection was performed for slightly smaller percentages of atypical (62.9%), anaplastic (60%), and hemangiopericytic or papillary (64.3%) tumors than for classic meningiomas (73%). The percentage of primary tumors that were retreated despite complete surgical removal increased from classic (2.5%) to hemangiopericytomas and papillary meningiomas

* Macintosh IIci computer manufactured by Apple Computer, Cupertino, California.

(11.1%), to atypical meningiomas (18.2%), and to anaplastic meningiomas (25%) (Table 2).

Tumor Size and Site

Considering the tumor size (largest diameter) in all histopathological subgroups (Table 3), the median size of classic meningiomas (4 cm) is significantly lower than that of atypical and anaplastic tumors (5 cm) (Kruskal-Wallis comparison: H corrected for 10 tied groups = 11.0; p = 0.004), although this did not have a detectable effect upon the extent of surgery.

Among atypical and anaplastic meningiomas, the percentage of tumors treated surgically at the falx or laterally is 68.6% and 70%, respectively, which is higher than the percentage of classic meningiomas (44.2%) (Table 4). Classic tumors were operated on more often at the skull base and in the posterior fossa than atypical and anaplastic ones. For falcine, lateral, and intraventricular tumors, complete resection was only slightly less frequent among the atypical than among the classic variety (75% vs. 80.6%).

Silver Staining of Nucleolar Organizer Region Proteins

Silver-stained nucleolar organizer region proteins are seen as well-defined black dots (Fig. 1) situated within and outside the nucleolus. They can also be identified in mitotic cells.

Correlation of Mean Number of Ag-NOR's With Malignancy

The Ag-NOR counts are plotted in Fig. 2 for each tumor subtype, separately for primary and recurrent tumors. In the Kruskal-Wallis comparison of all subtypes, a significant increase in Ag-NOR counts occurs

TABLE 4

*Site of 252 meningiomas by tumor subtype and extent of surgery**

Subgroup & Extent of Surgery	No. of Cases	Falx, Lateral, Intraventricular†	Skull Base	Tentorial Region	Posterior Fossa	Undetermined‡
classic						
all cases	163	72 (44.2)	52 (31.9)	20 (12.3)	18 (11)	1
complete	119	58	36	11	13	1
subtotal	32	7	12	9	4	0
partial	7	3	3	0	1	0
undetermined	5	4	1	0	0	0
atypical						
all cases	35	24 (68.6)	7 (20)	1 (2.9)	3 (8.6)	0
complete	22	18	4	0	0	0
subtotal	6	2	3	1	0	0
partial	3	1	0	0	2	0
undetermined	4	3	0	0	1	0
anaplastic						
all cases	40	28 (70)	7 (17.5)	4 (10)	0	1
complete	24	15	5	3	0	1
subtotal	9	6	2	1	0	0
partial	4	4	0	0	0	0
undetermined	3	3	0	0	0	0
hem/pap						
all cases	14	3 (21.4)	4 (28.6)	5 (35.7)	1 (7.1)	1
complete	9	1	4	4	0	0
subtotal	3	1	0	1	1	0
partial	0	0	0	0	0	0
undetermined	2	1	0	0	0	1

* Site of 252 meningiomas in subgroups of classic, atypical, and anaplastic meningiomas, and hemangiopericytomas and papillary meningiomas (hem/pap) in relation to extent of surgery.

† There were only three intraventricular tumors (all of classic type).

‡ Includes tumors that involve more than one region listed separately.

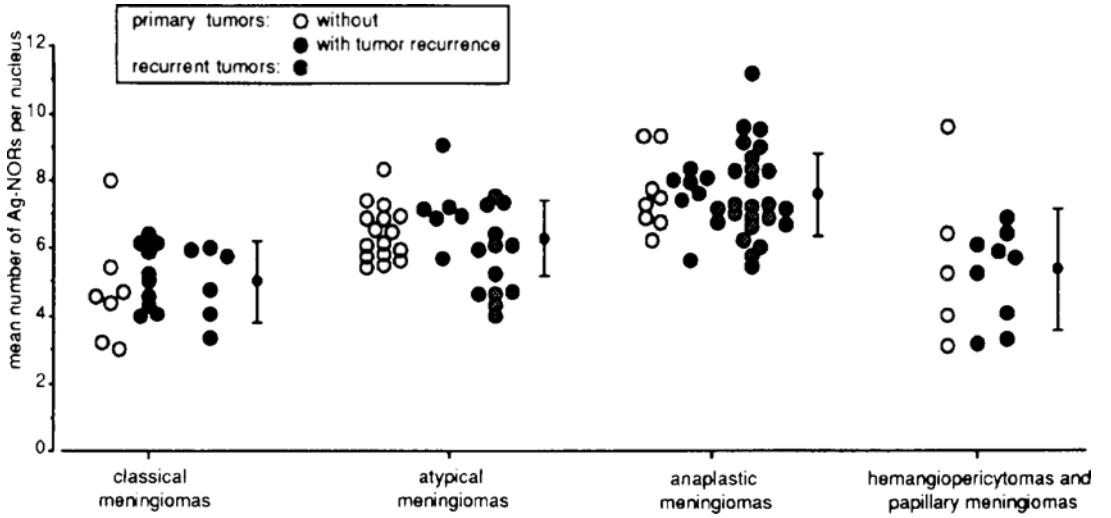

FIG. 2. Scattergram showing silver-stained nucleolar organizer region protein (Ag-NOR) counts in primary and recurrent tumors of classic, atypical, and anaplastic meningiomas, and of hemangiopericytomas and papillary meningiomas, with mean values and respective standard deviations of all cases are shown for each histological group.

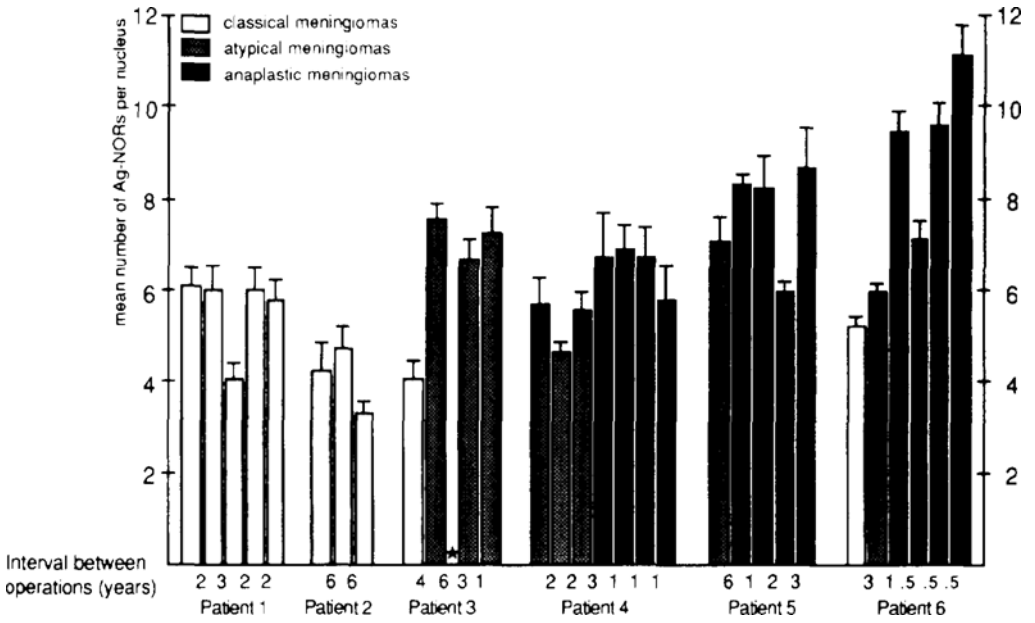

FIG. 3. Graph depicting silver-stained nucleolar organizer region protein (Ag-NOR) counts of primary tumors and recurrences in six patients according to their clinical course and histopathological subtypes. *Asterisk:* an Ag-NOR count of the second recurrent tumor in Case 3 was not made.

from classic to atypical and to anaplastic meningiomas (3 df; H corrected for 11 tied groups = 47.3; $p = 0.0001$). In the comparison of individual groups (Nemenyi's test), atypical tumors were significantly different from classic meningiomas when all tumors (Dijmod = 22.5; $p < 0.05$) or only primary tumors (Dijmod = 12.34; $p < 0.01$) were considered; however, recurrent tumors showed no significant differences (Dijmod = 5.5). Anaplastic meningiomas were significantly different from all other types of meningiomas: from classic tumors when all (Dijmod = 47.5; $p < 0.0001$), primary (Dijmod = 28.17; $p < 0.0001$), and recurrent (Dijmod = 20.02; $p < 0.001$) tumors were considered; from atypical meningiomas in the total group (Dijmod = 25; $p < 0.001$) and in subgroups of primary (Dijmod = 11.86; $p < 0.01$) and recurrent (Dijmod = 13; $p < 0.01$) tumors. Hemangiopericytomas and papillary meningiomas had significantly lower Ag-NOR counts than anaplastic meningiomas (Dijmod = 33.75; $p < 0.05$). The Ag-NOR numbers for all four categories of meningiomas showed some degree of overlapping (Fig. 2).

Within groups of classic, atypical, and anaplastic meningiomas, and in hemangiopericytomas and papillary meningiomas, Ag-NOR counts showed no statistically significant difference between primary and recurrent tumors (Fig. 2). When all recurrences, irrespective of subtype, were compared with all primary tumors, no significant difference was found (Mann-Whitney U-test).

Counts in Tumors of Patients with Multiple Recurrences

In six patients with more than two tumor operations, an eventual stepwise progression of Ag-NOR's could be evaluated. Figure 3 plots the number of Ag-NOR's against time intervals between operations and against histopathological types. A prominent progressive increase of Ag-NOR's in recurrent tumors was seen in only one case. This was a 68-year-old woman with a left parietal classic meningioma and a first atypical recurrence after 3 years, followed by four recurrent anaplastic meningiomas within 2 years (Fig. 3, Case 6).

Discussion

Histopathology and Prognostic Factors for Recurrence

Histopathological signs prognostic for future recurrence in meningiomas have frequently been considered.[8,19–24,52,53] There is broad agreement that the most important predictor for the patient's course is the extent of radical removal of the tumor;[5,21,24,33,52] this is also suggested by the neurosurgical data given in our series on classic meningiomas which rarely recurred after complete resection. However, primary atypical and malignant meningiomas recurred, even after complete resection, up to 10 times more frequently than classic tumors, demonstrating that the extent of surgery may not be the only prognostically significant factor.

It is well known that the rate of reoperations is also influenced by the individual anatomical situation, making radical removal more difficult or even impossible (for instance, for tumors arising in the tentorial region or invading the skull-base venous sinuses and the orbita). In this series, atypical and malignant meningiomas occurred more frequently than classic tumors

at lateral and falcine sites, which are usually more amenable to complete resection. Thus, the tumor site is unlikely to contribute to the worse recurrence rate for atypical and malignant meningiomas.

Although classic meningiomas of our series were found to be smaller at surgery than atypical and anaplastic tumors, primary tumors without reoperation among classic and atypical meningiomas did not differ in size from those that required reoperation. Only anaplastic primary tumors with reoperation were significantly larger than tumors not requiring reoperation, suggesting that tumor size is prognostically more important in anaplastic meningiomas than in classic and atypical tumors.

An increase in mitotic rate, high cellularity, sheeting of tumor cells with loss of typical histological pattern, prominent nucleoli, focal necrosis, tumor invasion into cortex or bone, and hypervascularity have all been described as suspicious histomorphological features.[8, 19,20,24,53] Numbers of macrophages and T and CD8 lymphocytes in meningiomas have also been related to atypical histology.[47] There is no relation of recurrence rate with histological patterns[20,22,53] or with cell counts and nuclear area.[5]

Atypical Histology

Jääskeläinen, *et al.*,[19] described a four-grade tumor classification scale constructed by combining six histological criteria, including cellularity and mitotic rate. A similar concept has been proposed most recently by Chin and Hinton.[3] In both publications, the authors describe more rapid growth in their atypical and anaplastic groups as compared with classic tumors, confirming the relevance of histopathological subtyping of meningiomas. A histopathological categorization of atypical and anaplastic meningiomas was also proposed by Chen and Liu[2] that considers high cellularity, pleomorphism, and one of the additional features including presence of mitotic figures. Those authors did not differentiate between atypical and anaplastic meningioma. Considering this body of published data and our own experience, we found it most useful to restrict the definition of atypical meningioma to two major histopathological features: increased cellularity and a significant and defined increase of mitotic activity. Use of these simple and reproducible criteria allowed the easy recognition of a meningioma subtype having a definitive increase of risk for recurrence over classic tumors, but a lower recurrence rate than anaplastic meningiomas. Atypical meningioma was recently included in the new World Health Organization (WHO) classification of central nervous system tumors[25] and is defined as "meningiomas in which often several of the following features are evident: frequent mitoses, high cellularity, small cells with high nuclear cytoplasmic ratios and/or prominent nucleoli, uninterrupted patternless or sheet-like growth, and foci of necrosis." Although this is an excellent description of ominous histopathological features, terms such as "often" and "several" might be considered somewhat vague for a detailed correlative study.

Meningioma Subtypes and Ag-NOR Counts

Studies of proliferation indices in meningiomas and other brain tumors have usually shown a good correlation with anaplasia or malignancy.[4,17,18,34,35,46] In a previous study, we could not find a clear-cut correlation of Ag-NOR values to labeling indices of Ki-67 and bromodeoxyuridine (BUdR) when all brain tumors were considered collectively.[31,32] In this study, however, the mean numbers of Ag-NOR's were highly significantly correlated with the three-step scale of classic, atypical, and anaplastic meningiomas.

Other studies investigating Ag-NOR numbers in meningiomas also showed some correlation with histopathological malignancy and recurrence.[1,3,40,44,49] However, Boon and Sharif[1] only distinguished "benign" and "atypical" tumors in their brief communication. Although Ag-NOR counts differed between "benign" and "atypical" tumors, no difference was found between primary and recurrent tumors. The term "atypical" as used by those authors encompassed tumors with features differing from meningiomas with classic histology, but it remains unclear whether their "atypical" tumors reflect definitive malignancy or not.

Orita, *et al.*,[40] described correlations between Ag-NOR numbers and BUdR labeling indices in meningiomas. Following the original staining protocol,[7] they obtained Ag-NOR numbers strikingly lower than the values found in our series. We suspect that their low counts may be caused by the formation of large silver-stained structures apparently corresponding to nucleoli in which no Ag-NOR's can be identified. This phenomenon has been described in our previous study[31,32] and by other authors.[13,36] Evaluation of Ag-NOR's within silver-stained nucleoli is difficult and attempts have led to severe interobserver disagreements,[13] so that application of the Ag-NOR method to routinely fixed paraffin-embedded tissue was even claimed to be nonspecific and unreliable.[14] However, experiments on incubation time, concentration of silver solution, and incubation temperature by Hittmair, *et al.* (in preparation), resulted in the identification of certain combinations of time, temperature, and concentration to achieve a much clearer presentation of Ag-NOR's within the nucleolus; the present study was performed using this optimized method. We recently found by chance that an Ag-NOR staining result very similar to that obtained by our optimized protocol can also be achieved by the modified Bielschowsky impregnation method, which is used in neuropathological laboratories for demonstration of Alzheimer histopathology, but which is much more laborious and expensive than our protocol.

In further studies of the Ag-NOR technique, meningiomas were investigated among other non-neural[49] and intracranial[44] tumors. Meningiomas, including a small number of nonbenign tumors, were "graded fol-

lowing the WHO classification." The authors obtained a correlation of Ag-NOR numbers, and inverse correlation of Ag-NOR area, with malignancy. However, the WHO grading[57] never did appropriately define the criteria for meningiomas of Grades 2 and 3; thus, it remains obscure whether WHO Grade 2 tumors comply with our atypical meningiomas.

We were not able to demonstrate differences in Ag-NOR numbers in classic meningiomas with or without later recurrence, in accordance with other authors[1] but in contrast with another recent, albeit much smaller, series.[3] A distinct increase of Ag-NOR values in recurrent tumors related to dedifferentiation could be observed in only one case.

Papillary Meningiomas and Hemangiopericytomas

Most neuropathologists agree that the meningeal hemangiopericytoma is a tumor entity separate from the group of meningiomas. It has some similarities to papillary meningioma, a histologically characteristic variant of malignant meningioma.[30,42] Both tumors are known to show a significantly higher tendency to recur in comparison with classic meningioma;[24,53] this is also comfirmed by our study. However, tumors of this group had significantly lower Ag-NOR numbers than anaplastic meningiomas, with counts similar to those in classic tumors. Nuclei did not form a few large silver-stained nucleoli, as noted in anaplastic meningiomas, but revealed small, clearly defined Ag-NOR's. It remains unclear whether this difference reflects histogenetic differences. If so, then it might support separation of the two tumor groups.

Conclusions

Atypical meningiomas, defined by increased cellularity and mitotic rate, have recurrence rates intermediate between those of classic and anaplastic meningiomas. The extent of surgery and tumor size and site are unlikely to account wholly for these differences. Correlation of Ag-NOR counts with such a three-step histopathological malignancy scale further supports the introduction of the atypical meningioma as a tumor with simple definition and intermediate biological behavior. For the individual tumor patient, however, the overlapping of Ag-NOR counts in all three groups of malignancy limits clinical use of these data for prognostic considerations of a given tumor specimen.

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Address reprint requests to: Herbert Budka, M.D., Neurological Institute, University of Vienna, Schwarzspanierstrasse 17, A-1090 Vienna, Austria.