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Histological Subtypes and Prognostic Problems in Meningiomas*

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Summary. The incidence of the various histological subtypes of meningiomas was examined in 1238 patients with surgically treated meningiomas, about 80% arising within the cranial cavity. The histological classification used was that of Courville (1950) and Rubinstein (1972), but "angioblastic" meningiomas were segregated into 3 groups: highly vascularized meningiomas, hemangioblastomas, and hemangiopericytomas. Endotheliomatous and transitional forms constituted 85% of the total (71.5% of intracranial tumors), fibroblastic forms 6.6 and 7.5%, respectively, and highly vascularized (endotheliomatous or transitional) meningiomas 5.2% of the intracranial tumors, while true "angioblastic" meningiomas (hemangioblastomas and hemangiopericytomas) amounted to 2.8% of the total (3.1% of the intracranial tumors). 1.2% were "atypical" (so-called malignant) meningiomas; true meningeal sarcomas were excluded.

The incidence of recurrence in patients surviving at least 5 years after apparently complete removal of the tumor was 13% for all sites, and 14.2% for intracranial tumors, but almost twice as high after partial removal. There were no significant differences in the recurrence rate and intervals between first and second operation according to the various histological subtypes of meningiomas, except for hemangiopericytomas which recurred with significantly higher frequency and, together with atypical meningiomas, at much shorter intervals than the others.

The prognostic significance of some histological criteria in "non-angiomatous" meningiomas was examined in 211 patients surviving at least 5 years after apparently complete removal of the tumor. Among the recurrences, there was a significantly higher degree of cellularity and increased mitotic rate and, probably, of cortical invasion, while nuclear pleomorphism, increased vascularity, and focal necroses showed no definite differences. The presence of mitotic figures alone appeared to be of no prognostic value.

While most recurrent meningiomas did not change their basic morphological type significantly, about 12.5% of the recurrences appeared to have a different rate of growth as suggested by increased cellularity and mitotic rates. In 2 cases an isomorphic (benign) meningioma became a true spindle cell sarcoma.

Key words: Meningioma — Hemangioblastoma — Hemangiopericytoma — Recurrence rate — Atypical meningioma — Cytology brain tumors.

* Dedicated to Prof. P. Röttgen on the occasion of his 65th anniversary.

Zusammenfassung. Die Häufigkeit der verschiedenen histologischen Meningiomtypen wurde bei 1328 Patienten mit chirurgisch behandelten Meningiomen, darunter 80% intrakraniellen Geschwülsten, untersucht. Die histologische Klassifikation erfolgte nach Courville (1950) und Rubinstein (1972), doch wurden „angioblastische" Meningiome in 3 Gruppen untergliedert: gefäßreiche Meningiome, Hämangioblastome und Hämangiopericytome. Endotheliomatöse und Mischformen umfaßten 85% des Materials (71,5% der intrakraniellen Geschwülste), fibroblastische Formen 6,6 bzw. 7,5% und gefäßreiche (endotheliomatöse und Mischtyp-)Meningiome 5,2% der intrakraniellen Geschwülste, während echte „angioblastische" Meningiome (Hämangioblastome und Hämangiopericytome) 2,8% des Gesamtmaterials (3,1% der intrakraniellen Tumoren) ausmachten. 1,2% waren „atypische" (sog. maligne) Meningiome; echte Meningealsarkome wurden ausgeschlossen.

Die Rezidivhäufigkeit bei Patienten mit mindestens 5 Jahren Überlebenszeit nach offenbarer Totalresektion des Tumors betrug 13% für alle Lokalisationen und 14,2% für die intrakraniellen Tumoren, war aber nach Partialresektion fast doppelt so hoch. Es fanden sich keine signifikanten Unterschiede in der Rezidivhäufigkeit und den Intervallen zwischen Erst- und Zweitoperation bei den verschiedenen histologischen Untergruppen der Meningiome. Eine Ausnahme bildeten die Hämangiopericytome, die signifikant höhere Rezidivraten boten und gemeinsam mit den atypischen Meningiomen wesentlich kürzere Rezidivintervalle aufwiesen.

Die prognostische Bedeutung einiger histologischer Kriterien bei „nichtangiomatösen" Meningiomen wurde bei 212 Patienten mit mindestens 5jähriger Überlebenszeit nach kompletter Tumorresektion geprüft. Die Rezidivfälle boten signifikant höhere Zelldichte und Mitoserate sowie vermutlich häufigere Rindeninvasion, während Kernpleomorphie, gesteigerter Gefäßgehalt und Fokalnekrosen keine Unterschiede zeigten. Der Nachweis von Mitosen allein erschien ohne prognostische Bedeutung.

Während die meisten Meningiomrezidive keine wesentliche Änderung des morphologischen Grundtyps boten, zeigten 12,5% der Rezidive erhöhte Zelldichte und Mitoseraten als offenbare Hinweise auf eine geänderte Wachstumsrate. In 2 Fällen wurde die Umwandlung eines isomorphen (benignen) Meningioms in ein echtes Spindelzellsarkom beobachtet.

Introduction

Recurrence of intracranial meningiomas after apparently complete removal of the tumor is estimated to range from 5 to 21% (Hoessly and Olivecrona, 1955; Simpson, 1957), the figures being higher when resection was incomplete (Skullerud and Löken, 1974). The average postoperative period at which such recurrences become evident is 5 years (Simpson, 1957; Crompton and Gauthier-Smith, 1970). Recurrence of a spinal meningioma is far rarer (Svien and Wood, 1957). While the extent of tumor extirpation is agreed to be the most important prognostic factor in meningiomas, the prognostic significance of the histological character of the growth is controversial. While Crompton and Gauthier-Smith (1970), using the classification of Courville (1950), found that the syncytial meningiomas were most likely to recur and the fibroblastic ones least so, other authors found no significant differences in the recurrence rate and length of postoperative survival according to the various histo-

logical subtypes, but a small group of "angioblastic" meningiomas has a poorer prognosis (Bailey *et al.*, 1928; Simpson, 1957; Earle and Richany, 1969). These tumors having the appearance of hemangiopericytomas were found to recur with significantly higher frequency than the others (Pitkethly *et al.*, 1970; Gullotta and Heller, 1974; Skullerud and Löken, 1974).

The prognostic value of other histological features in meningiomas is also controversial. While Henschen (1955), Simpson (1957) and others found little correlation between the cytological criteria and the growth rate of the tumors, most authors agree that high mitotic rates, high cellularity, focal necroses, and cortical infiltration are suggestive of rapid growth and increased recurrence rate (Gullotta and Wüllenweber, 1968; Crompton and Gauthier-Smith, 1970; Rubinstein, 1972). High cellularity was found significantly more often among recurring syncytial tumors (Skullerud and Löken, 1974).

Although most recurrent meningiomas, as demonstrated by repeated biopsies, do not change their basic type significantly (Gullotta and Wüllenweber, 1968; Crompton and Gauthier-Smith, 1970), in some examples the morphological features of the tumor may be markedly altered (Russell and Rubinstein, 1971). A benign and endotheliomatous tumor may very rarely become a malignant spindle cell sarcoma (Russell, 1950).

Atypical (so-called malignant) meningiomas showing some cellular pleomorphism and increased mitotic rate, indicative of aggressive growth, are quite rare and the more frankly invasive examples cannot be easily distinguished from primary meningeal sarcomas by light microscopy (Rubinstein, 1972). The ultrastructure of these latter tumors is very similar to the basic type of "benign" meningiomas, although meningeal sarcomas also show some architectonic features suggestive of their arachnothelial origin (Matakas and Cervós-Navarro, 1973).

The purpose of this paper is to present further information about the incidence of the various histological types of meningiomas and the possible prognostic value of histological assessment as seen in a large consecutive series of such tumors.

Material and Methods

The material consisted of 1238 surgically treated cases of meningiomas coded from January 1, 1964 to December 31, 1973 in the files of the Neurological Institute, University of Vienna, and the State Institute of Neurosurgery, Budapest. The former material was received mainly from the Department of Neurosurgery, University of Vienna (746 cases), and a small number from the Division of Neurosurgery, Wagner-Jauregg-Krankenhaus, Linz (49 cases).

The total material was divided into 2 groups. The first group included those patients where the surgical removal of the tumor was believed to be complete, and the second one those with only partial or subtotal removal. A follow-up study

was performed in the patients of the Vienna series who had been treated between 1964 and 1969. Of 372 patients of this group, 34 died within the first 4 postoperative weeks. 26 died within 5 years from unrelated causes. Sufficient information was obtained in 297 patients. In 268 of them "complete" removal was reported by the neurosurgeons, and partial removal in 29. No follow-up data of the Budapest material or of the Vienna patients surviving less than 5 years were obtained, but all recurrences were included.

The surgical and autopsy material was fixed in formalin. Paraffin sections were stained with hematoxylin-eosin, Gomori's reticulin, and van Gieson's elastic stains and, if necessary, with trichrome and periodic acid Schiff (PAS).

All tumors were histologically re-examined and classified independently by both authors. The histological classification proposed by Rubinstein (1972) was largely used in this study. However, "angioblastic" meningiomas were divided into 3 groups: highly vascularized meningiomas, hemangioblastomas, and hemangiopericytomas. Fibrosarcomas and undifferentiated, high-grade malignant primary meningeal tumors were excluded, whereas meningiomas showing some criteria suggesting rapid growth, i.e. high cellularity, slightly increased mitotic rate, and invasion of the bone or cortex, were included.

The histological type of meningiomas and additional features registered in non-angioblastic meningiomas were compared with regard to the frequency of the clinical recurrence. The differences between these groups were evaluated by the χ^2 test. Correlations between the histological features and intervals between first operation and reoperation or death from recurrence were also examined.

Results

The total material of 1237 cases of meningiomas treated surgically, and examined during the past 10 years in two Neuropathology departments, included 989 patients with intracranial (79.4%), 41 primary intraorbital (3.3%), and 208 spinal tumors (16.9%). Of the total series, 70.7% (876 patients) were females. In the cranial cavity there was a ratio of females to males of 2:1; the spinal examples showed a much greater incidence of females with a ratio of almost 10:1. The average age at hospital admission was 50.56 ($\pm$ 10.9) years for intracranial, and 60.98 ($\pm$ 6.5) years for spinal tumors. The regional incidence of the tumors is given in Table 1.

Courville's (1950) histological classification adopted by Russell and Rubinstein (1971) and Rubinstein (1972), which was used in the present study, divides the meningiomas into syncytial (endotheliomatous), transitional, fibroblastic, angioblastic, and atypical (malignant) forms. Many tumors showed the features of two or more of the above categories, and in these cases the tumor was classified on the dominant pattern. The most frequent examples showed overlapping between the endotheliomatous and transitional types, the latter being rich in stroma.

"Angioblastic" meningiomas (Cushing and Eisenhardt, 1938) include at least 3 different histological categories: a) highly vascularized me-

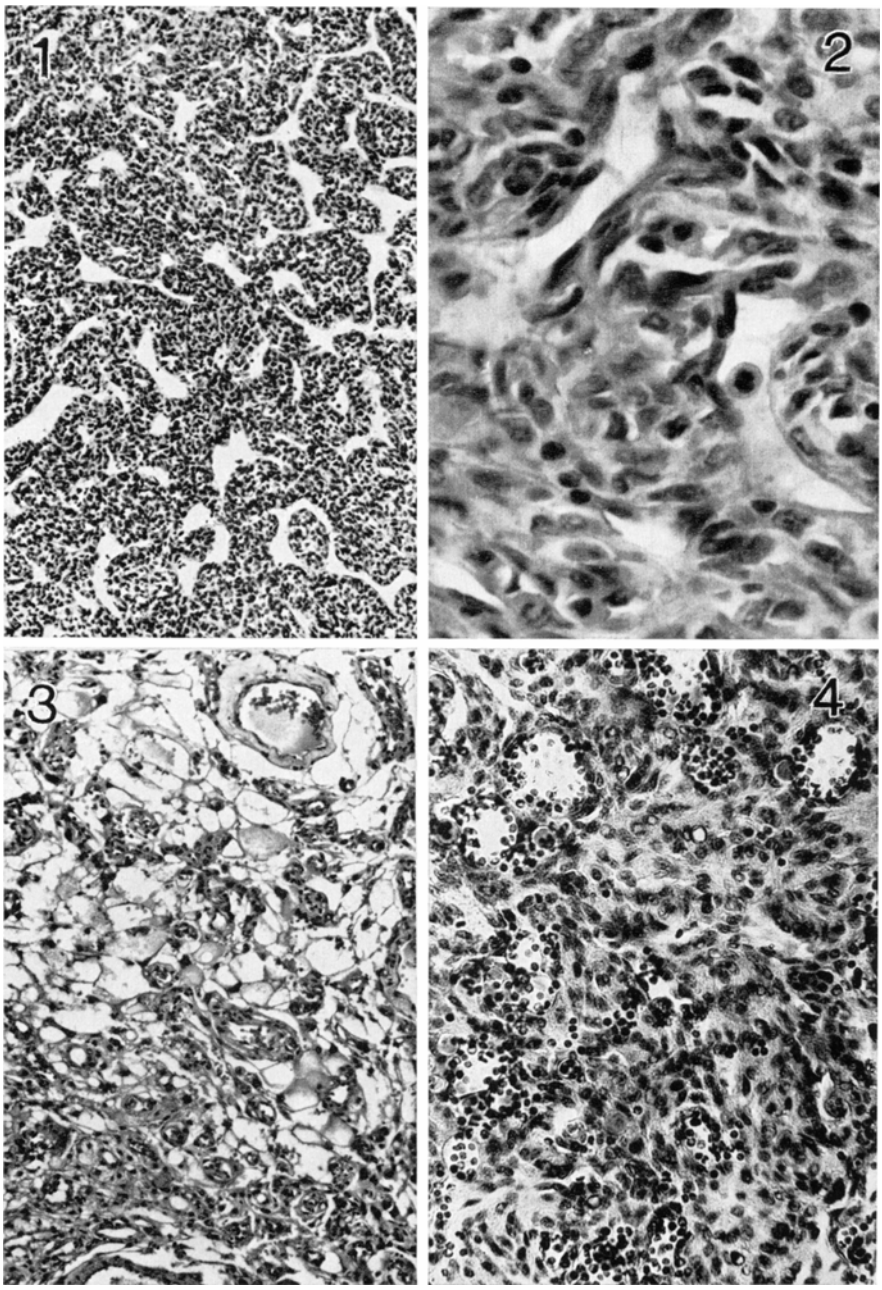
Table 1. Location of meningiomas (total series)

Site	Vienna series		Budapest series		Total series	
	number	percent	number	percent	number	percent
Convexity						
Frontal	81	14.6	95	21.6	176	17.1
Parietal	77	14.0	71	16.1	148	14.9
Occipital	18	3.3	19	4.3	37	3.8
Temporal	37	4.8	62	14.1	99	10.0
Falx, parasagittal	132	24.0	62	14.1	194	19.7
Olfactory groove	49	9.0	33	7.5	82	8.3
Supra/parasellar	31	5.6	19	4.3	50	5.1
Sphenoid ridge	73	13.3	34	7.7	107	10.8
Intraventricular	3	0.6	3	0.7	6	0.6
Tentorial and posterior fossa	48	8.8	42	9.6	90	9.1
Intracranial	549	79.0	440	81.0	989	79.8
Intraorbital	24	3.4	17	3.2	41	3.3
Spinal	122	17.6	86	15.8	208	16.9
Total	695	100.0	543	100.0	1238	100.0

ningiomas, b) the "hemangioblastic" type (Fig. 3), having the light and electron microscopical appearance of the capillary hemangioblastoma of the cerebellum (Castaigne *et al.*, 1968; Cervós-Navarro, 1971; Leu and Rüttner, 1973), and c) the "hemangiopericytic" variant (Figs. 1 and 2) similar if not identical to hemangiopericytomas arising elsewhere in the body (Pitkethly *et al.*, 1970; Rubinstein, 1972).

Richly vascularized meningiomas showing nests of arachnothelial cells between the dense vascular meshwork (Fig. 4) can be separated from the two other types which are suggested to originate from vasoformative elements (Kawamura *et al.*, 1973; Battifora, 1973; Jellinger and Denk, 1974).

The term "atypical" (malignant) meningioma was applied to those tumors which showed somewhat atypical cytological features indicating rapid and agressive growth (high cellularity, cellular pleomorphism, increased numbers of mitoses) without, however, presenting the distinctive features of sarcomas (Figs. 5—7). In one of these patients (Fig. 8), extracranial metastasis was reported (Fenyes and Slowik, 1972). This group does not include primary "typical" meningiomas showing recurrences with a tendency towards dedifferentiation or increased rate of growth (Figs. 9—13).



Figs. 1—4

Table 2 shows the number of tumors in each of the histological categories. Endotheliomatous and transitional forms, representing 84.9% of the total series, comprised 71.5% of the intracranial, 94.5% of the spinal, and 97.5% of the intraorbital meningiomas. Fibroblastic tumors occurred in 7.5% of the intracranial, and in 4.5% of the spinal tumors. Richly vascularized meningiomas, usually showing admixture with syncytial or transitional forms (5.2% of the total), hemangioblastomas (1.2% of the total), and "atypical" meningiomas (1.2% of the total) were restricted to the cranial cavity, while hemangiopericytomas (1.6% of the total) occurred in intracranial and spinal locations.

The incidence or *recurrence* in the total series (uncorrected material including early postoperative deaths) was 10.5%. Table 3 shows the distribution of the recurrent meningiomas according to their site of origin. Falcine and convexity tumors recurred with higher frequency

Fig. 1. Recurrent hemangiopericytoma in occipital region of male aged 74. Endothelial lined vascular channels are surrounded by densely arranged tumor cells. H.-E., × 90

Fig. 2. Parasagittal hemangiopericytoma in male aged 28 showing two recurrences. Network of slit-like capillaries lined by endothelial cells are surrounded by plump pericytes. H.-E., × 540

Fig. 3. Hemangioblastoma over right parietal lobe in male aged 64 showing hyalinized and stromal cells. H.-E., × 100

Fig. 4. Highly vascularized endotheliomatous meningioma in right frontal region of female aged 61. H.-E., × 225

Figs. 5—7. Atypical (malignant) endotheliomatous meningioma in female aged 65

Fig. 5. Processes of parasagittal tumor infiltrating into cerebral cortex. First operation. H.-E., × 100

Fig. 6. Recurrence of same tumor showing somewhat pleomorphic cytologic features and mitotic figures. H.-E., × 328

Fig. 7. Third recurrence of same tumor with considerable pleomorphism, nuclear hyperchromasia and increased mitotic rate. H.-E., × 90

Fig. 8. Atypical (malignant) endotheliomatous meningioma in occipital region of female aged 51, showing pleomorphism and increased number of mitoses. H.-E., × 225

Figs. 9—11. Recurrent and dedifferentiating parasagittal meningioma in male aged 67

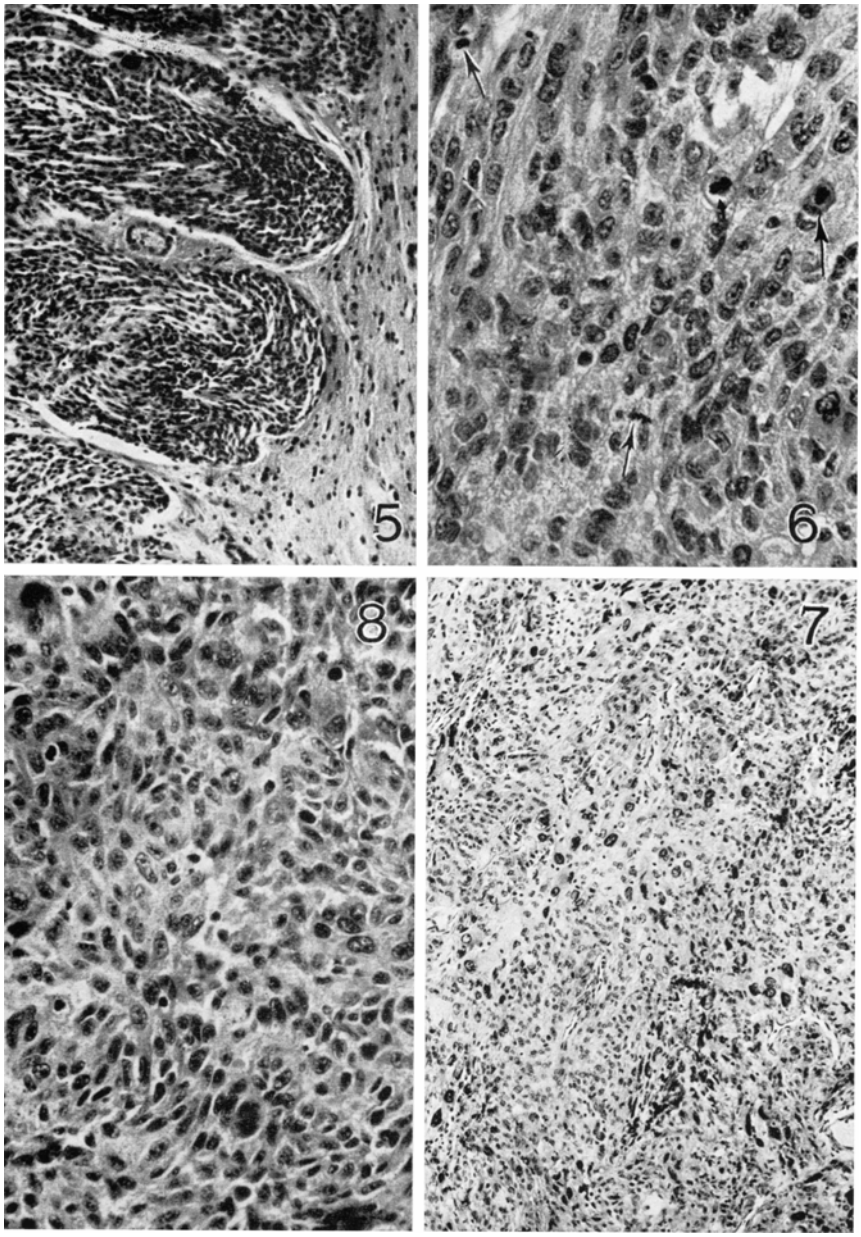
Fig. 9. First surgical specimen. Isomorphic picture of transitional type. H.-E., × 67

Fig. 10. Recurrence showing isomorphic arrangement with occasional mitosis (arrow). H.-E., × 225

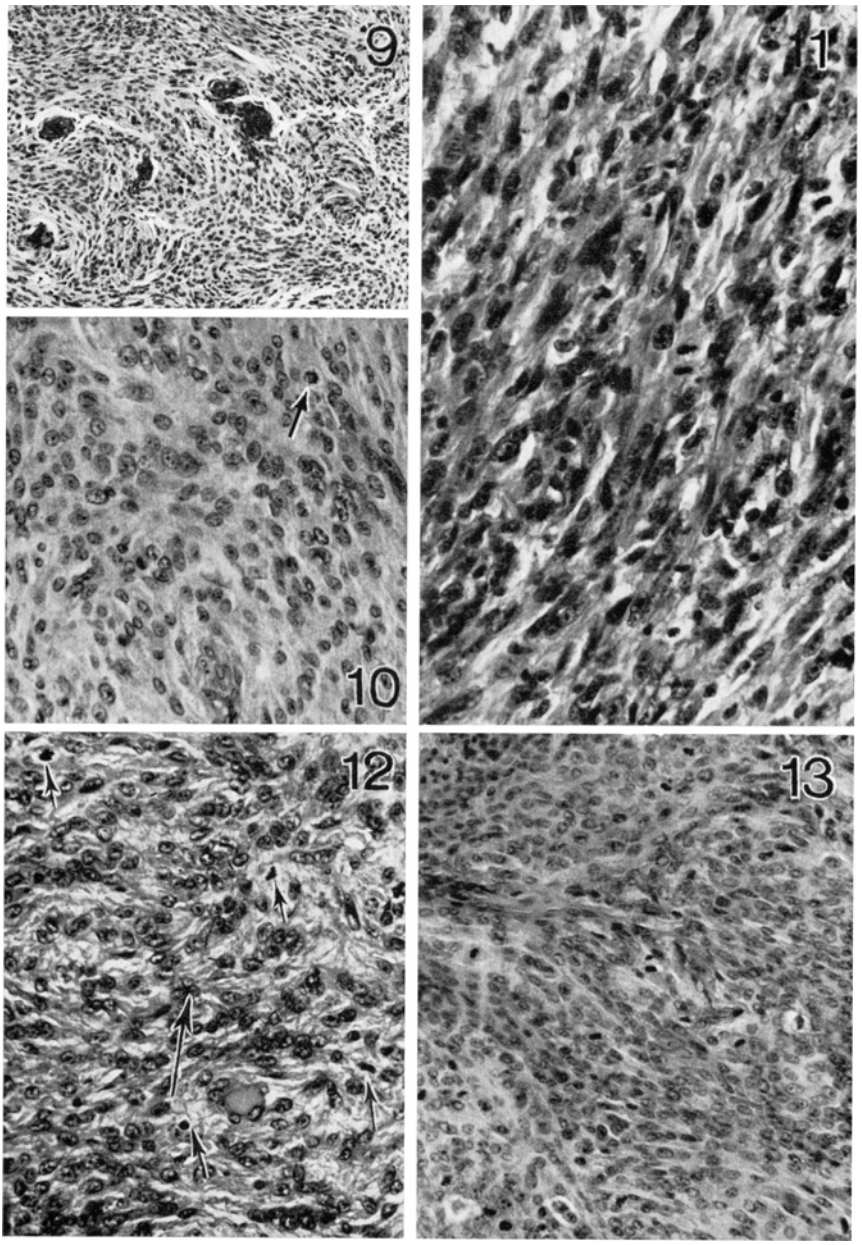
Fig. 11. Second recurrence showing fibrosarcoma-like picture with many mitotic figures. H.-E., × 252

Fig. 12. Second recurrence of previously amitotic endotheliomatous meningioma in female aged 49, showing many mitoses. H.-E., × 225

Fig. 13. Second recurrence of previously amitotic endotheliomatous parasagittal meningioma in female aged 33, showing many mitotic figures. H.-E., × 225



Figs. 5—8 (for legends see page 285)



Figs. 9—13 (for legends see page 285)

Table 2. Types of meningiomas in total material

Histology	Intracranial tumors				Intraorbital				Spinal tumors				Total series all locations	
	Vienna	Budapest	total		Vienna	Budapest	total		Vienna	Budapest	total			
			n	%			*n*	%			*n*	%	*n*	%
Endotheliomatous	287	293	580	58.5	20	17	37	90.0	114	55	169	81.2	786	63.3
Transitional	152	72	227	23.0	3	—	3	7.5	5	23	28	13.3	254	20.9
Fibroblastic	27	46	73	7.5	—	—	—	—	2	7	9	4.5	82	6.6
Highly vascularized	57	7	64	6.5	—	—	—	—	—	—	—	—	64	5.2
Hemangioblastoma	11	3	14	1.4	—	—	—	—	—	—	—	—	14	1.2
Hemangiopericytoma	8	9	17	1.7	1	—	1	2.5	1	1	2	1.0	20	1.6
Atypical (malignant)	6	8	14	1.4	—	—	—	—	—	—	—	—	14	1.2
Total	549	440	989	100.0	24	17	41	100.0	122	86	208	100.0	1238	100.0

Table 3. Site of recurrent meningiomas

Site	Vienna series		Budapest series		Total material		Percent of total series
	complete removal	partial removal	complete removal	partial removal	complete removal	partial removal	
Frontal	10	—	5	2	15	2	9.1
Parietal	6	—	5	1	11	1	8.0
Occipital	5	1	4	—	9	1	28.0
Temporal	3	—	8	—	11	—	11.1
Parasagittal	11	2	9	1	20	3	11.8
Olfact. groove	6	2	1	—	7	2	10.8
Parasellar	3	4	—	1	3	5	16.0
Sphenoid r.	3	2	3	1	6	3	8.8
Poster. fossa	3	1	3	—	6	1	7.8
Intracranial	49	12	38	6	87	18	16.2
Orbital	8	3	4	1	12	4	39.0
Spinal	8	1	1	—	9	1	4.8
Total	66	16	43	7	109	23	10.5

than those on the base of the skull. The mean interval between first operation with "complete" removal of the tumor and reoperation was 6.6 years (range 0.5 to 32 years). The recurrence rate of orbital tumors was 39%, and of spinal meningiomas 4.8%.

Table 4 shows the overall frequency of the various histological subtypes of meningiomas in recurrences after complete and partial removal of the tumor. It demonstrates the limited prognostic value of general histological criteria including the presence or absence of mitoses, except for the comparatively frequent recurrence rate of hemangiopericytomas and "atypical" (so-called malignant) meningiomas.

For prognostic purposes, the Vienna series of patients surviving at least 5 years was evaluated. Of 694 patients, 65 died within the first 4 postoperative weeks, and 26 within 5 years from unrelated causes. Of the remaining 603 patients, 81 (13.5%) had recurrence of the tumor. However, 10% of the recurrences occurred after partial removal of the growth. The incidence in these patients after complete removal of the tumor was 13% for all sites, and 14.2% for intracranial tumors, while after partial removal, the incidence was 27 and 26%, respectively. Parasagittal tumors recurred with higher frequency than those on the convexity and base of the skull (Table 5).

The frequency of recurrences in the various histological types of tumors after "complete" removal, in patients surviving at least 5 years,

Table 4. Site and type of recurrent meningiomas (total series)

Type (first biopsy)	Intracranial		Intraorbital		Spinal		Total	
	complete removal	partial removal	complete removal	partial removal	complete removal	partial removal	complete removal	partial removal
Endotheliomatous								
a) no mitoses	32	5	6	2	4	—	42	7
b) with mitoses	22	3	4	1	3	—	29	4
Transitional								
a) no mitoses	10	4	1	—	2	—	13	4
b) with mitoses	7	2	—	—	—	—	7	2
Fibroblastic								
a) no mitoses	3	—	—	—	—	—	3	—
b) with mitoses	3	1	—	—	—	—	3	1
Atypical (malignant)	3	3	1	—	—	—	4	3
Hemangioblastoma	2	—	—	—	—	—	2	—
Hemangiopericytoma	6	—	—	1	—	1	6	2
Total	88	18	12	4	9	1	109	23

Table 5. Location of meningiomas in 297 patients surviving at least 5 years

Site	"Completely" removed (268 cases)				Partially removed (29 cases)			
	with recurrence		no recurrence		with recurrence		no recurrence	
	number	percent	number	percent	number	percent	number	percent
Frontal	5	13	31	87	—	—	1	100
Parietal	3	11	24	89	—	—	3	100
Occipital	2	25	6	75	3	100	—	—
Temporal	1	5	20	95	—	—	3	100
Parasagitt.	9	17	43	83	1	33	2	67
Olfact. gr.	2	11	16	89	1	50	1	50
Parasellar	—	—	10	100	1	50	1	50
Sphenoid r.	4	15	23	85	1	17	5	83
Post. fossa	1	8	12	92	—	—	4	100
Intracranial	27	14.2	186	85.8	7	26	20	74
Orbital	3	75	1	25	—	—	—	—
Spinal	2	4	50	96	4	50	1	50
Total	32	13.1	236	86.9	8	27.0	21	73.0

Table 6. Types of meningiomas in 268 patients surviving at least 5 years where tumor was thought to be completely removed. Intracranial tumors in parenthesis

Histological type	With recurrence		Without recurrence	
	number	percent	number	percent
Endotheliomatous	19 (16)	58	161 (114)	68
Transitional	5 (5)	16	50 (47)	21
Fibroblastic	3 (2)	10	18 (17)	8
Atypical (malignant)	3 (2)	3	1 (1)	0.5
Hemangioblastoma	0	0	5 (5)	2
Hemangiopericytoma	4[a] (3)	13[a]	1 (1)	0.5
Total	32 (27)	100	236 (185)	100

[a] $P < 0.005$.

Table 7. Additional histological features in completely removed intracranial non-angioblastic meningiomas (survival time 5 years and over)

Histological features	Recurrences (26 cases)		No recurrence (185 cases)	
	number	percent	number	percent
High cellularity	12[a]	46	21	11
High vascularity	4	15	25	14
Nuclear pleomorphism	3	11	6	3
Increased mitotic rate	10[b]	38	6	3
Focal necroses	7	26	18	10
Cortical invasion	4[a]	15	6	3
Bone invasion	5	18	9	5

[a] $P < 0.05$. [b] $P < 0.001$.

is shown in Table 6. Only hemangiopericytomas were found to recur with a significantly higher frequency than the others, which confirms previous observations (Pitkethly *et al.*, 1970; Skullerud and Löken, 1974).

Certain additional histological features in "non-angioblastic" meningiomas were evaluated with regard to the recurrence in 211 patients surviving at least 5 years (Table 7). High cellularity and the presence of mitotic figures were found more frequently among the recurrent tumors, and these differences were statistically significant. The significant preponderance of invasion of the cortex among recurrent meningiomas appears conjectural due to insufficient investigation of this fact in many non-recurring tumors. Nuclear pleomorphism and small focal necroses occurred more often in recurrent growths, but these differences were not significant. High vascularity was equally seen in both groups.

Table 8 gives the average time elapsing between primary operation and second or further surgical interventions in various types of menin-

Table 8. Average intervals between first operation and reoperations in different types of "completely" removed intracranial meningiomas

Histological type (first biopsy)	Number cases	Interval to 2nd operation (years)	Interval to 3rd operation (years)	Number cases	Interval to 3rd or 4th operation (years)	Number cases
Endotheliomatous						
a) no mitoses	30	8.9 (0.5—32)	7.5 (2.0—13)	2	1.0 (0.5—3.0)	5
b) with mitoses	17	5.5 (1.0—25)	1.6 (1.0—3)	5		
Transitional						
a) no mitoses	9	6.9 (0.5—15)	1.0	1		
b) with mitoses	6	6.8 (3.0—12)	1.6 (1.0—2)	3	1.0	1
Fibroblastic						
a) no mitoses	2	6.5 (4.0—9)	5.0	1		
b) with mitoses	3	8.6 (2.0—16)	1.5 (1.0—3)	2		
Atypical (malignant)	4	1.5 (1.0—3)	7.0	1	0.5	1
Hemangioblastoma	2	10.5 (6.0—15)	2.5 (1.0—4)	2		
Hemangiopericytoma	6	4.0 (1.0—8)				
Total	78			17		7

giomas (as seen in the first biopsy specimen). A series of 79 cases of completely removed meningiomas, with sufficient data, was evaluated. The longest intervals were seen in hemangioblastomas and in endotheliomatous meningiomas without mitoses, while the shortest were in cases with atypical (malignant) meningiomas. The differences between endotheliomatous meningiomas with and without mitoses were not significant. No differences were seen in transitional types. The intervals between the second and third intervention (17 patients) were usually shorter than the above intervals, and showed considerable differences between tumors with and without mitoses. In 7 cases with three and more recurrences the subsequent intervals were short (0.5 to 3 years).

In most of the recurrent meningiomas, including the hemangiopericytomas, no definite changes in the basic morphological type of tumor were seen in the second or further specimens, although they may have appeared to have a different rate of growth as suggested by more or fewer mitoses and focal necroses. Only in 11 out of 88 cases with completely removed "typical" (isomorphic) intracranial meningiomas (listed in Table 3), were some histological signs of rapid growth or cytological dedifferentiation observed in recurrent biopsies (Table 9). In 7 cases the first biopsy specimen showed the silent picture of various types of "non-angiomatous" meningiomas without mitoses; in 4 other tumors high cellularity and few mitotic figures were seen. In 8 patients, the tumor

Table 9. Recurrent meningiomas with tendency towards dedifferentiation

	Case No.	Age, sex	Site	Duration sympt.	Extent of removal	Histology (first biopsy)	First recurrence			Second recurrence			Course
							interval	removal	histology	interval	removal	histology	
1	N 75—64 N 3—74 N216—74	57 M	falx	14 mo.	compl.	syncytial high cellul. no mitoses	9 yr.	compl.	syncytial high cellul. mitoses!	5 mo.	part.	invasive fibro- sarcoma	died 2 weeks later fibrosarcoma
2	N260—65 N206—72	63 F	tento- rium	4 yr.	compl.	fibroblast. no mitoses	7 yr.	compl.	fibrillary sarcoma				unknown
3	N310—67 N206—72	65 F	front. left	2 yr.	compl.	transitory no mitoses cort. invas.	20 mo.	compl.	transitory polymitotic necroses				unknown
4	N104—70 N294—72 N284—73 N 21—74 N256—74	49 F	par.- occ. left	?	compl.	cytoplast. highly cell. no mitoses no invasion	28 mo.	compl.	cytoplast. highly cell. polymitotic no invasion	12 mo.	compl.	same	2 further recurrences after 6 and 6 months same histology as 1st recurr.
5	N 27—71 N311—71 N449—71 N319—72 NI388—72	56 M	front. par. left	3 mo.	compl.	syncytial no mitoses no invasion no necroses	7 mo.	compl.	syncytial high cellul. polymitotic no invasion	13 mo.	compl.	same	died after 4th operation; invasion of sup. sag. sinus same histology

Table 9 (continued)

	Case No.	Age, sex	Site	Duration sympt.	Extent of removal	Histology (first biopsy)	First recurrence			Second recurrence			Course
							interval	removal	histology	interval	removal	histology	
6	138—40 N123—72	38 F	front. left	?	compl.	syncytial no mitoses	32 yr.	compl.	syncytial polymitotic		none		
7	1955 N 29—64 N422—71 N447—74	53 F	front. lat.	?	compl.	syncytial no mitoses	5 yr.	compl.	syncytial highly cell. no mitoses	7 yr.	compl.	same	died after 4th operation (3 years interval); sync. polymitotic tumor
8	B354—65 B208—68 B396—70	42 F	front. convex.	?	compl.	transitory some mitoses no invasion	3 yr.	compl.	transitory highly cell. polymitotic	18 mo.	compl.	same	no further recurrence
9	B 4—67 B359—68	61 F	front.	?	compl.	syncytial few mitoses	19 mo.	compl.	syncytial polymitotic	—			unknown
10	B 45—69 B 54—70	36 F	front.	?	compl.	transitory few mitoses	13 mo.	compl.	transitory polymitotic				unknown
11	B187—70 B 55—73 B485—73	43 M	occip.	?	compl.	syncytial few mitoses no invasion	2 yr.	compl.	syncytial polymitotic foc. necroses	3 yr.	compl.	same	3rd recurrence after 10 months same histology

removed at the second or a further operation displayed increased cellularity and mitotic rate, and/or focal necroses without, however, having changed its basic type of architecture (Figs. 12 and 13). 2 cases showed the frank appearance of a fibrosarcoma; one falcine meningioma recurring 9 years after complete removal showed high cellularity and many mitotic figures. 5 months later, a diffuse spindle cell sarcoma invading the brain was partially removed (Figs. 9—11). The diagnosis was confirmed at autopsy 2 weeks later. In another patient, a typical fibrillary meningioma without mitoses converted into a polymitotic spindle celled sarcoma, which was removed 7 years later. No clinical follow-up was possible.

Discussion

In the present series of meningiomas (about 80% arising within the cranial cavity), endotheliomatous and transitional forms comprised 85% of the total and 71.5% of the intracranial tumors; the fibroblastic type was seen in 6.6 and 7.5%, respectively. Richly vascularized meningiomas accounted for 5.2%, while true "angioblastic" forms of primary meningeal tumors suggesting an origin from vasoformative elements (hemangioblastomas and hemangiopericytomas) constituted 2.8% of the total and 3.1% of the intracranial tumors. This is less than in other series, where these types represented 4.2 to 4.7% of intracranial meningiomas (Pitkethly *et al.*, 1970; Skullerud and Löken, 1974), while Gullotta and Wüllenweber (1968) described 3 hemangiopericytomas among 423 meningiomas (0.7%). "Atypical" (so-called malignant) meningiomas restricted to the cranial cavity constituted 1.4% of our series. Cushing and Eisenhardt (1938) described 6 malignant variants in 313 meningiomas (1.9%). Mennel and Zülch (1974), in a study of 1400 meningiomas, found about 10% polymitotic examples, while Tytus *et al.* (1967) reviewing 37 intracranial meningiomas disclosed 4 with malignant features (10.8%). Fibrosarcomas of the dura and primary meningeal sarcomas were excluded from our series.

The overall recurrence rate in the total (uncorrected) series was 10.5%. In a series of patients surviving 5 years or more, the incidence of recurrence after apparently complete removal of the tumor was 13% for all sites and 14.2% for intracranial growths, but was about twice as high after partial removal. The average interval between the first and second operation was 6.6 years and usually decreased in further recurrences. This is in line with the results of other large series (Simpson, 1957; Skullerud and Löken, 1974).

There was no significant difference in the length of the intervals according to the various histological subtypes, except for hemangiopericytomas and atypical (malignant) meningiomas which recurred more

rapidly than the others. These data confirm previous observations on the limited prognostic value of the various histological subtypes of "non-angioblastic" meningiomas compared to the extent of removal (Simpson, 1957; Crompton and Gauthier-Smith, 1970; Skullerud and Löken, 1974).

Of the angioblastic meningiomas the "hemangioblastic" type (supratentorial hemangioblastomas) showed a natural history and prognosis similar to other meningiomas with little tendency to recur. These vascular tumors, attached to the meninges but derived from endothelial cells (Cervós-Navarro, 1971), can be separated from the majority of highly vascularized meningiomas, although combinations of transitional forms between hemangioblastomas and common meningiomas are likely to occur (Rubinstein, 1972; Jellinger and Denk, 1974).

On the other hand, the "hemangiopericytic" type of angioblastic meningiomas recurred with significantly higher frequency and shorter intervals than the others. The unfavorable prognosis of this type has been emphasized repeatedly (Cushing and Eisenhardt, 1938; Kernohan and Uihlein, 1972; Pitkethly *et al.*, 1970; Skullerud and Löken, 1974), but its classification is still controversial. Although the frequent attachment of cerebrospinal hemangiopericytomas to meninges and the finding of meningiomatous whorls in tissue culture (Muller and Mealey, 1971), not confirmed by others (Gullotta and Wüllenweber, 1969; Gaszo, 1974), lend support for their inclusion with the meningiomas, their histological and ultrastructural features, identical to those of vascular tumors arising in the soft tissues (Hahn *et al.*, 1973; Battifora, 1973), justify their separation from the general group of "angioblastic" meningiomas (Jellinger and Denk, 1974). This is supported by the fact that, unlike the supratentorial hemangioblastomas, we never observed any transitions or features intermediate between meningiomas and hemangiopericytomas suggestive of a common origin for both tumors.

While no definite relationship between the other subtypes of meningiomas and their tendency to recur was found, there were correlations between some histological criteria and the recurrence rate in "non-angiomatous" meningiomas. Among the recurrences, there was a statistically significantly higher degree of cellularity, increased mitotic rate and, probably, of cortical invasion, while other details, e.g. nuclear pleomorphism, high vascularity and the presence of focal necroses, showed no definite differences. These data, in line with observations on falcine meningiomas (Crompton and Gauthier-Smith, 1970) and syncytial tumors (Skullerud and Löken, 1974), suggest that the detailed assessment of histological and cytological criteria may give some indications about the biological behavior of these tumors. On the other hand, the presence of mitoses alone appears to be of no prognostic value, as small numbers of mitotic figures are seen in a considerable proportion of otherwise typical

meningiomas (Crompton and Gauthier-Smith, 1970; Zülch, 1971; Rubinstein, 1972). No difference in the recurrence rate nor in the intervals between first and second operation were observed in our material. Thus, the prognostic significance of histological criteria in meningiomas has to be considered critically, except for hemangiopericytomas and atypical tumors showing distinct features of rapid growth.

Similar problems arise in the evaluation of recurrent biopsies. While most recurrent meningiomas do not change their basic type, the possibility of marked alteration in the behavior of previously benign non-angioblastic meningiomas should be borne in mind. In about 12.5% of recurrent meningiomas in our series some changes in the rate of growth were suggested by the presence of increased cellularity and mitotic rates. In exceptional cases, a syncytial or fibroblastic meningioma, without previous signs of aggressive growth, may even become a frank sarcoma. The propensity of such rare changes in the biological behavior of meningeal tumors is apparently not predictable from the routine examination of the first biopsy specimens, and the causal problems of such transformation remain unresolved.

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