Neurosurgery 1992-98
December 1993, Volume 33, Number 6
955 Atypical and Malignant Meningiomas: A Clinicopathological Review
Clinical Study

AUTHOR(S): Mahmood, Asim, M.D.; Caccamo, Dario V., M.D.; Tomecek, Frank J., M.D.; Malik, Ghaus M., M.D.

Departments of Neurological Surgery (AM, FJT, GMM) and Pathology (Neuropathology) (DVC), Henry Ford Hospital, Detroit, Michigan

Neurosurgery 33; 955-963, 1993

ABSTRACT: THERE HAS BEEN continuing debate on the subject of malignant meningiomas, but few studies of large series have been reported. We present our experiences with 25 atypical and malignant meningiomas operated on at Henry Ford Hospital between 1976 and 1990. A total of 319 primary intracranial meningiomas were operated on during this period; of these, 294 (92%) were benign, 20 (6.26%) atypical, and 5 (1.7%) malignant. We used a modified histological grading system, based primarily on World Health Organization criteria of malignancy (hypercellularity, loss of architecture, nuclear pleomorphism, mitotic index, tumor necrosis, and brain invasion), to define atypical and malignant meningiomas. Each of these criteria was given a score from 0 to 3, and then partial scores were added to obtain cumulative scores. These total scores were then used to determine what is benign, atypical, and malignant. The peak incidence of atypical and malignant meningiomas was in the seventh and sixth decades, respectively. The predominance of female patients with benign meningiomas was not observed in the nonbenign group. The male:female ratio for atypical and malignant meningiomas was 1:0.9 versus 1:2.3 for benign meningiomas ($P = 0.024$). The most common presenting symptom and physical sign in our patients was paresis. In reviewing their radiographic features, all patients showed moderate or marked edema on computed tomography. Calcification was exhibited by one patient only and "mushrooming" was seen in three cases. Of the 25 patients, 11 (44%) died during follow-up: 2 in the perioperative period, 8 within the first 5 years, and 1 died 11 years after the diagnosis. There were recurrences in 14 cases (51.85%), 10 (71.42%) of which had undergone gross total resection. Tumor recurrence was accompanied by dedifferentiation from a more benign histological finding in five cases (1.63% of the total number of meningiomas). The 5-, 10-, and 15-year recurrence rates each were 50% for atypical meningiomas and 33%, 66%, and 100% for malignant meningiomas. These recurrence rates far exceeded those for benign meningiomas, which were 2% each ($P = 0.0001$). Radiation therapy did not prevent or delay the recurrence of tumors. However, because there were a small number of patients receiving radiation therapy in our series, we cannot conclude that radiation therapy has no role in the postoperative management of meningiomas.

KEY WORDS: Atypical and malignant; Meningiomas; Recurrence; Radiation

Meningiomas comprise 13 to 19% of primary intracranial neoplasms [3,6,8,12], and their incidence is second only to gliomas. They are generally benign; malignant subtypes, although long recognized [14], are not always easy to define. We are all well aware of the case of Dorothy May Russell who was operated on 17 times by Harvey Cushing [3] and finally died of pulmonary metastases. Malignant meningiomas remain a controversial topic because of a lack of universally accepted histological criteria for malignancy and because few large series to evaluate the problem of malignancy have been published [5,9,10,16,32]. Older literature on the subject has also been considered unreliable because erroneous diagnoses have been reported [26]. We have adopted and expanded the criteria outlined by the World Health Organization (WHO). When these criteria are employed, our results show that an important subgroup of meningiomas with aggressive behavior can be identified and their natural history can be predicted to a large extent.

PATIENTS AND METHODS

The neuropathological records of 319 cases of intracranial meningiomas operated on at our institution from 1976 to 1990 were reviewed. All cases originally described as showing atypical or malignant features, such as hypercellularity, high mitotic count, necrosis, or brain invasion, were retrieved from the archives of the department of pathology. The number of microscopic slides examined in each case ranged from 3 to 16, and, on average, 7 large sections of each tumor were reviewed. Cases of hemangiopericytomas of the meninges or papillary meningiomas were specifically excluded because there is agreement that these tumors pursue an aggressive behavior. All cases were reviewed by one of us (D.V.C.) without a previous knowledge of the patient's outcome after surgery. These nonbenign cases were subsequently classified into atypical and malignant meningiomas, according to the grading system detailed below. The clinical records, including comprehensive follow-up, were closely examined. For those patients not recently seen in the department, their most recent status was assessed via correspondence.

Histological grading of tumors

Criteria to classify meningiomas as benign, atypical, or malignant were listed but not defined by the WHO classification of brain tumors of 1979 [33] and its revision of 1990 [13]. The six criteria are hypercellularity, loss of architecture (described as "sheeting" by some authors), nuclear pleomorphism, mitotic index, tumor necrosis, and brain invasion. Jaaskelainen et al. [9] and Rohringer et al. [19] proposed that each of the WHO parameters be given a score from 0 to 3, and the partial scores added for a total score. According to these authors, tumors with a

total score of 0 to 2 were classified as benign, 3 to 6 as atypical, 7 to 11 as anaplastic, and ≥12 as sarcomatous. However, neither of these groups defined the criteria to be used to assign a score of 1, 2, or 3 for each of the parameters mentioned above. Therefore, the following criteria for grading were established at the beginning of the study.

Nuclear pleomorphism

This feature was graded as 0 when neoplastic cells showed uniform and bland nuclei, with dense chromatin and no nucleoli; Grade 1 when occasional clusters of cells showed nuclei that were two or three times larger with irregular nuclear contours, folded or notched (*Figs. 1 and 2*); Grade 2 when the neoplastic cells predominantly displayed nuclei that were clearly larger than those of typical meningothelial cells, with pale chromatin, clearly defined nuclear membrane, and small, nonprominent or absent nucleoli (*Figs. 3 and 4*); and Grade 3 when most of the neoplastic cells displayed vesicular nuclei, with considerable variation in size, clear chromatin, and, most important, the presence of distinct prominent nucleoli, usually large and sometimes multiple (*Figs. 5 and 6*). Of note, the presence of occasional neoplastic cells with large, hyperchromatic nuclei with dense chromatin and no nucleolus, a common finding in many otherwise typical meningiomas, was not considered as an indicator of nuclear pleomorphism for the purpose of this study.

Hypercellularity

This feature was the most difficult to assess objectively, and its grading was more subjective than the others. This feature also showed the most pronounced variation in different areas of tumor, and it was not unusual to observe adjacent medium- and high-power fields (HPFs) in which the cellularity of tumor varied considerably. Grade 0 was assigned to tumors almost entirely composed of well-formed whorls, where the cells displayed large, bland nuclei separated by abundant cytoplasm (*Fig. 1*). In these tumors, approximately 10 loosely packed large whorls occupied one HPF. Grade 1 was assigned to tumors predominantly composed of large whorls, as described for Grade 0, except for perivascular areas where this pattern was lost and the cells became perceptibly smaller, with less cytoplasm, but were more compactly packed (*Fig. 2*). Grade 2 was assigned to tumors predominantly composed of smaller and less defined concentric whorls, each of which was composed of correspondingly smaller and more closely packed cells. Approximately 30 of these smaller whorls occupied one HPF (*Fig. 3*). A tumor Grade 3 showed tightly packed cells with dense, crowded, and sometimes overlapping nuclei, with little intervening cytoplasm and no distinct whorl formation, giving a very cellular appearance (*Figs. 5 and 6*).

Mitotic rate

In each case, all available slides were scanned, and the areas of the tumor with the highest cellularity, especially those showing loss of architecture, were chosen to evaluate the mitotic rate of tumor. The mitotic count was established by counting mitotic figures in 50 consecutive, nonoverlapping microscopic fields (a total surface of approximately 2 cm^2), and the average number of mitotic figures per 10 HPFs was obtained by dividing the total number of mitotic figures observed in 50 HPFs by 5. Mitotic count was graded as 0 if no mitosis was identified per 10 HPFs, as Grade 1 if 1 to 2 mitoses were identified per 10 HPFs, as Grade 2 if 3 to 4 mitoses were identified per 10 HPFs, and as Grade 3 if ≥ 5 mitoses were identified per 10 HPFs (*Figs. 4 and 6*).

Necrosis

Necrosis was assessed by scanning at low and at medium magnification all available slides from each case and identifying areas of coagulation necrosis of neoplastic cells. A grade of 0 was established when no areas of necrosis were seen; Grade 1 when the foci of necrosis were small and scarce, each involving less than half of an HPF; Grade 2 when the foci of necrosis were readily found after examining several medium-power magnification fields, but were predominantly small, each encompassing less than 1 HPF (*Fig. 2*); Grade 3 when large, confluent foci of necrosis were readily found, each involving areas larger than one HPF.

Loss of architecture

This feature consists of the partial or complete loss of the regular arrangement into the concentric whorls of neoplastic cells in meningotheliomatous meningioma or of intersecting bundles of spindle-shaped meningothelial cells found in typical fibroblastic meningiomas. Instead, the neoplastic cells form large, solid sheets with a syncytial appearance not interrupted by fibrovascular septa. This feature was graded as 0 when it was completely absent; Grade 1 when it was detected only as an incipient loss of the lobular or fascicular arrangement (*Figs. 1 and 2*); Grade 2 when this pattern was found throughout most of the tumor as a readily identifiable loss of the normal arrangement, with each area confined only to 1 or 2 adjacent HPFs (*Figs. 3 and 4*); Grade 3 when it consisted of multiple large and confluent areas of uninterrupted solid pattern, each of them involving several contiguous HPFs (*Figs. 5 and 6*).

Brain invasion

The mere presence of brain parenchyma attached to the tumor, separated by a thin layer of compressed leptomeninges, was not interpreted as brain invasion. Brain invasion was considered to be present when large, rounded tumor masses produced a pushing margin directly against brain tissue (Grade 1) or, even more evidently, when thick cords of neoplastic cells infiltrated the underlying parenchyma, entrapping islands of neuroglial tissue (Grade 2). A summary of this scoring system is described in *Table 1*.

Partial scores were added to obtain cumulative scores. Tumors with total scores ranging from 0 to 4 were considered benign, 5 to 11 atypical, and > 11 malignant.

Radiographic criteria

Although computed tomography (CT) had been performed in all the cases since the late 1970s and reports were in the records, actual films were available in nine cases. Only these were used in analyzing the radiographic data. CT scans were examined for the degree of peritumoral edema, the density of the tumor including the presence of hypodense or cystic areas, calcification, the pattern of enhancement, and the presence of irregular margins and fringes. All tumors were analyzed for the presence of a special growth pattern termed *mushrooming* that was defined as the presence of prominent tumor pannus extending away from the globoid mass [18] (*Fig. 7*).

Treatment

A total of 50 operations were performed on 25 patients. Eight patients were operated on once, 10 twice, and 7 more than twice. The extent of surgical resection was graded according to Simpson's classification [23], with Grade 1 being complete resection and Grade 5 simple decompression. Primary resection was gross total (Simpson's Grade 1 or 2) in 16 tumors and subtotal (Simpson's Grades 3 to 5) in six tumors. Three tumors that underwent primary resection at a different hospital, even though the referring hospital's records reported a complete removal, were not included in the final analysis of recurrences.

Ten patients received radiation therapy (six atypical and four malignant). The dosage ranged from 50 to 62 Gy. Six of these patients (four atypical and two malignant) had undergone total resection, whereas resection was subtotal in four (two atypical and two malignant). Radiation was administered after the first surgery in four patients, and the rest were irradiated at the time of recurrence. Only two patients received chemotherapy.

RESULTS

Incidence, age, and sex distribution

In the 15-year period, 319 meningiomas were operated on at Henry Ford Hospital; of these, 294 (92%) were benign, 20 (6.26%) atypical, and 5 (1.7%) malignant. The peak incidence for benign meningiomas was in the ninth decade (range, 11 to 84 yr), whereas for atypical and malignant meningiomas, the peak incidence occurred in the seventh decade (range, 29-81 yr) and sixth decade (range, 30-60 yr), respectively. This difference in age distribution between the groups was not statistically significant. The male:female ratio was 1:2.3 for benign meningiomas, 1:0.9 for the group of atypical and malignant meningiomas, and 1:1 and 1:0.67, respectively, for atypical and malignant meningiomas separately. This lack of a female predominance in nonbenign meningiomas was statistically significant ($P = 0.024$). A nonparametric χ^2 test was employed to test the differences between the distribution of sexes.

Clinical manifestations

No difference was noted between atypical and malignant meningiomas regarding their presenting signs and symptoms, with limb weakness (10 cases) and headache (9 cases) being the most common complaints. Limb paresis was the most common clinical sign (13 cases). The clinical features are detailed in *Table 2*.

Location of tumors

Tumor site was determined by radiographic studies and operative findings (*Table 3*). The most common location was the cerebral convexities (48%) followed by the parasagittal areas (20%). Although there were two tumors with supra- and infratentorial extensions, no tumor was confined solely to the posterior fossa.

Radiological findings

As mentioned, CT scans were available in nine patients. The tumors were either isodense (five patients) or slightly hyperdense (four patients). Hypodense or cystic areas within the tumor were not seen in any case. Calcification, commonly seen in benign meningiomas, was present only in one case. All tumors exhibited homogenous dense contrast enhancement. Peritumoral edema was either moderate or marked, but never mild. Tumor margins were irregular in five patients, and mushrooming was seen in three patients (*Table 4*).

Angiograms were available in 19 cases. Two tumors were avascular, and the rest showed a homogenous vascular blush. The tumors were supplied primarily by the external carotid artery in 14 cases (73.36%), with some contribution from the internal carotid artery and vertebral artery in 6 (31.5%) and 2 (10.5%) cases, respectively. The vascular supply was entirely from the internal carotid artery in three (15.8%) cases.

Survival and recurrence

The median follow-up was 38 months (range, 3-186 mo; mean, 46.08 mo). For patients with atypical meningiomas, the median survival time was 5.95 years, and 5-, 10-, and 15-year survival rates were 58.33, 41.67, and 27.78%, respectively (*Fig. 8*). For malignant meningiomas, the median survival time was 8.75 years, and 5-, 10-, and 15-year survival rates were 60, 30, and 30%, respectively (*Fig. 9*).

A distinction was made between recurrence (reappearance of tumor after total resection) and regrowth (enlargement of tumor after subtotal removal). Among the atypical meningiomas, 13 underwent total resection, whereas 4 were subtotally resected (the extent of primary resection was unknown in 3). For totally resected tumors, the mean recurrence time was 3.32 years, and 5-, 10-, and 15-year recurrence rates were 50, 67, and 67%, respectively. For subtotally resected tumors, the mean regrowth time was 0.72 years, and 5-, 10-, and 15-year regrowth rates were each 50%. Of the malignant meningiomas, three underwent complete resection and two were subtotally resected. The 5-, 10-, and 15-year rates were 33, 66, and 100%, respectively, for recurrence and 100% each for regrowth. The mean recurrence time was 7.77 years, whereas the average time for regrowth was 3.08 years (*Figs. 10 and 11*).

(Although the mean recurrence time of 7.77 years was relatively long, this was solely the result of one patient's tumor recurring 15 years after total resection.) Among the patients with benign meningiomas, the mean recurrence time was 3.15 years, and 5-, 10-, and 15-year recurrence rates were each 2%. A statistically significant difference was observed in recurrence rates between benign and atypical meningiomas ($P = 0.0001$) as well as between benign and malignant meningiomas ($P = 0.0001$). There was no statistically significant difference among recurrence rates for atypical and malignant meningiomas ($P = 0.68$).

Six atypical meningiomas were irradiated, four after total resection and two after subtotal removal. In the completely resected and irradiated group, the mean recurrence time was 0.48 years, and 5- and 10-year recurrence rates were 50% each. In comparison, nine completely resected and nonirradiated atypical meningiomas had 5- and 10-year recurrence rates of 22 and 48%, respectively, and a mean recurrence time of 4.41 years. However, the difference between the two groups was not statistically significant ($P = 0.153$). Among the subtotally resected and irradiated atypical meningiomas, 5- and 10-year regrowth rates were each 50% and the mean regrowth time was 3.83 years. The two patients with subtotally resected and nonirradiated meningiomas died within 6 months after surgery. Therefore, it was difficult to compare the regrowth rates between the irradiated and nonirradiated subtotally removed atypical meningiomas.

Four malignant meningiomas were irradiated, two after complete and two after incomplete resections. All four recurred. The average recurrence time among completely resected tumors was 2.5 years, whereas the average regrowth time for subtotally resected tumors was 3.08 years. The only nonirradiated malignant meningioma had undergone a total resection, and it recurred after 15 years. Because of the small number of cases, we were not able to perform a statistical analysis of recurrence rates for irradiated and nonirradiated malignant meningiomas.

The product-limit estimator was used to estimate the survival and recurrence rates in this report. The log rank test was used to test for homogeneity between groups.

Extracranial metastasis

Extracranial metastases were seen in two patients, one within a lumbar vertebral body and the other within the spinal subarachnoid space.

DISCUSSION

Meningiomas have been recognized as a clinical entity for nearly 200 years [24]. Their origin is generally believed to be from arachnoid cap cells. Of all the meningioma subtypes, malignant meningiomas represent 1 to 11% [5,9,10,16,32]. This varying incidence partly represents the lack of uniformly agreed on histological criteria for malignancy. Alhough Jaaskelainen et al. [9] and later Rohringer et al. [19] attempted to classify tumors by using a numerical grading system, their grading criteria were not completely elucidated and are therefore subjective. Even more confusing, their numerical grading system was called the *WHO classification system* [20,25], which is not correct. The WHO classification provides the broad criteria for malignancy without suggesting a numerical scoring system. We have used a system of scoring similar to that proposed by Jaaskelainen et al. [9] and Rohringer et al. [19], but we have made the system more reproducible by establishing objective histological criteria. These authors [9,19] separated meningiomas into four groups (benign, atypical, anaplastic, and sarcomatous) according to the histological criteria, but when studying the clinical course, they combined anaplastic and sarcomatous meningiomas into one group called *malignant*. We believe this is confusing and of little clinical utility, and therefore we do not distinguish between anaplastic and sarcomatous types. Hemangiopericytomas of the meninges and papillary meningiomas were excluded from our study because there is agreement that these tumors behave aggressively. Their inclusion would have biased our series and the survival rates of the patients. Moreover, hemangiopericytomas of the meninges are probably not meningiomas; in the revised WHO classification, they are classified as tumors of uncertain origin [13].

In our series, atypical and malignant meningiomas presented at an earlier age than benign meningiomas. This may be because nonbenign meningiomas grow more rapidly and become symptomatic at an earlier age. It is also generally believed that in children, malignant meningiomas represent a higher percentage of all meningiomas [21,28]. However, meningiomas as a whole are so uncommon in children [19] that this does not affect the age distribution of malignant meningiomas. We did not have any pediatric patients in our series, which is reflective of the predominance of adults in our patient population. Regarding gender distribution, the female predominance seen in benign meningiomas is not found in their malignant counterparts. The absence of female predominance in malignant meningiomas suggests that endocrinological influences apparently important in the genesis of benign meningiomas are not active in malignant ones. In fact, some biochemical studies have shown that progesterone activity correlates inversely with malignancy in meningiomas [30].

Clinical features were not helpful in differentiating benign from malignant meningiomas. According to Rohringer et al. [19], patients with malignant meningiomas are more likely to have objective neurological deficits, but this may simply be a reflection of increased peritumoral edema associated with malignant meningiomas.

CT, while useful in showing certain trends indicative of malignancy [1,19], is by no means completely reliable in differentiating benign from malignant meningiomas [22]. Earlier reports seem to have overstated the utility of CT in this aspect [4,27]. CT signs suggestive of nonbenign behavior include marked peritumoral edema, heterogenous contrast enhancement, minimal or no calcification, indistinct or irregular margins, and mushroom-like projections

from the main tumor mass [15]. Although some or all of these features were present in most of our cases, we believe that the aggressive potential of a meningioma cannot be predicted by CT alone.

Malignant meningiomas occur most commonly over cerebral convexities [19,24,31]. There have been few reports of tumors situated either infratentorially [26] or intraventricularly [11]. In our series, only one tumor was located within the ventricles and there were two tentorial meningiomas with supra- and infratentorial extensions. This may simply be a representation of the lower incidence of meningiomas in these locations.

The role of radiation therapy (RT) in the treatment of meningiomas remains controversial. The conventional teaching has been that ordinary meningiomas are radioresistant [7]. However, in view of high recurrence rates, RT has continued to be used in benign as well as malignant meningiomas. Carella et al. [2] had recommended RT for all malignant meningiomas regardless of whether the resection was total or subtotal. Of their 11 patients, 3 had died and 8 were free of tumor recurrence. Unfortunately, this report did not have a control group of nonirradiated patients and details such as the follow-up period and the extent of surgical resection were absent from the study. In our series, RT did not prevent or retard the recurrence of tumors regardless of the extent of resection. However, our patient population was small, and we cannot conclusively comment on the efficacy of RT. In fact, data in the literature support the use of RT for incompletely excised meningiomas [29]. Therefore, we believe that all subtotally resected malignant meningiomas should be irradiated. Regarding completely resected tumors, there is no similar study to suggest the benefits from RT, but some authors still recommend its use because of the invasive potential of the tumor [20]. At our institution, we no longer use RT for completely resected malignant meningiomas because of the complications of RT and because there is no proven benefit of RT for such cases in our experience or the experience of others. However, we cannot overstate the need to wait for results from larger series before drawing any significant conclusions on the role of postoperative RT in treating completely resected malignant meningiomas. Regarding chemotherapy, two of our patients who received chemotherapy did not show any response and the literature does not recommend it [20].

Malignancy in meningiomas has been a subject of controversy, and some have even stated that biological behavior cannot be predicted on histopathological analysis [10,17]. We believe this is simply a reflection of the absence of criteria for defining malignancy. Our study demonstrates that histological parameters permit an accurate identification of atypical and malignant meningiomas with high growth potential and recurrence rates that far exceed that of benign meningiomas. We hope that the use of these relatively simple histological criteria will help to further the understanding of the biology of this important group of tumors.

Received, November 30, 1992.
Accepted, June 29, 1993.
Reprint requests: Asim Mahmood, M.D., F.R.C.S., c/o Editorial Office, Department of Neurological Surgery, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, MI 48202.

REFERENCES: [1-33]

1. Alvarez F, Roda JM, Romero MP: Malignant and atypical meningiomas: A reappraisal of clinical, histological, and computed tomographic features. **Neurosurgery** 20:688-694, 1987.
2. Carella RJ, Ransohoff J, Newall J: Role of radiation therapy in the management of meningioma. **Neurosurgery** 10:332-339, 1982.
3. Cushing H, Eisenhardt L (eds): Meningiomas: *Their Classification, Regional Behaviour, Life History and Surgical End Results.* Springfield, IL, Charles C Thomas, 1938.
4. Dietman JL, Heldt N, Burquet JL, Medjek L: CT findings in malignant meningiomas. **Neuroradiology** 23:207-209, 1982.
5. Fabiani A, Trebini F, Favero M: The significance of atypical mitosis in malignant meningiomas. **Acta Neuropathol (Berl)** 38:229-231, 1977.
6. Grant FC: Intracranial meningiomas, surgical results. **Surg Gynecol Obstet** 85:419-431, 1947.
7. Guthrie BL, Carabell SC, Laws ER: Radiation therapy for intracranial meningiomas, in Al-Mefty O (ed): *Meningiomas*. New York, Raven Press, 1991, pp 255-262.
8. Hoessly GF, Olivecrona H: Report on 280 cases of verified parasagittal meningiomas. **J Neurosurg** 12:614-626, 1955.
9. Jaaskelainen J, Haltia M, Servo A: Atypical and anaplastic meningiomas: Radiology, surgery, radiotherapy, and outcome. **Surg Neurol** 25:233-242, 1986.
10. Jellinger K, Slovik F: Histologic subtypes and prognostic problems in meningiomas. **J Neurol** 208:279-298, 1975.
11. Kamiya K, Inagawa T, Negasako R: Malignant intraventricular meningioma with spinal metastasis through the cerebrospinal fluid. **Surg Neurol** 32:213-218, 1989.
12. Katsura S, Suzuki J, Wada I: A statistical study of brain tumors in the neurosurgical clinics in Japan. **J Neurosurg** 16:570-579, 1959.
13. Kepes JJ: Review of the WHO's new proposed classification of brain tumors. Proceedings of the XIth International Congress of Neuropathology, Kyoto, Japan, 1990, pp 87-97.
14. Lebert H: Uber Krebs und die mit Krebs verwechselten Geschwulstate im Gehirn und seinen Hullen. **Virch Arch** 3:463-569, 1851.
15. Latchaw RE, Hirsch WL: Computerized tomography of intracranial meningiomas, in

Al-Mefty O (ed): *Meningiomas*. New York, Raven Press, 1991, pp 195-207.
16. MacCarty CS, Taylor WF: Intracranial meningiomas: Experiences at the Mayo Clinic (in Japanese, English abstr) **Neurol Med Chir (Tokyo)** 19:569-574, 1979.
17. May PL, Broome JC, Lawry J: The prediction of recurrence in meningiomas. **J Neurosurg** 71:347-351, 1989.
18. New PF, Hesselink JR, Carrol CP: Malignant meningiomas: CT and histologic criteria, including a new CT sign. **Am J Neuroradiol** 3:267-276, 1982.
19. Rohringer M, Sutherland GR, Louw DF, Sima AA: Incidence and clinicopathological features of meningioma. **J Neurosurg** 71:665-672, 1989.
20. Salcman M: Malignant meningiomas, in Al-Mefty O (ed): *Meningiomas*. New York, Raven Press, 1991, pp 75-85.
21. Sano K, Wakai S, Ochiai C: Characteristics of intracranial meningiomas in children. **Child's Brain** 8:98, 1981.
22. Servo A, Porras M, Jaaskelainen J, Paetau A, Haltia M: Computed tomography and angiography do not reliably discriminate malignant meningiomas from benign ones. **Neuroradiology** 32:94-97, 1990.
23. Simpson D: The recurrence of intracranial meningiomas after surgical treatment. **J Neurol Neurosurg Psychiatry** 20:22-39, 1957.
24. Su CF, Shih CJ, Tsou CK: Malignant meningiomas: Clinical and pathological study of 10 cases. **Taiwan I Hsueh Hui Tsa Chih** 85:608-623, 1986.
25. Sutherland GR, Sima AA: Incidence and clinicopathologic features of meningioma, in Schmidek HH (ed): *Meningiomas and Their Surgical Management*. Philadelphia, W.B. Saunders Co., 1991, pp 10-21.
26. Thomas HG, Dolman CL, Berry K: Malignant meningioma: Clinical and pathological features. **J Neurosurg** 55:929-934, 1981.
27. Vassiloutis J, Ambrose J: Computerized tomography scanning of intracranial meningiomas. **J Neurosurg** 50:320-327, 1979.
28. Wakai S, Ochiari C, Takakura K: Meningiomas in childhood. **Nervous System in Children (Jap)** 5:1, 1980.
29. Wara WM, Sheline GE, Newman H, Townsend JJ, Boldrey EB: Radiation therapy of meningiomas. **AJR** 123:453-458, 1975.
30. Whittle IR, Foo MS, Besser M: Progesterone and estrogen receptors in meningiomas: Biochemical and clinicopathological considerations. **Aust NZ J Surg** 54:325, 1984.
31. Wong G, Harper C: Atypical meningiomas: Clinical pathological correlation. **Aust NZ J Surg** 54:331-336, 1984.
32. Zulch KJ, Mennel HD: Malignant meningiomas. **Adv Neurosurg** 2:3-11, 1975.
33. Zulch KJ (ed): Histologic Typing of Tumors of *the Central Nervous System*. Geneva, World Health Organization, 1979.

COMMENTS

I am sure that neuropathologists will have considerable discussion about this article. The reproducibility of the criteria and the concept of separating specific criteria to predict aggressive behavior are both controversial.

It is of the utmost importance that this endeavor go forward. Whether by 5-bromodeoxyuridine labeling, histopathological criteria, or other criteria, the identification of potentially aggressive meningiomas will be very important for future work. This article by Mahmood et al. continues the discussion in this important area.

Peter McL. Black
Boston, Massachusetts

The study of a larger series of intracranial meningiomas with regard to the relationship between the histology and prognosis of these tumors is a valuable undertaking. The authors are quite correct in stating that predicting the prognosis of a given meningioma case from the histological features of the tumor is not a hopeless task. I think that the problem of histologically benign but hard-to-resect meningiomas (e.g., a meningioma occupying the foramen magnum area or one growing around the intracranial portion of an internal carotid artery) has not been adequately stressed.

In this day and age, the examining pathologist should be informed about preoperative embolization procedures. From my own experience, I know that this information does not always automatically accompany the submitted operative specimen and it is possible to find massive areas of coagulation necrosis in tumors "pretreated" in this fashion without actually finding the material used for embolization in the slides. The presence of such necrosis can easily lead to the unjustified diagnosis of malignant meningioma.

I also think that "papillary" meningiomas should not have been excluded from the series because doing so has skewed the overall statistics toward a more benign constellation. Contrary to the general understanding of the term, there are no "papillary meningiomas" as such. Papillary formations may occur in meningothelial as well as in other types of meningiomas (including hemangiopericytic forms) and may be seen as an occasional focus or as being present extensively throughout the tumor. The former is probably a less significant sign of malignancy than the latter. Furthermore, they may not be present from the outset. Harvey Cushing's famous patient, Dorothy May Russell, referred to in the introduction of this article had to undergo 17 operations for her meningioma and its recurrences; there were no papillary structures in the early specimens, only in

the late recurrences and in the pulmonary metastases! So was the malignancy of her course determined by papillarity or by other factors? I suggest that future studies should not exclude "papillary meningiomas," but rather mention the foci of papillarity as a bad prognostic sign in any meningioma, possibly in the same class as large numbers of mitotic figures or necroses. There is obviously no justification to create new histological subtypes of meningiomas called *mitotic* or *necrotic* meningiomas.

John J. Kepes
Kansas City, Kansas

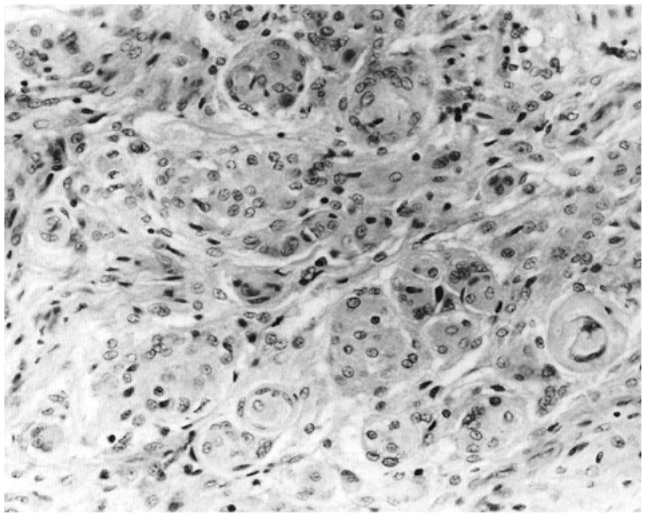

Figure 1. This meningioma displays mild nuclear pleomorphism (score, 1), normal cellularity (score, 0), no necrosis (score, 0), no mitotic activity (score, 0), and an incipient loss of normal whorled pattern (score, 1). This tumor did not recur after complete excision (hematoxylin-eosin, ×250).

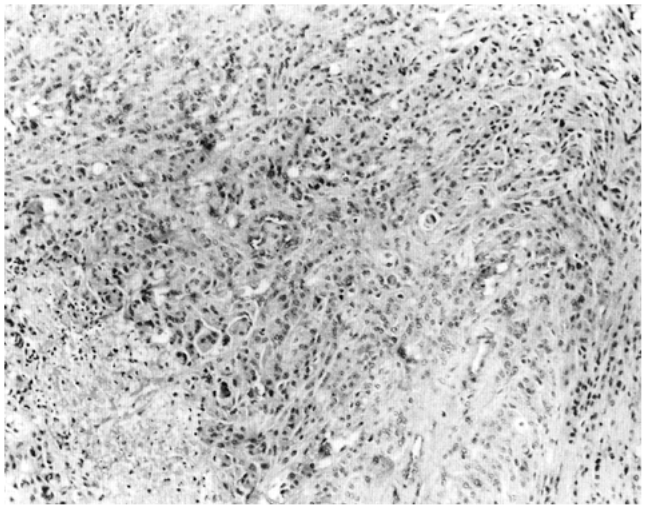

Figure 2. This meningioma shows mild nuclear pleomorphism (score, 1), several areas of necrosis (score, 2), incipient loss of lobular pattern (score, 1), and mild hypercellularity (score, 1). There was no mitotic activity (score, 0) or brain invasion (score, 0). This tumor did not recur (hematoxylin-eosin, ×150).

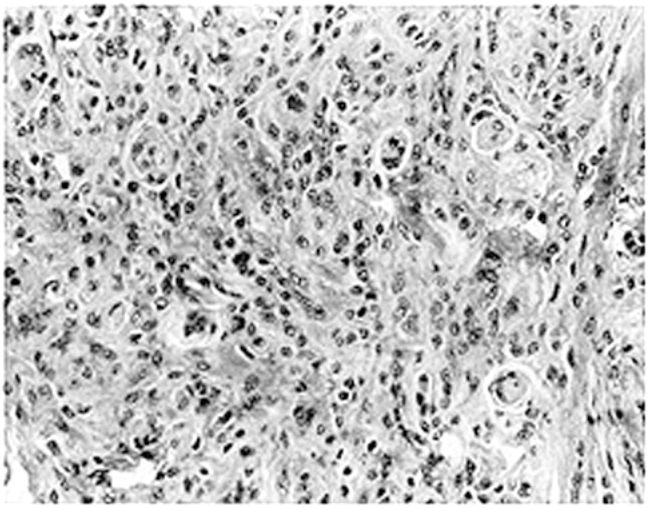

Figure 3. An example of a meningioma with moderate nuclear pleomorphism (score, 2), moderate hypercellularity with small indistinct whorls (score, 2), loss of architecture (score, 2), and frequent mitosis (score, 2). There was no necrosis or brain invasion. The tumor recurred after complete resection (hematoxylin-eosin, ×250).

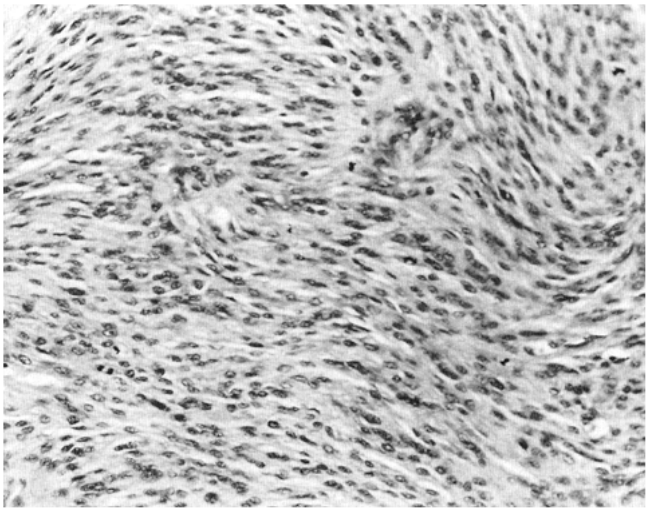

Figure 4. A fibroblastic meningioma with advanced loss of architectural pattern (score, 2), moderate nuclear pleomorphism (score, 2), and hypercellularity (score, 1). There was no necrosis or brain invasion but mitotic activity was brisk (score, 3) (hematoxylin-eosin, ×150).

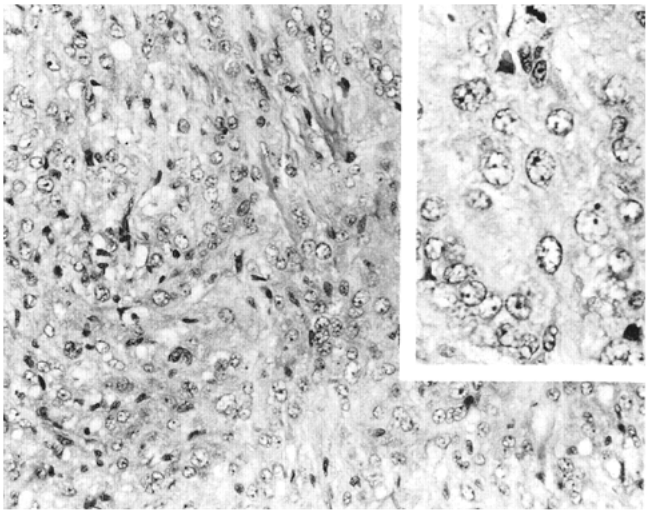

Figure 5. This meningioma reveals a complete loss of architecture with uninterrupted sheets of neoplastic cells (score, 3) and hyperchromatic nuclei with prominent nucleoli (score, 3). In the inset, the tumor displays increased cellularity (score, 3) and brisk mitotic activity (score, 3). The foci of necrosis were small (score, 1), and brain invasion was not detected (hematoxylin-eosin, ×250; inset, ×450).

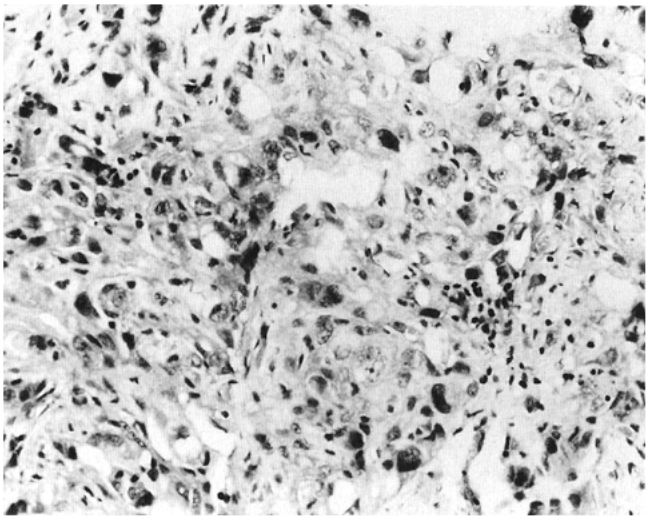

Figure 6. This malignant meningioma shows a complete loss of architecture (score, 3), hypercellularity (score, 2), severe nuclear pleomorphism (score, 3), extensive areas of necrosis (score, 3), and high mitotic activity (score, 3) (hematoxylin-eosin, ×250).

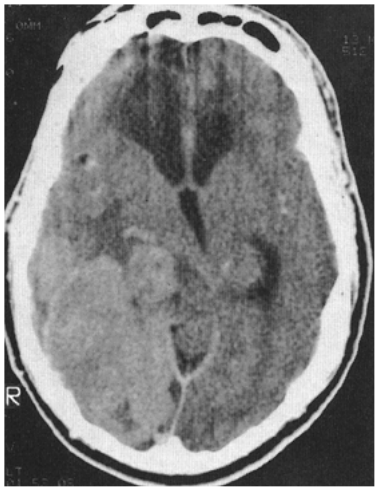

Figure 7. Contrast-enhanced CT scan of a patient with malignant meningioma showing the mushrooming pattern.

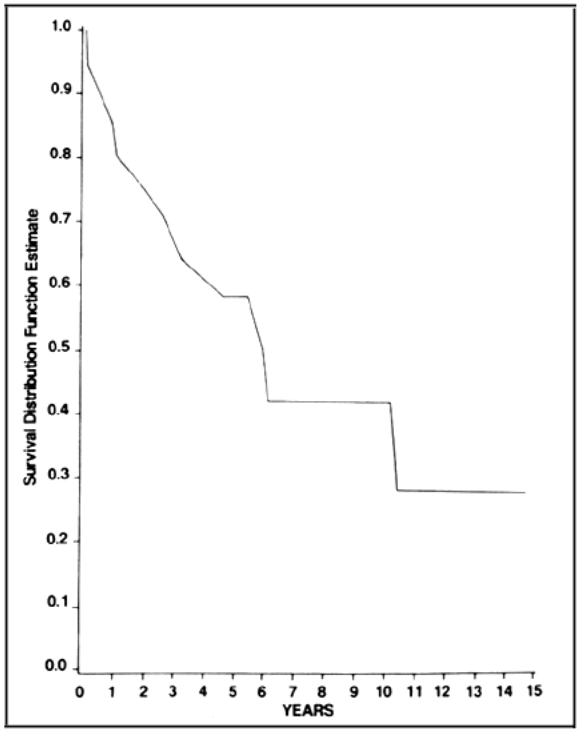

Figure 8. Graph illustrates the survival periods from the date of surgery in patients with atypical meningiomas

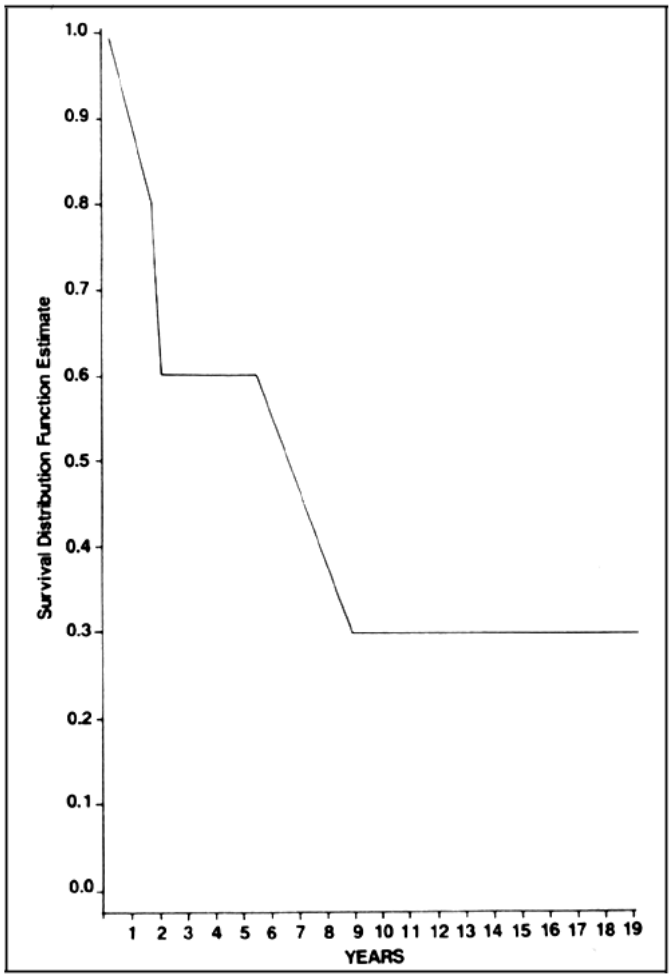

Figure 9. Graph shows the survival periods from the date of surgery in patients with malignant meningiomas.

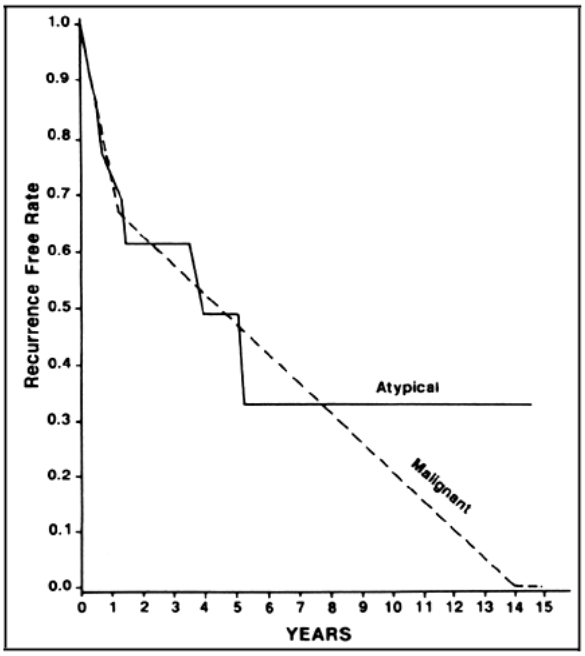

Figure 10. Graph illustrates the cumulative proportion of all patients with atypical and malignant meningiomas who did not have a recurrence after total resection.

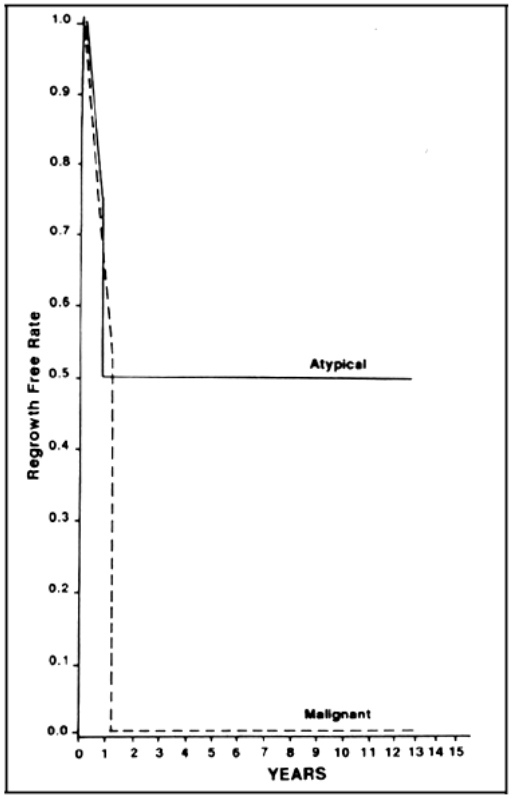

Figure 11. Graph illustrates the cumulative proportion of all patients with atypical and malignant meningiomas who were free of regrowth after subtotal resection.

Histological Feature	Grade[a]			
	0	1	2	3
Hypercellularity	10 whorls/HPF	Same, except increased cellularity in perivascular areas	Less defined small, more closely packed whorls (up to 30 per HPF)	Densely crowded overlapping nuclei with loss of whorls
Nuclear pleomorphisms	Uniform, bland nuclei, no nucleoli, "pepper and salt" chromatin	Occasional larger nuclei, 2 or 3 times larger with irregular contours	Many cells with large pale nuclei, small nonprominent nucleoli	Most cells with large, vesicular nuclei, variable size, prominent nucleoli
Mitosis	None	1–2 per 10 HPFs	3–4 per 10 HPFs	≥5 per 10 HPFs
Necrosis	None	Rare, each involving less than ½ of HPF	Frequent foci involving more than ½ but less than 1 HPF	Large, confluent areas of necrosis more than 1 HPF
Loss of architecture	None	Incipient loss	Involving 1–2 adjacent HPF	Involving more than 2 adjacent HPFs
Brain invasion	Absent	Tumor pushing the brain without intervening meninges	Cords infiltrating the brain	

[a] HPF, high-power field.

Table 1. Histological Grading of Meningiomas

	No. of Patients	%
Symptoms		
Paresis	10	40
Headache	9	36
Personality change	7	28
Speech problem	3	12
Ataxia	3	12
Generalized seizures	2	8
Visual impairment	2	8
Decreased hearing	2	8
Focal seizures	1	4
Physical signs		
Paresis	13	52
Visual field deficit	4	16
Pappiledema	4	16
Memory impairment	3	12
Cranial nerve deficit	3	12
Aphasia	3	12
Cerebellar dysfunction	1	4
Decreased visual acuity	1	4
Normal examination	3	12

Table 2. Clinical Features of Patients with Atypical and Malignant Meningiomas

Location	No. of Patients	%
Convexity	12	48
Parasagittal	5	20
Sphenoid ridge	5	20
Tentorium	2	8
Lateral ventricle	1	4

Table 3. Location of Atypical and Malignant Meningiomas

Computed Tomographic Feature	No. of Patients	%
Isodense	5	55
Hyperdense	4	44
Moderate edema	4	44
Marked edema	5	55
Homogenous enhancement	9	100
Calcification	1	11
Irregular margins	5	55
Mushrooming	3	33
Cystic areas	0	

Table 4. Computed Tomographic Findings in 9 Patients with Atypical and Malignant Meningiomas