Journal of Neuropathology and Experimental Neurology

Vol. 56, No. 5
May, 1997
pp. 551–556

Atypical Central Neurocytoma

FIGEN SÖYLEMEZOGLU, BERND W. SCHEITHAUER, JACQUES ESTEVE, AND PAUL KLEIHUES

Abstract. The proliferative potential of central neurocytomas was determined in a biopsy series of 36 cases and compared with clinical outcome. The mean size of the growth fraction, as determined by MIB-1 labeling index (MIB-1 LI) at first biopsy, was 2.8 ± 2.5 with a range of 0.1 to 8.6%. Neurocytomas with an MIB-1 LI >2% comprised 39% of cases and showed a close correlation with the presence of vascular proliferation ($p = 0.0006$). The Kaplan-Meier analysis showed a highly significant difference in disease-free survival between the 2 groups ($p = 0.0068$). Over an observation time of 150 months, there was a 22% relapse among patients with an MIB-1 LI less than 2% and a 63% chance of relapse among those with an MIB-1 LI greater than 2%. We propose the term "atypical central neurocytoma" for the latter subset, corresponding to WHO grade II.

Key Words: Brain Neoplasms; Central neurocytoma; Disease-free survival; Growth fraction; Ki-67; Monoclonal antibody MIB-1.

INTRODUCTION

The central neurocytoma is defined as an intraventricular tumor composed of uniform round cells with neuronal differentiation (1–3). On the basis of their histopathology and the usually benign clinical course, neurocytomas have been designated grade I in the new WHO classification (2, 4). It has, however, been noted that some neurocytomas show mitotic activity (5–7), vascular proliferation (5–8), and focal necrosis (6, 7, 9–13). Whether or not these features justify the designation "anaplastic neurocytoma" (5–7) has remained a subject of controversy (11). The objective of this study was to determine the proliferative potential of central neurocytomas and to correlate this with clinical behavior.

MATERIAL AND METHODS

Investigations were carried out on a total of 41 neoplasms from 36 patients (Table 1). They were diagnosed as central neurocytoma on the basis of their location in the lateral ventricles, their typical histopathological features and the immunohistochemical detection of synaptophysin.

Immunohistochemistry

Surgical specimens were routinely fixed in formalin and embedded in paraffin. For immunohistochemistry, sections were incubated with monoclonal antibodies to synaptophysin (SY 38; Boehringer, Mannheim, FRG; dilution, 1:30), neuron-specific enolase (NSE, Dakopatts; 1:100), neurofilament proteins (70 and 200 kD NFP, Bio-Science, Emmenbrucke, Switzerland; 1:20), and with polyclonal rabbit antisera to glial fibrillary acidic protein (GFAP; Dakopatts; 1:150). Primary antibodies were visualized with an avidin-biotin-staining kit for mouse IgG (Dakopatts) and with a peroxidase-antiperoxidase sandwich to rabbit IgG (Dakopatts), respectively. The monoclonal antibody MIB-1 requires repetitive heating of slides in a microwave oven (14–16). Briefly, 4-μm sections from paraffin-embedded tissues were mounted on 3-aminopropyltri-ethoxysilan-(Sigma; A-3648) coated slides. Deparaffinization and rehydration to water were carried out through xylol, acetone, 70% alcohol, 40% alcohol to distilled water. Then slides were placed in plastic jars containing 10 mM citrate buffer (pH6). Loosely covered jars were incubated in the microwave oven in 3 to 5 five-minute (min) cycles. Between every cycle the level of the fluid in the jars was checked. After heating, the jars were allowed to cool for 20 min and then rinsed in distilled water twice and in PBS for 5 min. Sections were immunostained with monoclonal antibody MIB-1, diluted 1:10 (Dianova GmbH, D-2000 Hamburg). Immunohistochemical staining was carried out according to the avidin-biotin technique. The representative areas of the lesion were photographed at a final magnification of ×250 to determine the fraction of labeled cells. A minimum of 1000 cells were counted in each case, and labeled cells were expressed as a percentage of the total number of cells. If labeled tumor cells were unevenly distributed (e.g. the 2nd biopsy of case 16), regions with highest proliferative activity were analyzed.

RESULTS

A total of 41 biopsies from 36 patients were evaluated (Table 1). The mean age of the patients at the time of first surgery was 29.9 ± 12.2 years, with a range of 6 to 55 years. The male/female ratio was 1:1.1. Histologically, tumors displayed the typical features of neurocytoma, i.e. monotonous cells with uniform small round nuclei, inconspicuous nucleoli and a fine chromatin pattern. The cytoplasm, small in quantity, was clear or weakly eosinophilic and uniform in appearance. Prominent neuropil islands were present in some of the cases. Occasionally, a perivascular arrangement of tumor cells was noted, resembling ependymoma. There were no Homer-Wright rosettes. In 2 neoplasms (cases 6 and 36), some scattered

From the Institute of Neuropathology, Department of Pathology, University Hospital, 8091 Zürich, Switzerland (FS, PK), the Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN 55905 (BWS), and the International Agency for Research on Cancer, World Health Organization, 69732 Lyon, France (JE, PK).

Correspondence to: P. Kleihues, MD, International Agency for Research on Cancer, 150 Cours Albert Thomas, 69732 Lyon Cedex 08, France.

TABLE 1
Summary of Patient and Biopsy Data

Case	Biopsy	Age	Sex	Syn	GFAP	Vasc. prol.	Necrosis	MIB-1 (%)	RT (Gy)	Status	Survival (months)
1	R3215	9	M	+	+	−	−	0.1	−	Alive	12
2	R3524	53	F	+	−	−	−	0.2	−	Alive	14
3	Z8807	27	M	+	−	−	−	0.7	−	Alive	84
4	Z7851	47	M	+	+	−	−	0.7	−	Alive	96
5	R3939	35	M	+	−	−	−	0.8	−	Alive	10
6	R2336	53	F	+	−	−	−	0.8			
7	R2924	39	F	+	−	−	+	1.1	46.8	Alive	4
8	R3305	6	M	+	−	+	−	1.3			
9	R3195	36	F	+	−	−	−	1.3	−	Alive	21
10	Z862	18	M	+	−	−	−	1.5	−		11
	Z1434	19	M	+	−	+	−	3.2	−	Alive	36
11	Z16556	19	F	+	−	−	+	1.7	−	Alive	204
12	Z21549	19	F	+	−	−	−	1.7	−		73
	Z1065	25	F	+	−	−	−	2.3	−	Alive	48
13	R4071	17	F	+	−	−	−	1.8	−	Alive	4
14[a]	R4211	18	F	+	−	−	−	3.1	−	Died	1.5
15	Z29186	19	F	+	−	−	−	3.5	−	Alive	156
16	R4113	23	F	+	+	+	−	4.4	−		4
	R4253	23	F	+	−	+	−	21	−	Alive	0.5
17	Z20740	27	F	+	−	+	−	5.3	54.0	Alive	60
18	R3402	20	F	+	−	−	−	5.5	−	Alive	12
19	Z12827	21	F	+	−	−	−	6.1			38
	Z17878	24	F	+	−	+	+	4.6	50.0	Alive	96
20	R3422	32	M	+	−	−	−	6.1	−		14
	R4191	33	M	+	−	+	−	5.0	+	Alive	3
21	Z16428	39	M	+	+	+	+	7.0			
22	Z4573	39	M	+	−	+	+	7.4	54.0	Alive	60
23	R3928	55	F	+	−	+	−	8.6			
24[b]	4-125-562	34	F	+	−	−	−	0.7	55.0	Alive	48
25	4-153-356	20	F	+	−	−	−	0.7	+	Alive	48
26	HR93-2626	33	M	+	−	−	−	0.8	50.0	Alive	24
27	3-912-901	37	F	+	−	−	+	0.9	−	Alive	102
28	1-804-192	38	M	+	−	−	−	1.0	+	Alive	20
29	4-088-942	28	M	+	−	−	+	1.6	−	Alive	70
30[c]	3-308-422	27	M	+	−	−	+	1.6	−	Died	
31	3-982-783	29	M	+	−	−	+	1.7	−	Alive	72
32	3-995-943	28	F	+	−	−	−	1.8	−	Alive	96
33[d]	4-185-036	35	M	+	+	−	+	2.6	60.0	Alive	72
34[e]	4-173-705	25	F	+	−	−	+	3.4	−	Died	5
35	4-294-696	50	M	+	−	+	+	7.0	+	Alive	24
36[f]	4-326-026	20	M	+	+	+	−	8.1	34.0	Alive	54

Abbreviations: Syn, synaptophysin immunoreactivity; Vasc. prol., vascular proliferation; RT, radiotherapy.

[a] The patient died of bilateral massive intraventricular hemorrhage 6 weeks after the operation.

[b] Following a stereotactic biopsy, the patient received 55 Gy radiotherapy. Due to the residual mass, a definitive operation was performed.

[c] The patient died of cerebral edema during the postoperative period.

[d] Nine months after the first operation, the patient received another operation and was irradiated (60 Gy brain and 30 Gy spinal) due to an evidence of recurrence in MR. The sample is from the first operation.

[e] Four months after the gross total surgery, a recurrence was noted, and the patient died of brain stem infarction within 1 month.

[f] Following a biopsy, the patient received 34 Gy whole brain and 20 Gy spinal RT. Four years later, a gross total resection was performed. Six months thereafter, the patient was doing well. The sample is from the definitive operation.

ganglion cells were seen. In 2 tumors (recurrent tumor of cases 16 and 17) there were multinucleated cells (Fig. 1D). In all tumors, uniform synaptophysin (Fig. 1E) and NSE immunostaining were detected. Focal GFAP expression (Fig. 1F) by tumor cells was observed in 6 cases; 7 tumors immunostained for neurofilament, while only 1 biopsy (case 6), which contained scattered ganglion cells, stained positive for neurofilament antibody.

The mean MIB-1 labeling index of all biopsies was 3.4 ± 3.7 and showed a skewed distribution, ranging from 0.1 to 8.6, with one outlier at 21. The latter value was observed in a recurrent lesion (case 16) with nodular pattern and

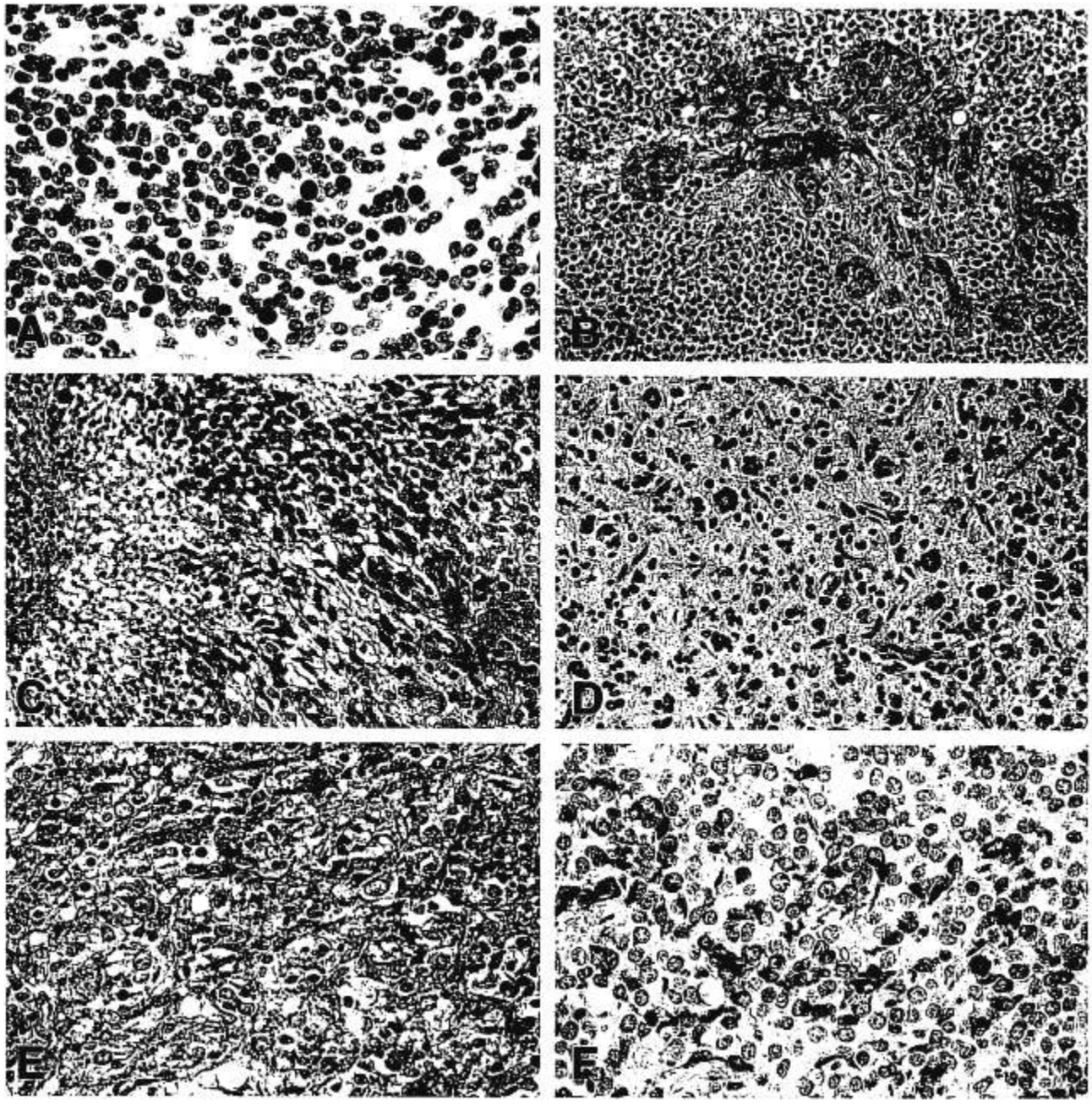

Fig. 1. Histopathologic features of the atypical neurocytoma include (A) high proliferative activity (MIB-1) and (B) prominent vascular proliferation (hematoxylin and eosin [H&E]). Necrosis (C) may occur (H&E), while multinucleated tumor cells (D) are rare (H&E). Synaptophysin expression (E) is a diagnostic feature, while GFAP immunoreactivity of tumor cells (F) occurred only in 15% of biopsies.

multinucleated tumor cells, suggesting the unusual occurrence of malignant progression. The graph of the values of the MIB-1 LI against the normal distribution clearly showed the existence of 2 populations, with 22 biopsies (54%) below the cut-off value of 2% (Fig. 2). Tumors with an MIB-1 LI of >2% usually contained mitoses (3 or more per 10 HPF). Tumor cells immunoreactive to MIB-1 usually showed an even distribution throughout the neoplasm (Fig. 1A). A notable exception was the recurrent tumor of case 16, which grew in a nodular pattern. Within the highly cellular nodules, an MIB-1 labeling index of up to 21% was observed, while the less cellular internodular areas showed a significantly smaller proliferative fraction.

The value of MIB-1 LI decreased with age of the patient among those biopsies with an MIB-1 LI of less than 2%, but increased in the cases with an MIB-1 staining

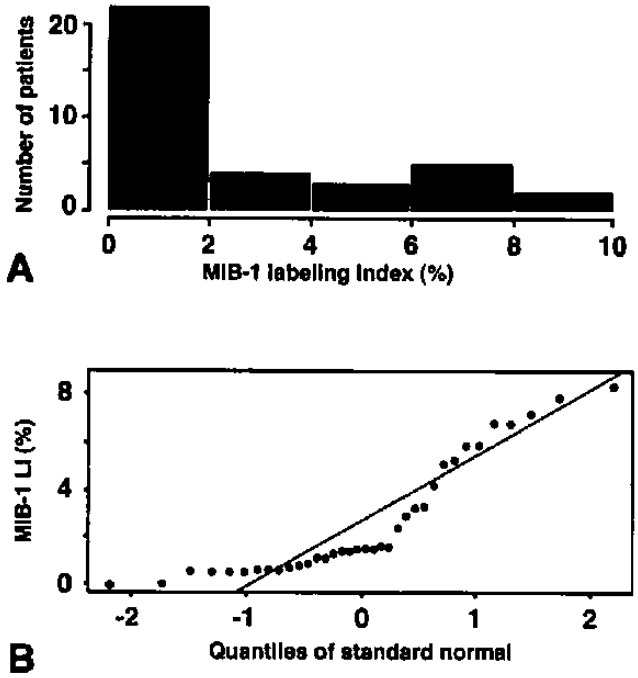

Fig. 2. Distribution of the MIB-1 labeling index (A). Comparison with the normal distribution (continuous line) suggests the presence of 2 tumor populations (B).

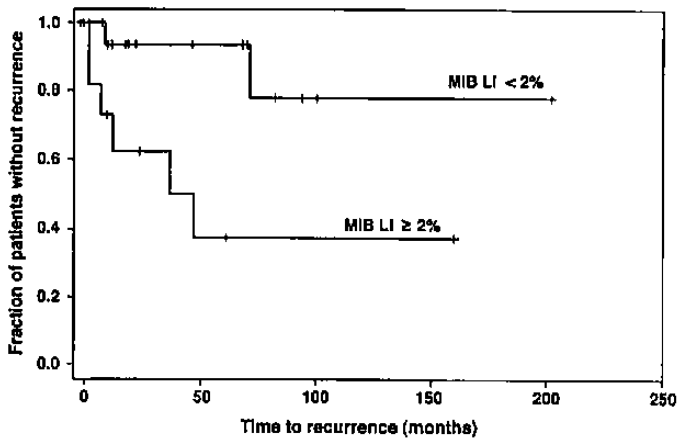

Fig. 3. Kaplan-Meier analysis of the recurrence of central neurocytomas. Tumors with an MIB-1 labeling index greater than 2% are associated with a significantly less favorable clinical course.

index greater than 2%. The sex distribution did not differ significantly between high and low MIB-1 staining groups.

There was a highly significant correlation between MIB-1 labeling index and the presence of vascular proliferation ($p = 0.0006$). This feature was present in 12 of 41 tumors (29.3%), and all but 1 of these (92%) had an MIB-1 staining index of greater than 2% (Fig. 1B). The median MIB-1 LI was 7.00 among those tumors with vascular proliferation and was 1.55 among the others. No such correlation was apparent for focal necrosis (Fig. 1C), which was observed at an overall frequency of 29.3%, but occurred at a similar incidence in neurocytomas with a low and high MIB-1 index. However, it was noted that necroses were less frequent among the biopsies from Zurich (cases 1 to 23) than in those from Mayo Clinic (cases 24 to 36), which were mainly consultation cases.

Eight out of 36 patients had a recurrence during the observation period. Two of these occurred in the group with low MIB-1 values and 6 in the group with high MIB-1 values. In the statistical analysis of recurrence, 1 case (case 36 in Table 1) from the high MIB-1 group was omitted since MIB-1 data could only be obtained for the second intervention. The Kaplan-Meier analysis showed a marked difference between the 2 groups with an MIB-1 labeling index of $<2\%$ and $\geq 2\%$ (Fig. 3). The difference was highly significant, the chi-square value being 7.3 for 1 degree of freedom ($p = 0.0068$). Even if the only death in the low MIB-1 group had been classified as a recurrence (assuming that it obscured the occurrence of a relapse), the difference between both groups would still be significant. Over an observation time of 150 months, there was a 22% chance of relapse in patients with an MIB-1 LI less than 2% and a 63% chance of relapse in those with an MIB-1 LI greater than 2%.

DISCUSSION

The antibodies MIB-1/Ki-67 allow the direct assessment of the size of a tumor's growth fraction, since nuclei in all phases of the cell cycle (G_1, S, G_2, M) are immunoreactive; only cells in G_0 show no immunoreactivity (14, 17). There are numerous reports demonstrating that the growth fraction, as defined by Ki-67 immunostaining, allows reliable estimation of a neoplasm's proliferative potential for a variety of neuroectodermal tumors (18–26). As a rule, the labeling index is in general agreement with the histologic grade and known biologic behavior of the lesions. Its predictive value is usually higher in neoplasms with little cell loss, e.g. meningiomas (20) and low-grade astrocytomas (19, 22), than in malignant gliomas with extensive areas of necrosis.

Previous reports containing data on Ki-67 immunostaining of central neurocytomas include the work of Barbosa et al, who published a case with a Ki-67 index of less than 1% (27), and Zentner et al (28), who mentioned values $<5\%$ in 2 cases and $>5\%$ in 1 case, without exact determination of the labeling index. In 7 cases, low MIB-1 indices were also observed by Robbins et al (29). Casadei et al (30) observed a low cell proliferation rate in 4 central neurocytomas using proliferating cell nuclear antigen (PCNA) immunostaining. Similarly, an assessment of the proliferative potential of neurocytomas by silver colloid staining for nuclear organizer regions

(AgNORs) revealed low values, even in a recurrent lesion (31).

The present study clearly shows that the proliferative activity of central neurocytomas varies considerably, with approximately 40% of cases having an MIB-1 labeling index of >2% (Fig. 2A) The statistical analysis strongly suggests a significant deviation from normal distribution and the presence of 2 distinct tumor populations (Fig. 2B). The follow-up of 36 patients from 2 centers (Mayo Clinic and University Hospital Zurich) clearly showed that the proliferative potential of central neurocytomas does indeed correlate with clinical behavior. The Kaplan-Meier survival plot (Fig. 3) demonstrates a highly significant difference in relapse-free survival time between patients whose tumors show low (<2%) or high (≥2%) MIB-1 labeling indices, indicating that the MIB-1 LI may serve as a predictive parameter of clinical outcome in this tumor entity. Over a period of 150 months, 22% of patients whose tumors had a low MIB-1 LI showed a relapse, whereas the percentage of the recurrence increases to 63% for those in the high MIB-1 LI group. Although follow-up data are still incomplete and the number of cases with clinical follow-up is still too small to allow a definitive conclusion, there was a trend toward higher relapse of neoplasms with a high MIB-1 index. Of 7 patients with recurrent tumors included in the statistical analysis, 2 (cases 10 and 12 in Table 1) showed an MIB-1 labeling index <2% in the primary tumor. The interval between first and second operations was 11 and 73 months, respectively. In the remaining 5 cases (16, 19, 20, 33, 36), all of which had tumoral labeling indices greater than 2%, the mean interval was 22.6 months (range, 4 to 48 months). Only 1 patient showed a sharp increase in the MIB-1 index between the first (4.4%) and second operations (21%), and it was in this case that the interval was unusually short (4 months). Follow-up was done on two of the cases previously designated "anaplastic neurocytoma" (5, 7); it was of note that their recurrence-free interval or survival was within the range observed in neurocytomas with low proliferative potential. Thus, in retrospect the term "anaplastic" appears exaggerated when the patients' long term follow-up is taken into consideration.

In diffuse astrocytomas, vascular proliferation is a strong and reliable indicator of histologic and clinical malignancy (32–34), but this correlation is less significant in other neuroepithelial neoplasms. Vascular proliferation has been observed in central neurocytomas (5–8) and a variety of extracranial neural and neuroendocrine neoplasms (35), but its clinical significance has remained obscure. The present study showed a highly significant correlation between the MIB-1 labeling index and the presence of vascular proliferation ($p = 0.0006$). This feature was present in 12 of 41 tumors (29.3%), all but one of which (92%) had an MIB-1 labeling index of greater than 2%. No such correlation was apparent for focal necrosis, which was observed at an overall frequency of 29.3% but occurred at a similar incidence in neurocytomas with low and high MIB-1 indices.

Focal GFAP expression in central neurocytomas has been somewhat controversial and was initially reported in only a few cases (5, 6, 36). Some of these showed marked mitotic activity and vascular proliferation or necrosis, which led to the suspicion that these lesions belong to the group of primitive neuroectodermal tumors (11) or that they occupy a middle ground between neurocytoma and neuroblastoma (36). Of the 41 biopsies analyzed in the present study, 6 (15%) unequivocally showed GFAP expression by neoplastic cells; 2 of these (cases 3 and 21) have been reported earlier (5, 6). Four of these cases had an MIB-1 LI greater than 2% (Table 1). The concept that central neurocytomas have the capacity for astrocytic differentiation is supported by coexpression with synaptophysin (5, 6, 37) and the observation that neurocytoma cells typically express GFAP and synaptophysin within 1 day after in vitro culture even if the primary neoplasm showed no evidence of glial differentiation (38).

In conclusion, the present study shows that the proliferative potential of central neurocytomas varies considerably and correlates with recurrence-free survival. We propose the term "atypical central neurocytoma" for those exhibiting a Ki-67/MIB-1 index of ≥2% and/or vascular proliferation, as these are associated with a somewhat less favorable clinical course. Future studies may reveal that this subset of neurocytomas warrants different treatment, e.g. postoperative radiotherapy, which in some neurocytomas has been shown to cause a significant reduction in tumor mass (3, 9, 27). However, clinical follow-up data are still scarce and additional observations will be required to reliably estimate the biologic behavior of this variant of central neurocytoma.

REFERENCES

1. Hassoun J, Gambarelli D, Grisoli F, et al. Central neurocytoma. An electron-microscopic study of two cases. Acta Neuropathol (Berl) 1982;56:151–56
2. Kleihues P, Burger PC, Scheithauer BW. Histological typing of tumours of the central nervous system. World Health Organization international histological classification of tumours. 2nd ed. Berlin Heidelberg: Springer Verlag, 1993
3. Hassoun J, Soylemezoglu F, Gambarelli D, Figarella Branger D, von Ammon K, Kleihues P. Central neurocytoma: A synopsis of clinical and histological features. Brain Pathol 1993;3:297–306
4. Kleihues P, Burger PC, Scheithauer BW. The new WHO classification of brain tumours. Brain Pathol 1993;3:255–68
5. von Deimling A, Kleihues P, Saremaslani P, et al. Histogenesis and differentiation potential of central neurocytomas. Lab Invest 1991;64:585–91
6. von Deimling A, Janzer R, Kleihues P, Wiestler OD. Patterns of differentiation in central neurocytoma. An immunohistochemical study of eleven biopsies. Acta Neuropathol Berl 1990;79:473–79

7. Yasargil MG, von Ammon K, von Deimling A, Valavanis A, Wichmann W, Wiestler OD. Central neurocytoma: Histopathological variants and therapeutic approaches. J Neurosurg 1992;76:32–37
8. Kim DG, Chi JG, Park SH, et al. Intraventricular neurocytoma: Clinicopathological analysis of seven cases. J Neurosurg 1992;76: 759–65
9. Ferreol E, Sawaya R, de Courten Myers GM. Primary cerebral neuroblastoma (neurocytoma) in adults. J Neurooncol 1989;7:121–28
10. Kubota T, Hayashi M, Kawano H, et al. Central neurocytoma: Immunohistochemical and ultrastructural study. Acta Neuropathol Berl 1991;81:418–27
11. Figarella Branger D, Pellissier JF, Daumas Duport C, et al. Central neurocytomas. Critical evaluation of a small-cell neuronal tumor. Am J Surg Pathol 1992;16:97–109
12. Hessler RB, Lopes MB, Frankfurter A, Reidy J, VandenBerg SR. Cytoskeletal immunohistochemistry of central neurocytomas. Am J Surg Pathol 1992;16:1031–38
13. Louis DN, Swearingen B, Linggood RM, et al. Central nervous system neurocytoma and neuroblastoma in adults—report of eight cases. J Neurooncol 1990;9:231–38
14. Cattoretti G, Becker MH, Key G, et al. Monoclonal antibodies against recombinant parts of the Ki-67 antigen (MIB 1 and MIB 3) detect proliferating cells in microwave-processed formalin-fixed paraffin sections. J Pathol 1992;168:357–63
15. Gerdes J, Becker MH, Key G, Cattoretti G. Immunohistological detection of tumour growth fraction (Ki-67 antigen) in formalin-fixed and routinely processed tissues. J Pathol 1992;168:85–86
16. Shi SR, Key ME, Kalra KL. Antigen retrieval in formalin-fixed, paraffin-embedded tissues: An enhancement method for immunohistochemical staining based on microwave oven heating of tissue sections. J Histochem Cytochem 1991;39:741–48
17. Gerdes J, Lemke H, Baisch H, Wacker HH, Schwab U, Stein H. Cell cycle analysis of a cell proliferation-associated human nuclear antigen defined by the monoclonal antibody Ki-67. J Immunol 1984;133:1710–15
18. Burger PC, Shibata T, Kleihues P. The use of the monoclonal antibody Ki-67 in the identification of proliferating cells: Application to surgical neuropathology. Am J Surg Pathol 1986;10:611–17
19. Raghavan R, Steart PV, Weller RO. Cell proliferation patterns in the diagnosis of astrocytomas, anaplastic astrocytomas and glioblastoma multiforme: A Ki-67 study. Neuropathol Appl Neurobiol 1990;16:123–33
20. Roggendorf W, Schuster T, Peiffer J. Proliferative potential of meningiomas determined with monoclonal antibody Ki-67. Acta Neuropathol 1987;73:361–64
21. Schroder R, Bien K, Kott R, Meyers I, Vossing R. The relationship between Ki-67 labeling and mitotic index in gliomas and meningiomas: Demonstration of the variability of the intermitotic cycle time. Acta Neuropathol Berl 1991;82:389–94
22. Jaros E, Perry RH, Adam L, et al. Prognostic implications of p53 protein, epidermal growth factor receptor, and Ki-67 labelling in brain tumours. Br J Cancer 1992;66:373–85
23. Giangaspero F, Doglioni C, Rivano MT, Pileri S, Gerdes J, Stein H. Growth fraction in human brain tumors defined by the monoclonal antibody Ki-67. Acta Neuropathol Berl 1987;74:179–82
24. Maruno M, Kovach JS, Kelly PJ, Yanagihara T. Transforming growth factor-alpha, epidermal growth factor receptor, and proliferating potential in benign and malignant gliomas. J Neurosurg 1991;75:97–102
25. Louis DN, Edgerton S, Thor AD, Hedley Whyte ET. Proliferating cell nuclear antigen and Ki-67 immunohistochemistry in brain tumors: A comparative study. Acta Neuropathol Berl 1991;81:675–79
26. Zuber P, Hamou MF, de Tribolet N. Identification of proliferating cells in human gliomas using the monoclonal antibody Ki-67. Neurosurgery 1988;22:364–68
27. Barbosa MD, Balsitis M, Jaspan T, Lowe J. Intraventricular neurocytoma: A clinical and pathological study of three cases and review of the literature. Neurosurgery 1990;26:1045–54
28. Zentner J, Peiffer J, Roggendorf W, Grote E, Hassler W. Periventricular neurocytoma: A pathological entity. Surg Neurol 1992;38: 38–42
29. Robbins P, Segal A, Narula S, et al. Central neurocytoma. A clinicopathological, immunohistochemical and ultrastructural study of 7 cases. Pathol Res Pract 1995;191:100–111
30. Casadei GP, Arrigoni GL, Versari P, Gambacorta M, Giangaspero F. Central neurocytoma. A clinico-pathologic study of five cases. Tumori 1991;77:323–27
31. Hara A, Araki Y, Shinoda J, et al. Central neurocytoma: Proliferative assessment by nucleolar organizer region staining. Surg Neurol 1993;39:343–47
32. Russell DS, Rubinstein LJ. Pathology of tumours of the nervous system. 5th ed. London: Edward Arnold, 1989
33. Burger PC, Scheithauer BW. Tumors of the central nervous system. Washington: Armed Forces Institute of Pathology, 1994
34. Daumas Duport C, Scheithauer B, O'Fallon J, Kelly P. Grading of astrocytomas. A simple and reproducible method. Cancer 1988;62: 2152–65
35. Gaudin PB, Rosai J. Florid vascular proliferation associated with neural and neuroendocrine neoplasms. A diagnostic clue and potential pitfall. Am J Surg Pathol 1995;19:642–52
36. Mrak RE. Malignant neurocytic tumor. Hum Pathol 1994;25:747–52
37. Tsuchida T, Matsumoto M, Shirayama Y, Imahori T, Kasai H, Kawamoto K. Neuronal and glial characteristics of central neurocytoma: Electron microscopical analysis of two cases. Acta Neuropathol 1996;91:573–77
38. Westphal M, Stavrou D, Nausch H, Valdueza JM, Herrmann HD. Human neurocytoma cells in culture show characteristics of astroglial differentiation. J Neurosci Res 1994;38:698–704

Received September 3, 1996
Revision received January 12, 1997
Accepted January 18, 1997