PILOCYTIC AND PILOMYXOID HYPOTHALAMIC/ CHIASMATIC ASTROCYTOMAS

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OBJECTIVE: Pilocytic astrocytoma (PA) is a common type of pediatric brain tumor that can arise within the hypothalamic/chiasmatic region and typically has an excellent outcome. We identified a group of tumors, previously classified as PAs, with unique histological features and aggressive behavior. This article describes the clinicopathological features of these unusual neoplasms, which are currently known as pilomyxoid astrocytomas (PMAs), to better differentiate them from typical PAs.

METHODS: Medical information and surgical specimens were obtained for 42 PA cases and 21 PMA cases. Patient demographic features, treatment modalities, progression-free survival (PFS) times, overall survival (OS) times, and outcomes were compared between the groups with nonparametric tests.

RESULTS: The PMA group included 12 male and 9 female patients. The PA group included 27 male and 15 female patients. The mean ages at diagnosis for the PMA and PA groups were 18 months (range, 2–84 mo) and 58 months (range, 4–189 mo), respectively ($P < 0.01$). The mean PFS times for the PMA and PA groups were 26 and 147 months, respectively ($P < 0.001$). The mean OS times for the PMA and PA groups were 63 and 213 months, respectively ($P < 0.001$). Sixteen patients with PMAs (76%) experienced local recurrence, and three of those patients demonstrated evidence of cerebrospinal fluid dissemination. Twenty-one patients with PAs (50%) experienced local recurrence, none with evidence of cerebrospinal fluid dissemination. Within the follow-up period, seven patients with PMAs (33%) and seven patients with PAs (17%) died as a result of their disease. In an age-matched set, the mean PFS times for the PMA and PA groups were 25 and 163 months, respectively ($P < 0.01$), and the mean OS times for the PMA and PA groups were 60 and 233 months, respectively ($P < 0.001$).

CONCLUSION: Hypothalamic/chiasmatic PMAs occurred in a significantly younger population and were associated with substantially shorter PFS and OS times than were typical PAs. Increased recognition of these lesions could affect the prognosis and treatment of pediatric astrocytomas.

KEY WORDS: Astrocytoma, Hypothalamic, Optic chiasm, Pilocytic, Pilomyxoid

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Pilocytic astrocytomas (PAs) represent the most common type of brain tumors in the pediatric population (7). These neoplasms can occur anywhere along the neuraxis and can involve the hypothalamic/chiasmatic region. In general, hypothalamic/chiasmatic tumors pose a treatment challenge; they may not be amenable to gross total resection (GTR), because of the high morbidity and mortality rates associated with surgery in this region. Fortunately, PAs in this location have a better prognosis than do other tumor types. Patients with PAs who undergo subtotal resection demonstrate 20-year survival rates of 70 to 80% (32). In contrast, infiltrating astrocytomas diffusely invade the parenchyma and have a worse long-term prognosis (2, 22).

We recently identified a unique group of tumors that were previously diagnosed as PAs (31). In contrast to the typical biphasic

pattern of PAs, these neoplasms demonstrated monomorphous piloid cells in a loose fibrillary and myxoid background. Furthermore, they did not display Rosenthal fibers, which are characteristic of PAs (24, 31). We designated such neoplasms pilomyxoid astrocytomas (PMAs), on the basis of their typical histological appearance. In our initial study, PMAs displayed higher recurrence rates and greater potential for cerebrospinal fluid (CSF) dissemination, compared with typical PAs (31). Although it seemed that PMA could be a distinct tumor type with more aggressive behavior, compared with PA, additional investigations with larger groups are needed to determine whether this neoplasm is a variant of PA or a distinct entity. In this article, we present our experience with 63 hypothalamic/chiasmatic tumors in the PA and PMA categories, to better differentiate these neoplasms.

MATERIALS AND METHODS

Surgical specimens from 21 hypothalamic astrocytomas with monomorphous pilomyxoid features (*Table 1*) were obtained from the personal consultation files of the authors (15 cases) and from Pediatric Oncology Group files (6 cases). All cases were previously diagnosed as PAs.

Surgical specimens from 42 hypothalamic astrocytomas with typical pilocytic features (*Table 1*) were selected from among all pediatric brain tumors diagnosed at the Johns Hopkins Hospital between 1966 and 1996. Clinical information for these cases was obtained from the patient files and the records of the referring physicians.

Histological and immunohistochemical studies were performed with formalin-fixed, paraffin-embedded tissues. Immunohistochemical staining for glial fibrillary acidic protein (1:6000; Dako, Carpinteria, CA) and Ki-67 (MIB-1, 1:100; Dako) was performed with the avidin-biotin-peroxidase method, with appropriate positive and negative control samples. Histological diagnosis and grading were performed by two of the authors (PCB and TT), after a consensus review. The evaluators were blinded with respect to all clinical information, such as age, tumor location, treatment, and subsequent course. The diagnostic criteria are listed in *Table 1*.

We retrospectively compared clinical characteristics, such as patient demographic features and treatment modalities, between the PMA and PA groups with nonparametric Mann-Whitney tests. The progression-free survival (PFS) time, defined as the time from the initial diagnosis to radiological progression, and overall survival (OS) time, defined as the time from the initial diagnosis to the final follow-up assessments, were calculated with Kaplan-Meier curves. Standard errors (SEs) for the curves were determined with Greenwood's formula. Curves were compared with log-rank tests. The SPSS software package (version 10.0; SPSS, Chicago, IL) was used for statistical analysis. PFS and OS times were also compared for 42 age-matched (within 5 mo) patients (21 with PMAs and 21 with PAs), to control for patient age as a possible confounding variable.

RESULTS

Clinical Characteristics

In the PMA group (*Table 2*), there were 12 male and 9 female patients. In the PA group (*Table 3*), there were 27 male and 15 female patients. The mean patient ages at the time of diagnosis for the PMA and PA groups were 18 months (range, 2–84 mo) and 58 months (range, 4–189 mo), respectively ($P < 0.01$). All tumors were located in the hypothalamic/chiasmatic region, with rare cases extending to the thalamus and temporal lobes. Patients with neurofibromatosis were excluded from this study. Radiologically, tumors in both groups were well circumscribed and had solid and/or cystic components, without gross evidence of parenchymal infiltration (*Fig. 1*). The most common presenting symptoms for patients in both groups

TABLE 1. Histological features of pilocytic and pilomyxoid astrocytomas

Histological feature	Pilocytic	Pilomyxoid
Cellular composition	Heterogeneous/biphasic	Monomorphous/monophasic
Oligodendroglioma-like pattern	Occasional	Absent
Piloid cells, "pilocytes"	Abundant	Abundant
Plump/"protoplasmic" cells	Present	Rare
Myxoid background	Focal/infrequent	Diffuse/predominant
Rosenthal fibers	Often present	Absent
Eosinophilic granular bodies	Often present	Often absent
Angiocentric pattern	Rare	Frequent
Calcification	Often present	Uncommon

TABLE 2. Clinical features of patients with pilomyxoid astrocytomas[a]

Age (mo)/sex	Location	Initial operation	Adjuvant therapy	Recurrence		Follow-up period (mo)	Outcome
				Site	Time (mo)		
2/M	Hypothalamus	BX	None	None			AWD
3/F	Chiasm	PSX	CT	CSF	9	12	DOC
3/M	Chiasm	PSX	CT	Local	4	9	DOD
4/F	Chiasm	PSX	CT	Local	4	24	DOD
4/M	Hypothalamus	PSX	None	Local	2	2	AWD
5/M	Hypothalamus	PSX	CT, RT	CSF	10	13	DOD
5/F	Thalamus	PSX	None	CSF	10	14	DOD
6/F	Hypothalamus	PSX	CT, RT	Local	5	14	AWD
6/M	Hypothalamus	PSX	CT	Local	38	60	AWD
6/M	Hypothalamus	PSX	CT	Local	60	61	DOD
8/F	Hypothalamus	PSX	None	Local	32	40	AWD
9/M	Hypothalamus	PSX	CT	Local	13	36	AWD
11/M	Chiasm	PSX	RT	Local	13	21	DOD
12/F	Hypothalamus	PSX	CT	Local	4	15	AWD
22/M	Hypothalamus	BX	CT	Local	25	82	AWD
22/M	Hypothalamus	PSX	CT, RT	Local	4	31	DOD
24/F	Hypothalamus	PSX	None	None		5	AWD
27/M	Hypothalamus	PSX	CT	None		6	AWD
28/M	Hypothalamus	BX	CT, RT	None		32	AWD
36/F	Hypothalamus	PSX	None	Local	9	11	AWD
84/F	Hypothalamus	BX	CT	None		5	AWD

[a] BX, biopsy only; PSX, partial resection; CT, chemotherapy; RT, radiotherapy; CSF, cerebrospinal fluid; AWD, alive with disease; DOC, died as a result of other causes; DOD, died as a result of disease.

were a failure to thrive, developmental delays, altered levels of consciousness, vomiting, feeding difficulties, and generalized weakness. The presenting symptoms did not differ between the groups.

Treatment

In the PMA group, 17 patients (81%) underwent partial resection and 4 patients (19%) underwent biopsy only. Ten patients (47%) received chemotherapy, one patient (5%) received radiotherapy, four patients (19%) received both chemotherapy and radiotherapy, and six patients (29%) received no adjuvant therapy. In the PA group, 36 patients (86%) underwent partial resection and 6 patients (14%) underwent biopsy only. Three patients (7%) received chemotherapy, 15 patients (36%) received radiotherapy, 11 patients (26%) received both chemotherapy and radiotherapy, and 13 patients (31%) received no adjuvant therapy. The criteria for operative intervention were clinical progression and worsening symptoms.

Pathological Findings

Tissue samples from patients with PMAs were small and compact and appeared rather myxoid. Histologically, the tumors were composed of highly monomorphous and piloid cells in a markedly myxoid background (*Fig. 2*). Tumor cells were often arranged around vessels, perpendicular to the vascular axis, in an angiocentric pattern. Tumor fragments often appeared solid, without Rosenthal fibers and with only rare eosinophilic granular bodies. Infiltration of tumor cells

TABLE 3. Clinical features of patients with pilocytic astrocytomas[a]

Age (mo)/sex	Location	Initial operation	Adjuvant therapy	Recurrence		Follow-up period (mo)	Outcome
				Site	Time (mo)		
4/M	Hypothalamus	PSX	None	None		68	AWD
4/F	Chiasm	PSX	RT	Local	21	232	DOD
4/F	Hypothalamus	PSX	None	None		8	DOD
5/M	Hypothalamus	PSX	None	None		67	AWD
6/M	Hypothalamus	PSX	CT	None		118	NED
7/M	Hypothalamus	PSX	None	None		74	AWD
9/F	Hypothalamus	PSX	CT, RT	Local	95	102	DOD
10/F	Chiasm	PSX	CT, RT	None		185	DOD
10/M	Chiasm	PSX	None	Local	4	80	LFU
12/M	Hypothalamus	PSX	None	None		301	AWD
13/F	Hypothalamus	PSX	RT	Local	4	100	AWD
14/M	Hypothalamus	PSX	CT, RT	Local	69	117	LFU
14/M	Hypothalamus	PSX	CT, RT	None		161	AWD
15/M	Hypothalamus	BX	CT, RT	Local	115	135	AWD
19/M	Hypothalamus	PSX	CT, RT	Local	22	106	AWD
22/F	Hypothalamus	PSX	None	None		136	AWD
22/M	Hypothalamus	PSX	CT	Local	26	123	AWD
28/M	Hypothalamus	PSX	CT, RT	Local	52	103	AWD
29/M	Hypothalamus	PSX	None	None		237	NED
38/M	Chiasm	PSX	RT	Local	33	121	AWD
40/F	Hypothalamus	PSX	CT, RT	Local	83	89	AWD
42/M	Hypothalamus	BX	None	Local	15	16	LFU
48/M	Hypothalamus	PSX	CT, RT	Local	97	156	LFU
48/M	Hypothalamus	BX	RT	Local	89	123	DOD
50/M	Hypothalamus	PSX	CT, RT	Local	71	96	AWD
54/M	Hypothalamus	PSX	CT, RT	None		160	DOD
67/F	Hypothalamus	BX	RT	None		61	LFU
67/M	Hypothalamus	BX	RT	Local	41	170	AWD
79/M	Hypothalamus	PSX	RT	None		134	AWD
85/F	Hypothalamus	PSX	None	None		68	AWD
89/F	Chiasm	PSX	RT	Local	27	31	LFU
92/F	Hypothalamus	BX	RT	Local	94	126	AWD
95/M	Hypothalamus	PSX	RT	None		46	LFU
112/M	Hypothalamus	PSX	RT	Local	4	33	AWD
116/M	Chiasm	PSX	None	None		87	AWD
120/F	Hypothalamus	PSX	CT	None		82	AWD
125/F	Hypothalamus	PSX	None	None		59	AWD
127/M	Hypothalamus	PSX	RT	None		62	AWD
155/F	Hypothalamus	PSX	RT	Local	47	148	DOD
168/M	Hypothalamus	PSX	None	None		125	AWD
178/F	Hypothalamus	PSX	RT	Local	30	95	AWD
189/M	Hypothalamus	PSX	RT	None		6	LFU

[a] BX, biopsy only; PSX, partial resection; CT, chemotherapy; RT, radiotherapy; AWD, alive with disease; DOD, died as a result of disease; NED, no evidence of disease; LFU, lost to follow-up monitoring.

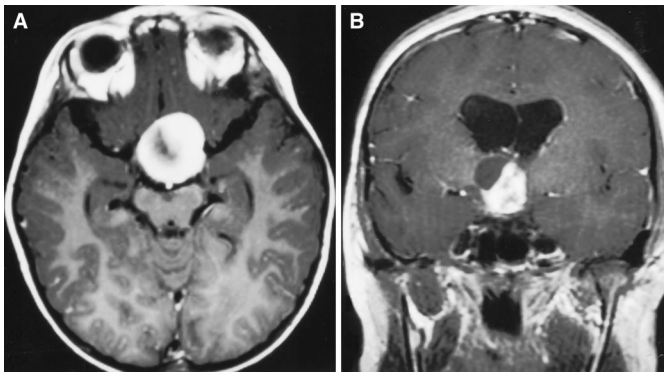

FIGURE 1. A, *axial, contrast-enhanced, T1-weighted magnetic resonance imaging scan for a patient with a PMA. The tumor exhibited solid architectural features, marked contrast enhancement, and a hypodense central region suggesting a hypovascular or necrotic core. The histological features were consistent with PMA.* B, *coronal, contrast-enhanced, T1-weighted magnetic resonance imaging scan for a patient with a typical PA. Associated hydrocephalus was noted in the lateral ventricles. The solid/cystic neoplasm in the hypothalamic region exhibited histological features typical of a PA, with Rosenthal fibers and eosinophilic granular bodies.*

into the surrounding neuropil at the tumor periphery occurred in some cases. Rare mitotic figures could be observed in some tumors, but no mitotic figures were identified in the majority of cases.

The PA group displayed histological characteristics typical of pilocytic tumors with compact biphasic architectural features, demonstrating densely cellular areas alternating with loose cystic regions (*Fig. 2*). All tumors displayed Rosenthal fibers, and most also demonstrated eosinophilic granular bodies. Mitotic figures could not be identified in most tumors. In some cases, cyst formation was accompanied by granulation tissue-type vascular proliferation along the cyst wall. Microcalcifications were present in approximately one-half of the tumors.

Outcomes

In the PMA group, 16 patients (76%) experienced local recurrence and five patients (24%) experienced no recurrence. Three patients demonstrated evidence of CSF dissemination. In the PA group, 21 patients (50%) experienced local recurrence and 21 patients (50%) experienced no recurrence. No patient demonstrated evidence of CSF dissemination. The PFS times (mean ± SE) for the PMA and PA groups were 26 ± 7 and 147 ± 22 months, respectively ($P < 0.001$). The OS times (mean ± SE) for the PMA and PA groups were 63 ± 10 and 213 ± 23 months, respectively ($P < 0.001$). In the PMA group, 7 patients (33%) died as a result of their disease, 13 patients (62%) were alive with disease, and 1 patient died as a result of other causes. In the PA group, 7 patients (17%) died as a result of their disease, 25 patients (59%) were alive with disease, 2 patients (5%) demonstrated no evidence of disease, and 8 patients (19%) were lost to follow-up monitoring.

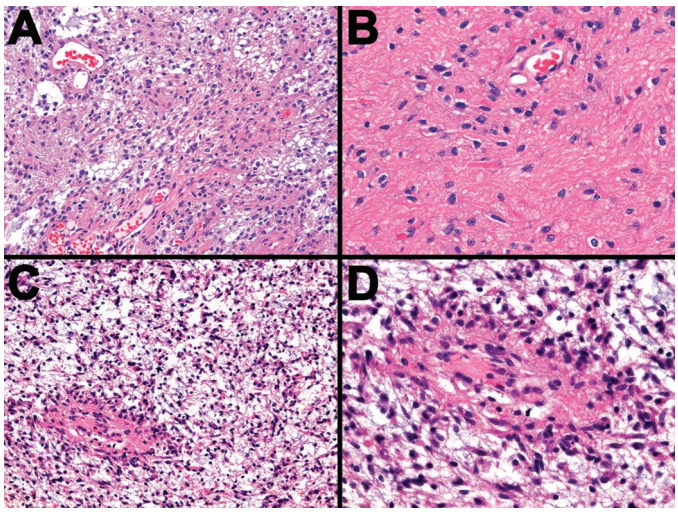

FIGURE 2. A, *histological appearance of a typical PA. The tumor demonstrated a biphasic pattern, with compact and loose areas. There was no particular predilection of tumor cells for an angiocentric arrangement. The tumor demonstrated a moderate degree of nuclear variability (original magnification, ×200).* B, *histological appearance of a typical PA, with high-power magnification of the compact area. The tumor cells were arranged in a haphazard manner. Numerous Rosenthal fibers can be identified in this field (original magnification, ×400).* C, *histological appearance of a PMA. The tumor was composed of monomorphous bipolar astrocytic cells in a rich myxoid background, with prominent increases in cell density around vascular structures, i.e., angiocentric pattern (original magnification, ×200).* D, *histological appearance of a PMA, with high-power magnification of the perivascular arrangement of tumor cells (angiocentric pattern) and the myxoid background. The tumor cells often exhibited dark condensed chromatin (original magnification, ×400).*

In an age-matched set (n = 42), the PFS times (mean ± SE) for the PMA and PA groups were 25 ± 6 and 163 ± 31 months, respectively ($P < 0.01$) (*Fig. 3*). The OS times for the PMA and PA groups were 60 ± 10 and 233 ± 26 months, respectively ($P < 0.001$) (*Fig. 4*).

DISCUSSION

PAs can occur anywhere in the central nervous system but exhibit a predilection for the cerebellum, optic nerve, and hypothalamic/chiasmatic region (4, 7). Complete resection is the goal in surgical treatment of PAs (12). In the hypothalamic/chiasmatic region, however, GTR is difficult and carries a risk of damage to the pituitary gland, optic apparatus, hypothalamic structures, and carotid arteries (28). This raises several important questions regarding the long-term behavior of residual tumor.

The majority of pediatric low-grade astrocytomas in the hypothalamic/chiasmatic region are typical PAs. These well-circumscribed tumors are indolent in nature and rarely exhibit an aggressive course (9). Although GTR provides the best opportunity for longer PFS times, studies demonstrated that even children who undergo partial resection of PAs have

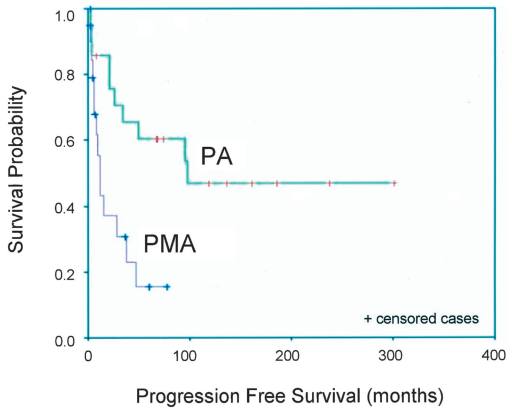

FIGURE 3. *Kaplan-Meier curve comparing the PFS times for patients with PMAs and PAs in age-matched groups. The PFS times (mean ± SE) for the PMA and PA groups were 25 ± 6 and 163 ± 31 months, respectively (P < 0.01).*

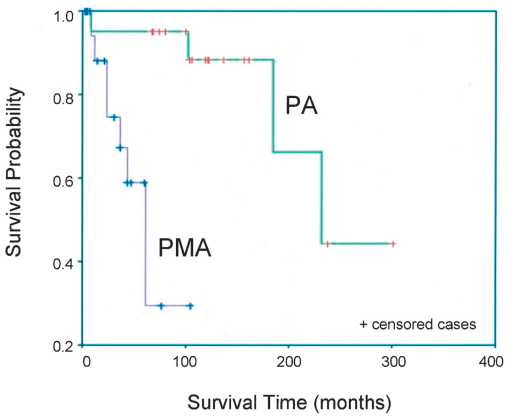

FIGURE 4. *Kaplan-Meier curve comparing the OS times for patients with PMAs and PAs in age-matched groups. The OS times (mean ± SE) for the PMA and PA groups were 60 ± 10 and 233 ± 26 months, respectively (P < 0.001).*

excellent long-term prognoses (29). CSF dissemination is uncommon for typical PAs, and malignant progression of these lesions is rare (3, 18–20).

In contrast, PMAs exhibit a distinctive monomorphous pilomyxoid pattern and demonstrate aggressive behavior in some cases (31). In this study, PMAs occurred in a significantly younger population than did PAs (mean ages at diagnosis of 18 and 58 mo, respectively; $P < 0.01$). Patients with PMAs demonstrated a slightly higher rate of local recurrence than did patients with PAs (76 and 50%, respectively). Furthermore, the PMA group demonstrated a substantial rate of CSF dissemination (14%), whereas none of the tumors in the PA group exhibited such spread. Patients with PMAs demonstrated significantly shorter PFS times than did patients with typical PAs (mean PFS times of 26 and 147 mo, respectively; $P < 0.001$). Patients with PMAs also demonstrated significantly shorter OS times than did patients with typical PAs (mean OS times of 63 and 213 mo, respectively; $P < 0.001$). Even when matched for age, patients with PMAs demonstrated significantly shorter PFS times (mean PFS times of 25 and 163 mo, respectively; $P < 0.01$) and OS times (mean OS times of 60 and 233 mo, respectively; $P < 0.001$) than did patients with typical PAs. Furthermore, 33% of patients with PMAs died as a result of their disease, compared with 17% of patients with PAs.

In addition to intrinsic biological behavior, several other variables may affect the prognosis for patients with gliomas, including tumor location, patient age at diagnosis, extent of resection, use of adjuvant therapy, and sex. These factors must be controlled for in comparisons of the clinical characteristics of the PMA and PA groups.

The tumor location has obvious implications for surgical management and outcome. Hypothalamic/chiasmatic lesions are rarely amenable to GTR and are associated with high operative risks. In addition, midline gliomas demonstrate shorter PFS times and higher rates of CSF spread than do lesions located in the cerebral hemispheres or cerebellum (12, 18). All patients in our study had hypothalamic/chiasmatic lesions. Therefore, tumor location does not account for the less favorable outcomes of patients with PMAs.

The age at the time of the initial diagnosis may affect long-term survival rates among patients with gliomas. Younger patients have worse prognoses after surgical resection, regardless of tumor location and histological features (12). To control for the possible confounding effect of age, we compared the clinical characteristics of the PMA group with those of an age-matched PA group. The results of this analysis demonstrated significantly shorter PFS (*Fig. 3*) and OS (*Fig. 4*) times in the PMA group, compared with the PA group. Therefore, the difference in age at the time of diagnosis does not seem to account for the less favorable outcomes of patients with PMAs.

The extent of resection is a critical determinant of prognosis after tumor surgery (3, 22). Patients who undergo partial resection of low-grade gliomas have shorter PFS times than do patients who undergo GTR. Diencephalic tumors pose a surgical challenge; therefore, approximately 80% of patients in both groups underwent partial resection and no patient underwent GTR. The extent of resection was comparable in the PMA and PA groups and did not affect the observed differences in PFS and OS times.

Although surgery remains the best treatment for circumscribed gliomas, the use of postoperative adjuvant therapy can alter disease progression and recurrence rates. The efficacy of radiotherapy among PAs is unclear. Although some studies demonstrated improved outcomes after irradiation of residual tumor (8, 30), suggesting that radiotherapy may be beneficial for subsets of patients, other investigations demonstrated no significant change in OS times (22). Furthermore, radiotherapy is associated with anaplastic changes in the original tumor and may cause cognitive and endocrine dysfunction (6, 22).

The role of chemotherapy in the treatment of unresectable low-grade gliomas has expanded, especially for very young

children (<5 yr of age), for whom the morbidity of irradiation of the developing nervous system can be severe and irreversible (6, 16, 23). Chemotherapy is increasingly being used to delay radiotherapy for partially resected tumors and seems to produce improvements in OS rates, even for low-grade astrocytomas with neuraxis dissemination (3, 11, 21). In our investigation, the majority of patients with PMAs received chemotherapy and the majority of patients with PAs received radiotherapy. This was expected, considering the mean age at diagnosis for each group. In the age-matched groups, however, the proportions of patients receiving chemotherapy and radiotherapy were comparable. Therefore, variability in the use of adjuvant therapy does not seem to account for the less favorable outcomes of patients with PMAs.

The effect of sex on outcomes for patients with gliomas remains unresolved. Although certain studies demonstrated that the sex of patients had significant effects on long-term survival rates (14, 25), others refuted such results (1, 27, 30). Although the literature data are inconclusive, the sex distributions of our PMA and PA groups were similar (57 and 64% male, respectively). We think that sex differences do not account for the less favorable outcomes of patients with PMAs.

PMAs display a histological pattern that is correlated with worse prognosis. There have been other reports of tumors with similar pathological features. Janisch et al. (15) reported on 11 children with hypothalamic/chiasmatic astrocytomas that, in addition to typical piloid cells, displayed "degenerative changes" such as mucoid degeneration and angioma-like structures. Cottingham et al. (5) presented an abstract that documented a series of PAs in infants with a more aggressive course, which the authors called the infantile type. Another study noted increased perivascular cellularity in some PAs, similar to the angiocentric pattern of PMAs observed in our study (17). A more recent abstract by Fuller et al. (10) discussed two cases of aggressive myxoid lesions in the suprasellar region that were interpreted as a variant of myxopapillary ependymoma. Those studies are consistent with our observation that pilomyxoid histological features were associated with more aggressive tumor biological features.

Tumor cell proliferation rates can be measured as Ki-67 labeling indices. Typical PAs often demonstrate low proliferation rates, ranging from 0 to 4% (measured on the basis of Ki-67 labeling with the MIB-1 antibody) (13). In our PA group, no tumor exhibited a MIB-1 labeling index of more than 3%. In the PMA group, all tested tumors demonstrated labeling indices of less than 5% (range, 2–5%). No significant difference in MIB-1 labeling indices was observed between the groups; therefore, proliferation indices are unlikely to be useful in distinguishing PMAs from PAs.

Although PMAs have some features that distinguish them from typical PAs (*Table 1*), there are a number of similarities that indicate a close association. Recently noted cases of PMAs that recurred as typical PAs further complicate this dilemma (MK Rosenblum, personal communication). Additional investigations involving larger groups and longer follow-up periods are necessary to determine the relationship between PAs and PMAs.

Currently, very little is known regarding the role of genetic abnormalities in the development of PAs and PMAs (26). In a preliminary analysis using comparative genomic hybridization, we observed no abnormalities in a small group of PAs and PMAs. Our ongoing investigations aim to identify genetic differences between the tumors in more detailed studies.

In conclusion, PMAs are lesions with distinctive histological features that exhibit a predilection for the hypothalamic/chiasmatic region, a tendency to occur among young children, and less favorable outcomes, compared with typical PAs. Better recognition of these neoplasms could affect both the prognosis and treatment of pediatric low-grade astrocytomas.

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COMMENTS

The authors report a series of patients with a pediatric glioma variant, pilomyxoid astrocytoma, that seems to have a more aggressive course than typical juvenile pilocytic astrocytoma. The authors contrast the outcome between these two tumor types by comparing a series of cases of pilomyxoid astrocytoma from their consultation files and the Pediatric Oncology Group with a selected cohort of patients treated at a single institution over an interval of 30 years that were found on review to truly represent pilocytic astrocytomas. Given that these cohorts represent quite different patient groups, they differ substantially in terms of age and treatment. The authors have therefore identified an age-matched pilocytic astrocytoma subgroup to compare with the pilomyxoid cohort. Clearly, there are limitations to this sort of analysis. Nonetheless, the authors have called attention to a potentially distinct subgroup of tumors and highlight the importance of attempting to validate their data in a larger study of pediatric gliomas, which should be feasible within the context of the current pediatric cooperative group study (A9952) for these tumors. The present data provide a strong rationale for such an analysis.

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It has always been somewhat curious that low-grade astrocytomas of the hypothalamic/chiasmatic region behave variably depending on patient age. We have known for some time that children under the age of 3 years have a far more unpredictable clinical course and response to therapy than do older children with similar-appearing lesions on magnetic resonance imaging. Here, the authors have shown nicely that this variability in patient response may be related to the presence of a newly described histopathological variant of pilocytic astrocytoma known as pilomyxoid astrocytoma. Pilomyxoid astrocytoma is characterized, as the name implies, by a markedly myxoid background on histopathology. This is an important observation and one that may influence diagnoses and treatment protocols in the future. An important question that remains, however, is why young children under age 3 tend to develop pilomyxoid astrocytomas as opposed to pilocytic astrocytomas in this region of the central nervous system.

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This is a review of 42 histology samples obtained from children biopsied for hypothalamic/chiasmatic astrocytomas. All had previously been classified as "pilocytic," and fibrillary astrocytomas were excluded. Retrospective pathology review was performed by consensus of two neuropathologists who were blinded to outcome and clinical variables. On the basis of earlier work on astrocytomas obtained from various locations, they divided the group into pilocytic and pilomyxoid subtypes. The major finding was that patients harboring the pilomyxoid subtype tended to belong to younger groups, but even when age-matched analysis was performed, this subtype carried a worse prognosis.

This is potentially important work, if the subclassification proves to be reproducible by other neuropathologists. Low-grade chiasmatic/hypothalamic astrocytomas are notably variable in their outcome, and previous attempts to classify them have been unsuccessful in predicting outcome. Many have assumed that there is some unknown "biological" variable that accounts for the difference in outcome among affected individuals. Clearly, dividing this group into high-risk and low-risk groups will be helpful in assessing the value of treatment and tailoring the aggressiveness of treatment on the basis of risk.

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Komotar et al. review the histology and outcome of 63 children with tumors in the hypothalamus/chiasm. Forty-two of these children's tumors were classic pilocytic astrocy-

tomas, whereas 21 tumors had distinctly different histological features (in a previous article, the authors named this tumor a *pilomyxoid astrocytoma*) (1). Most impressive is the clear difference in survival for the two groups. This is an important observation that perhaps explains the unusual behavior sometimes observed with juvenile pilocytic astrocytomas, and it should be kept in mind when considering their management.

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1. Tihan T, Fisher PG, Kepner JL, Godfraind C, McComb RD, Goldthwaite PT, Burger PC: Pediatric astrocytomas with monomorphous pilomyxoid features and a less favorable outcome. **J Neuropathol Exp Neurol** 58:1061–1068, 1999.

The authors collected 63 cases of hypothalamic/optic chiasm astrocytomas covering the years 1966 to 1996. On the basis of histological criteria (their *Table 1*), they divided their group into two subsets consisting of 21 patients with what they are calling pilomyxoid astrocytomas and those with the typical pilocytic astrocytomas. When comparing these two subsets, they noted that the patients with the pilomyxoid astrocytomas were younger children and had a distinctly poor progression-free survival and overall survival probability compared with those patients with the typical pilocytic astrocytoma. Also, three of the patients with the pilomyxoid astrocytoma had cerebrospinal fluid dissemination, whereas this was not the case for the pilocytic astrocytomas.

It should be possible to validate the authors' observations with one of the Children's Oncology Group studies. The knowledge of distinct subsets of hypothalamic/chiasmic astrocytomas with better or worse prognoses would be beneficial to directing appropriate adjuvant chemotherapy and/or radiation therapy, because surgical removal of these tumors is not a possibility.

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Athena and Pegasus *by Theodor van Thulden, 1644, oil on canvas. The Greek goddess Athena slips a bridle around the neck of Pegasus, the wild winged horse born from the blood that fell to earth when the hero Perseus cut off Medusa's head. Athena's renown for horse training stemmed from her capture and taming of Pegasus. This feat reflects Athena's wisdom (symbolized by the owl standing at her feet) and also her physical ability (represented by her full suit of armor). (Courtesy, J. Paul Getty Museum, Los Angeles, California.)*