Pilocytic astrocytomas are generally benign, typically showing 20-year survival rates of 70 to 80%, even when only a subtotal resection is achieved. These highly treatable and potentially curable pediatric tumors are considered Grade I neoplasms according to the World Health Organization tumor classification system. Prior to its recognition, PMA was grouped with PA, because the two display similar histological features. The PMA was first described by Tihan and colleagues in 1999. Earlier reports pointed out unusual features of some pediatric astrocytomas, particularly those within the hypothalamic/chiasmatic region, but did not specifically use a term to distinguish them. Our group reported that PMA demonstrates a more variable clinical course and tends to behave more aggressively than PA, with a decreased duration of disease-free survival and higher mortality rates. Their histological features distinguish PMAs from typical PAs. In this paper we describe the clinicopathological characteristics of PMA, as well as its prognostic implications and management strategies. Increased awareness of this recently described pediatric low-grade astrocytoma in the pediatric population is important for accurate diagnosis and treatment of low-grade astrocytomas.

DIAGNOSIS

Clinical Manifestations

The original report on PMA consisted of tumors located exclusively in the hypothalamic/chiasmatic region. Subsequently, PMA was also described in the posterior fossa and in the spinal cord. Although the mean age at diagnosis for patients with PMA is 18 months, it may present throughout childhood. This tumor typically causes focal neurological symptoms, such as visual disturbances and endocrine dysfunction. The clinical manifestations of PMA also parallel those of other pediatric brain tumors, and include failure to thrive, developmental delay, altered level of consciousness, vomiting, feeding difficulties, and generalized weakness. If the tumor involves the posterior fossa, gait abnormalities, dysmetria, and nystagmus may be present, with tumor extension into the foramen magnum leading to neck stiffness or head tilt.

Radiographic Findings

Radiographic findings for PMA appear similar to those for PA (Figs. 1 and 2); PMA tends to be well-circumscribed, demonstrates solid or cystic components, and has little to no calcification on computerized tomography scans. These lesions are commonly isointense on T<sub>1</sub>-weighted sequences, hyperintense on T<sub>2</sub>-weighted ones, and exhibit variable enhancement on MR images with addition of Gd. Furthermore, PMAs may exhibit peritumoral edema, mass effect, and necrosis. No radiographic characteristics have yet been identified that reliably differentiate PMA from PA. Preliminary investigations with the use of proton MR spectroscopy in two cases of pediatric optic/chiasmatic PMA revealed decreased concentrations of total choline, creatine, and N-acetylaspartate. In comparison, proton MR spectra of PAs revealed elevated choline and decreased creatine and N-acetylaspartate signals. Although larger studies are clearly necessary, the use of proton MR spectroscopy may provide a useful tool for the diagnosis of PMA.
needed, MR spectroscopy may prove to be useful in the future to help distinguish this tumor from PA.

Histological Features

The diagnosis of PMA is made predominantly on the basis of histological features (Fig. 3). Whereas classic PA is a compact neoplasm with biphasic architecture, PMA is composed of piloid and highly monomorphous cells. Even though myxoid change is commonly encountered in PAs, PMAs display a much more uniform and extensive myxoid background. A PMA often lacks Rosenthal fibers and only rare cases have eosinophilic granular bodies, both of which are characteristic of PA. In PMA, the neoplastic cells display an angiocentric pattern that remotely resembles the perivascular rosettes seen in ependymomas. The tumor cells can infiltrate into the surrounding neural parenchyma. In contrast with typical PA, mitoses can be readily seen in PMA and necrosis is not uncommon.

Recent anecdotal evidence has demonstrated that biopsy samples obtained in patients with PMA who underwent a repeated operation at a later date may resemble more typical PAs. These cases have initiated a discussion about the possibility of “maturation” of PMAs into typical PAs. Even though there is very limited experience in this area, such cases underline the association between PMA and PA.

PROGNOSIS

Although limited clinical experience makes it difficult to generate conclusive prognostic data regarding this recently described pediatric tumor, PMA has been shown to behave more aggressively than PA. A preliminary investigation addressed this topic by comparing the long-term clinical outcomes (mean follow-up duration 26 months) for 21 patients with hypothalamic PMAs with the outcomes in 42 patients with PAs in the same location. Patients with PMA had a higher rate of local recurrence than those with PA (76 and 50%, respectively), despite having undergone equal degrees of GTR. Notably, the PMA group had a substantial rate of dissemination (14%) in the cerebrospinal fluid, an event not recognized in the PA group. Patients with PMA also demonstrated significantly shorter progression-free (mean duration 26 and 147 months for those with PMA and PA, respectively; \( p > 0.001 \)) and overall (mean duration 63 and 213 months, respectively; \( p < 0.001 \)) survival times than those with PA (Fig. 4). Even when matched for age, patients with
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PMA continued to demonstrate significantly shorter progression-free duration (mean duration 25 and 163 months for those with PMA and PA, respectively; \( p < 0.001 \)) and overall survival for PMA and PA cohorts was 60 ± 10 and 233 ± 26 months, respectively (mean ± standard error; \( p < 0.001 \)). Figure reprinted with permission from Komotar RJ, et al: Pilocytic and pilomyxoid hypothalamic/chiastic astrocytomas. *Neurosurgery* **54**:72–80, 2004

**CONCLUSIONS**

Because PMA generally exhibits more aggressive biologic behavior, physicians have been inclined to implement adjuvant therapy earlier in the course of treatment. At our institution and others, unless a GTR is achieved, adjuvant therapy is started immediately after surgery, without waiting for tumor growth or recurrence. Chemotherapy is most often used because of the young age of patients at diagnosis, and it can delay the need for radiation. For older children, radiotherapy administered concomitantly with chemotherapy may prove to be a more effective method of treatment for PMA, although side effects can be severe in certain cases. Given the uncertainties about the prognostic significance of PMA overall and the possible maturation of some tumors into typical PA, it is not possible to provide strict management guidelines at this stage. More definitive guidelines are certain to emerge as clinicians gain more experience with PMA in the future.

**References**


**Fig. 4.** A: Kaplan–Meier curve comparing the progression-free survival of patients with PMA and PA in age-matched cohorts. The mean progression-free survival duration for PMA and PA cohorts was 25 ± 6 and 163 ± 31 months, respectively (mean ± standard error; \( p < 0.01 \)). B: Kaplan–Meier curve comparing the overall survival duration of patients with PMA and PA in age-matched cohorts. The mean duration of overall survival for PMA and PA cohorts was 60 ± 10 and 233 ± 26 months, respectively (mean ± standard error; \( p < 0.01 \)).


Manuscript received February 28, 2005. Accepted in final form May 16, 2005.

Dr. Ricardo J. Komotar was supported by a National Institutes of Health Research Training Fellowship, Dr. J Mocco was supported by the Congress of Neurological Surgeons Wilder Penfield Fellowship, and Jess E. Jones was supported by an American Heart Association Research Fellowship.

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