Pleomorphic Xanthoastrocytoma, a Distinctive Astroglial Tumor: Neuroradiologic and Pathologic Features

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PURPOSE: To analyze and discuss CT and MR features of pleomorphic xanthoastrocytoma (PXA) and present salient histopathologic features of this distinctive astroglial tumor. **METHOD:** CT, MR, and histopathologic studies on seven patients with the histologic diagnosis of PXA were reviewed retrospectively. **RESULTS:** All patients were in their first 3 decades of life when first diagnosed and demonstrated peripherally situated supratentorial tumors of varying size involving the superficial cortex and leptomeninges. Five of six cases examined with CT showed areas of mixed attenuation with four demonstrating well-demarcated enhancement. MR demonstrated low or mixed signal intensity on T1-weighted and high or mixed signal intensity on T2-weighted sequences. All five who received gadopentetate dimeglumine showed well-defined enhancement. Three showed cyst formation. Typical histologic features included marked cellular pleomorphism with giant cells, bizarre nuclei, variable cytoplasmic lipidization and positive immunoreactivity for glial fibrillary acidic protein. Necrosis and endothelial-pericytic cell proliferation were absent. **CONCLUSION:** PXA has a highly suggestive neuroradiologic and distinctive histopathologic appearance.

Index terms: Brain neoplasms, magnetic resonance; Brain neoplasms, computed tomography; Brain, occipital lobe

AJNR 14:1397–1404, Nov/Dec 1993

Pleomorphic xanthoastrocytoma (PXA) was described in 1979 as a histologically distinctive, benign supratentorial astrocytoma occurring in young patients (1). Since then a number of reports have appeared in the neurosurgery, neurology, neuropathology, and oncology literature describing this entity, which consists of well-defined superficially located tumors involving the leptomeninges and superficial cortex. In this report we describe computed tomography (CT) and magnetic resonance (MR) findings in seven cases of this rare type of astrocytoma. PXAs differ from the more common types of low-grade astrocytoma in their location and enhancement with both CT and MR contrast media. The histologic features of this tumor are described.

Received September 18, 1992; accepted and revision requested November 3; revision received November 24.

D.E.A. is supported by National Institute of Neurological Disorders and Stroke grant T32 NS7236.

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AJNR 14:1397–1404, Nov/Dec 1993 0195-6108/93/1406–1397

Materials and Methods

Imaging studies of seven patients given histopathologic diagnoses of intracranial PXA and imaged between 1988 and 1992 were evaluated retrospectively. The cases were taken from neuropathology, neuroradiology, neurosurgery, and consultation case files. CT and MR scans were obtained before surgery in six patients and only an MR scan in one. All CT studies were obtained on late-generation General Electric (Milwaukee, Wis) or Siemens (Iselin, NJ) scanners before and after the intravenous administration of contrast material (100 ml of iohexol, 350 mg of iodine/mL). Six of the seven MR studies available for interpretation consisted of T1-weighted, 500–750/15–20/2 (repetition time/echo time/excitations) and T2-weighted 2500–3000/20–90, spin-echo sequences; in one only a T1-weighted sequence was evaluated. Five had T1-weighted sequences after the intravenous administration of gadopentetate dimeglumine (0.1 mmol/kg). MR studies were performed on 1.0- or 1.5-T Siemens or 1.5-T GE units. Two patients had undergone previous craniotomy with initial misdiagnosis of the tumors.

CT and MR studies were reviewed with attention to the following features: location of lesion, size, CT attenuation,

MR signal intensity, presence of edema, cyst formation, calcification, and enhancement pattern.

The histopathologic diagnosis of PXA was based on the presence of meningeal invasion and histologic appearance consisting of a wide variety of cytologic morphology including giant cells; bizarre, enlarged, hyperchromatic nuclei; and variable cytoplasmic lipidization.

Results

The clinical presentations and radiologic findings for the seven patients are summarized in Table 1. All were in the first three decades of life and presented with symptoms of seizures, headaches, or hemiparesis. There were four women and three men in the series. All lesions were supratentorial in location.

On CT five out of six available studies demonstrated peripheral supratentorial lesions of mixed high and low attenuation, two with well-defined and three with ill-defined margins. One lesion, a small tumor situated in the inferior portion of the right anterior temporal lobe, was not seen on CT, presumably because of its location on the floor of the middle cranial fossa with resultant bone artifact and partial volume averaging. Calcification was not a prominent feature and was seen in one postoperative case. In the four of six instances in which intravenous contrast material was administered, well-defined homogeneous enhancement of the noncystic component was noted (Fig 1). One patient (case 5) who had normal CT findings on his more recent presentation had been shown to have a small enhancing nodule on six scans performed between 5 and 13 years before this admission.

T1-weighted MR findings were varied, with three showing ill-defined low signal, one well-defined low signal, one ill-defined mixed signal, and two well-defined mixed signal intensities. These mixed signal intensity lesions consisted of areas of hypo- and isointensity. There were no lesions with increased signal intensity on T1-weighted images. On T2-weighted MR, three demonstrated ill-defined mixed signal intensities (Fig 2), and three showed well-defined high signal intensity (Fig 3); in one instance, a T2-weighted sequence was not available. The mixed signal consisted of areas of hyperintensity mixed with areas of isointensity. Edema was significant in two cases and mild to moderate in five. Gadopentetate dimeglumine was administered in five cases. Enhancement was significant and well marginated in four; in one (Fig 4) only mild enhancement was seen. This case also showed dural enhancement. Three of the lesions showed cyst formation, which was significant in one patient (Fig 5).

TABLE 1: Imaging features of PXA

Case	Age	Sex	Presenting Symptoms	Location	CT Features	T1-Weighted MR	T2-Weighted MR	Edema	Enhancement	Cyst Formation
1	23	F	Seizures	Peripheral R. Parietooccipital	Ill-defined Mixed attenuation	Ill-defined Low signal	Well-defined High signal	±	CT ++ MR ++	–
2	15	F	Seizure Headache	Peripheral R. temporal	Well-defined Mixed attenuation	Well-defined Low signal	Well-defined High signal	+	CT ++ MR ++	+
3	4[a]	M	Headache R. hemiparesis							
	5[b]		L. III N. palsy Slurred speech	Peripheral L. temporal	Ill-defined Mixed attenuation	Ill-defined Low signal	Ill-defined Mixed signal	++	CT ++ MR NE	–
4	14	M	Seizure	Peripheral L. parietooccipital	Well-defined Mixed attenuation	Well-defined Mixed signal	Well-defined High signal	+	CT ++ MR NE	+
5	7[a]	M	Seizures							
	26[b]		Seizures L. hemiparesis	Peripheral R. parietal	Ill-defined Mixed attenuation Calcification	Ill-defined Mixed signal	Ill-defined Mixed signal	++	CT –[c] MR +	–
6	28	F	Seizures	Peripheral R. occipital	NE	Well-defined Mixed signal	NE	±	CT NE MR ++	++
7	25	F	Seizures	Peripheral R. temporal	Negative	Ill-defined Low signal	Ill-defined Mixed signal	+	CT – MR +[d]	–

Note.—R indicates right; L, left; and NE, not evaluated.

[a] At first presentation.

[b] At second presentation.

[c] Small enhancing nodule seen on six CT scans performed 5 to 13 years before this admission.

[d] Dural enhancement.

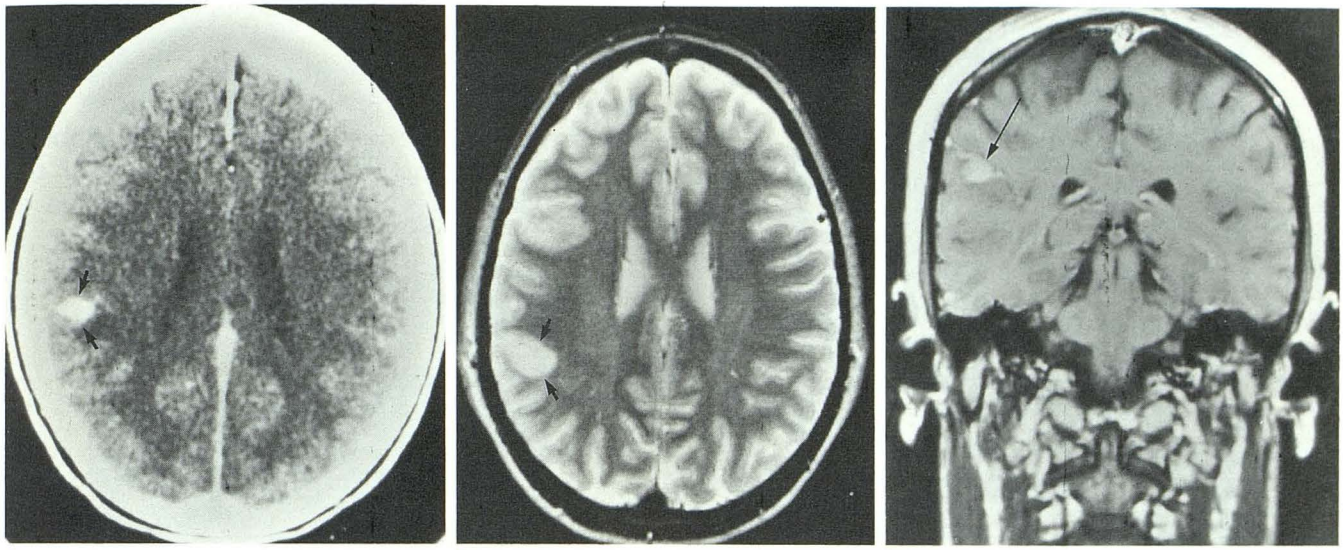


Fig. 1. Case 1.

A, Contrast-enhanced CT scan shows a well-defined enhancing peripheral lesion in the right parietal lobe (*arrows*).

B, On this axial T2-weighted MR image (2500/90), the lesion appears as a well-defined region of high signal intensity (*arrows*) with a small amount of surrounding edema.

C, A coronal T1-weighted contrast-enhanced section (570/20) demonstrates marked well-defined enhancement of the lesion (*arrow*).

Two of the cases were interesting in that they were recurrences of lesions initially given diagnoses other than PXA. In case 3 a four-year-old boy from East Africa experienced headaches and a right hemiparesis after a motor vehicle accident and was found on angiography to have an avascular left temporal mass, which after surgical debulking was diagnosed as a meningioma. He was brought to the United States 1 year later for further evaluation and care, at which time he was suffering from slurred speech and a left third-nerve palsy. CT and MR scans performed at this time revealed a large, strongly enhancing mass overlying the left temporal lobe and infiltrating the underlying brain. At surgery, the tumor was adherent to the overlying dura and extended largely along the surface of the brain. Histopathologic diagnosis of the excised tumor was PXA.

In case 5, a man who first presented at the age of 7 with a left focal seizure, underwent subtotal resection of a lesion diagnosed at that time as meningeal sarcoma. A silastic dural prosthesis was inserted to reconstitute the dura. He received postoperative radiotherapy and was followed for 19 years for treatment of his seizures. He presented again at the age of 26 with sudden onset of left hemiparesis due to a right frontoparietal chronic subdural hematoma and an intraparenchymal hematoma apparently caused by the prosthesis. An enhanced MR study demonstrated a small, mildly enhancing nodule adjacent to the dura and medial to the subdural hematoma (Fig 6). This patient was the only one in our series who underwent cerebral angiography, which showed a small tumor blush and puddling of contrast. The enhancing nodule was surgically removed when the hematoma was drained. After this nodule was found on histology to be a PXA, blocks of fixed tissue removed at the initial surgery were obtained. On reexamination, the original tumor was histologically identical to the later specimen and was immunopositive for glial fibrillary acidic protein, confirming the identity of the lesion as PXA.

All except one case completely conformed to the histologic description of PXA given below. The exception was case 2, a cystic lesion that showed a number of degenerative features common to the more cellular forms of pilocytic astrocytoma (Fig 7).

Discussion

The term pleomorphic xanthoastrocytoma was suggested by Kepes et al to describe a specific type of astrocytoma involving both the leptomeninges and superficial cortex (1, 2) and thus also has been called meningocerebral xanthoastrocytoma (3). It is composed of cells displaying a wide morphologic spectrum including multinucleated

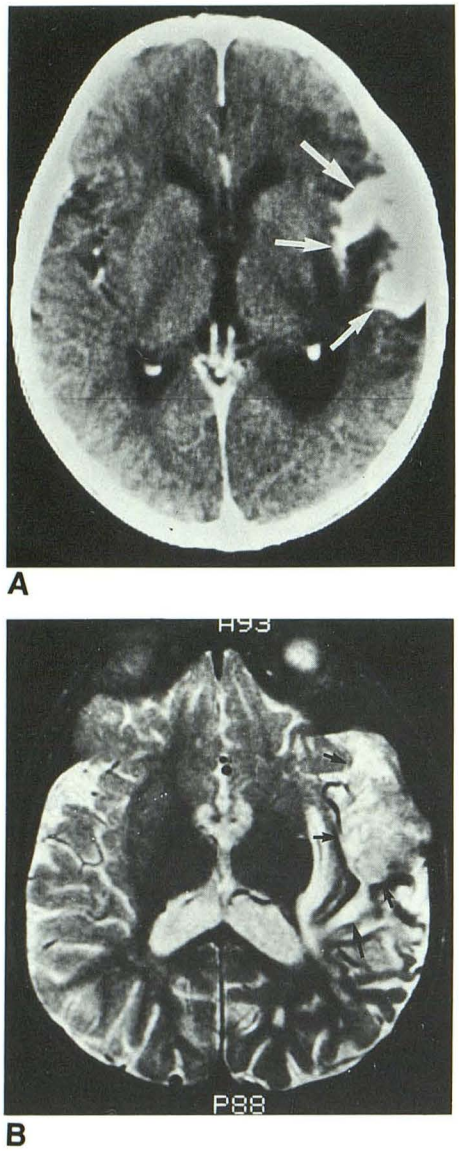


Fig. 2. Case 3.

A, Contrast-enhanced CT shows well-marginated strongly enhancing lesion (*arrows*) in the left temporal region.

B, Axial T2-weighted MR image (2800/80) demonstrates a poorly marginated left temporal mixed-signal-intensity lesion (*short black arrows*) with a moderate amount of high-signal-intensity edema (*long black arrows*).

giant cells with cytoplasmic lipidization, but which lack other histologic features of malignancy. These tumors usually occur during the first 3 decades of life (3–5), most commonly in the second decade. Rarely, PXA has been described in older patients (6, 7). The age range in our series was 4 to 28 years. As confirmed in our patients, there appears to be no definite gender predilection. The most common presenting feature is seizures, and six of our patients presented in this fashion. Other presentations include headache and motor and sensory deficits related to the location of the lesions.

Of the radiologic features seen on CT and MR, the most constant is the location of this neoplasm, with all of our cases showing a peripheral supratentorial location with involvement of the cortex and gray-white matter junction. Five of

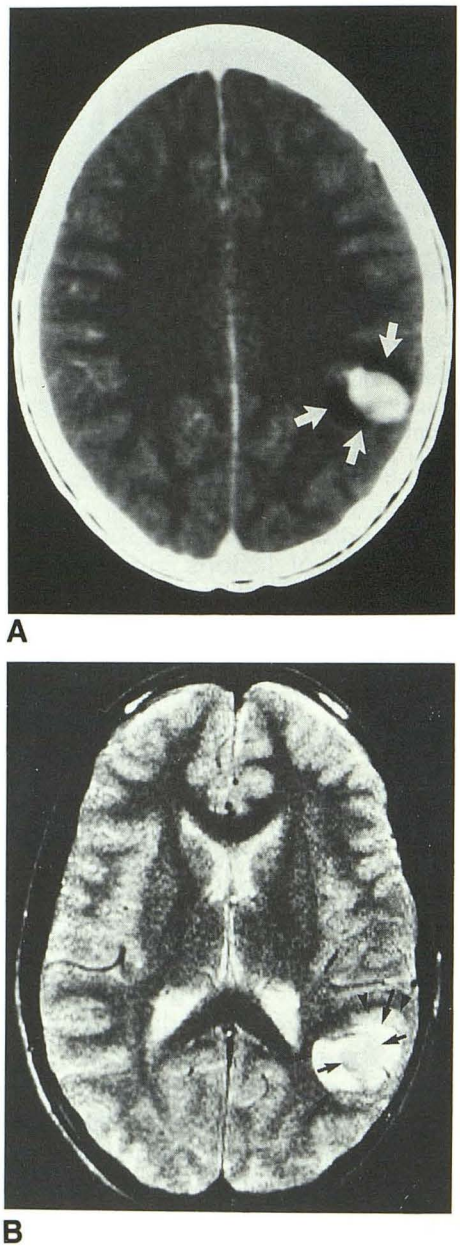
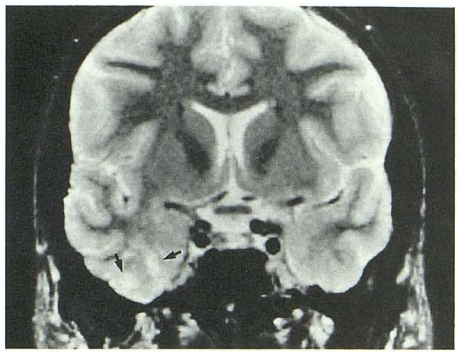


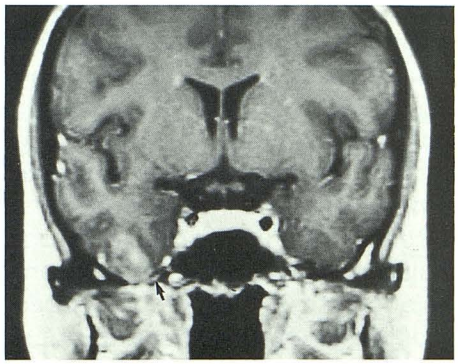
Fig. 3. Case 4.

A, Contrast-enhanced CT shows a well-defined enhancing PXA with surrounding cystic element (*arrows*) in the left parietal lobe.

B, Axial T2-weighted MR section (3000/90) shows a well-defined high-signal-intensity lesion (*short black arrows*) with the surrounding cystic element appearing as areas of higher signal intensity (*long black arrows*) and mild surrounding edema (*arrowheads*).



A



B

Fig. 4. Case 7.

A, Coronal T2-weighted MR image (2500/90) shows an ill-defined mixed-signal-intensity right inferior temporal lesion (*arrows*).

B, Coronal T1-weighted postcontrast MR (500/15) demonstrates a mildly enhancing tumor in this region. Also noted is a small area of dural enhancement (*arrow*).

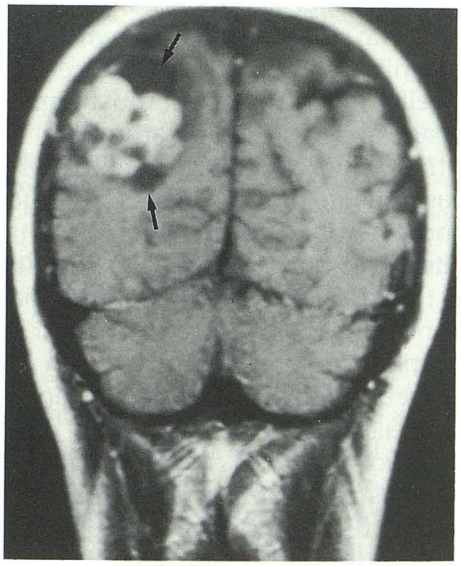


Fig. 5. Case 6. Coronal contrast-enhanced T1-weighted MR image shows a lobulated strongly enhancing peripheral right occipital lesion with a large cystic component (*arrows*).

seven (71%) showed radiologic evidence of extension to the leptomeningeal surface of the brain.

On CT these lesions appear as either ill- or well-defined masses of varying size, showing mixed high and low attenuation. Calcification is rare and was seen in one of our patients (case 5), possibly related to previous surgery. Cyst formation can occur (8) and was present in three of our patients (43%). Edema was present in all cases, varying between mild to moderate, extending centrally into the white matter (9). Well-defined homogenous contrast enhancement of the solid component of the tumors, which has been described as a constant feature (9), was seen in four of six patients who had received intravenous contrast material.

The macroscopic surgical appearance is usually that of superficial tumor involving the cortex and leptomeninges and firmly attached to the dura (2). The solid portions of the tumor have been grossly described as ivory-colored or gray and white firm avascular masses without gross evidence of necrosis. The cysts are uni- or multiloculated, contain clear, yellow, or xanthochromic fluid, and are usually deep to the solid portion.

The MR appearance is equally varied. Signal intensity is equally low or mixed (hypo- and

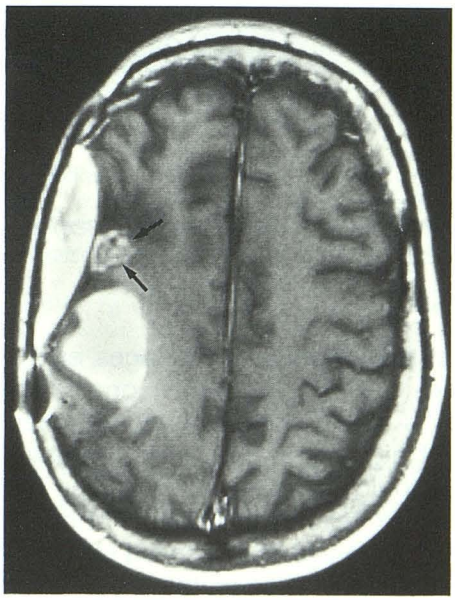


Fig. 6. Case 5. Axial T1-weighted postcontrast image (570/20) shows large, high-signal-intensity (presumably caused by methemoglobin content) chronic right parietal subdural and intraparenchymal hematomas with an adjacent small mildly enhancing tumor (*arrows*).

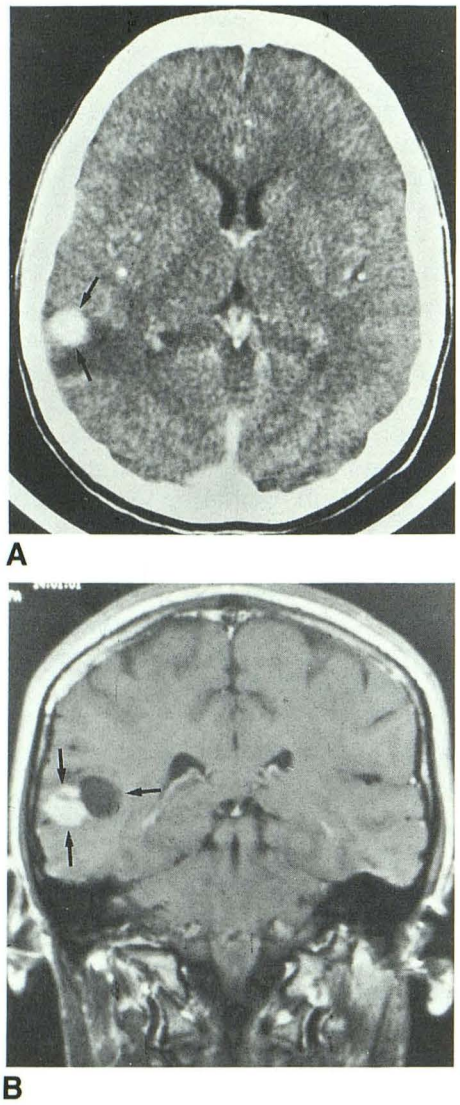


Fig. 7. Case 2.

A, Contrast-enhanced CT demonstrates an enhancing peripheral right posterior temporal tumor (*arrows*).

B, Coronal T1-weighted postcontrast MR (680/20) shows a well-defined enhancing lesion with a medial cystic component (*arrows*).

isointense) on T1-weighted images and high or mixed (iso- and hyperintense) on T2-weighted images. It is interesting to note that there were no areas of high signal intensity on T1-weighted images as could be expected from the high lipid content of the cells on histology. The finding of edema, seen as areas of increased signal intensity on T2-weighted images in the underlying white matter, is more obvious on MR than CT and was present in all cases. Enhancement is similar to that seen on CT, being homogeneous and well defined, and was present in all five patients who were imaged after contrast administration.

Microscopic examination (Fig 8) demonstrated moderately cellular astrocytic tumors with a wide variety of cellular morphologies including spindle cells, polygonal or round cells, cells with scant cytoplasm, and multinucleated giant cells (Fig 8A). Nuclear pleormorphism included bizarre, enlarged, and hyperchromatic forms. Cytoplasmic lipidization was present in at least some of the larger cells but was inconspicious in case 2. Typically, a stroma containing reticulin delineated small groups of cells and individual cells, but the prominence of the stroma varied between regions within a given tumor and between cases. Perivascular aggregations of mononuclear inflammatory cells were sometimes present but were not associated with necrosis. The cystic areas arising within the tumors did not contain necrotic debris but were filled with proteinaceous fluid. PXA invariably invaded the overlying meninges. At the deeper margins, microinfiltration of tumor cells into the adjacent brain could be demonstrated, even in lesions with a well-circumscribed radiographic and gross appearance. It is not uncommon for PXA to coexist with regions showing pilocytic or fibrillary astrocytic features (1, 10). Case 6 of our series contained some areas with pilocytic morphology, and case 2 displayed a histologic appearance intermediate between that of PXA and pilocytic astrocytoma.

The differential diagnosis includes lipidized glioblastoma, which must be ruled out by careful microscopic examination. Although the high degree of nuclear and cytoplasmic pleomorphism in PXA might suggest anaplasia, other features associated with astroglial malignancy such as significant mitotic activity, vascular endothelial-pericytic cell proliferation, and, most importantly, necrosis, are absent. The pleomorphic qualities of PXA thus can be ascribed to degeneration rather than malignancy, because the behavior of these tumors tends to be less aggressive than the cytoarchitectural features would suggest (7, 8). However, transformation of PXA into a malignant astrocytoma or glioblastoma can occur (6, 11). The infiltrating tumor cells at the brain interface usually appear more anaplastic in tumors that recur with malignant progression. The differential diagnosis also includes nonastrocytic tumors such as fibrous xanthoma or sarcoma, which can be excluded by demonstrating glial fibrillary acidic protein immunoreactivity within tumor cells.

In summary, the diagnosis of PXA should be considered in patients presenting with superficial

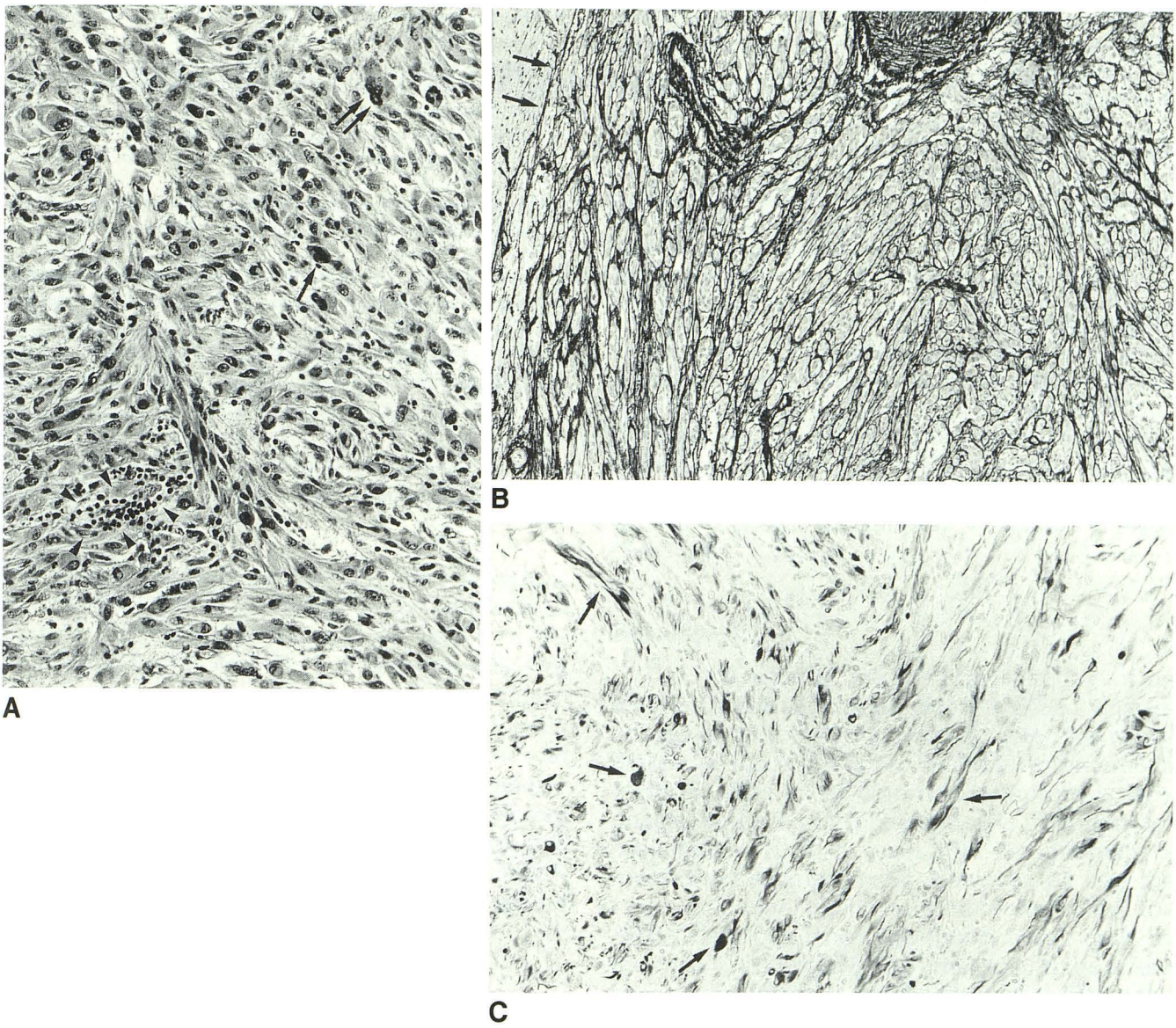


Fig. 8. Case 1.

A, Typical histologic appearance of PXA with extreme nuclear and cytoplasmic pleomorphism including large hyperchromatic nuclei (*single arrow*) and multinucleated cells (*double arrows*). At the *lower left* is a focal lymphocytic infiltrate (*arrowheads*) (hematoxylin and eosin, magnification ×300).

B, Stromal reticulin fibers form a network surrounding small groups of tumor cells. At the *upper left corner*, the tumor is sharply demarcated (*arrows*) from adjacent brain (Wilder's reticulin, magnification ×120).

C, Glial fibrillary acidic protein imunopositivity within tumor cells (*arrows*) of various shapes and sizes is demonstrated (glial fibrillary acidic protein, magnification ×300).

cerebral hemispheric tumors showing meningeal involvement, particularly at a young age and with a history of seizures (12). The differential diagnosis consists primarily of other varieties of astrocytoma (including pilocytic astrocytoma and glioblastoma, especially the giant-cell subtype), and ganglioglioma, meningioma, meningiosarcoma, and fibrous xanthoma (9, 13). The distinctive histopathologic features of PXA confirm the diagnosis. These patients should enjoy a favorable prognosis with conservative management.

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