Pleomorphic xanthoastrocytoma: Favorable outcome after complete surgical resection[1]

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To describe the clinical features, histologic characteristics, and management of patients with pleomorphic xanthoastrocytoma (PXA), we reviewed data on 13 children who had histologically confirmed PXA and were referred to the neuro-oncology service between 1985 and 1999. Neuro-imaging with CT and/or MRI documented the anatomic location, tumor extent, and degree of resection. There were 3 males and 10 females; median age was 12.9 years (range, 8.2-17.2 years). The most frequent presentations included seizures (n = 8) and headache (n = 5). Tumor sites included temporal (n = 5), parietal (n = 3), frontal (n = 1), frontoparietal (n = 1), parieto-occipital (n = 1), and temporoparietal (n = 1) lobes and the spinal cord (n = 1). CT/MRI revealed a cystic component in 6 patients, with cyst wall enhancement in 3 patients. The solid component was uniformly enhancing in 11 patients. Vasogenic edema was present in 9 patients, and calcification was noted in 4 patients. Histopathologic findings included meningeal invasion in 12 patients, calcifications in 4, and necrosis in 2. Mitotic figures (1-12 per high-power field) were seen in 8 patients. Gross total resection was achieved in 8 patients, near total resection in 1, and subtotal resection in 4. Ten patients were alive with a median follow-up of 41 months at this writing. Two patients died of progressive disease, and 1 died of an unrelated cause. In conclusion, pleomorphic xanthoastrocytoma is a rare neoplasm in childhood, commonly presenting with seizures. Gross total resection without adjuvant therapy provides prolonged disease control, as seen in 6 of 7 patients (85%) in our series. *Neuro-Oncology 3, 184–192, 2001 (Posted to Neuro-Oncology [serial online], Doc. 00-068, May 25, 2001. URL <neuro-oncology. mc.duke.edu>)*

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[3]Abbreviations used are as follows: EFS, event-free survival; GTR, gross total resection; NTR, near total resection; OS, overall survival; PXA, pleomorphic xanthoastrocytoma; STR, subtotal resection.

PXA,[3] first described by Kepes et al. (1979), is a rare neoplasm that accounts for 1% of all astrocytic tumors (Kepes et al., 1997). PXAs are often supratentorial and may be superficial in location and frequently involve the leptomeninges (Kepes, 1993). Typical clinical presentation includes seizures as well as signs and symptoms of a mass lesion (Kepes et al., 1979, 1993, 1997; Kleihues et al., 1993; Lipper et al., 1993; Tien et al., 1992; Kawano, 1992; Giannini et al., 1999; Davis et al., 1994). The histologic appearance of these tumors, which are positive for glial fibrillary acidic protein, may be quite aggressive, characterized by marked cellular pleomorphism, nuclear atypia, mitotic figures, necrosis, and multinucleated giant cells (Glasser et al., 1995; Grant and Gallagher, 1986; Herpers et al., 1994; Iwaki et al., 1987; Kepes et al., 1979; Kleihues et al., 2000; Kros et al., 1991; Lach et al., 1996; Lindboe et al., 1992; Macaulay et al., 1993; Maleki et al., 1983; Powell et al., 1996). These features, initially, led to the lesions' being regarded as giant cell astrocytomas, glioblastomas, or tumors of

Table 1. Diagnostic characteristics of pleomorphic xanthoastrocytoma

A.	Pleomorphic cells
	1. Large
	2. Somewhat bipolar
	3. Copious glassy cytoplasm
	4. Dark, lobulated nuclei
	5. Similar appearance to malignant fibrous histiocytoma
B.	Prominent eosinophilic granular bodies
C.	Lipidized astrocytes
	1. Fine or large vacuoles
	2. Scanty lipid (in many lesions)
D.	Focal perivascular lymphocytes
E.	Abundant reticulin network
	1. In peripheral lesions, is most abundant
	2. In compact regions, extends into parenchyma, invests individual cells
F.	Absent or scant mitoses
G.	Absent necrosis
H.	Immunohistochemical qualities
	1. Neoplastic cells positive for GFAP, though often weakly
	2. Neoplastic cells positive for a histiocyte marker
I.	Electron microscopy
	1. Cytoplasm contains lipid
	2. Cytoplasm contains intermediate filaments
	3. Tumor cell junctions are incomplete
	4. Basal lamina surrounds tumor cells

Abbreviations: GFAP, glial fibrillary acidic protein.

mesenchymal origin called fibrous xanthomas or xanthosarcomas. Despite this appearance, however, PXAs possess a relatively favorable prognosis with a 10-year survival of 70% (Giannini et al., 1999). Thus, it is important to recognize and distinguish this entity from more biologically aggressive neoplasms, because the treatment and prognosis differ significantly from the high-grade astrocytomas. Presently, PXAs are histologically designated as grade II in the World Health Organization classification, with lesions that demonstrate significant mitotic activity and/or areas of necrosis being designated as "PXA with anaplastic features." The term "*anaplastic PXA,*" corresponding to a WHO grade III classification, is not recommended (Kleihues and Cavenee, 2000).

Here we report the clinicopathologic and radiologic features, treatment, and outcome of 13 children who had PXA and were studied in a single institution in the era of modern surgery and neuro-imaging.

Materials and Methods

Clinical Materials and Methods

Between January, 1984, and June, 1999, a total of 866 patients with primary CNS tumors were newly diagnosed at St. Jude Children's Research Hospital. Among these patients, 13 were diagnosed with PXA based on the criteria of the 2000 World Health Organization classification of tumors of the nervous system (Kleihues and Cavenee, 2000). We conducted a retrospective chart review to document the clinical, radiologic, and pathologic features at diagnosis; the pattern of relapse and therapy; and the outcome of this cohort of patients.

All patients underwent diagnostic and serial follow-up CT or MRI scans on a regular basis. These scans were reviewed for the extent of resection and leptomeningeal involvement and the presence of solid and cystic components, vasogenic edema, and calcification. The intent of surgery in all patients was to achieve a GTR. The extent of resection was defined as follows: GTR, no surgical or imaging evidence of residual disease; NTR, <10% residual tumor by surgical report and postoperative imaging; and STR, <50% residual tumor by surgical report and postoperative imaging. Two independent pathologists (J.J., P.B.) reviewed all the histologic specimens with special emphasis on presence of meningeal invasion, calcification, mitosis, and necrosis. The histopathologic criteria used to make a diagnosis of PXA are presented in Table 1.

Kaplan-Meier Curves

EFS was calculated from the date of diagnosis to the date of death or last follow-up. OS was calculated from the date of diagnosis to the date of last contact or death. One patient died of a cause unrelated to his disease 24 months after diagnosis. He was disease free at the time of death.

Results

Clinical Characteristics

Table 2 summarizes the clinical characteristics of the 13 patients included in the study. Symptoms at presentation were seizures (n = 8), headache only (n = 3), and headache and neurologic deficits (n = 2). Except for 1 patient who had a spinal cord tumor, all other patients presented with tumor in the supratentorial hemispheres. The site of the primary tumor included the temporal lobe in 5 patients, parietal lobe in 3 patients, frontal lobe in 1 patient, frontoparietal area in 1 patient, parieto-occipital area in 1 patient, temporoparietal area in 1 patient, and spinal cord in one patient. No patients had disseminated or multifocal disease at the time of presentation.

Neuroradiology

Neuroradiologic findings are summarized in Table 3. Three patients had a CT only, and 11 patients had an MRI. Imaging revealed a cystic component in 6 patients, with cyst wall enhancement in 3. The solid component was uniformly enhancing in 11 patients (Fig. 1). The tumor extended to the brain surface in 11 patients, and there was evidence of bony remodeling of the inner table of the skull in 3 (Fig. 2). Vasogenic edema, ranging from 10-35 mm in diameter beyond the enhancing tumor, was present in 9 patients. Calcification was noted in 4 patients. The T1 signal was isointense relative to the cortex in 7 patients and hyperintense in 1 patient. The T2 signal was isointense relative to the cortex in 4 patients and hyperintense in 4 patients.

Table 2. Clinical characteristics and treatment outcome for patients diagnosed with pleomorphic xanthoastrocytoma

Patient	Sex/age at diagnosis (/y)	Symptoms	Site	Extent of resection	Further therapy	Recurrence	Extent of repeat surgery	Outcome/months of follow-up
1	M/8.2	Seizures	R temporal	GTR	None	—	—	NED/73.6+
2	F/8.6	Seizures	L temporal	STR	RT	—	GTR	NED/103.6+
3	F/9.9	Seizures	L parietal	GTR	None	—	—	NED/44.8+
4	F/11.9	Seizures	L temporal	STR	None	Local	GTR	NED/140.4+
5	F/12	Headaches	R temporal and parietal	GTR	None	—	—	NED/28.0+
6	F/12.3	Headaches	R temporal occipital	GTR	None	Local L + D	GTR + RT chemotherapy	DOD/30.4
7	M/12.9	Headaches	Spinal cord	STR	RT	L + D	Chemotherapy	DOD/22.7
8	F/13.4	Headaches; L arm numbness	R parietal	STR	Chemotherapy + RT			NED/33.9+
9	F/15.1	Seizures	R temporal	NTR	—	—	—	NED/37.2+
10	M/16.2	Seizures	L parietal	GTR	RT	—	—	DNOD/24.9
11	F/17	Headache; blurred vision	R temporal	GTR	None	—	—	NED/32.1+
12	F/17	Seizures	R parieto-occipital	GTR	None	—	—	NED/12.6+
13	F/17.2	Seizures	L frontal	GTR	None	—	—	NED/49.2+

Abbreviations: R, right; NED, no evidence of disease; L, left; RT, radiation therapy; L + D, local and distant metastases; DOD, died of disease; DNOD, dead but not of disease.

Histopathology

Histopathologic findings in the 13 patients are summarized in Table 4. All lesions were pleomorphic, with a focal perivascular chronic inflammatory infiltrate. Eosinophilic granular bodies were seen in almost all cases. In 12 patients, at least part of the neoplasm was localized to the meninges. Calcification was present in 4 patients; necrosis was present in 3. In the 12 cases examined for the presence of reticulin, all were positive. Eight of 9 pathology specimens examined were positive for glial fibrillary acidic protein. Lipidization was present in 11 cases. A fibrillary component was present in 4 cases. There was no histopathologic evidence of neuronal differentiation.

Mitoses were uncommon and often absent in all but 2 patients, who had 6 and 12 mitoses per high-power field, respectively. One of these 2 patients with >5 mitoses per high-power field had both local and leptomeningeal recurrence and died 24 months later despite chemotherapy. Among the patients whose tumor recurred, 1 had a mitotic index >5, 1 had <5, and 1 had 0.

The pathologic findings of the tumors of the 2 patients who succumbed to the disease deserve special comment. The initial lesion in patient 6 was a typical PXA with abundant eosinophilic granular bodies, a spindle-cell component, and no mitoses (Fig. 3). In the specimen obtained at the time of recurrence, the pleomorphic component had not changed, but was now accompanied

Table 3. CT and MRI characteristics of tumors

				Solid tumor		Cyst						
Patient	Imaging modality	Extending to brain surface	Inner table modeling	Size (mm^2)	Enhancement	Size (mm^2)	Wall enhancement	Vasogenic edema (mm)	Calcification	CT density relative to brain	T1 signal relative to cortex	T2 signal relative to cortex
1	MRI	Y		8 × 13	Uniform	4 × 9	N	15		—	Iso	Hyper
2	CT	Y	N	15 × 15	Uniform	20 × 20	N	—	Absent	Indeterminate	—	—
3	MRI	Y		14 × 23	None	None	N/A	25		—	Hyper	Iso
4	MRI	N		12 × 12	N/A	10 × 15	Y	35		—	Iso	Hyper
5	CT	Y	N	20 × 20	Uniform	50 × 70	N	35	Absent	Iso	—	—
6	CT/MRI	Y	Y	24 × 30	Uniform	60 × 80	Y	10	Absent	Iso	Iso	Iso
7	CT/MRI	N/A	N/A	4	Uniform	Absent	NA	NA	Absent	NA	NA	NA
8	CT/MRI	Y	Y	4.5 × 5	Uniform	Absent	NA	None	Absent	Iso	—	—
9	CT/MRI	Y	N	10 × 12	Uniform	Absent	NA	None	Absent	Iso	Iso	Iso
10	CT	Y	Y	40 × 55	Uniform	Absent	NA	15	Absent	Iso	—	—
11	MRI	Y		40 × 52	Uniform	50 × 60	N	15		—	Iso	Iso
12	CT/MRI	Y	N		Uniform		Y	10	Absent	Iso	Iso	Hyper
13	CT/MRI	Y	*	18 × 22	Uniform	Absent	NA	12	Absent	Iso	Iso	Hyper

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; Y, yes; N, no; Iso, isointense; Hyper, hyperintense; NA, not applicable.

*No bone windows obtained.

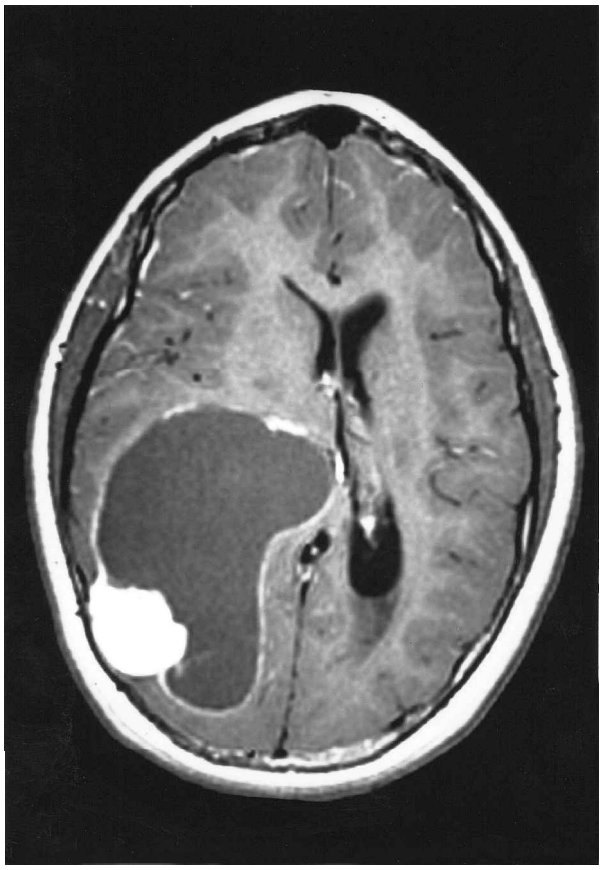

Fig. 1. Postcontrast T1-weighted image showing uniform enhancement of the solid component of the tumor and partial enhancement of the cyst wall.

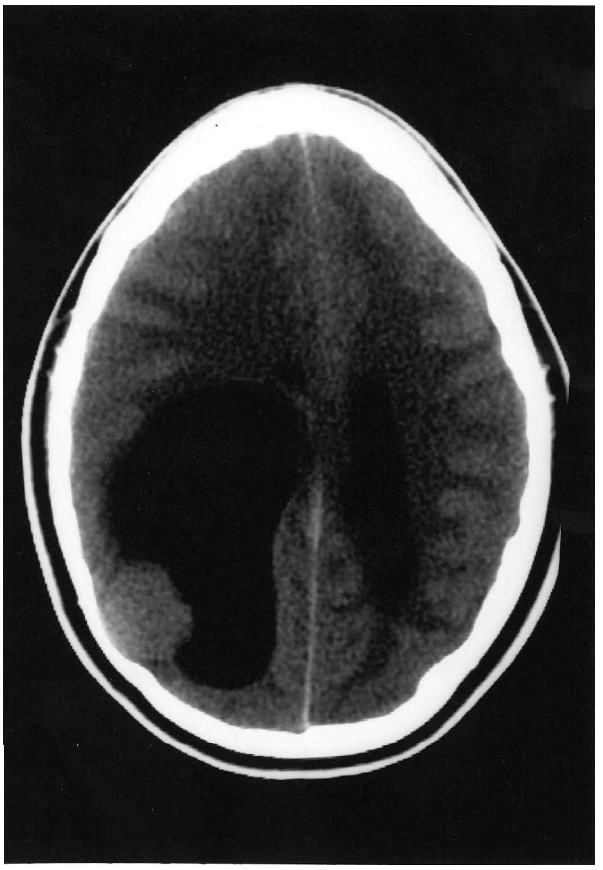

Fig. 2. A 2.5-cm temporo-occipital tumor isodense to the cortex on CT with a large cyst and remodeling of the inner table of the calvarium.

by widespread malignant areas with marked cytologic atypia, necrosis, and many mitoses. The lesion was highly invasive at this point (Fig. 4).

The neoplasm in case 7 was a compact, reticulin rich, pleomorphic lesion with xanthomatous change and prominent eosinophilic granular bodies. Unlike most of the other lesions, however, mitoses were found readily (6-10 per high-power field; original magnification ×40).

Treatment

The intent of surgery in all supratentorial tumors was to achieve a GTR. As noted in Table 1, 8 patients underwent GTR, 1 had NTR, and 4 had STR. Four patients received further therapy after surgery. Among those with GTR, 7 patients were observed without any further therapy, and 1 patient received postoperative radiation therapy. The patient with NTR was observed without further therapy. Of the 4 patients with STR, 2 received radiation therapy only, and 1 received both radiation therapy and chemotherapy.

Patient Outcome

The median follow-up for the entire cohort was 33.9 months (range 12.6-140.4 months). Overall, 10 patients remained alive as of this writing, with a median follow-up time of 41 months (range 12.6-140.4 months). Two died of their disease at 24 and 29 months after diagnosis; 1 died of an unrelated cause. OS at 5 years was 74%

Table 4. Histopathologic findings in the original neoplasms

Patient	Meningeal invasion	Calcification in adjacent brain	Mitoses/ 10 hpf	Necrosis
1	Prominent	Present	1	Absent
2	Present	Absent	0	Absent
3	Present	Absent	1	Absent
4	Indeterminate	Absent	0	Absent
5	Present	Present	1	Rare microfocal
6	Present	Absent	1	Absent
7	Present	Absent	6	Absent
8	Present	Present	12	Focal
9	Present	Absent	0	Absent
10	Present	Present	2	Absent
11	Present	Absent	0	Absent
12	Present	Absent	0	Absent
13	Present	Absent	1	Absent

Abbreviation: hpf, high-power field.

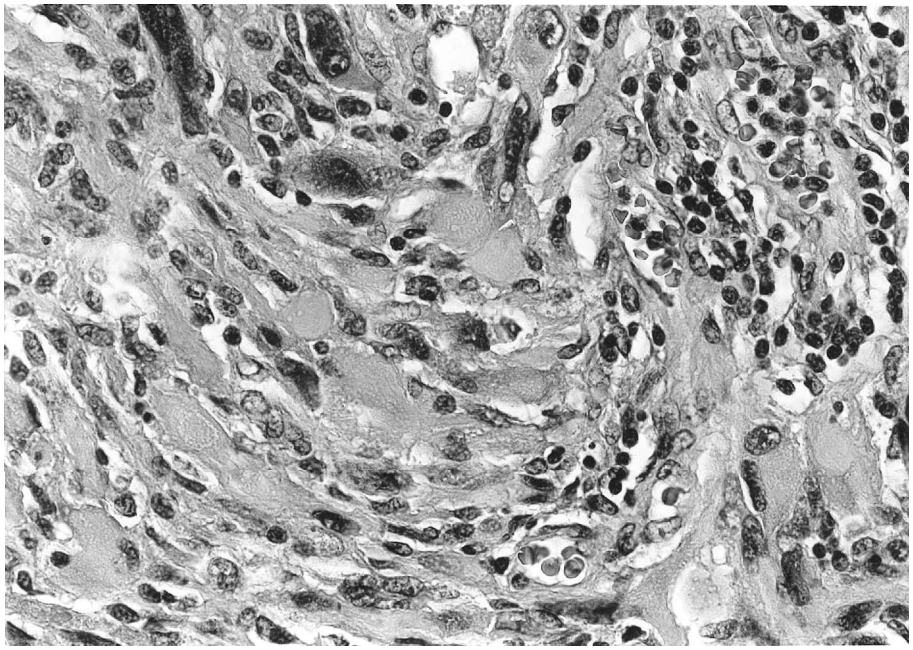

Fig. 3. Pathology specimen of patient 6 at the time of diagnosis. The original lesion was an entirely low-grade, typical pleomorphic xanthoastrocytoma with compact architecture, pleomorphic cells, and inflammatory infiltrate.

with an EFS of 50%. The Kaplan-Meier curves of overall and event-free survival are shown in Fig. 5.

Of the 8 patients who had a GTR, 1 received postoperative radiation therapy, and 7 were observed. Six of the 7 patients (85%) remained disease free with a median follow-up of 34 months (12.6-103 months). One patient died of recurrent disease. The patient who received postoperative radiation therapy died of unrelated causes 24.9 months later. He was free of disease at the time of his death.

The 1 patient who underwent an NTR remains free of disease at 37.2 months. Of the 4 patients with an STR, 1 was observed, 2 also received radiation therapy, and 1 received radiation therapy and chemotherapy. Overall, 2 patients continued to be free from disease. Of the 2 who had a recurrence, 1 remains alive after a second GTR.

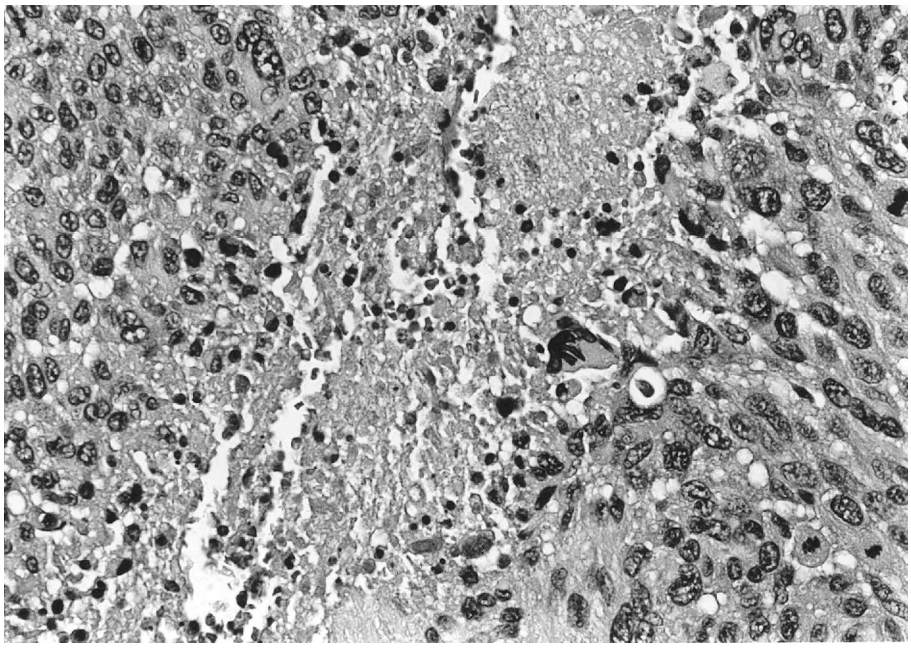

Fig. 4. Pathology specimen of patient 6 at recurrence. Recurrence occurred 2 years after the initial lesion, at which time there were large areas that were highly cellular, cytologically malignant, and mitotically active. Necrosis was present. Focally, typical well-differentiated areas of the neoplasm, similar to those seen in the original specimen, were found as well.

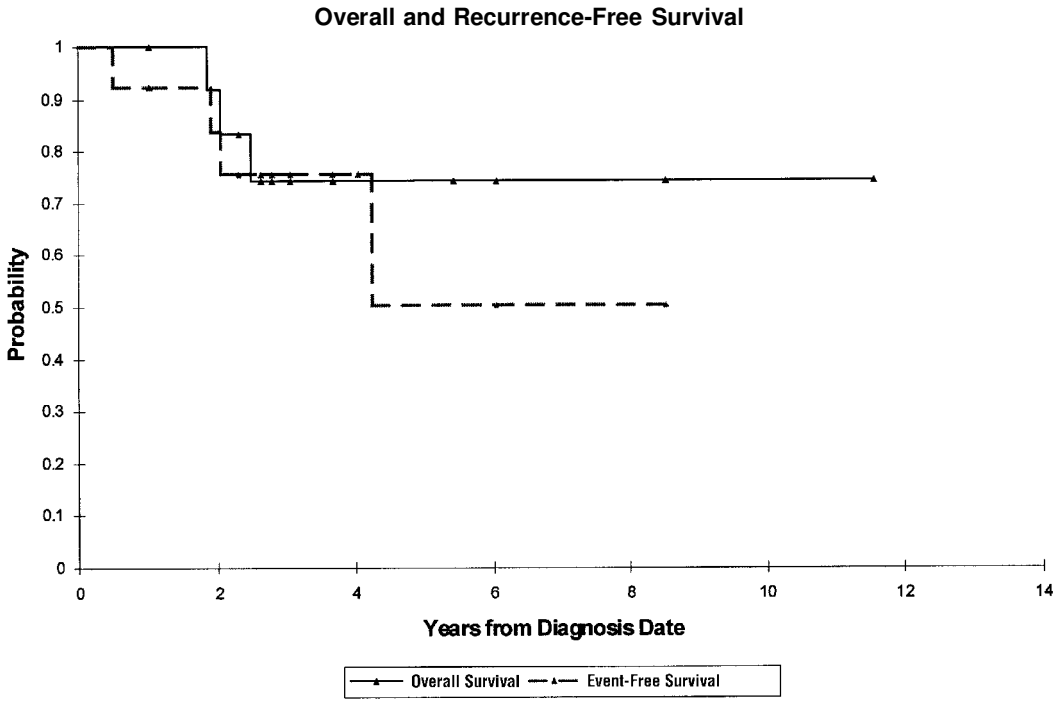

Fig. 5. Kaplan-Meier survival curve for overall survival and event-free survival in patients with pleomorphic xanthoastrocytoma.

Treatment at Tumor Recurrence

Three patients had recurrent disease at a median time of 8 months after initial surgery. Among the 3, 1 previously had GTR (with no further therapy) and 2 had STR (including 1 who received postoperative radiation therapy). All 3 patients with recurrent tumor failed at the initial site of involvement; 1 patient, in addition, showed leptomeningeal disease at the time of first failure.

The patient with a previous GTR (Patient 6, see Table 1) had a local recurrence, underwent a repeat GTR and received radiation therapy, relapsed a second time with leptomeningeal disease, and died 24 months after diagnosis of progressive disease despite chemotherapy. Of the 2 patients with previous STRs (Patients 4 and 7), 1 was followed, relapsed locally, had a GTR, and remains disease free at 140 months postdiagnosis. The second patient underwent radiation therapy at the time of initial diagnosis, but went on to have both a local and disseminated recurrence, received chemotherapy, and died of his disease at 24 months after diagnosis.

Discussion

PXAs were originally described by Kepes et al. in 1979. In 1993, the World Health Organization recognized PXA as a distinct diagnosis (Kleihues et al., 1993). Although surgery is the treatment of choice, there is no consensus regarding the role of adjuvant chemotherapy or radiotherapy (Giannini et al., 1999). The current series is the largest single institution pediatric series to date. It is marked by an evaluation of the disease in the era of modern neuroimaging and a consistent and conservative treatment approach after aggressive surgical resection. Despite a histologic appearance that may suggest an aggressive tumor, overall survival of 70%-80% can be expected after a GTR. In our series, 6 of 7 patients (85%) with imaging-confirmed GTR remained free of recurrence. However, despite the low-grade biology, it is important to follow cases with confirmed PXA, since cases of recurrence with anaplastic evolution have been reported in our series as well as in others (Kepes et al, 1989). The role of further surgery alone or requirements for added irradiation and/or chemotherapy are yet undefined for cases with disease recurrence.

Because of the rich reticulin background often seen in PXAs (Giannini et al., 1999; Herpers et al., 1994; Kepes et al., 1979; Lipper et al., 1993; Macaulay et al., 1993; Powell et al., 1996), these tumors were originally considered to be of mesenchymal origin and were often classified as fibrous xanthomas (Kepes et al., 1973; Paulus and Peiffer, 1991). The cells are pleomorphic and often large, somewhat bipolar, with copious glassy cytoplasm and dark, lobulated nuclei reminiscent of malignant fibrous histiocytoma. However, the presence of glial fibrillary acidic protein identified these tumors as variants of astrocytomas (Kepes, 1993). PXAs also exhibit many similarities to the desmoplastic cerebral astrocytoma of infancy (de Chadarevian et al, 1990). Both tumors are generally superficial in location with leptomeningeal involvement. Both are generally cystic and have a relatively good prognosis. The differences between the two entities include, for PXAs, the older age at presentation and the pleomorphic, xanthomatous appearance of the astrocytes. Thus, de Chadarevian et al. (1990) have suggested that PXAs represent the lipidized form of desmoplastic cerebral astrocytoma of infancy in older children and adults.

Although mitotic activity has been reported to be uncommon in PXAs (Allegranza et al., 1991; Giannini et al., 1999; Jones et al., 1983; Kros et al., 1991; Kuhajda et al., 1981; Macaulay et al., 1993; Paulus and Peiffer, 1988; Yoshino and Lucio, 1992; Zorzi et al., 1992), both Macaulay et al. (1993) and Giannini et al. (1999) have suggested that this feature may possess prognostic significance. The mitotic index was the most significant predictor of recurrence and survival in multivariate analysis reported by Giannini et al. (1999). The mitotic index was defined as the maximum number of mitotic figures present in 10 high-power fields at original magnification ×400 . The groups included mitotic indices of 0, <5, and >5 mitoses per 10 high-power fields. The number of patients in the current series is insufficient to confirm the association of mitosis and prognosis.

Several investigators have studied the prognostic significance of necrosis (Giannini et al., 1999; Papahill et al., 1996). Papahill and colleagues' (1996) literature review of 79 patients with PXAs noted that 9 of 15 deaths occurred in association with histologic evidence of necrosis at initial presentation or at recurrence. In contrast, Giannini and colleagues' (1999) review of 71 cases from multiple institutional reports demonstrated that, although in univariate analysis the presence of atypical mitoses and necrosis were significantly associated with overall survival ($P = 0.04$), in multivariate analysis mitotic indices was the only independent histologic parameter predictive of survival (Giannini et al., 1999). In our series, 2 patients had tumors that demonstrated necrosis, but the numbers were too small to correlate with outcome.

The clinical presentations of patients in our series were in keeping with other series. In our series, the male to female ratio was 1:3, somewhat different from other reports where an equal distribution between the sexes was reported. Patients presented predominantly with seizures (Davis et al., 1994; Giannini et al., 1999; Kepes et al., 1979, 1993, 1997; Kleihues et al., 1993; Kawano, 1992; Lipper et al., 1993; Tien et al., 1992). Tumors involved predominantly the temporal lobe. Of those patients who had GTR and presented with seizures, all became seizure free or were significantly improved within a year after surgery. These results are similar to those of Packer et al. (1994) in that 45 of 47 patients who had cortical low-grade gliomas and were treated with GTRs or NTRs were seizure free, and 2 were significantly improved, 1 year after surgery.

In the 7 patients studied by Lipper et al. (1993), 5 of 6 cases examined by CT demonstrated areas of enhancement. MRI demonstrated low- or mixed-signal intensity on T1-weighted image and high- or mixed-signal intensity on T2 sequences. All showed well-defined enhancement. Three showed cyst formation. Tien et al.'s (1992) study of the MRI features of 6 patients with PXA demonstrated that the tumors were cortically based and isointense with gray matter on T1-weighted images, and mildly hyperintense on T2-weighted images. All masses enhanced with contrast material. Cystic components and leptomeningeal enhancement were seen in 2 patients. Similarly, in our series, cysts were present in over 50% of cases, with high- or mixed-signal intensity on T2-weighted sequences on MRI and 87% of the solid component of the tumor enhanced with contrast. Thus, despite the imaging characteristics of a higher grade malignancy suggested by a higher T2 signal intensity, these tumors behaved as low-grade tumors. Certain imaging characteristics, such as the presence of cysts with enhancing cyst walls, are more typical of juvenile pilocytic astrocytomas.

The EFS of 50% and OS of 74% at 5 years in our cohort of patients is very similar to other reports (Giannini et al., 1999; Macaulay et al., 1993; Papahill et al., 1996). We concur with others that the treatment of choice in patients with PXAs is surgery. Giannini et al. (1999) reported that the single most significant predictor of recurrence-free survival in multivariate analysis was the extent of resection ($P = 0.007$). Recurrence-free survival was significantly longer for patients who underwent GTR (>80% at 15 years) rather than STR (>50% at 15 years) ($P = 0.003$). However, it is unclear how many patients in each group received adjuvant therapy. Even though 42% of the entire cohort received adjuvant therapy, the impact of this factor was not apparent in the multifactorial analysis. Although the extent of resection did not appear to be a predictor of OS in multivariate analysis, the former series was handicapped in presenting data from multiple institutions, with likely differing treatment approaches and less consistent availability of operative information and immediate postoperative imaging. Macaulay et al. (1993) reviewed 48 previously cited cases in the literature in which intraoperative assessments of the extent of surgical resection were available. No difference in OS was noted between those with GTR and those with less than GTR. In contrast, Papahill et al. (1996) reported that, for patients whose tumors were not necrotic, those who underwent a GTR had a significant overall survival advantage ($P < 0.05$). EFS was not reported in this group.

Data regarding the use of adjuvant therapy (radiation or chemotherapy) are controversial (Macaulay et al., 1993; Paulus and Peiffer, 1988). Macaulay et al. (1993) reviewed all the previously published cases of PXA and addressed the role of radiotherapy in the treatment of PXAs. They compared the survival of 23 patients receiving adjuvant radiotherapy with that of 34 patients who received no radiotherapy or who were irradiated only after tumor recurrence. No difference in overall survival rate between the 2 groups was apparent at up to 15 years after the initial resection. Similarly, there was no statistically significant difference in the recurrence-free survival of the group. Extent of resection, which may have been a confounding variable, was not reported in either group. Papahill et al. (1996) also noted that survival curves for those receiving adjuvant radiotherapy were not significantly different from those who did not. Giannini et al. (1999) did not address this question specifically in their cohort, because the number of patients receiving adjuvant therapy was too small to make any conclusions. The apparently high EFS among the small cohort of patients in the current series with imaging-confirmed GTR who did not receive adjuvant irradiation, combined with the literature series summarized above, indicate no apparent role for postoperative irradiation in patients with GTR. In the absence of a multivariate analysis looking at extent of resection and adjuvant radiotherapy as separate

variables in patients with PXA, we cannot draw any conclusions regarding the role of adjuvant radiotherapy in those with less than a GTR. It is important to document both secondary disease control in a proportion of recurrent cases with secondary GTR alone, and a proportion of children who demonstrate aggressive disease recurrence and dissemination in an otherwise low-grade neoplasm. Few data are available in the literature to support the role of adjuvant chemotherapy in PXAs.

Thus, we concur with Giannini et al. (1999) and others that GTR is the treatment of choice in PXAs leading to OS of 70%-80%. Further surgery is recommended in the case of recurrent disease. The role of radiotherapy as adjuvant therapy at diagnosis or recurrence remains controversial, but may be considered in the setting of residual disease or with features such as necrosis or high mitotic index.

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