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# Glioblastoma multiforme masquerading as a pleomorphic xanthoastrocytoma

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**Abstract.** Since its first description by Kepes in 1979, pleomorphic xanthoastrocytoma (PXA) has been considered a tumor with a benign course. Two cases are presented here that support the concept that PXA may be more accurately considered part of a spectrum of astrocytomas that occasionally may act aggressively. These cases represent astrocytomas with PXA components and are characterized by meningeal proximity, a high number of mitoses, and subsequently aggressive clinical behavior. The importance of recognizing the potential of a "benign" PXA to transform into a malignant entity has obvious implications for the therapeutic management of these tumors.

**Key words:** Pleomorphic xanthoastrocytoma – Astrocytoma – Tumor.

Kepes first described pleomorphic xanthoastrocytomas (PXA) in 1979 [3]. Since that time, several reports of these neoplasms in the literature have clearly established them as a distinct pathological entity. They commonly demonstrate a predilection for children and young adults, frequently presenting with seizures. Typically, they occur in a superficial location (most frequently in the temporal and parietal regions), so that gross inspection leads one to suspect a meningioma or an extra-axial astrocytoma. Pathologically, they have a highly cellular quality with a mixture of spindle-shaped cells, large foamy (highly lipidized) polygonal cells, and giant cells with marked cellular atypia and relatively few mitoses. A reticulin network is frequently present as well [4]. These tumors are characterized by a benign course [1, 3, 6]. This report, however, presents two cases that had features of PXA at some time during their course and yet eventually became highly malignant and aggressive tumors.

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## Case reports

### *Case 1*

This 2-year-old female initially presented with focal seizures on the right side and irritability. The initial workup included a computed tomography (CT) scan (normal) and an electroencephalogram, which revealed a parietal seizure focus on the right. The child was treated with phenobarbital and lost to follow-up. She returned 6 months later with daily vomiting, headaches, lethargy, and irritability. At that time she had papilledema, palsy of the right third nerve and left seventh nerve with mild left-sided hyperreflexia. CT now disclosed a large enhancing lesion of the right temporal fossa (Fig. 1). At surgery, an extra-axial tumor arising from the temporal fossa and adherent to the dura of the temporal fossa and sphenoid wing was found. Gross total removal was accomplished and the patient did well.

Histologically, the tumor was extremely cellular with areas of focal necrosis scattered throughout (Fig. 2). The cell type was highly variable with a variety of spindle-shaped cells, histiocytic-appearing cells with abundant eosinophilic foamy cytoplasm, and some giant cells (Figs. 3, 4). Cellular palisading and a reticulin network were present. The S100 stain was weakly positive in spindle cells while the glial fibrillary acidic protein (GFAP) was strongly positive in all types of cells.

Based on immunological and histological findings, there was some debate regarding the appropriate classification of the tumor, which had some malignant features. Except for the remarkable mitotic activity, the histological picture was consistent with PXA. Due to the extra-axial location an initial diagnosis of meningeal sarcoma was made.

Within 3 months follow-up CT scan confirmed a large tumor recurrence in the right temporal fossa (Fig. 5). The tumor was again resected and a temporal lobectomy performed.

The second specimen was also a very cellular tumor with numerous areas of necrosis (Fig. 6). It was composed of pleomorphic cells with numerous giant cells and frequent normal and abnormal mitoses (Figs. 7, 8). Large-sized vacuolated tumor cells (sudan IV negative) were present but not as prominent as those seen in the first surgical specimen. GFAP stain was again strongly positive with the greatest response seen in the more spindle-shaped cells. S100 stain was weakly positive and keratin, factor VIII-related antigen, and NSE were negative. The surgical margin of the right temporal lobe showed gliosis and perivascular cuffing. The histology was now felt to be consistent with glioblastoma multiforme.

Despite chemotherapy – vincristine, CCNU, and prednisone – she had a progresive downhill course. A postoperative CT scan showed an enhancing lesion in the area of previous resection. Radiation therapy was initiated. Due to the evolution of quadra-

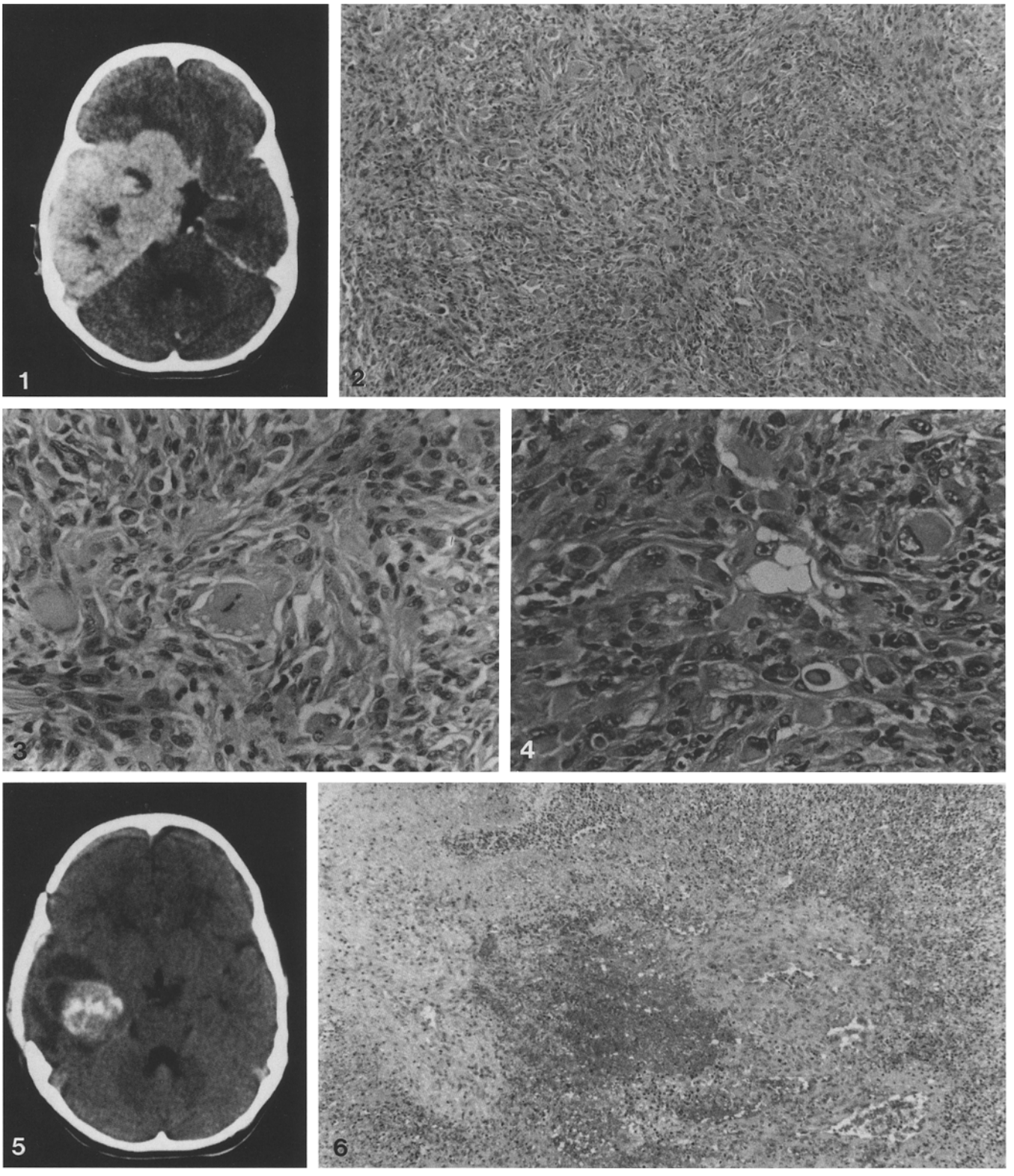


**Fig. 1.** CT showing the large enhancing tumor

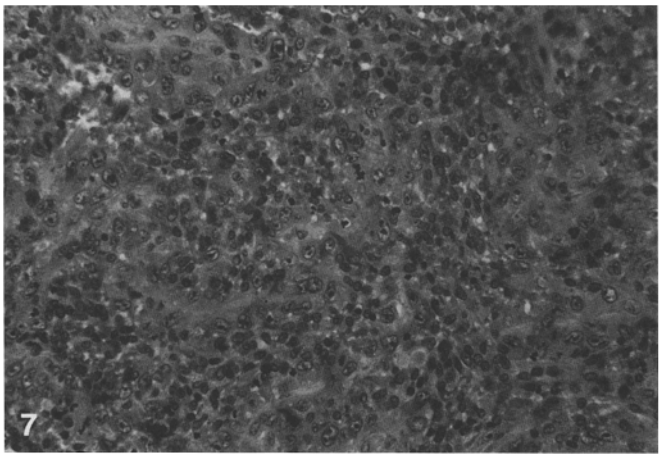
**Fig. 2.** Low-power CT of the first surgical specimen, demonstrating the pattern of spindle-shaped cells (H & E, ×60)

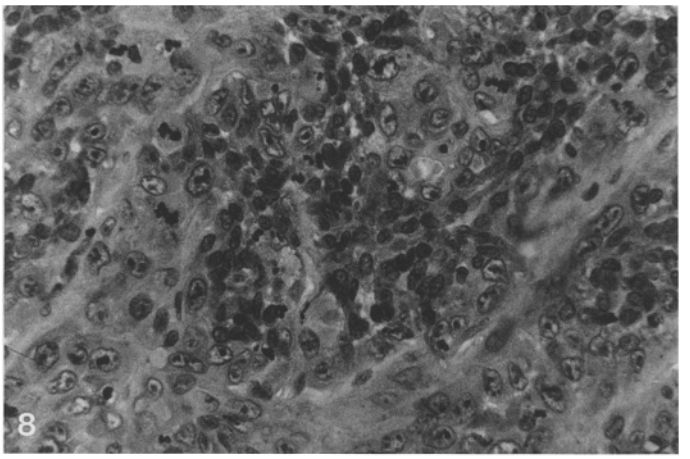
**Fig. 3.** High power CT of Fig. 2, demonstrating both a histiocytic appearance and giant cells (H & E, ×470)

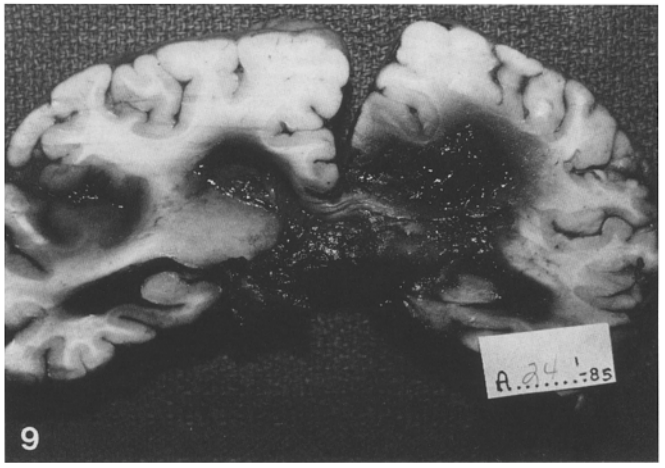
**Fig. 4.** High power CT of Fig. 2 with prominent, large vacuolated cells (H & E, ×470)

**Fig. 5.** CT 3 months after the initial operation, confirming tumor recurrence

**Fig. 6.** Low-power micrograph of the second specimen showing large areas of necrosis (H & E, ×40)







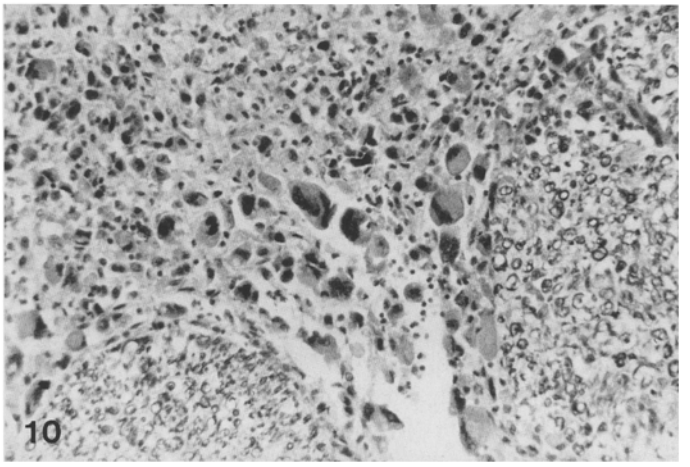


**Fig. 7.** Another field of the second specimen, showing a large number of normal and abnormal mitoses (H & E, ×235)

**Fig. 8.** H & E stain of the second specimen is representative of the pleomorphic character of the tumor. Mitoses are evident in this photomicrograph as well (×575)

**Fig. 9.** Autopsy specimen revealing gross hemorrhage and necrosis

**Fig. 10.** Autopsy histology of the tumor demonstrated a number of bizarre giant tumor cells with abundant eosinophilic cytoplasm

paresis, myelography was performed, which showed marked thickening of the cauda equina, consistent with tumor metastasis. Amitryptyline, steroids, and spinal radiation were used for palliation of pain. She died just 11 months after the onset of seizures and 5 months after her presentation, with significant signs of increased intracranial pressure and cranial nerve involvement by the tumor. Postmortem examination revealed a gray-tan tumor coating the temporal lobe, spinal cord, and nerve roots. Necrosis and hemorrhage with extension into the cerebral cortex were clearly evident (Fig. 9).

Histologically, a highly cellular tumor consisting of a disorganized mass of spindle-shaped cells and large tumor giant cells with abundant eosinophilic cytoplasm were demonstrated. Large polygonal tumor cells with a granular-to-foamy appearance and frequent bizarre tumor giant cells were present (Fig. 10). The mitotic index was high (24/10 HPF). Hemorrhage and necrosis were abundant with associated neutrophilic infiltration. The cauda equina was encased by tumor. S100 antibody stain was negative and only rare tumor cells exhibited positive GFAP (versus the first two specimens in which GFAP was strongly positive).

*Case 2*

This is a recent case of a 10-year-old female who presented with a 3-week history of headaches. Despite a normal neurological examination, CT showed a large hyperdense mass in the posterior temporal parietal lobe. It appeared to have a superficial base and extended to the midline. At surgery, the tumor was adherent to the dura. Histological examination revealed a highly pleomorphic tumor with a multiplicity of histological patterns, some compatible with juvenile pilocytic astrocytoma, and others with glioblastoma multiforme. Oil red-0 stains were positive, suggesting a lipid component and perhaps a diagnosis of lipidized glioblastoma. There were large areas of necrosis throughout the specimen with areas of palisading round vessels. Because of the age of the patient and the dural adhesion of the tumor noted at surgery, the possibility that this tumor may have been a PXA was considered. The tumor was classified as a lipidized glioblastoma; however, it may have originated as a PXA and evolved into a more malignant entity (J. Kepes, personal communication).

## Discussion

The rapid downhill course of the child in the first case could have been predicted both by the gross development of the tumor within a 6-month period, documented on CT as well as by the initial histological appearance with an unusually high rate of mitoses. The tumor's initial behavior was more predictive of the prognosis than its histology. It is of interest that in tissue culture the tumor grew for

only 3 weeks and then died. Also of note in this case is the negative oil red-0 stain in the frozen tissue sections of the second surgical specimen (usually positive in PXA but negative in gliomas) and the positive GFAP, pointing toward a diagnosis of a malignant glioma. The reactivity of the tumor cells to GFAP and the extra-axial location were indicative of an extra-axial glioma but, because of the rarity of such a presentation, the possibility of a histologically aggressive PXA was considered more likely. The second case study is not as definitive as the first; however, it does support the possibility that a PXA has the potential to turn into an aggressive and malignant entity.

Since Kepes original description [3], PXA has been thought of as a relatively benign neoplasm with a good prognosis. The only case study present in the literature which contradicts this notion is that by Weldon-Linne et al. in 1982 [9], in which there was a fatal outcome. In this case there was the question of possible radiation-induced malignant transformation. In each of the present cases, radiation therapy was not introduced until after malignancy had been demonstrated. Therefore, we are forced to consider the possibility that a histological classification of PXA does not necessarily mean a benign prognosis. Alternatively, the fact that this neoplasm had striking mitotic activity not typical of PXAs noted previously may mean that tumors demonstrating features of PXA may, in fact, be part of a spectrum of astrocytoma and that those with an inordinate number of mitoses are malignant. Cases will thus need to be considered individually – histologically and clinically – before associating PXAs with a benign course and hence treat them as such.

In conclusion, this case supports the consideration of PXA as part of the spectrum of astrocytoma in which particular attention to the location, mitotic activity, and clinical behavior must be evaluated before prognosticating and considering adjuvant therapy.

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