PET-FDG of Pleomorphic Xanthoastrocytoma

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A young patient with pleomorphic xanthoastrocytoma (PXA), a usually benign cerebral tumor, had two recurrences in a short time period. The clinical, pathological and neuroradiological features, including PET with [^{18}F]-fluorodeoxyglucose (FDG), are presented. The PET-FDG study revealed the recurrent tumor to be hypermetabolic. The diagnosis was confirmed histopathologically. As the clinical outcome of patients harboring PXA is not easy to predict because of possible recurrence and/or transformation into more aggressive gliomas, we discuss the predictive indicators of more aggressive clinical behavior.

Key Words: pleomorphic xanthoastrocytoma; tumor recurrence; PET, fluorodeoxyglucose

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The pleomorphic xanthoastrocytoma (PXA) was first described by Kepes et al. in 1979 (*1*). Histologically, this glioma is characterized by pleomorphic, lipid-laden neoplastic cells with surrounding reticulin layers. Typically, necrosis and a high mitotic rate are absent at the first evaluation (*2*). PXAs are usually located superficially in the temporal lobe and leptomeningeal involvement is frequent (*2*). Children and young adults are more often affected by this neoplasm, which generally has a benign course, with long, symptom-free, postoperative survival. However, both recurrence (*3,4*) as well as anaplastic transformation to more aggressive histology have been described (*5*).

Performing partial rather than total resections of PXAs does not appear to adversely affect the long-term survival and, therefore, the value of total resection is controversial (*6–8*). Some skepticism is also found in the literature about the efficacy of radiation therapy (*8,9*). However, it is commonly accepted that cases of PXA which are not treated with radiotherapy after partial removal have a higher probability of recurrence (*7*).

The CT and MRI findings in patients with PXA have already been reported (*5,6,10,11*). In this article we describe PET with [^{18}F]-fluorodeoxyglucose (PET-FDG) findings in a patient with a recurrent PXA.

CASE REPORT

A 19-yr-old male with a 6-wk history of worsening headaches and diplopia was first evaluated in January 1991. Clinical examination revealed florid papilledema of the left optic disc.

Postcontrast CT scans showed a left parieto-temporal mass with a posterior cystic component. The mass enhanced inhomogeneously and was associated with marked edema. Similar features were seen on post-Gd-DTPA MRI (Fig. 1).

The patient underwent subtotal surgical resection in February 1991. At first the histological diagnosis was oligodendroglioma but after review of the specimen, the diagnosis was changed to PXA because of the reticulin pattern and the lipid-loaded neoplastic cells. Postoperative CT demonstrated enhancement in the remaining tumor. Radiation therapy (54 Gy) was then carried out.

The patient remained clinically stable until June 1991, when he had a seizure and experienced speech difficulty. A repeat post-Gd-DTPA MRI study showed that the left parieto-temporal lesion was now larger and caused marked mass effect (Fig. 2). The lesion also extended deeper into the temporal lobe, where it appeared multicystic and involved the temporal pole. A second craniotomy, in October 1991, confirmed tumor recurrence (new growth spurt). Microscopically, mitotic figures were inconspicuous, but numerous necrotic foci were seen which were not present in the tissue removed at the first operation. The patient remained clinically stable, but in April 1992 new changes were observed on MRI. An

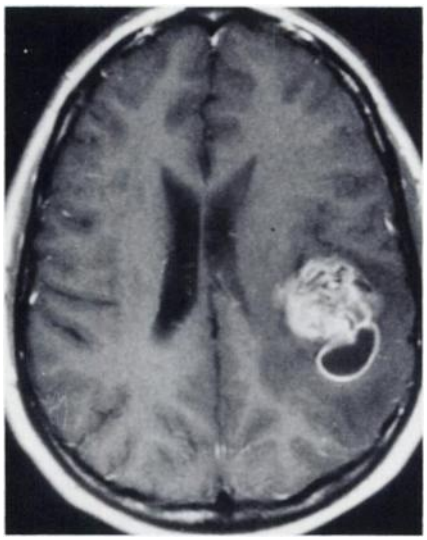

FIGURE 1. February 1991. Axial, preoperative postcontrast (Gd-DTPA) T1-weighted (TR 420, TE 19) MR image of the brain shows left parietal temporal lesion with a posterior cystic component. Notice edema surrounding the enhancing mass.

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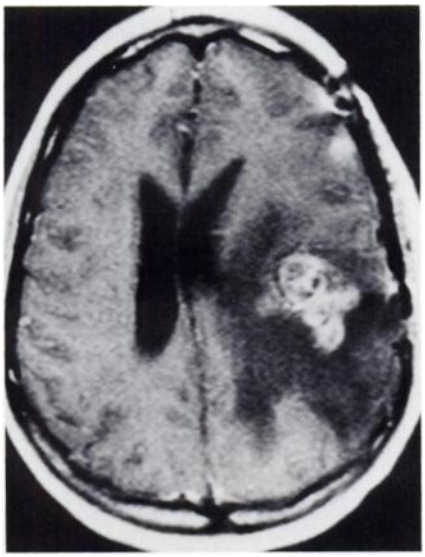

FIGURE 2. June 1991. Postcontrast (Gd-DTPA) T1-weighted (TR 417, TE 16) axial MR image of the brain shows marked mass effect with compression and displacement of the lateral ventricles. Also, the surrounding edema has increased. At this level, we do not see an obvious cyst associated with the tumor. However, lower in the temporal lobe (not shown) the neoplasm appears multicystic.

enhancing nodule, of more than 2 cm in diameter, was seen in the cortex of the posterior left temporal lobe (Fig. 3A). The patient was then referred for a PET-FDG scan. Prior to the PET examination, an MRI was repeated in the same plane as that used for the PET scan, although the MRI slice thickness was half that of the PET-FDG scan.

The PET study was performed on a Scanditronix PC1024-7B-Scanner (Uppsala, Sweden), a 7-slice brain scanner with a resolution of 5.2 mm at the center and a slice thickness of 10.5 mm. A transmission scan with ^{68}Ge was performed for attenuation correction. Fluorine-18-FDG (185 MBq (5 mCi)) was injected intravenously, and arterial blood samples were taken periodically from a radial artery opposite the injection side. Throughout the study, the patient's eyes and ears were patched, and the patient's head was immobilized by a thermoplastic mask molded to the contours of the face.

After a 30-min uptake period, emission data were acquired. The imaging plane was parallel to the cantho-meatal line. The regional cortical glucose metabolic rate (rCGMR) was calculated according to standard rate and lumped constant values (grey matter rate constants: $k_1 = 0.1020$, $k_2 = 0.1300$, $k_3 = 0.0620$ and $k_4 = 0.0068$; lumped constant = 0.4180) as described previously (*12,20*). The rCGMR in the lesion was assessed with a circular 8-mm diameter region of interest (ROI) which was placed in the region of maximal tracer accumulation. This value was then normalized to the rCGMR of white matter in the contralateral hemisphere. We use normalization to minimize systematic errors. Thus the tumoral rCGMR is divided by the white matter rCGMR. White matter rCGMR was calculated by placing three ROIs, identical in size to the ROI used for the lesion, in the contralateral centrum semi-ovale. The white matter was separated into thirds and one ROI was placed in the anterior, middle and posterior third of the centrum semi-ovale. The white matter ROIs were always placed at least 20 mm above the bodies of the caudate nuclei to exclude a partial volume from the bodies of the lateral ventricles. The three ROI values were then averaged.

The PET-FDG study was evaluated visually and quantitatively. There was a small focus on visual inspection of increased glucose utilization seen over several contiguous images anterior to a hypometabolic area in the left temporo-parietal lobe (Fig. 3B). This region was within the area of Gd-DTPA enhancement on the MRI studies (Fig. 3A). Regional analysis showed a rCGMR of 8.93 mg/100 g/min in the lesion and 11.40 mg/100 g/min in the contralateral gray matter. The normalized value for the rCGMR within the tumor, was 3.5. Since gliomas are derived from neuroglia, our practice is to visually compare tumoral FDG uptake to FDG uptake in the normal contralateral white matter. For quantitation, we also compare lesional rCGMR to rCGMR in the contralateral white matter rather than cerebral cortex, because white matter rCGMR mainly reflects glucose metabolism in normal neuroglia. Cortical rCGMR, on the other hand, reflects glucose utilization in both synaptic terminals and neuroglia. Low-grade tumors display glucose metabolism which is equal to or slightly greater than the glucose metabolism of the white matter. When compared to data previously reported from our branch (*20*), the normalized value 3.5 is consistent with a high-grade lesion (low-grade astrocytoma 1.32 ± 0.30, anaplastic astrocytoma 4.19 ± 2.15, glioblastoma multiforme 6.46 ± 2.67; values are ±1 s.d.).

The patient underwent a third craniotomy, in May 1992, with total tumor resection. Immuno-histopathology again showed typ-

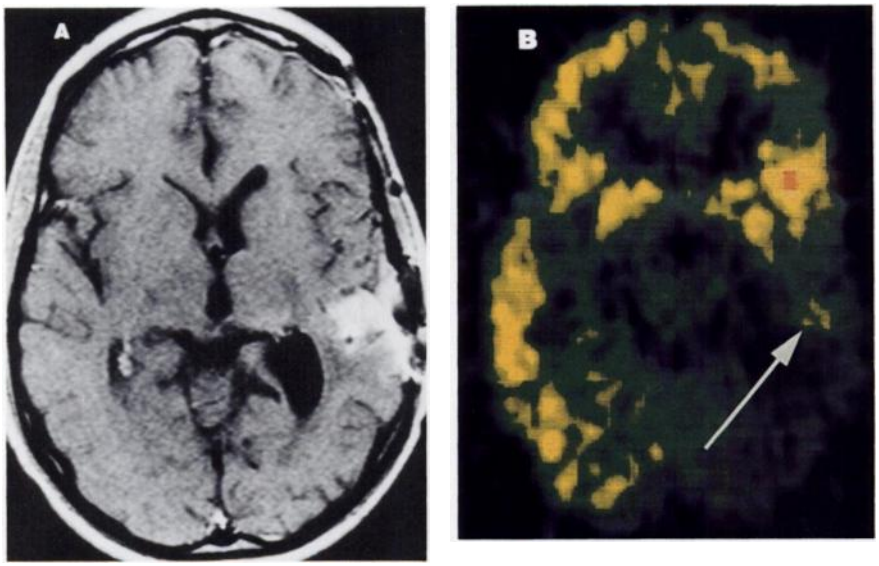

FIGURE 3. April 1992. Postcontrast (Gd-DTPA) T1-weighted (TR 600, TE 16) axial MR image of the brain (A) shows an enhancing cortical/subcortical nodule in the left posterior-temporal lobe. A PET-FDG study (B) shows a heterogeneous, ill-defined area (arrow) of slightly increased tracer activity anterior to a region of decreased FDG localization.

ical features of PXA together with necrotic and reactive areas. Since then, the patient has remained clinically stable.

DISCUSSION

PXA is considered to be a relatively benign variant of astrocytoma, but in each case the prognosis remains uncertain because of possible recurrence and/or anaplastic transformation. Although neuroimaging features, as well as immuno-histologic findings, have been used as prognostic criteria, there is no agreement about their value.

Tien et al. (*6*) proposed peri-tumoral edema as a predictive factor for more aggressive clinical behavior. However, Kros et al. (*13*) reported a postsurgical survival of up to 11 yr in patients with extensive peri-tumoral edema. Lipper et al. (*14*) found edema, mostly mild, in all seven patients, but they did not assign a prognostic value to this finding. In our patient, the initial CT and MRI features were consistent with the previously described appearance of PXA, but marked peri-lesional edema and mass effect were considered to be indicative of aggressive clinical behavior. This was confirmed by the clinical course.

Although slight mitotic activity has been reported before (*5,8*), this is not considered as a strong indicator of aggressiveness. However, increasing mitotic activity, found in recurrent PXAs may be associated with anaplastic transformation (*7*). The immuno-histochemical findings in all tissue samples obtained from the different craniotomies in our patient were typical for PXA. Negligible mitotic activity was evident at the first surgical evaluation, as well as at the later surgeries.

While necrotic areas are not encountered at first in PXA, in recurrences they are indicative for anaplastic transformation (*1,2,3*). Several necrotic areas were found in our patient after radiation therapy. This finding, along with increased mitosis rate and the loss of reticulin fibers, is usually associated with malignant dedifferentiation (*3*). In our patient, however, we feel that the necrotic areas may have been induced by radiation therapy.

Previous studies (*15,16*) have demonstrated the utility of PET-FDG in patients with brain tumors to assess tumor aggressiveness, effects of treatment (radiation necrosis, gliosis), tumor recurrence and/or malignant dedifferentiation. Although we have no experience in PXAs, and there are no studies available, we expect tumors of high grade and aggressive clinical behavior to express higher glucose utilization rates (*12,20*). In our patient, the lesion was clearly hypermetabolic with respect to white matter and easily detected within an area of hypometabolism which resulted from previous treatment (surgery, radiation) (*16*). Although the rCGMR of the lesion was less than the contralateral cerebral cortex, the normalized rCGMR was indicative of an aggressive lesion (*20*). Thus, visual inspection together with quantitative analysis indicated tumor recurrence.

Recently, there has been an increasing interest in analyzing cases of subtypes of primary brain tumors occurring in young patients, such as PXA (*1–11*), juvenile pilocytic astrocytoma (JPA) (*17–20*), dysembryoplastic neuroepithelial tumor (DNT) (*21*) and gangliogliomas (*22,23*). These neoplasms often show peculiar discordant and inconsistent neuroimaging findings. Continuing research aimed at establishing criteria of expected biological and clinical behavior, is to be encouraged.

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