Abstract  We report a case of a 24-year-old woman with left temporal pleomorphic xanthoastrocytoma (PXA) with atypical neuronal cells. Many neoplastic cells, otherwise typical of PXA, expressed glial fibrillary acidic protein, while neuronal cells with marked atypia were immunopositive for synaptophysin and neurofilament protein. This report supports a notion that PXA, like other astrocytic tumors, may have its gangliogliomatous counterpart.

Key words  Pleomorphic xanthoastrocytoma
Ganglioglioma

Introduction

Cases of pleomorphic xanthoastrocytoma (PXA), were originally reported as “fibrous xanthoma of the meninges” and, thus, regarded as mesenchymal tumors [13]. However, the finding of glial fibrillary acidic protein (GFAP) expressed in such tumors subsequently necessitated modification of this opinion and in 1979 Kepes et al. [14] established PXA as originating from glial cells. Ultrastructurally, many neoplastic astrocytes were found to be covered by basal laminae, so these investigators proposed its origin to be from subpial astrocytes which are known to elaborate basal laminae in non-neoplastic condition [14]. The possibility of a histiocytic origin for these neoplasms has also been debated. Immunopositivity for such markers as α-1-antitripsin, α-1-antichymotripsin, common leukocyte antigen and OKM-1 was quoted to support this opinion [24, 25]. These markers, however, are of low specificity and, therefore, their presence does not exclude a glial origin for PXA [7]. Moreover, the existence of complex tumors containing components with neuronal differentiation, may also support a hypothesis of neuroectodermal origin of PXA [3, 6, 15, 20].

Most PXA are localized superficially and supratentorially, with frequent involvement of the leptomeninges but sparing of the dura mater [11]. They often exhibit a cystic appearance and occur in young patients – with a few notable exceptions [17, 22]. Microscopically, marked cellular pleomorphism is a consistent finding. Lipidization of neoplastic cells, absence of, or low incidence of mitotic figures, abundant reticulin deposits and perivascular chronic inflammatory cells are consistent findings of PXA [9, 10, 12, 14, 16–19, 27, 28, 30]. Necrosis should cause one to refrain from diagnosing PXA since its presence points to glioblastoma [14]. In contrast to marked pleomorphism, the clinical course in most cases appears to be relatively favorable, although anaplastic changes have been described [3, 33]. Furthermore, PXA should be discriminated from the “desmoplastic” glioblastoma [2, 12].

Two cases of mixed PXA and gangliogliomas have been reported [6, 20], and in two other cases a few scattered abnormal ganglion cells in otherwise typical PXA were found. We report here an additional case of PXA with a large number of atypical ganglion cells – the gangliogliomatous variant of PXA.

Case report

A 24-year-old woman had suffered from headaches since 1974 and epileptic seizures of the “absence” type for 3 weeks. In 1980 she complained of an exacerbation of the headache of 3-week duration, and was admitted to the Department of Neurosurgery, Regional “Copernicus” Hospital, Lodz. Left carotid angiography showed a mass lesion, displacing the anterior and medial cerebral arteries to the right. Computerized tomography (CT) was not available at that time. At surgery, a cystic cavity superficially located in the left temporal lobe was found. After aspiration of 25 ml of xan-
impregnated with silver for reticulin. For immunohistochemistry, embedded in paraffin. Sections were stained routinely with HE and

delivered a normal child and later was lost to follow-up.

Whole brain. She remained asymptomatic for 4 years after surgery, subsequentl the patient received radiation therapy of 40 Gy to her whole brain. She remained asymptomatic for 4 years after surgery, delivered a normal child and later was lost to follow-up.

Materials and methods

The surgical specimen was fixed in 10% buffered formalin and embedded in paraffin. Sections were stained routinely with HE and impregnated with silver for reticulin. For immunohistochemistry, slides were incubated with monoclonal antibodies against GFAP, a 200-kDa subunit of neurofilament protein (NFP), chromogranin A and synaptophysin, p53(D07; DAKO) and proliferating cell nu-
clear antigen (PCNA, PC10 clone; DAKO). The streptavidin-bi-
tin complex method was used. Fresh material was fixed in 2.5% glutaraldehyde in cacodylate buffer (pH7.2) and used for ultra-
structural examination.

Results

Histopathological features

The tumor was composed of compactly arranged partly spindle-shaped, partly pleomorphic, multinucleated and sometimes bizzare cells. Numerous large foamy cells were scattered in the tumor parenchyma. Despite a careful search, neither mitotic figures nor foci of necrosis were found. Robust lymphocytic infiltration was present at the periphery of the tumor. Furthermore, several large, round and occasionally bi- or multinucleated cells with vesicular nuclei and prominent nucleoli, reminiscent of atypical ganglion cells, were observed diffusely in all specimens. Silver reticulin staining revealed a dense reticulin network surrounding individual tumor cells. These features met the criteria of PXA, but with an admixture of a population of atypical neuron-like cells.

Immunohistochemistry

The majority of the bizzare multinucleated tumor cells and foamy tumor cells were GFAP positive (Fig. 1a). The ganglion-like cells were GFAP negative. The frequently seen binucleated cells, diffusely dispersed in all specimens, were synaptophysin and, weakly, chromogranin A positive (Fig. 1b). Using synaptophysin as a marker, we found one to four positive ganglion cells in virtually every high-power field (×1000). NFP staining revealed a network of altered axons (Fig. 1c) and numerous large spheroids, indistinguishable from those of reactive axonal swellings [8]. There was no p53 immunoreactivity but isolated astrocytic nuclei expressed PCNA (data not shown). There was no PCNA immunopositivity detected in the bizzare lipidized cells or in the ganglion cells.

Ultrastructural examination

Electron microscopy revealed innumerable astrocytes and their processes containing large numbers of glial filaments. Astrocytic processes, connected by plaque-like long junctions were intermingled with dense bundles of collagen fibers. Numerous Rosenthal fibers of different shapes and in different stages of development were observed. Furthermore, we also noticed some astrocytic processes containing dense amorphous structures, not unlike those recently described in glioblastomas of granular appearance [5]. Many astrocytes were covered with basal laminae, which formed a complicated labyrinth invagi-
nated into astrocytic cytoplasm (Fig. 1d). Other astrocytes contained numerous vacuoles containing myelin figures and whorls. These vacuoles probably represented the ultrastructural correlate of foamy cells seen by light microscopy. The second neoplastic component consisted of cells with pale cytoplasm, with no intermediate fila-
ments but a few microtubules and prominent stacks of ri-
bosomes. Infrequent dense-cored vesicles were also ob-
erved. We regarded these cells as being neuronal.

Discussion

We have documented here a case of PXA with an admix-
ture of gangliomatous components. Ganglion cells were of unequivocal neoplastic appearance. Neuronal compo-

nents in PXA have been recognized only recently. Furuta et al. [6] described a case of a tumor with two different components, ganglioglioma and PXA, in a 16-year-old boy. A similar case was reported by Lindboe et al. [20]. Reinhardt and Nahser [26] reported a tumor resembling PXA, but with a peculiar growth of neurons. They diag-

nosed it as a gliofibroma because of the scarcity of true ganglionic cells. Maleki et al. [23] described PXA with a few atypical ganglion cells containing membrane-bound neurosecretory granules. These cells were regarded as too sparse to warrant such a tumor being considered as gan-

gliogliomatous. Kros et al. [17] also found neoplastic NFP- and synaptophysin-positive neuronal cells in one of their five PXA cases. These cells were often binucleated, randomly oriented and clustered. We found a large num-
ber of similar cells in our case, and this tumor should be regarded as the gangliogliomatous variant of PXA. Be-
cause of the characteristic desmoplasia, young age of the patients, and possible origination from subpial astrocytes, a similarity of these gangliomatous PXA cases with an-
other novel neurooncologic entity, desmoplastic infantile ganglioglioma (DIG) is plausible [31, 32], although they clearly differ in several clinico-pathological features. In particular, in DIG, small, primitive cells with the promi-
nent desmoplasia are present and this tumor occurs in younger patients than those with PXA [31]. The latter also shows a higher degree of atypia and lipidization of the tu-
mor cells. DIG seems to be a gangliogliomatous variant of superficial cerebral astrocytoma of infancy (SCAI) [4], which has also a favorable prognosis. Furthermore, SCAI