Epithelial properties of pleomorphic xanthoastrocytomas determined in ultrastructural and immunohistochemical studies*

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Summary. Three cases of pleomorphic xanthoastrocytoma (PXA), one of which showed anaplastic evolution, are described. In all three the PXA tumors were well circumscribed and could be totally removed. Light-microscopically, pleomorphic tumor cells clustered gregariously and often formed alveolar structures. Electron microscopy revealed various epithelial properties, such as junctions and interdigitations between apposing tumor cells, and prominent basal laminae surrounding tumor nests. The circumscribed growth of PXA, as contrasted with an infiltrative growth of usual astrocytoma, can be attributed to the cellular cohesion based on the epithelial properties of the tumor cells. In the third patient, tumor recurred 6 months postoperatively. Although the recurrent tumor retained the alveolar structures, pleomorphism and various degenerative features of the tumor cells diminished with advance in the proliferative activities.

Key words: Pleomorphic xanthoastrocytoma — Epithelial properties — Circumscribed growth — Electron microscopy — Immunohistochemistry

In 1979, Kepes et al. [8] described distinctive supratentorial gliomas of young patients. These tumors were designated “pleomorphic xanthoastrocytoma” (PXA) on the basis of their superficial location in the brain, marked cellular pleomorphism, and prominent lipid-laden cells. Twenty-seven such cases have been reported [2, 5-7, 11, 15, 18, 22, 25, 26]. Most had a relatively favorable outcome, despite the bizarre cellular pleomorphism. Most PXAs showed a circumscribed growth with desmoplastic change, while a great majority of astrocytomas showed diffuse infiltration into the adjacent brain areas. In these reports, many characteristic pictures of PXA were viewed by light microscopy. As there are few reports on fine structure of PXA [7, 8, 11, 15, 26], we investigated three cases of PXAs by electron microscopy and immunohistochemistry. The objective of our study was to shed some light on morphological characteristics of PXA in relation to its biological behavior.

Case reports

Case 1 (NS681096)
An 11-year-old girl presented with a 1-year history of convulsive seizure. Neurological examination on admission revealed early papilledema, hypesthesia of the left lower extremity, and hearing disturbance in the right ear. Plain skull X-ray films showed mild cranial suture separation and bulging of the right temporal bone. Cerebral angiograms demonstrated a slightly vascular lesion in the right temporal lobe. At operation a fairly well-demarcated tumor with a portion exposed on the cortical surface was present in the right temporal lobe. The tumor was accompanied by a large cyst. Total removal of the tumor was macroscopically performed and a total of 40 Gy of postoperative radiation was administered. She has been doing well with no recurrence for 17 postoperative years.

Case 2 (NS790783)
A 7-year-old girl presented with a 1-month history of convulsive seizure. CT scan revealed an iso-density mass in the parasagittal portion of the right parietal lobe, which was homogeneously enhanced with contrast media. Cerebral angiograms revealed a hypovascular mass. At craniotomy, there was a well-demarcated tumor associated with a cyst. The tumor was embedded in the brain like an extra-axial mass but was not attached to the dura matter. The tumor was easily removed and a total of 50 Gy of radiation therapy was administered. Another tumor was found in the right frontal lobe 6 years after surgery. The second tumor was located mainly in the cerebral cortex and was exposed on
the cortical surface. The tumor was round, elastic firm, and well demarcated. The tumor was totally removed. At the second craniotomy, there were neither subarachnoid dissemination nor local recurrence of the previous tumor. She has been doing well postoperatively.

Case 3 (NS840818)

A 30-year-old man complained of headache 2-months duration prior to admission. This man was an uncle of case 2. Neurological examination on admission revealed bilateral papilledema with retinal hemorrhage and right homonymous hemianopsia. CT scan showed a slightly high density mass occupying the posterior half of the left cerebral hemisphere and this mass was irregularly enhanced with contrast media. Cerebral angiograms showed a somewhat dumbbell-shaped large mass. The anterior one third of the tumor was hypervascular, but the posterior two thirds hypovascular. At operation, the tumor was located 5-10 mm deep from the cortical surface and reached the trigone of the left lateral ventricle. There were several small cysts between the tumor and the adjacent brain areas. The tumor was sharply demarcated from the surrounding tissue and was totally removed. Histological findings of the posterior two thirds of the tumor were those of PXA with few mitoses, but the anterior one third showed evidence of malignant astrocytoma with increased mitotic activities. The tumor recurred at the same site 6 months after surgery. At the second operation, the recurrent tumor consisted of many nodules of various sizes and was removed. A total of 60 Gy of irradiation to the brain was given. Four months later, subarachnoid dissemination of the tumor occurred and irradiation to the spinal area was given.

Materials and methods

For light microscopic examination, surgical specimens were fixed in 10% formalin or chilled 70% ethanol and embedded in paraffin. Sections were stained with hematoxylin and eosin (H&E), Masson trichrome, periodic-acid-Schiff (PAS), phosphotungstic acid hematoxylin (PTAH), and silver reticulin stains. Frozen-section material from case 3 was stained with Sudan III.

For immunohistochemical analysis, peroxidase anti-peroxidase (PAP) method for glial fibrillary acidic protein (GFAP), S-100 protein, neurofilament triplet proteins (68 kDa, 160 kDa, 210 kDa), neuron-specific gamma-enolase, myelin basic protein (PAP) method for glial fibrillary acidic protein (GFAP), S-100 protein, neurofilaments, and neuron specific gamma-enolase were established in our laboratory [12, 16, 23, 27]. For immunohistochemical staining with anti-laminin antibody, formalin-fixed sections were predigested with 0.4% pepsin in 0.01 M HCl at 37°C for 120 min.

For electron microscopic examination, fresh tissues from the surgical specimens were fixed in 3% glutaraldehyde, postfixed in 1% osmium tetroxide, and embedded in Epon. Ultrathin sections were double-stained with uranyl acetate and lead citrate, then examined under a Hitachi HU-12AS electron microscope at 75 kV.

Results

Light microscopy

The original tumors of case 1 and case 2 showed similar microscopic structures. The tumor cells were pleomorphic with mixtures of polygonal, spindleshaped, and multinucleated giant cells (Fig. 1a). Mitoses were scarce and necrosis was absent. Vacuolated or xanthomatous cells were occasionally seen. In addition, eosinophilic hyaline granules (hyaline globules) and round granulated bodies were often evident (Fig. 2a). Eosinophilic hyaline granules were strongly stained red with PAS and with Masson trichrome and dark blue with PTAH. The pleomorphic tumor cells often formed alveolar structures and were sometimes arranged in a trabecular pattern. Reticulin fibers encased each nest of tumor cells (Fig. 1b). The loose connective tissue, which was mainly composed of spindle-shaped fibroblast-like cells and vessels, surrounded clusters of tumor cells. In portions of the alveolar or trabecular patterns, the tumor cells did not directly extend cytoplasmic processes to the blood vessels, since they were surrounded by the connective tissue. Trichrome stains demonstrated increased interstitial collagen. Although there was no capsule, the margin of each tumor was relatively clear. Gliosis was present in the contiguous brain tissue. There was no endothelial proliferation in the tumors, but perivascular lymphocytes were occasionally present. The microscopic structure of the second tumor in case 2 was essentially similar to that of the original tumor.

On the other hand, the original tumor in case 3 was composed of two different parts. The microscopical structures of the posterior two thirds of the original tumor were similar to those of cases 1 and 2 (Figs. 1c, 2b). In addition, the tumor showed marked desmoplastic change, despite no meningeal involvement. Reticulin fibers often surrounded each group of tumor cells. In part, spindle-shaped tumor cells were arranged in bundles or in a storiform pattern. Many Rosenthal fibers were encountered in the marginal area of the tumor and in the brain adjacent to the tumor. Some tumor vessels were fibrously thickened and were associated with calcification.

The anterior one third of the original tumor in case 3 was composed of monomorphic proliferation of small anaplastic cells with numerous mitoses, and of a central necrosis. In some areas, the nests of anaplastic cells were surrounded by thick collagenous septa (Fig. 1d). There was marked endothelial proliferation in the anaplastic foci. Neither vacuolation of the tumor cell nor eosinophilic hyaline granules were seen. The microscopical structures of the recurrent tumor were similar to that of anaplastic foci of the original tumor. The recurrent tumor was also composed of relatively monomorphic tumor cells with numerous mitoses, and showed distinct alveolar structures encased by the collagenous tissue (Fig. 1e). In the recurrent tumor, there was neither endothelial proliferation nor necrosis.