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Desmoplastic Cerebral Astrocytoma of Infancy
: A Case Report

We present a case of desmoplastic cerebral astrocytoma of infancy (DCAI) in a 9-month-old boy including immunohistochemical and proliferative activity studies. It was mainly composed of glial fibrillary acidic protein (GFAP)-positive astrocytes and desmoplastic stroma. Studies with Ki-67 and synthetic phase fraction disclosed a low proliferative activity. Flow cytometric study revealed diploidy pattern. These findings suggest a positive correlation with the favorable prognosis.

Key Words : *Astrocytoma; Infant; Glial fibrillary acidic protein*

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INTRODUCTION

Intracranial tumors in early childhood are malignant in 85% of cases. However, desmoplastic cerebral astrocytoma of infancy (DCAI) is a rare tumor that presents itself as a hemispheric mass of voluminous size in infants. It reveals well-circumscribed dural-based cystic structure and has a biphasic histologic pattern consisting of neoplastic astrocytes embedded in a desmoplastic stroma (1-7). The tumors are associated with a good prognosis. It is known that most patients have survived a long period of time with surgical resection and radiation therapy, or with surgery alone. We report a case of DCAI in a 9-month-old boy presenting with generalized weakness of left upper and lower extremities for 3 months. This is the first report of DCAI in Korea.

CASE REPORT

A 9-month-old boy presented with a generalized weakness of left upper and lower extremities for 3 months. His birth and past development have been unremarkable. Brain magnetic resonance (MR) T1-weighted and T2-weighted images showed a lobulating iso- or slightly hypointense mass, 9 cm in its largest diameter, in the fronto-temporo-parietal area, compressing the ipsilateral cerebral hemisphere and the mass extended into the centrum semiovale forming cystic mass (Figs. 1, 2). There was a widening of cerebrospinal fluid (CSF) space adjacent to the mass. It looked like an extraaxial mass with some intraaxial portion. The tumor mass was partially removed via the temporo-parietal craniotomy.

Grossly, the solid portion of the tumor mass showed homogeneously grayish white fishflesh cut surface. Histological examination revealed densely cellular tumor composed of spindle cells embedded within a dense fibrous stroma. The tumor cells were arranged in fascicle and whorls forming storiform pattern resembling a meningioma or fibrous histiocytoma (Fig. 3). Masson trichrome stain showed a prominent collagenous network. Some areas exhibited plump tumor cells having more abundant eosinophilic cytoplasm and astrocytic appearance (Fig. 4). Focal collection of foamy histiocytes with necrosis and calcification were present but no mitotic figure was identified (Fig. 5). There was no ganglion cell. Immunohistochemically, both spindle and polygonal neoplastic cells were positive for glial fibrillary acidic protein (GFAP: DAKO, 1:100) (Fig. 5) and vimentin (BioGenex) but not stained for epithelial membrane antigen (DAKO), cytokeratin (Becton Dickinson) and neuron specific enolase (DAKO). Ki-67 (DAKO, 1:100) labelling index was less

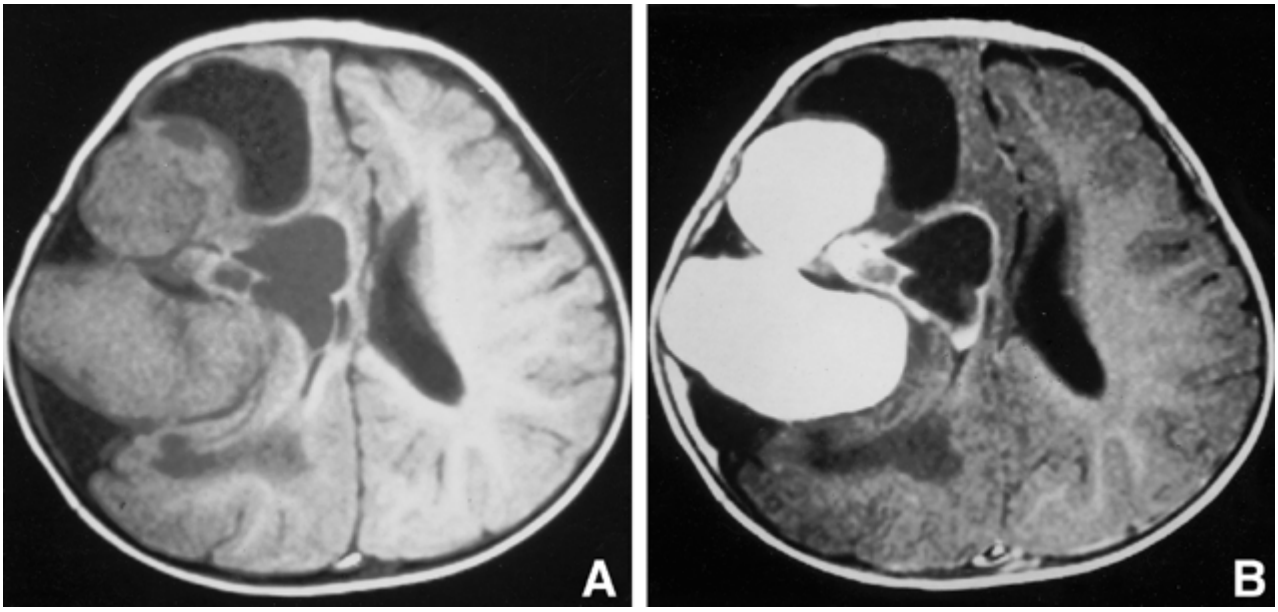

Fig. 1. (A) MR T1-weighted image of brain showed an iso- or hypointense lobulating mass with cystic lesion in the right fronto-temporo-parietal lobe. (B) MR T1-weighted contrast-enhanced image revealed enhancement of solid portion.

than 1%. DNA content of this tumor in fresh state by flow cytometry disclosed diploidy with low synthetic phase fraction (9.8%) (Fig. 6).

Two years after surgery, the brain tumor mass recurred. Histological finding was similar to the first biopsy, but multinucleated giant cells and mitoses were focally presented. However, Ki-67 labelling index was still less than 1% positivity. Flow cytometric analysis revealed DNA diploidy pattern. At follow up examination, 4 years after the first operation, the patient is developing normally.

DISCUSSION

DCAI was first described as a distinct pediatric neo-

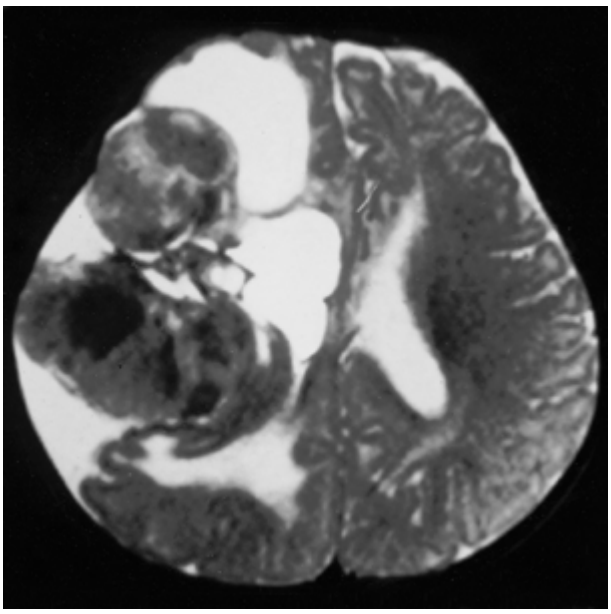

Fig. 2. MR T2-weighted image of brain demonstrated a heterogeneous signal in solid and cystic mass.

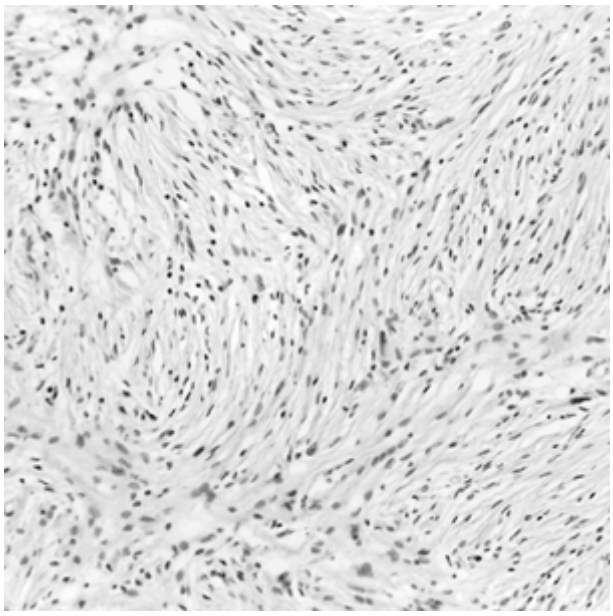

Fig. 3. The neoplastic cells were arranged in fascicle and whorls forming a storiform pattern (H&E, ×100).

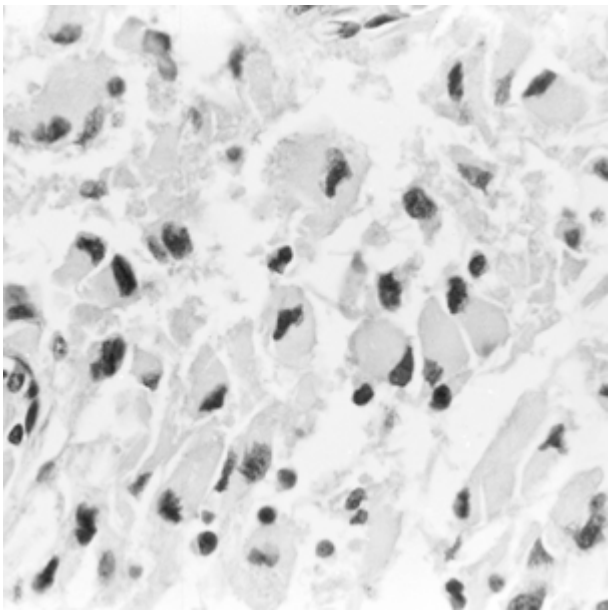

Fig. 4. Some neoplastic cells revealed astrocytic appearance having abundant eosinophilic cytoplasm with eccentric nuclei (H&E, ×400).

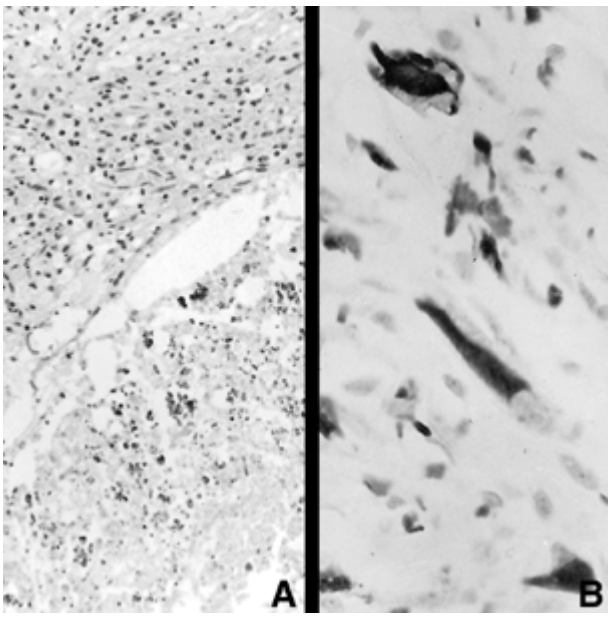

Fig. 5. (A) Focal necrosis and microcalcification (H&E, ×40). (B) Both spindle and polygonal neoplastic cells were positive for GFAP (×400).

plasm occurring under 1 year of age by Taratuto et al. (2). These cases were composed of a GFAP-positive astrocytic component without neuronal participation intermixed with a dense dural stroma, and revealed only astrocytic component without neuronal participation. Because of their rarity, debate exists over their nosologic position

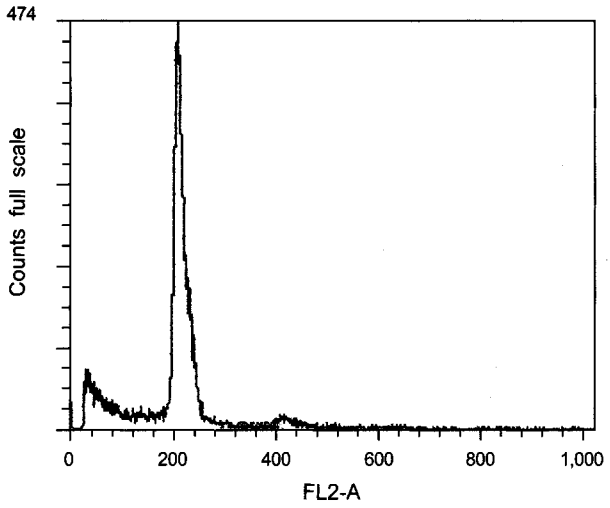

Fig. 6. Flow cytometric analysis of tumor revealed DNA diploidy pattern (CV=4.1%).

relative to entities such as desmoplastic infantile ganglioglioma (DIG) and gliofibroma (3-6). VandenBerg et al., who coined the term DIGs, suggested that superficial cerebral astrocytomas were either incomplete DIGs with differentiation restricted to the astrocytic line, or true gangliogliomas, having not identified the neuronal component (5). However, even after examination for neuronal differentiation using silver impregnation and immunohistochemical stain, no neuronal component was found in the original cases.

DCAI and DIG are almost identical with respect to age distribution, radiologic finding, macroscopic appearance, main histological features, and prognosis. Both tumors are usually found prior to 18 months of age, usually within the first 4 months of life. It is more common in males than in females. Seizure is the common mode of presentation. These tumors usually involve the parietal or frontal lobes (5). The superficial portions have a variable attachment to the dura. Typical imaging features are large cystic and small cortical solid component which is enhanced by contrast medium intensely. Those are apposed to a meningeal surface and/or contrast enhancement along the meningeal side of the mass (8). None of them communicated with the ventricles. In this case, the outer wall of the cyst was focally continued with the CSF space. This finding is probably caused by entrapment of CSF, probably in the subarachnoid space by some check-valve mechanism (9). Similar mechanisms explain the etiology of the intraparenchymatous, disproportionately large cysts in DCAI, because the leptomeninges were commonly involved in the tumor (5). The only difference between DCAI and DIG is the presence of neurons or neuronal differentiation in the latter. The histologic

appearance resembles a cellular, mesenchymal tumor, raising the differential diagnosis of meningeal neoplasm but the strong GFAP immunostaining gives unequivocal support to the glial nature of the tumor cells (2).

There is an important correlation between the neoplastic astrocytes and desmoplastic stroma in DCAI. The histogenesis of childhood desmoplastic tumors remain controversial. Some of the mechanisms try to explain the production of basal lamina and collagen in the purely astrocytic tumors, including aberrant glial metaplasia, meningial fibroblastic participation, and involvement of subpial astrocytes which are known to produce basal lamina in the normal brain (5). Astrocytes are capable of producing laminin, type-IV collagen and fibronectin which are essential components of the basal lamina structure (6, 10, 11). The components of the extensive tumor basal lamina may contribute in an autocrine fashion to the slow growth of these lesions (6). This phenomenon is related to the good prognosis of DCAI. The basal lamina of the glial limitans externa at the pial-glial junction is similar to those of other basal laminae (12). Therefore, it has been postulated that the DCAI arises from subpial astrocytes (6). In vitro studies have demonstrated that both immature astrocytes and leptomeningeal cells have the ability to produce many macromolecules of the basal lamina (13), and have demonstrated that the extracellular matrix proteins inhibit the growth and promote the differentiation of malignant glioma cells (10). The presence of large amounts of external laminal material and collagen fibers between neoplastic astrocytes, corresponding to the reticulin fibers seen by light microscopic study. The pleomorphic xanthoastrocytoma (PXA) also has a superficial cerebral location with leptomeningeal involvement and contains a rich reticulin-basal lamina meshwork (3). It also exhibits many similarities with the DCAI. Both tumors are often cystic and seem to have a good prognosis (14). Although DCAIs contain spindle-shaped cells and gemistocytic cells, lipidized cells are sporadic and the degree of pleomorphism is not as pronounced as in PXAs. The essential difference is the age of PXA detection, and the pleomorphic and usually xanthomatous appearance of its astrocytes. The coexistence of ganglioglioma and PXA within a single lesion has been documented (14-17). The capacity of PXA for malignant transformation have become increasingly appreciated, whereas such behavior in ganglion cell tumors is exceptional.

Most reported DCAIs did not have increased mitotic activity, severe pleomorphism, necrosis, and any other strong evidence favoring malignancy, but there were foci of micronecrosis in this case. Aydin et al. reported a case of clinically benign DCAI with high mitotic rate, cellular pleomorphism and an elevated S-phase fraction (13). Despite their large size and presumably rapid growth rate, DCAI have a generally good prognosis. Recurrence-free intervals have ranged from 6 months to 14 years. Surgical mortality and morbidity have been high due to hypervascularity of the tumors. None the less, if total surgical resection can be achieved, further therapy may not be needed (18, 19).

We suggest that the recurrence of this case is related to postoperative remnant neoplasm or a presence of micronecrosis. DCAI is a rare but quite interesting neoplasm which leads us to look at the glia-matrix interaction to better understand the growth and differentiation characterastics of the astrocytes.

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