***Subependymal Giant Cell Astrocytoma
Associated with Tuberous Sclerosis:
With Special Reference to Cell Kinetic Studies
—Case Report—***

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Abstract

The authors report a case of subependymal giant cell astrocytoma associated with tuberous sclerosis in a 15-year-old boy. Computed tomographic scans showed a large intraventricular mass with peritumoral calcification and a cyst in the left lateral ventricle. Left dominant unilateral hydrocephalus was also revealed. Magnetic resonance images clearly demonstrated the lesion. The tumor was subtotally removed and a ventriculoperitoneal shunt was performed because of the hydrocephalus. The proliferation potential was assessed by measuring the bromodeoxyuridine (BUDR) labeling index employing the *in vitro* labeling method, and determining the deoxyribonucleic acid (DNA) content by flowcytometry. BUDR-positive cells were found to be rare, and the DNA histogram demonstrated no evidence of high proliferative activity or aneuploidy.

Key words: subependymal giant cell astrocytoma, BUDR, flowcytometry

Introduction

Subependymal giant cell astrocytoma is considered morphologically to be a benign tumor, showing mitotic figures or endothelial proliferation only infrequently. However, to our knowledge, the cell kinetics of this tumor have not been investigated. In this study, we describe a case of subependymal giant cell astrocytoma associated with tuberous sclerosis. Moreover, we investigated and evaluated the proliferative activity of a subependymal giant cell astrocytoma by *in vitro* labeling using anti-bromodeoxyuridine (BUDR) monoclonal antibody and by flowcytometric deoxyribonucleic acid (DNA) analysis of paraffin-embedded material.⁴⁻⁶⁾

Case Report

A 15-year-old boy was admitted to our hospital in April, 1987, complaining of severe headache and vomiting. At the age of 1 month, angioma and angiofibroma on the cheek, and white, leaf-shaped maculae on his back had been noted, and diagnosed as tuberous sclerosis. Despite slight mental retardation, he had entered school and performed well.

On admission, physical examination demonstrated the dermatological abnormalities as described above. Neurological examination produced no remarkable findings except for bilateral papilledema. Computed tomographic (CT) scans revealed a large, markedly enhanced intraventricular mass with peritumoral calcification and a cyst in the left lateral ventricle, accompanied by left dominant unilateral hydro-

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Fig. 1 *upper*: Precontrast CT scans revealing a large intraventricular mass with calcification in the left lateral ventricle. *lower*: Postcontrast CT scans demonstrating a greatly enhanced mass accompanied by cyst and hydrocephalus.

Fig. 2 *left*: Axial T_1 -weighted MR image revealing a hypointense region near the left lateral ventricle. *right*: T_2 -weighted MR image demonstrating a high signal intensity in same region.

cephalus (Fig. 1). An axial T_1 -weighted magnetic resonance (MR) image revealed a hypointense region near the left lateral ventricle, and a T_2 -weighted MR image demonstrated a high signal intensity (Fig. 2). Angiography showed a lightly stained shadow in the capillary and venous phases. The preoperative

Fig. 3 Photomicrograph showing a mixture of gemistocytic and multinucleated cells (arrow). No morphological evidence of malignancy such as mitosis or endothelial proliferation is shown. The S-phase fraction of the tumor accounted for less than 1%. Anti-BUdR stain, $\times 200$.

diagnosis was subependymal giant cell astrocytoma.

He underwent a craniotomy *via* the right contralateral midline transcassal approach. A whitish-gray, soft and vascularized tumor was found to occupy the anterior part of the left lateral ventricle and was subtotally removed. Two weeks later, hydrocephalus developed, so a ventriculoperitoneal shunt operation was performed.

Histologically, many tumor cells were gemistocytic with plump cytoplasm, and multinucleated giant cells were also observed in some places (Fig. 3). No morphological evidence of malignancy such as mitosis or endothelial proliferation was present. In sections stained for glial fibrillary acidic protein and vimentin, cells were stained moderately and mildly, respectively. Positive reaction to 68-kDa neurofilament staining was located in the cytoplasm of globoid or angulated cells with large cytoplasm. The histological diagnosis was subependymal giant cell astrocytoma. The *in vitro* labeling method using BUdR⁴⁻⁶⁾ showed BUdR-positive cells were rare and the S-phase fraction of this tumor accounted for less than 1%.

Flowcytometric DNA analysis using ethanol-fixed paraffin-embedded material⁴⁾ was performed. No aneuploid line was observed and the populations of S and G_2M phases were very small (Fig. 4).

Postoperatively, no neurological deficit was observed, and he was subsequently able to return to school. No relapse has occurred during the 2.5 years since the tumor removal.

Fig. 4 DNA histogram of flowcytometric DNA analysis using ethanol-fixed paraffin-embedded BUdR labeled specimen. No aneuploid line was observed. C: channel number.

Discussion

Generally, surgical removal only is an adequate treatment of subependymal giant cell astrocytoma because this tumor is benign in its clinical course and morphology.^{2,8)} We consider that surgical removal is the best method, even if only subtotal, because a tumor near the foramen of Monro tends to cause hydrocephalus easily³⁾ and the possibility of malignancy or tumor bleeding cannot be ruled out. Some cases of malignant glioma¹⁾ combined with tuberous sclerosis or cases of massive tumor hemorrhage⁷⁾ in subependymal giant cell astrocytomas have been reported.

The investigation into proliferative activity in the present case showed the labeling index was extremely low and the DNA histogram demonstrated no

aneuploidy and a low percentage of cells in the S and G₂M phases. These results suggest that this tumor has a low proliferative potential.

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