Anaplastic astrocytoma and anaplastic oligodendroglioma occurring 6 years after subtotal resection of a central neurocytoma

Case report

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The authors present the case of a 51-year-old man who presented with an anaplastic astrocytoma and anaplastic oligodendroglioma that developed 6 years after subtotal resection of a central neurocytoma in his right lateral ventricle. He had received neither radiation therapy nor chemotherapy after the original resection. On readmission, neuroimaging revealed a mass in the right parietal lobe and a diffuse lesion in the right temporal lobe, insula, and corona radiata. Because both lesions extended to the right lateral ventricle wall, they were regarded as recurrent rather than metachronous tumors. Histological examination revealed anaplastic oligodendroglioma in the parietal lobe and anaplastic astrocytoma in the insula. One year later, the anaplastic astrocytoma was found to have transformed into a glioblastoma multiforme. Fluorescence in situ hybridization analysis and immunohistochemical examinations detected deletions of the 1p36 and 19q13 loci, and nuclear accumulation of TP53 protein in the anaplastic oligodendroglioma but not in the glioblastoma multiforme. These findings suggest that central neurocytoma or progenitor cells have the potential for oligodendrocytic and astrocytic transformation with different genetic aberrations. (DOI: 10.3171/JNS-07/07/0185)

KEY WORDS • anaplastic astrocytoma • anaplastic oligodendroglioma • central neurocytoma

CENTRAL neurocytomas are a recently described8 rare neoplasm type that accounts for approximately 0.25% of tumors of the CNS.16 In general, central neurocytomas are regarded as having benign biological behavior and a favorable prognosis.9,27 However, cases of recurrence and rapid progression have been reported.2,15,17,18,22,23 Interestingly, the recurrent tumors exhibit various histological features5,7,21,22,29 such as less differentiated central neurocytomas,22 more differentiated central neurocytomas occurring as gangliocytomas,21 and central neurocytomas with glial differentiation and craniospinal dissemination.1,5

In our patient, anaplastic astrocytoma and anaplastic oligodendroglioma developed 6 years after resection of the central neurocytoma.

Case Report

History and First Presentation. This 45-year-old man presented to our institution after suffering a head injury in October 1994. On admission, no neurological deficits were identified. However, on computed tomography a calcified lesion was revealed in the right lateral ventricle (Fig. 1A). On T1-weighted MR imaging with Gd-DTPA enhancement and on T2-weighted MR imaging, a heterogeneous mass was revealed in the right lateral ventricle (Fig. 1B). The patient underwent subtotal resection via the transcallosal approach.

First Histological Examination. Histological examination of the surgical specimen revealed small round cells with clear cytoplasm and uniform round nuclei embedded in a fibrillary background. Honeycomb architecture and anuclear zones were observed. No cellular pleomorphisms, mitotic cells, vascular proliferations, or necrotic cells were found (Fig. 1D). Immunohistochemical studies revealed diffuse expression of synaptophysin in the cytoplasm in a neuropil pattern (Fig. 1E) but no expression of GFAP (Fig. 1F). Monoclonal antibody staining with MIB-1 showed expression of Ki 67 antigen in 0.5% of cells. The histological diagnosis was central neurocytoma.

Postoperative MR imaging showed residual tumor, but no radiation therapy or chemotherapy was administered. The residual tumor had disappeared spontaneously 6 months af-
ter subtotal resection. No evidence of recurrence was de-
tected on follow-up MR images obtained in March 2000
(Fig. 1C).

Second Presentation. When he was 51 years of age, the
patient presented again with a deep sensation distur-
bance in the left upper limb in October 2000. On T1-weighted MR
imaging with Gd-DTPA, an enhanced lesion was revealed
in the right parietal lobe, and on T2-weighted MR imaging
a diffuse lesion in the right temporal lobe, insula, and coro-
na radiata could be seen (Fig. 2A–C). Axial and coronal T2-
weighted MR imaging demonstrated that the high-intensity
areas of both lesions were in contact with the right lateral

![Fig. 1. A: Axial computed tomography scan obtained at admission demonstrating an intraventricular mass lesion with
calcification. B: Axial T1-weighted MR image with Gd-DTPA (left) and axial T2-weighted MR image (right) obtained
at admission demonstrating a mixed intensity mass in the right lateral ventricle. C: Axial T1-weighted MR image with
Gd-DTPA (left) and a T2-weighted MR image (right) obtained 5 years after initial resection demonstrating no enhanced
lesions or abnormal areas of high intensity. D: Photomicrograph showing tumor cells with round nuclei and clear cyto-
plasm proliferating in a honeycomb architecture. H & E, original magnification × 100. E: Immunohistochemical stain-
ing showing synaptophysin expression in the cytoplasm. Original magnification × 200. F: Immunohistochemical stain-
ing showing no detectable expression of GFAP, except in reactive astrocytes. Original magnification × 200.

![Fig. 2. A: Axial T1-weighted MR images with Gd-DTPA obtained at the first recurrence showing an enhanced lesion
in the right parietal lobe and an unenhancing low-intensity lesion in the right temporal lobe. B and C: Axial (B) and coro-
nal (C) T2-weighted MR images demonstrating a diffuse lesion in the right temporal lobe, insula, and corona radiata, and
high intensity areas of both lesions in contact with the right lateral ventricle wall. D: Axial T1-weighted MR image with
Gd-DTPA enhancement (left) and T2-weighted MR image (right) at second recurrence showing the enhanced lesion in the
right temporal lobe.]

ventricle wall (Fig. 2B and C). Gross-total resection of the mass in the right parietal lobe and stereotactic biopsy of the diffuse lesion in the right insula were performed.

Second Histological Examination. Histological examination showed that the specimen obtained from the right parietal lesion consisted of round small cells with clear cytoplasm, proliferating with a lobar pattern in a fibrous matrix. Atypical histological features including high cellularity, pleomorphism, high mitotic activity, microvascular proliferation, and areas of necrosis were noted (Fig. 3A). Immunohistochemical staining showed no expression of GFAP (D, ×400), but expression of nestin (G, ×400). Nuclear accumulation of TP53 protein was found (J, ×400). B, E, H, and K: Photomicrographs of right insula anaplastic astrocytoma tissue demonstrating diffuse proliferation of spindle-shaped cells in a loose fibrous matrix. Mitosis and nuclear atypia were present (B; H & E, original magnification ×200). There was expression of both GFAP (E, ×400) and nestin (H, ×400), but nuclear accumulation of TP53 protein was not found (K, ×400). C, F, I, and L: Photomicrographs of right temporal glioblastoma tissue demonstrating diffuse proliferation of pleomorphic cells and pseudopalisading necrosis (C; H & E, original magnification ×200). There was expression of GFAP (F, ×400) and nestin (I, ×400), but no nuclear accumulation of TP53 protein (L, ×400). M: Fluorescence in situ hybridization analysis of tissue from the right parietal anaplastic oligodendroglioma showing allelic loss of 1p36 (upper panel) and 19q13 loci (lower panel). The green areas show the SpectrumGreen-labeled probe for 1q25 (upper panel) or 19p13 (lower panel). The red areas show the SpectrumOrange-labeled probe for 1p36 (upper panel) or 19q13 (lower panel). N: Fluorescence in situ hybridization analysis of tissue from the right temporal glioblastoma multiforme showing no allelic loss of 1p36 (upper panel) or 19q13 (lower panel) loci. The green areas show the SpectrumGreen-labeled probe for 1q25 (upper panel) or 19p13 (lower panel). The red areas show the SpectrumOrange-labeled probe for 1p36 (upper panel) or 19q13 (lower panel).

The histological diagnosis of the parietal lesion was anaplastic oligodendroglioma. Histological examination of a biopsy specimen from the right insula revealed diffuse proliferation of spindle-shaped cells within a loose fibrous matrix. One or two mitotic cells per 10 hpf's and nuclear atypia were also found (Fig. 3B). Immunohistochemical examination revealed no expression of synaptophysin, but expression of GFAP and nestin was detected (Fig. 3E and H). Nuclear accumulation of TP53 protein was found in less than 5% of cells (Fig. 3K). Expression of Ki 67 antigen in 27.8% of cells was noted on staining with MIB-1 monoclonal antibody. The histological diagnosis of the diffuse lesion in the right insula was anaplastic astrocytoma.

Treatment. Chemotherapy with nimustine hydrochloride (100 mg/m²) and radiation therapy to the right hemisphere and bilateral lateral ventricles were administered. As a result, the diffuse lesion in the right temporal lobe disap-
peared. One year later, however, MR imaging with Gd-DTPA demonstrated a new enhanced lesion in the right temporal lobe (Fig. 2D). The patient underwent a right temporal lobectomy.

Histological examination of the specimen from the temporal lobectomy revealed poorly differentiated pleomorphic cells of a high cellularity with significant areas of mitosis, vascular proliferation, and pseudopapilisading necrosis (Fig. 3C). Immunohistochemical examination revealed expression of GFAP and nestin (Fig. 3F and I). Nuclear accumulation of TP53 protein was found in less than 5% of cells (Fig. 3L). The histological diagnosis of the recurrent temporal lesion was glioblastoma multiforme. Retention of both 1p36 and 19q13 loci (Fig. 3N) was revealed on fluorescence in situ hybridization analysis.

**Discussion**

There are two proposed mechanisms to explain the development of two histologically distinct tumors 6 years after complete remission of a central neurocytoma. First, the tumors could have developed independently of the central neurocytoma as metachronous tumors. Metachronous gliomas are known to develop spontaneously, especially in the presence of neurofibromatosis Type I, multiple sclerosis, or previous irradiation. In a previously reported case, an anaplastic astrocytoma developed in the right basal ganglia and temporal lobe of a patient 8 years after partial resection and irradiation of a central neurocytoma. However, the patient in the present study did not have a history of any of these predisposing factors.

Second, central neurocytoma or its progenitor cells may migrate and transform into astrocytic and oligodendrocytic tumors in the temporal and parietal lobes. Immunohistochemical, electron microscopy, and electrophysiological studies have demonstrated that central neurocytoma exhibits astrocytic, oligodendrocytic, and neuronal characteristics. These findings suggest that central neurocytomas could originate from multipotent progenitor cells located in the subventricular zone and retain the capacity for multipotent differentiation. In our patient, the anaplastic oligodendroglioma and anaplastic astrocytoma had developed in contact with the ventricle wall, suggesting that the tumor progenitor cells in the ventricle wall could migrate into the parietal and temporal regions.

Nestin is a commonly used marker for undifferentiated cells in the developing CNS and for dedifferentiated cells in CNS tumors. Therefore, we performed immunohistochemical staining for nestin expression to evaluate the involvement of undifferentiated progenitor cells in the development of the anaplastic oligodendroglioma and anaplastic astrocytoma. Considering that both of the recurrent tumors expressed nestin, dedifferentiated or undifferentiated progenitor cells may have migrated from the ventricle wall to the parietal and temporal lobes and then transformed into astrocytic and oligodendroglial cells. In addition, nuclear accumulation of TP53 protein was overexpressed only in the anaplastic oligodendroglioma cells. Unfortunately we could not analyze p53 expression in the specimen of central neurocytoma tissue because the biopsy sample was insufficient; however, inactivation of the p53 pathway is unusual in the development of a central neurocytoma. Therefore, inactivation of p53 may have been involved in the transformation of the progenitor cells into oligodendroglioma in this case.

Allelic loss of the 1p and 19q loci were found in the anaplastic oligodendroglioma, but not in the glioblastoma in this case. Similarly, synchronous oligodendroglioma in the frontal lobe and pilocytic astrocytoma in the cerebellum have been reported with allelic loss of the 1p36 locus in oligodendroglioma, but not in pilocytic astrocytoma cells. We were not able to analyze the status of 1p36 and 19q13 loci in the central neurocytoma because of an insufficient sample; however, allelic loss of 1p and 19q loci have not been detected in other cases of central neurocytomas reported in the literature.

We speculate that allelic loss at 1p or 19q loci in the progenitor cells and inactivation of p53 are involved in the development of oligodendrogliomas from progenitor cells, and that distinct unknown genetic aberrations are involved in astrocytic or neuronal differentiation. Further detailed molecular analysis may clarify the mechanisms of transformation and differentiation in these tumors.

**References**

Transformation of central neurocytoma


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