

# ***Glioblastoma Detected at the Initial Stage in its Developmental Process***

## **—Case Report—**

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### **Abstract**

**A 73-year-old male presented with a glioblastoma that was detected at the initial stage in the developmental process. He suffered cerebral infarction. Follow-up magnetic resonance (MR) imaging showed no abnormality. Ten months later, he had transient right hemiparesis. Diffusion-weighted and fluid-attenuated inversion recovery (FLAIR) MR imaging showed a hyperintense area in the left frontal lobe. The diagnosis was cerebral infarction and antiplatelet drug treatment was begun. The patient's right hemiparesis subsided. Ten days later, right hemiparesis reappeared. Diffusion-weighted and FLAIR MR imaging showed an enlarged hyperintense area in the left frontal lobe. Three weeks after the onset of right hemiparesis, MR imaging revealed an irregular ring-enhanced mass lesion that had further increased in size. The diagnosis was brain abscess and antibiotic treatment was initiated. However, the lesion did not respond and had further enlarged 5 weeks after the onset of right hemiparesis. The lesion was partially removed and the histological diagnosis was glioblastoma with Ki-67 labeling index of 26%. After surgical treatment, the patient received irradiation of 60 Gy and chemotherapy with temozolomide. Follow-up MR imaging showed regrowth of the tumor and aggravation of edema. The rapid progression of the tumor ultimately resulted in the patient's death 12 months after the onset of right hemiparesis. Diffusion-weighted imaging is a good method for the early detection of glioblastoma.**

Key words: glioblastoma, developmental process, diffusion-weighted magnetic resonance imaging, cerebral infarction, brain abscess

### **Introduction**

Glioblastoma may occur de novo or secondary to another tumor. The developmental process of a de novo glioblastoma remains obscure. We found only three previous reports in which the developmental process was observed at an early stage.<sup>5,18,23)</sup> There is accordingly no consensus regarding the best method of detecting a glioblastoma during its development. The early diagnosis of glioblastoma using magnetic resonance (MR) imaging is difficult. One case of de novo glioblastoma appeared as a well circumscribed hyperintense lesion without mass effect on T<sub>2</sub>-weighted MR imaging, which could not be differentiated from cerebral infarction, since gadolinium caused no contrast enhancement on T<sub>1</sub>-weighted MR imaging. Three months after onset, gadolinium disclosed a small enhanced lesion.<sup>23)</sup> Another case appeared as a poorly demarcated, hyperintense area on T<sub>2</sub>-weighted MR imaging, with no visible abnormalities or contrast enhancement by gadolinium on T<sub>1</sub>-weighted MR imaging. About 4 months after onset, brain MR imaging disclosed a ring-shaped, irregular enhanced lesion.<sup>18)</sup> Diffusion-weighted

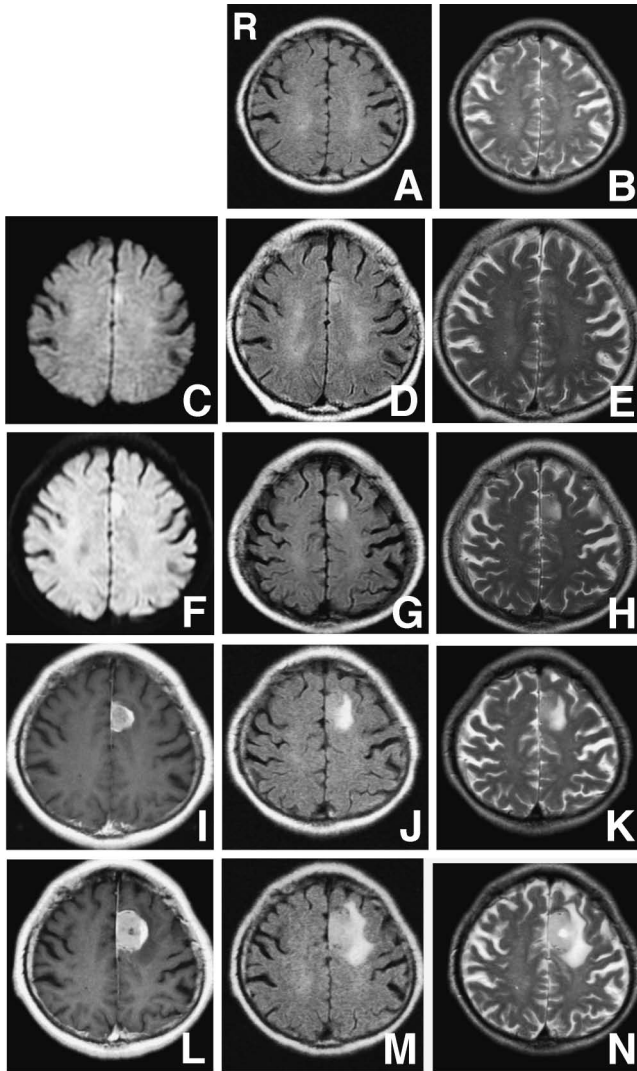
imaging and the tumor apparent diffusion coefficient may provide useful information about the anaplastic grade of glioblastomas.<sup>1,3,11,13)</sup> However, the differential diagnosis of a cerebral infarction and an abscess is also very important.<sup>11,17)</sup>

We report a case of de novo glioblastoma which was detected early in the course by diffusion-weighted imaging.

### **Case Report**

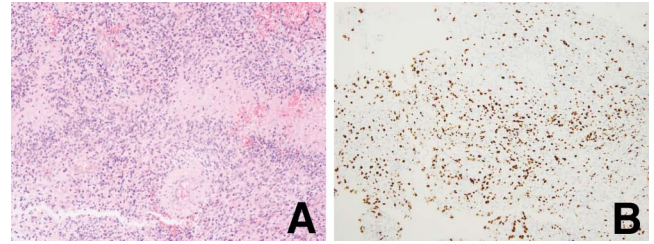
A 73-year-old male had previously suffered cardiac infarction, hypertension, and cerebral infarction. Follow-up head MR imaging using a 1.5 T MR unit showed no abnormality (Fig. 1A, B). Ten months later, the patient suffered transient right hemiparesis and was hospitalized. Diffusion-weighted and fluid-attenuated inversion recovery (FLAIR) MR imaging showed a hyperintense area in the left frontal lobe (Fig. 1C-E). The diagnosis was cerebral infarction. The patient's symptom subsided after treatment with glycerol, edaravone, and argatroban, followed by antiplatelet agent.

Ten days later, right hemiparesis reappeared and he was re-admitted. Diffusion-weighted and FLAIR MR imaging showed a hyperintense area in the left frontal lobe, which



**Fig. 1** Fluid-attenuated inversion recovery (FLAIR) (A, D, G, J, M), T<sub>2</sub>-weighted (B, E, H, K, N), diffusion-weighted (C, F), and T<sub>1</sub>-weighted with gadolinium (I, L) magnetic resonance images taken before and after onset of the symptoms. A, B: Images were taken 10 months before the onset of symptoms and show no abnormality. C–E: Images were taken at the onset of symptoms. Note the hyperintense area in the left frontal lobe on the diffusion-weighted and FLAIR images. F–H: Images were taken when right hemiparesis reappeared 2 weeks after symptom onset. Diffusion-weighted and FLAIR images show an increase in the size of the hyperintense area in the left frontal lobe, compared with the previous images. The lesion is also visible on the T<sub>2</sub>-weighted image. I–K: Images were taken 3 weeks after symptom onset. All images confirm a further increase in the size of the irregular ring-enhanced mass lesion. L–N: Images were taken 5 weeks after symptom onset. Note the lesion has further increased in size.

was larger than on the previous images. T<sub>2</sub>-weighted MR imaging also detected the lesion (Figs. 1F–H). Three weeks after the onset of right hemiparesis, MR imaging showed an irregular ring-enhanced mass lesion that had further increased in size (Fig. 1I–K). The diagnosis was brain ab-



**Fig. 2** A: Photomicrograph of the tumor which predominantly consists of proliferated atypical cells with irregular syncytium and chromatin-condensed heterogeneous nuclei. Hyperplasia of the vascular endothelium and pseudopalisading necrosis formation are also prominent. The tumor is a glioblastoma. Hematoxylin and eosin stain, original magnification  $\times 100$ . B: Photomicrograph showing the Ki-67 labeling index is 26%. Ki-67 stain, original magnification  $\times 100$ .

scs and antibiotic therapy was initiated. However, 5 weeks after the onset of right hemiparesis, the lesion had not responded to treatment and continued to increase in size (Fig. 1L–N). Therefore, the patient was admitted to our neurosurgical department with a diagnosis of possible tuberculoma or brain tumor.

Neurological examination found right hemiparesis, especially in the lower limb. The diagnosis was brain tumor. The patient underwent partial tumor resection 7 weeks after symptom onset. A vascular, soft, gray tumor was located in the left premotor and motor area. Histological examination revealed predominant proliferation of atypical cells with irregular syncytium and chromatin-condensed heterogeneous nuclei (Fig. 2A). Hyperplasia of the vascular endothelium and pseudopalisading necrosis formation were also prominent. The Ki-67 labeling index was 26% (Fig. 2B). Immunohistochemical staining for glial fibrillary acidic protein was positive. The histological diagnosis was glioblastoma.

The surgical treatment was followed by irradiation with 60 Gy and chemotherapy with temozolomide. Follow-up MR imaging showed regrowth of the tumor and aggravation of edema. Motor aphasia appeared and his right hemiparesis was aggravated with gait disturbance. Rapid progression of the tumor ultimately resulted in the patient's death 12 months after the onset of symptoms.

## Discussion

In our patient, diffusion-weighted imaging detected the glioblastoma in the early stage, whereas T<sub>1</sub>- and T<sub>2</sub>-weighted MR imaging showed almost no abnormality. Diffusion-weighted MR imaging is a useful technique for assessing a brain tumor,<sup>21)</sup> and shows glioblastoma, anaplastic astrocytoma, lymphoma, and metastases as hyperintense lesions, but these types of tumors are indistinguishable.<sup>3)</sup> Tumor cellularity correlates well with the intensity on diffusion-weighted imaging.<sup>11,21)</sup> Diffusion-weighted imaging can easily detect high-grade glioma, but not necessarily low-grade glioma.

Diffusion-weighted imaging also shows abscess or acute

cerebral infarction as a hyperintense lesion.<sup>2)</sup> Diffusion-weighted MR imaging shows almost no signal intensity abnormality in stroke patients more than 2 weeks after symptom onset since pseudo-normalization is occurring during the subacute stage of cerebral infarction.<sup>2)</sup> In our patient, cerebral infarction could be ruled out because diffusion-weighted imaging revealed continuous enlargement of the lesion.

Differentiation of brain abscess from malignant glioma can be difficult based on diffusion-weighted MR imaging.<sup>4,10,15)</sup> Brain abscess appears as markedly hyperintense and malignant glioma appears as moderately hyperintense on diffusion-weighted imaging.<sup>4,10,15,16)</sup> Furthermore, brain abscess appears as homogeneously hyperintense and malignant glioma appears as heterogeneously hyperintense.<sup>15)</sup> Diffusion-weighted imaging showed the lesion in our patient as moderately hyperintense and heterogeneous. Therefore, retrospective differential diagnosis was possible between malignant glioma and abscess. MR spectroscopy is another diagnostic method for the differential diagnosis between abscess and glioblastoma.<sup>15)</sup>

Uptake of L-methyl-<sup>11</sup>C-methionine (<sup>11</sup>C-methionine) is greater in glioma than in intact tissue. Therefore, methionine positron emission tomography (PET) is very useful for the evaluation of gliomas.<sup>7,19,22)</sup> The Ki-67 proliferation index is significantly correlated with <sup>11</sup>C-methionine uptake.<sup>9,22)</sup> Angiogenesis, as assessed by microvessel count, is also correlated with <sup>11</sup>C-methionine uptake.<sup>9,12)</sup> Therefore, methionine uptake is highly useful for detecting gliomas and for differentiating between benign and malignant gliomas.<sup>9,20)</sup> Furthermore, the metabolically active tumor volume (as reflected by methionine uptake) is greater than the volume of gadolinium-diethylenetriaminepenta-acetic acid enhancement in high-grade glioma, and complete resection of the tumor volume indicated by increased methionine uptake prolongs the survival.<sup>6,19)</sup>

FLAIR MR imaging sequence can show the complete extent of infiltrative gliomas with a sharp border.<sup>7,14,22)</sup> The fast FLAIR sequence can provide additional information about tumors with poor contrast enhancement and is useful for the evaluation of low-grade gliomas.<sup>9)</sup> In our case, the glioblastoma was clearly detected by diffusion-weighted MR imaging. However, the lesion was also demonstrated by FLAIR imaging.

Glioblastoma can progress very rapidly, as in our patient. T<sub>2</sub>-weighted and FLAIR MR imaging performed 10 months before the onset of symptoms did not detect the tumor. After detection by diffusion-weighted imaging, the tumor volume increased weekly. Prompt diagnosis is very important in cases of glioblastoma since total removal may be possible with an early and confident diagnosis. Combination of diffusion-weighted and FLAIR MR imaging with <sup>11</sup>C-methionine PET is important for the prompt diagnosis and treatment of glioblastomas.

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