Glioblastoma multiforme with diffusion-weighted magnetic resonance imaging characteristics mimicking primary brain lymphoma

Case report

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The authors report on the first case of corpus callosum glioblastoma multiforme (GBM) with diffusion-weighted (DW) magnetic resonance (MR) imaging findings that mimicked those for lymphoma but with MR spectroscopy results absent of lymphoma characteristics. This 68-year-old man presented with rapid, progressive impairment in short-term memory as well as slow responses and a change in his personality within 3 weeks of admission. Results of cranial computed tomography revealed a slightly hyperdense corpus callosum tumor with bihemispheric involvement. Magnetic resonance images showed a homogeneous mass with strong enhancement. The mass showed water restriction on DW MR images and apparent diffusion coefficient (ADC) maps but no markedly elevated lipid resonance on MR spectroscopy. The patient underwent tumor resection. Results of pathological studies with immunohistochemical analysis confirmed that the lesion was GBM.

Diffusion-weighted MR imaging together with ADC mapping and MR spectroscopy was reported to be useful in differentiating GBM and primary brain lymphoma. The lymphomas were hyperintense to gray matter on DW MR images and isointense to hypointense on ADC maps because of water restriction. In contrast, the GBMs were hyperintense to gray matter on both DW MR images and ADC maps because of the T2 shine-through effect. On MR spectroscopy, lipid resonance was markedly elevated in lymphoma but only slightly elevated in GBM.

KEY WORDS • glioblastoma multiforme • diffusion-weighted magnetic resonance imaging • apparent diffusion coefficient • magnetic resonance spectroscopy

T he differential diagnoses for a corpus callosum tumor with bihemispheric involvement, a so-called butterfly tumor, include GBM and lymphoma. Although lymphoma is one of the differential diagnoses, butterfly lesions are most commonly GBMs. Because conventional MR imaging may sometimes fail to distinguish between these lesions, DW MR imaging combined with ADC mapping, which can characterize water mobility in pathological tissues, has been used in an attempt to classify such tumors.14 Lymphomas are generally hyperintense to gray matter on DW MR images and isointense to hypointense on ADC maps, findings consistent with water restriction due to high cellularity. In contrast, GBMs are generally hyperintense to gray matter on both DW MR images and ADC maps because of a T2 shine-through effect rather than low diffusivity. Thus, high signal intensity of the solid portion of the tumor on DW MR images and low signal intensity on ADC maps favor the diagnosis of lymphoma rather than GBM.4,6,8,13,15 In addition to DW MR imaging and ADC mapping, MR spectroscopy, which provides metabolic information, has also been reported to be useful in the preoperative differentiation of primary brain lymphoma and astrocytoma.7 Markedly elevated lipid resonances have been considered the hallmark of lymphoma.

In this article, we report the neuroimaging findings in a patient with butterfly GBM, which was hyperintense on DW MR images and hypointense on ADC maps but lacked highly elevated lipid resonance on MR spectroscopy. To our knowledge, butterfly GBM with water restriction on DW images, mimicking lymphoma, has never been reported in the literature.

Case Report

History. This 68-year-old man with no prior medical illness began to experience rapid, progressive impairment in
short-term memory within 3 weeks of admission. At the same time, he demonstrated slow responses and a personality change.

Examinations. Computed tomography revealed a homogeneous mass in the genu of the corpus callosum together with bilateral involvement of the frontal lobes. The mass measured approximately 3.5 cm, appearing slightly hyperdense to gray matter and strongly enhanced after the intravenous administration of iodinated contrast medium. Magnetic resonance imaging was performed on a 1.5-tesla imaging system (Vision; Siemens, Erlangen, Germany). On axial T2-weighted MR images (TR 4000 msec, TE 98 msec), the mass was homogeneous and isointense to slightly hyperintense to gray matter. There was associated perifocal edema in the frontal lobes bilaterally. Diffusion-weighted MR imaging was performed using a spin echo–echo planar imaging sequence with the following parameters: TR, 5100 msec; TE, 137 msec; diffusion gradient encoding, three orthogonal directions; b values, 0, 500, and 1000 seconds/mm2; slice thickness, 5 mm; and matrix size, 96/11003128. The respective isotropic images and ADC maps were generated using software integrated with the MR imaging system. The mass was homogeneously hyperintense on DW MR images (Fig. 1A) and hypointense on ADC maps (Fig. 1B), indicating the presence of water restriction. A circular region of interest was placed in the corpus callosum. Data were processed using software provided by the manufacturer. The MR imaging spectra (Fig. 2) showed a high Cho peak and low Cr and NAA peaks. There was a slight increase in lipid resonance at 1.2 to 1.3 ppm. Calculated metabolite ratios for NAA/Cr, NAA/Cho, Cho/Cr, and lipids/Cr were 0.29, 0.08, 3.53, and 0.29, respectively.

Operation and Pathological Findings. A brain biopsy was performed and the results of frozen-section studies revealed a GBM. Therefore, a bilateral frontal craniotomy and tumor removal were performed. Results of the pathological studies (Fig. 3) demonstrated increased cellularity in the tumor cells with moderate nuclear pleomorphism. The vascularity of the tumor was increased and focal hemorrhagic necrosis was also apparent. Results of the immunohistochemical analysis demonstrated that tumor cells were negative for leukocyte common antigen CD45 and focally positive for glial fibrillary acidic protein. Thus, the diagnosis of GBM was confirmed.

Discussion

Diffusion-weighted MR imaging provides information on the mobility of water molecules in tissue. Highly mobile extracellular water shifts into cells, producing cytotoxic edema in the early stages of ischemic stroke. High sensitivity (94%) and specificity (100%) have been reported in the use of DW MR imaging to diagnose acute cerebral infarction. More recently, potential applications for DW MR imaging of central nervous system tumors have been established. A high signal intensity on DW MR images and a low signal intensity on ADC maps (that is, a decreased ADC value) imply the occurrence of water restriction and have been observed in lymphoma, medulloblastoma, and primitive neuroectodermal tumor. In the study by Gauvain, et al., the authors revealed a clear distinction in ADC values between gliomas and embryonal tumors (primitive neuroectodermal tumor, medulloblasto-
ma, and malignant teratoid-rhabdoid tumor). Tumor cellularity has been reported to be a major determinant of ADC values in brain tumors.\textsuperscript{5,6,17} Guo, et al.,\textsuperscript{6} compared the ADC values and the nuclear/cytoplasmic ratios in high-grade astrocytomas (two anaplastic astrocytomas and 15 GBMs) with those in lymphomas. In their study, the mean ADC ratio—that is, ADC values normalized by dividing the ADC value in lymphoma or in high-grade astrocytoma by the ADC value in seemingly normal white matter—in the lymphoma was significantly lower than that in the high-grade astrocytoma. Simultaneously, the mean nuclear/cytoplasmic ratio in lymphoma was significantly higher than that in high-grade astrocytoma. More recently, Yamasaki, et al.,\textsuperscript{17} reported that ADC values in lymphoma were significantly lower than those in GBM and metastatic tumor and concluded that the ADC is particularly useful in differentiating malignant lymphomas from GBMs and metastases. Thus, the presence of water restriction in the solid part of the tumor makes a diagnosis of lymphoma more likely than one of GBM.

Despite previous study data demonstrating the usefulness of the ADC in differentiating lymphoma from GBM, there have been two reported cases\textsuperscript{1} of GBMs, which were hypointense on DW MR images and hypointense on ADC maps—findings similar to those in lymphoma cases. One GBM was located in the left thalamus; the other, in the left parietal lobe. The patient in our case represents the first to harbor a butterfly GBM showing water restriction on DW MR images and ADC maps. The increased tumor cellularity found on pathological examination probably accounts for the water restriction. Given that high cellularity limits water diffusivity, a GBM with comparatively high tumor cellularity cannot be differentiated from a lymphoma by using DW MR images and ADC maps.

The MR spectroscopy images obtained in our patient showed high Cho and low Cr and NAA levels, which is suggestive of a high-grade brain neoplasm. There was a slight increase in lipid resonance at 1.2 to 1.3 ppm. Lipid resonance can be found in either high-grade astrocytoma or lymphoma. In a previous study,\textsuperscript{7} the MR spectroscopy images in all patients with primary brain lymphoma showed massive elevation in lipid resonance, with the lipids/Cr metabolite ratio ranging from 5.3 to 42.6. In contrast, the lipid resonance in solid GBMs in the same study was only slightly elevated, with the lipids/Cr ratio ranging from 0.43 to 0.51. The lipid resonance in the patient in our case was only slightly increased (lipids/Cr ratio 0.29), thus the lesion is more likely to be a GBM than a lymphoma. Lipids are physiologically not detectable in healthy brain and are found in areas of necrosis and in viable solid tissues in high-grade brain malignancies.\textsuperscript{10} Areas of necrosis as small as 3 \times 3 \times 6 \text{ mm} contribute significant lipid levels to the spectra, although such a small area may be difficult to visualize on MR imaging.\textsuperscript{11} Given that necrosis is one of the hallmarks of GBM, spectroscopic detection of lipids may increase tissue specificity on MR spectroscopy. Tumor necrosis and hemorrhage are not frequently seen in an immunocompetent patient with lymphoma. Thus, the mechanism of massive increased lipid resonance in lymphoma is different from GBM. The lipid resonance in lymphoma may be related to an increased turnover of membrane components in activated lymphocytes as well as the presence of numerous macrophages containing cellular debris.\textsuperscript{2}

**Conclusions**

In summary, GBM can appear hyperintense on DW MR images and hypointense on ADC maps because of high cellularity, which mimics primary brain lymphoma. Magnetic resonance spectroscopy may aid in the differentiation of GBM and lymphoma. The absence of markedly elevated
lipid resonance in MR spectroscopy favors the diagnosis of GBM rather than primary brain lymphoma. Larger series are needed to determine whether a combination of DW MR imaging and MR spectroscopy increases the preoperative diagnostic accuracy of GBM and lymphoma.

References

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