Splenial and White Matter Lesions Showing Transiently-reduced Diffusion in Mild Encephalopathy Monitored with MR Spectroscopy and Imaging

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We report the time course of magnetic resonance imaging and spectroscopy of a case with lesions of the splenium and white matter with transiently reduced diffusion in clinically reversible encephalopathy. Initially normal spectroscopy showed slightly elevated choline. Signal abnormality in T2-weighted and fluid-attenuated inversion recovery images persisted for 90 days. Lesions of the splenium and white matter with transiently reduced diffusion in clinically reversible encephalopathy are not always reversible and may reflect heightened glial cell-membrane turnover without neuronal damage.

Keywords: clinically mild encephalopathy, MRI, MRS, reversible splenial lesion, white matter

Introduction

Magnetic resonance (MR) imaging of reversible lesions with transiently reduced diffusion in the splenium of the corpus callosum (SCC) with lateral extension from the splenium into the subcortical white matter has been reported in patients with clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS).1 In previously reported cases of MERS, the lesions, demonstrating abnormal signal intensity disappeared within a short time. A recent case report described a lesion with abnormal signal in the SCC on MR imaging that persisted for over 5 months.2 MR spectroscopy (MRS) of MERS measured simultaneously following the initial MR imaging examination has been reported.3,4 Here, we report follow-up MR imaging and spectroscopy of clinically mild encephalopathy with lesions with transiently reduced diffusion in the splenium and white matter in which initial MRS appeared normal subsequent MR imaging and MRS showed abnormality for 90 days, and neurological symptoms did not reappear after 5 years.

Case Report

A previously healthy 23-year-old woman presented with subacute encephalopathy one month after delivering her first child. She caught a common cold several days before the neurological symptoms occurred. At the onset of flu-like symptoms, her body temperature was 37.8°C and she was subsequently drowsy (Glasgow Coma Scale; E2, V2, M4) for around 24 hours. These symptoms led to a clinical diagnosis of acute encephalopathy. Her neurological symptoms included numbness of the upper and lower limbs, delirium, ataxia, right facial palsy, dysphagia, and dysarthria. She had no family or personal history of neurological disorders. She did not drink alcohol. Results of urinary examination were normal. Blood chemistry revealed normal levels of white blood cells (7180/L), Na (141 mEq/L), and glucose (112 mg/dL). Examination of cerebrospinal fluid revealed normal cell counts and levels of protein and glucose. No serological abnormalities were detected in repeat blood chemistry examinations over her 27-day hospital admission.

MR imaging and spectroscopy were performed 2 days after she demonstrated neurological symp-
toms using a 3-tesla unit (Signa; GE Healthcare, Milwaukee, WI, USA). T$_2$-weighted images (T$_2$WI) and fluid-attenuated inversion recovery (FLAIR) images showed definite hyperintensity in the splenium and genu of the corpus callosum and surrounding white matter that extended laterally from the splenium. T$_1$-weighted images (T$_1$WI) showed hypointensity. Diffusion-weighted images (DWI) showed symmetric hyperintensity in the same area as the lesion that was hyperintense on T$_2$WI and FLAIR images. The apparent diffusion coefficient (ADC) map showed a low diffusion value. No contrast enhancement was seen (Fig. 1a–f). MRS was performed by volume-selective, inversion-recovery, water-suppressed, 90°-180°-90° point resolved spectroscopy with short echo time (TE), (repetition time

**Fig. 1.** Magnetic resonance (MR) imaging and spectroscopy (MRS) obtained 2 days after the first appearance of neurological symptoms (a) Axial T$_2$-weighted image shows hyperintensity in the splenium of the corpus callosum (SCC) and lateral extension from the splenium into the subcortical white matter (arrows). (b) Axial fluid-attenuated inversion recovery image shows SCC hyperintensity and bilateral white matter lesions extending laterally from the splenium into the subcortical white matter (arrows). Voxel indicates the position of MRS measurement. (c) Axial T$_1$-weighted image (T$_1$WI) shows hypointensity of the SCC and white matter lesions (arrows). (d) Diffusion-weighted image shows hyperintensity in the SCC, genu of the corpus callosum, and bilateral white matter (arrows). (e) Apparent diffusion coefficient (ADC) map shows a low diffusion value (arrows). (f) Axial contrast-enhanced T$_1$WI shows no contrast enhancement effect (arrows). (g) MRS measured from the lesion in the white matter (voxel in Fig. 1b) is normal.
MRS focused on the right deep white matter where signal intensity was abnormal on MR imaging. The voxel was set to 20 × 20 × 20 mm in 3 dimensions. MRS showed no definite abnormality (Fig. 1g). In our institution, normal values for N-acetylaspartate (NAA) to creatine (Cr) are 1.68 ± 0.11; for choline (Cho) to Cr, 0.79 ± 0.09; and for myoinositol (MI) to Cr, 0.55 ± 0.13.

We suspected encephalopathy caused by an unknown pathogen and treated the patient for 3 days with intravenous corticosteroid and intravenous fluid and reinstituted a vitamin supplement. She became alert on Day 3, and all neurological symptoms disappeared within one week.

She underwent follow-up MR imaging and MRS on Days 23 and 90. Diffusion MR imaging showed no signal abnormalities on either follow-up MR imaging (Fig. 2a). However, the lesions of the splenium and subcortical white matter remained hyperintense on FLAIR and T2WI on Day 90 (Fig. 2b, c), having almost the same appearance as on Day 23 (not shown). MRS metabolic ratios to Cr measured on Day 23 were 1.65 for NAA/Cr; 1.04 for Cho/Cr; and 0.45 for MI/Cr. Follow-up MRS on both Days 23 and 90 MRS showed elevated Cho peaks without NAA decrease or MI increase (Fig. 2d). Five years later, she consulted the Department of Obstetric Surgery of our university hospital to deliver her second child. Although MR imaging was not performed, she reported no repeat or new neurological symptoms during the 5-year follow-up period.

Discussion

Reversible splenial lesion is a clinical radiological syndrome associated with many diseases or conditions, such as postinfectious disorder, rapid withdrawal of antiepileptic drug, high altitude cerebral edema, and various metabolic disorders. The precise etiology remains unknown. The diagnosis is based on the characteristic reversibility of both the clinical symptoms and MR imaging abnormalities. MR imaging findings of splenial lesions are characteristic in both location and signal abnormality, especially low ADC value. Reversible lesions with transiently reduced diffusion have also been found extended laterally from the splenium into the subcortical white matter and in anterior extension in-
volving the entire corpus callosum; such lesions are designated MERS type 2. The lesion in our case was similar to MERS type 2 with regard to both the clinically benign course and initial MR imaging findings and the DWI time course during follow-up. A previous report described an atypical case of MERS that showed a splenial lesion with transiently reduced diffusion in clinically mild encephalitis but persistent abnormal signal in an SCC lesion in T2WI and FLAIR images. Our case showed persistent abnormal signals in the surrounding white matter as well as the splenium.

MRS is potentially useful for evaluating in vivo metabolic status in the live brain. Shimizu and colleagues reported a case of a transient lesion in the splenium of the corpus callosum that appeared normal on MRS. Another report describes the MRS demonstration of a reversible splenial lesion with elevated lactate (Lac) and MI. Although both cases reported with MRS were measured by a multi-voxel method, the results were completely different. In our case, the initial MRS appeared normal, the same as the MRS findings reported by Shimizu and colleagues, whereas follow-up MRS revealed a slight elevation of the Cho peak. We estimate that the initial normal MRS in the area of reduced diffusion reflects intramyelinic edema and not neuroaxonal damage or severe demyelination. The increase in Cho in follow-up MRS is thought to result from the heightening of cell membrane turnover in diseases with demyelination. Although Hashimoto’s group reported that the remaining abnormal signal in SCC in MERS may reflect gliosis, their speculation was limited to the MR imaging findings alone. Active demyelination initially showed NAA reduction and Cho elevation without MI elevation followed by an elevated MI peak with Cho reduction and NAA recovery in MRS. Moreover, previously reported demyelinating lesions showed various degrees of Cho elevation, NAA reduction, Lac elevation, and MI elevation that depended on the degree and time course of the follow-up, although our case did not show MI elevation on MRS on either Day 23 or 90. This means that massive gliosis was not present in the extensive white matter lesion where MRS was measured. Although it is difficult to define the exact histopathology of our MRS, we speculated that some heightening of glial cell turnover without neuronal damage or massive gliosis may have appeared in the abnormal signal during follow-up.

Diffusion-weighted imaging is particularly helpful in making the diagnosis because it permits detection of early changes in cellular function in the central nervous system. A low ADC value means irreversible cytotoxic edema in ischemic infarction. The reversibility of low ADC values in MERS cannot be attributed to cytotoxic edema, though intramyelinic edema is a possible etiology of MERS. However, a reversible SCC lesion with reduced diffusion has been observed in a 12-day-old neonate. Because of the immaturity of myelination, mechanisms other than intramyelinic edema should be considered. Follow-up MR imaging and spectroscopy in our case suggested the occurrence of some degenerative changes after intramyelinic edema in the residual abnormal signal in white matter.

Takanashi and associates reported the resolution of MERS type 2-exhibiting lesions in the white matter and entire corpus callosum through an isolated lesion of the splenium of the corpus callosum (type 1). They suggested that MERS types 1 and 2 have the same pathology. In our case, normal MRS findings of the white matter surrounding the splenial lesion did not reflect the reversibility of imaging findings, at least at the 90-day follow-up.

Acute disseminated encephalomyelitis (ADEM) should be considered in the differential diagnosis of postinfectious encephalopathy. Reversibility of both the neurological symptoms and MR imaging findings is a common feature of both MERS and ADEM. Although the corpus callosum may be involved in ADEM, these lesions are nearly always asymmetric. Balasubramanya and colleagues showed decreased ADC values without notable increase in Cho/Cr or decrease of NAA/Cr in the acute stage of ADEM findings that might reflect swelling of the myelin sheaths during the initial stage of ADEM.

In conclusion, although our diagnosis in this case may be controversial, we believe the normal metabolic pattern in the area of diffusion abnormality, symmetric appearance of the MR imaging findings, and 5-year stable clinical history of our patient suggest her lesions were MERS type 2. In addition, even if a lesion with abnormal diffusion initially reveals a normal metabolic appearance in MRS, an increase in Cho during the follow-up foretells the future appearance of a metabolic disorder caused by heightened cell membrane turnover.

References
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