Clinically Mild Encephalitis/Encephalopathy with a Reversible Splenial Lesion without Central Nervous System Disturbances: A Case Report

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Patients with clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) on the splenium of the corpus callosum (SCC) present with relatively mild central nervous system disturbances. A 41-year-old man was admitted with fever and headache and, his main symptoms were mild headache and fatigue. There were no neurological focal signs. Brain magnetic resonance imaging (MRI) showed abnormal signals in SCC. We report, for the first time, a MERS patient, detected on MRI, who did not present with central nervous system disturbances. Our experience suggests MERS should be considered as a differential diagnosis in patients with fever of unknown origin.

Keywords: corpus callosum, encephalopathy, fever of unknown origin, magnetic resonance imaging

Background
Patients with clinically mild encephalitis/encephalopathy and a reversible splenial lesion (MERS) usually present with mild central nervous system disturbances, such as seizure, drowsiness, delirium, tremor, ataxia, vertigo, and headache; they usually recover completely within a month without sequelae.1 Brain magnetic resonance imaging (MRI) is a sensitive technique that assists in the diagnosis of encephalitis/encephalopathy. A brain MRI finding of an ovoid reversible lesion in the central portion of the splenium of the corpus callosum (SCC) without any accompanying lesions has been reported in epilepsy patients receiving antiepileptic drugs.2 Hoshino et al advocate the diagnostic criteria of MERS (Table 1).3 It has also been reported in some cases of mild encephalitis/encephalopathy caused by various agents, such as influenza, mumps, rotavirus, adenovirus, human herpesvirus-6, measles virus, Escherichia coli, streptococcus, Salmonella enteritidis, Legionella, Hyponatremia, antiepileptic drug, and acute urinary retention.1–7 To our knowledge, this is the first report of a patient with MERS detected on a brain MRI who did not present with any central nervous system disturbances.

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Case Report

A 41-year-old Japanese man who was previously healthy was admitted at our institution with a 6-day history of headache and intermittent fever up to 38°C. He had already tested negative for the novel strains of the influenza virus by polymerase chain reaction of a nasopharyngeal swab. He was prescribed nonsteroidal anti-inflammatory drugs and oral antibiotics by a family physician, but the symptoms had not ameliorated.

On admission, the patient was alert (E4V5M6). His main symptoms were mild headache and fatigue. Neurological examination revealed no focal signs or neck stiffness. Physical examination revealed a temperature of 38.6°C, blood pressure 134/86 mmHg, a regular pulse of 86 beats per minute, and SpO2 of 99% on room air. Blood chemistry and urine analysis performed immediately on admission were almost normal except for a little low serum Na 130 mEq/L, as were electrocardiogram, chest X-ray and cranial computed tomography scanning showed no abnormality. Cerebrospinal fluid examination revealed a cell count of 117/mm³ (mononuclear cells 103/mm³, polymorphonuclear cells 14/mm³), protein 96 mg/dl, glucose 53 mg/dl, Cl 115 mEq/l and blood sugar was 105 mg/dl. Brain MRI performed on admission showed abnormal signals in SCC, which were hyperintense on diffusion-weighted and fluid-attenuated inversion recovery imaging, hypointense on apparent diffusion coefficient images, and isointense on T1-weighted images, without contrast enhancement (Figure 1A, B, C, D).

Thus, we clinically diagnosed mild, possibly virus-related, MERS. On the other hand, our second impression of this distinctive MRI finding was an acute disseminated encephalomyelitis which was foremost in our differential diagnosis. Therefore intravenous glucocorticoid pulse therapy with methylprednisolone (mPSL) was initiated. A daily dose of 500 mg of mPSL was prescribed three times a week and the patient received intravenous acyclovir for 7 days. Serum antibodies for mumps, Epstein–Barr virus, rubella virus, cytomegalovirus, herpes simplex virus, and varicella zoster virus were all negative. All symptoms disappeared after mPSL treatment. On day 10 of admission, brain MRI showed either disappearance or remarkable decrease in the previously observed abnormalities (Figure 2A, 2B) and the patient was discharged without medication.

Table 1. Diagnostic criteria for MERS

1. Onset with neuropsychiatric symptoms, such as abnormal speech and/or behavior, and impaired consciousness and convulsion, within one week after the onset of fever
2. Complete recovery without sequelae, mostly within ten days after the onset of neuropsychiatric symptoms
3. High signal intensity lesion in the splenium of corpus callosum, in the acute stage. T1 and T2 signal changes are mild
4. Lesion may involve the entire corpus callosum and the cerebral white matter in a symmetric fashion
5. Lesion disappears within a week, with neither residual signal changes nor atrophy
Discussion
This is the first report on the MRI findings of MERS in an adult case without central nervous system disturbances. The patient’s symptoms consisted only of fever, headache, and fatigue, which ameliorated within 10 days of treatment. In addition, the lesions of SCC on MRI completely disappeared. Our findings support previous studies stating that isolated reversible lesions in SCC are a good prognostic marker for a benign disease course in patients with MERS. Although we could not identify a causative virus in this patient, previous studies have shown similar MRI findings in the central SCC occurring in some cases of infectious encephalitis/encephalopathy with the various causative agents mentioned above, along with similar clinical manifestations. All these previously reported cases of encephalitis/encephalopathy were clinically mild, and the patients recovered completely. By brain MRI, the lesions are hyperintense on fluid-attenuated inversion recovery imaging and isointense on T1-weighted imaging with no contrast enhancement. On diffusion-weighted imaging, the lesions are hyperintense, with low apparent diffusion coefficient values, reflecting restricted diffusion due to cytotoxic edema. It has been speculated that the molecular mechanisms responsible for these reversible MRI findings on the SCC include intramyelinic edema caused by a cytokine storm, which resolve with steroid pulse therapy. As a previous clinical study reported that 138 patients (90.2%) of 153 patients with these findings usually recover completely, it has been suggested that MRI splenial lesions are a good prognostic radiological marker in patients with encephalitis/encephalopathy. All previously reported cases of MERS presented with neurological signs, including seizures and mildly altered states of consciousness, such as drowsiness (delirious behavior in 54%, consciousness disturbance in 35%, and seizures in 33%). As a case example, a previously healthy 35-year-old man contracted an influenza type A virus infection. He had a high fever with a mild painful throat, myalgia and arthralgia throughout his whole body. The next day, he had an acute progressive tetraplegia and transcortical motor aphasia with mildly altered mental status. However, our patient did not present with neurological signs. Although the pathogenesis of MERS is still unclear, we consider that the cytokine storm in the blood system may play an important role in the etiology of this disease process. Therefore, by aggressive and early steroid pulse therapy for the disease, our patient may have not presented central nervous system neurological signs. Indeed, if brain MRI had not been performed, we could not have diagnosed this patient as having MERS. The factor that led to the diagnosis by MRI was abnormalities on cerebrospinal fluid examination, which was performed despite the absence of neck stiffness. The details of our case, coupled with reports that some patients with MERS recover without treatment and have normal findings on cerebrospinal fluid examination, indicate that MERS can be difficult to diagnose and there may be undetected cases of MERS treated as fever of unknown origin (FUO). However, clues for diagnosing FUO can be obtained from the bedside, physical examination and pertinent laboratory tests. In this case, the patient did not present with central nervous system disturbances and his symptoms only included high fever, headache, and fatigue. In such cases, immediate brain MRI, with the suspected diagnosis of MERS, is not usually performed. However, because MRI is now a commonly available diagnostic test in Japan, the number of patients diagnosed with MERS might increase in future. In fact, although MERS has mainly been reported in Japan, the reason for this may simply be that it is easier to perform brain MRIs in Japan than in many other
countries. Therefore, when physicians treat FUO patients, it is necessary for them to consider MERS as a differential diagnosis.

To the best of knowledge, for the first time we report a case of a patient with MERS, as detected by brain MRI, who did not present with central nervous system disturbances. The appearance of abnormal signals in SCC is considered to be between 1 and 3 days after the prodromal symptoms, and that abnormal lesion disappears within a week. MRI splenial lesions may be a good prognostic radiological marker for patients with encephalitis/encephalopathy. Although it is difficult to diagnose such patients as having MERS, it is necessary to consider MERS as a differential diagnosis in patients with FUO.

Conflicts of Interest:
The authors declare that they have no competing interests.

References