Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.8997-17
Intern Med 56: 3093-3095, 2017
http://internmed.jp

【 CASE REPORT 】

Mild Encephalitis/Encephalopathy with a Reversible Splenial Lesion in an Adult Patient with Influenza

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Abstract:
We herein report the case of a 31-year-old Japanese woman who developed adult-onset clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) and presented with consciousness disorder and olfactory disturbance secondary to influenza A infection. The patient's neurological symptoms and the lesion in the splenium resolved within 14 days without therapy. Magnetic resonance images and the clinical course were consistent with a diagnosis of MERS; however, mental changes following the influenza infection always present a diagnostic dilemma for physicians. We considered various diagnoses, including viral encephalitis, medication-related encephalopathy, and MERS. A comprehensive assessment may be required to diagnose MERS, since it may mimic other neurological diseases, such as viral encephalitis and medication-related encephalopathy.

Key words: mild encephalitis/encephalopathy with a reversible splenial lesion, influenza, olfactory disorder

(Intern Med 56: 3093-3095, 2017)
(DOI: 10.2169/internalmedicine.8997-17)

Introduction

Influenza is common disease induced by a viral pathogen of the upper respiratory tract. In most cases, a fever, cough, myalgia, and arthralgia present early in the course of infection. However, influenza is under recognized due to central nervous system (CNS) dysfunction. In general, febrile seizure is common in infants and children with influenza. In young individuals, influenza infection may also be associated with acute onset brain dysfunction, characterized by decreased consciousness and delirious or abnormal behaviors. Such CNS dysfunction due to influenza infection has been reported worldwide (1). In patients with decreased consciousness after influenza infection, we should consider various diagnoses, including viral encephalitis, medication-related encephalopathy, and mild encephalitis/encephalopathy with a reversible splenial lesion (MERS). The management is challenging, as the differential diagnosis of encephalopathy is broad and often requires intensive supportive management.

Several investigators have reported that symptoms improved with the disappearance of the abnormalities in splenium of corpus callosum (SCC) in a patient with MERS, as in this case. To our knowledge, however, only a few studies have described adult cases of influenza-associated MERS (2-4). We herein report a case of influenza-associated MERS in an adult.

Case Report

A 31-year-old woman was admitted to Akashi Medical Center due to a fever and disordered consciousness. She had no remarkable medical or family history. She had had a high-grade fever and generalized fatigue for four days prior to admission. She had been diagnosed with influenza A infection based on the rapid antigen test and started on oseltamivir for two days by her primary care physician prior to admission. She was not taking any nonsteroidal anti-inflammatory drugs. On the day of admission, she was found foaming at the mouth and was not responsive. Her family consulted a doctor at a nearby hospital. Her mental state was scored at E2V2M4 for at least two hours. Her previous doctor considered encephalitis/encephalopathy associated with infection of influenza and referred the patient to our hospital. Her vital signs were within normal ranges, in-

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Received: February 7, 2017; Accepted: March 27, 2017; Advance Publication by J-STAGE: September 25, 2017
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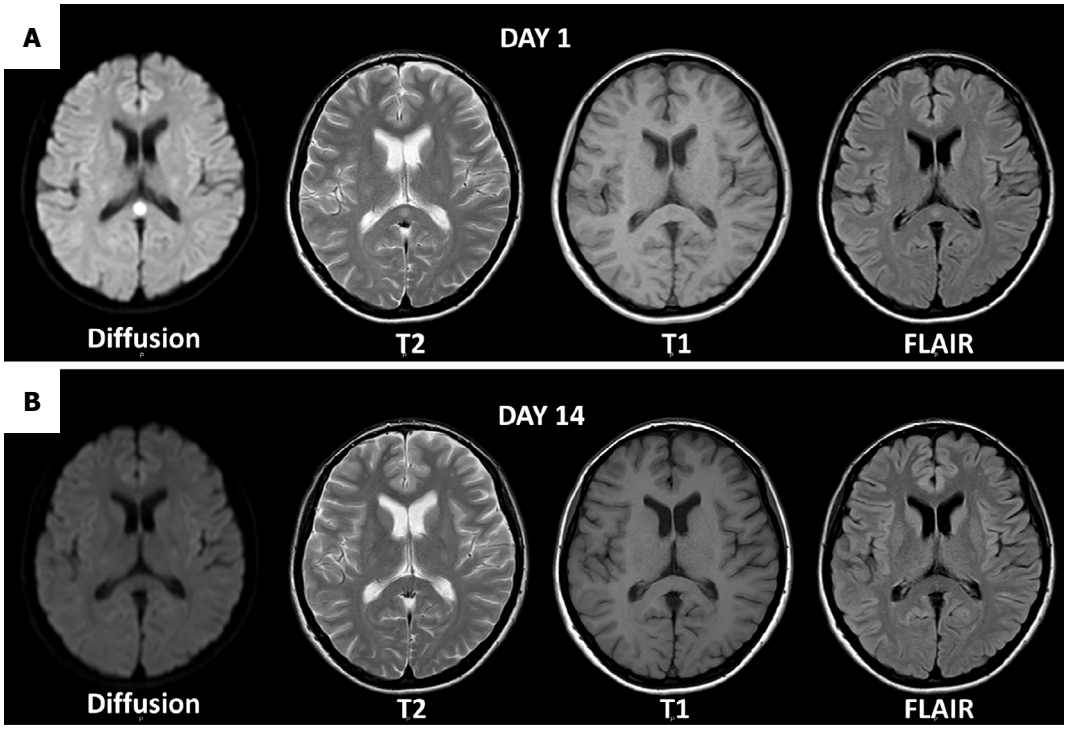

Figure. **Magnetic resonance imaging (MRI) of the brain. A: High intensity area in the center of splenium of corpus callosum (SCC) on diffusion image on admission. They are mildly hypointense on T1WI, displaying hyperintensity on T2WI and FLAIR. B: The T2WI and FLAIR image on day14 showed complete resolution of the abnormal finding.**

cluding her body temperature, which was 37.3℃. Without any treatment, her mental status improved after two hours, and she was able to follow all commands. A neurological examination did not reveal any focal deficit, except for decreased olfaction. She reported that she could not detect bathroom deodorant or sewage smells. There were no sensory disturbances or pathological reflexes.

There were no abnormalities in the complete blood count, glucose levels, blood biochemistry, or urinalysis, except for an elevated C-reactive protein level (CRP: 8.8 mg/dL). A cerebrospinal fluid examination showed a normal cell count (0/3 mm^3), normal protein level (18.5 mg/dL), and normal glucose level (61 mg/L). Chest X-ray was normal. Computed tomography on admission showed no masses or cerebral hemorrhage. Brain magnetic resonance imaging (MRI) on admission showed high intensity in the center of the splenium of SCC on diffusion imaging. Mildly hypointense lesions were noted on T1WI, displaying hyperintensity on T 2/FLAIR (Figure).

There were no abnormalities on electroencephalography on the patient's second hospital day. Based on the characteristic imaging findings and her clinical course, MERS was suspected. She was discharged on day 3 after close observation to rule out the possibility of encephalitis, encephalopathy and non-convulsive status epilepticus. Full recovery of olfaction was recognized at the follow-up visit, and the abnormal findings on MRI subsided.

Discussion

We described an influenza-associated MERS patient with a solitary lesion of the SCC on MRI. The patient's neurologic signs altered her mental status and decreased her olfaction, which dramatically improved after several days. The lesion of the SCC on MRI completely disappeared after 14 days.

In 2004, Tada et al. first described a group of conditions called MERS that were characterized by a transient splenial lesion of the MRI findings (5). The clinical symptoms of MERS include reversible consciousness disturbance, seizures, delirium and headaches (5). MERS is triggered by infections with pathogens such as influenza virus, rotavirus, mumps virus, varicella-zoster virus, *Salmonella enteritidis*, *Escherchia coli* O-157, *Mycoplasma pneumoniae*, or *Legionella pneumoniae* (6). In addition to infection, MERS has been caused by hypoglycemia and the administration of antiepileptic drugs (6). The typical features of the acute phase of MERS on diffusion-weighted MRI include high-intensity signals in the SCC. In a patient with altered mental status and lesions involving the SCC, ischemia, infections, posterior reversible encephalopathy syndrome, diffuse axonal injury, multiple sclerosis, hydrocephalus, Marchiafava-Bignami disease, adrenoleukodystrophy, AIDS dementia complex, lymphoma, epilepsy, and antiepileptic drug usage should be considered in the differential diagnosis (2). However, the quick recovery of the mental status in the present patient

could not explain these progressive illnesses. The MRI findings were not consistent with inflammatory diseases or malignancies. In cases of MERS, the symptoms improve with the disappearance of the abnormalities in the SCC (2). The most likely causes of these transient lesions of the SCC have been suggested to be rapidly resolving intramyelinic edema or the influx of inflammatory cells and macromolecules, combined with related cytotoxic edema (2). The anatomical vulnerability of the SCC is hypothesized as the reason for these changes. However, why only the SCC is affected remains unclear, calling for further research (2).

Previous reports described trigeminal neuralgia as a clinical symptom of MERS. Along with the decreased olfaction seen in the present case, this might be a consequence of the viral route of entry into the brain, as the olfactory and trigeminal nerves are the two most likely neuronal pathways of viral infection after intranasal inoculation (7).

Mental changes following influenza infection always present a diagnostic dilemma for physicians, as it is difficult to distinguish encephalitis/encephalopathy from simple signs of influenza infection at the first visit. Various diagnoses, including viral encephalitis, medication-related encephalopathy, and MERS, have been suspected. Detailed history taking, a physical examination, the results of lumbar puncture and brain imaging, as well as the clinical course are required to rule out potentially lethal etiologies, such as acute necrotizing encephalopathy or herpes virus encephalitis. In the present case, we diagnosed MERS based on the generic clinical course and imaging findings.

A recent report described a case of oseltamivir-induced neurotoxicity with elevated serum levels of active metabolite rather than the expected value after oseltamivir ingestion. In that report, a 15-year-old girl who had been diagnosed with influenza A developed delirium-like symptoms after taking oseltamivir for 3 days. She had neither previously taken oseltamivir nor developed neuropsychiatric symptoms prior to this point. She completely recovered within two weeks after cessation of oseltamivir and with the administration of benzodiazepine (8). In the present case, the patient received oseltamivir before admission. We therefore cannot completely rule out that the patient's clinical course was due to oseltamivir-induced neurotoxicity. However, as her mental state improved immediately after cessation, we stopped using oseltamivir with no further intensive treatment in the present case. Given the biphasic deterioration of her mental status, we continued to observe her.

MERS is a reversible syndrome with an excellent prognosis in most patients; however, some patients requiring ventilator support at the early stage might have severe neurological sequelae (3). In a case report, a previously healthy 35-year-old man with MERS due to influenza A was treated with methylprednisolone pulse therapy (1,000 mg/day) for three days because of acute progressive tetraplegia and transcortical motor aphasia with mildly altered mental status, which might suggest a diagnosis of acute disseminated encephalomyelitis (ADEM) on an initial examination (9). Patients with MERS require several days to recover. Therefore, we should consider treatment when encountering patients with a severe disease status, such as serious disturbance of consciousness and neurologic manifestations.

In conclusion, MERS is a relatively uncommon syndrome that manifests as a temporary neurological abnormality. A comprehensive assessment and close observation are required to diagnose MERS, since it can resemble other neurological diseases.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

We thank Shenli Hew from Akashi Medical Center for proofreading and editing the manuscript.

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