Transient Hemiparesis and Hemianesthesia in an Atypical Case of Adult-onset Clinically Mild Encephalitis/Encephalopathy with a Reversible Splenial Lesion Associated with Adenovirus Infection

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Abstract

We herein report the case of a previously healthy 24-year-old Japanese woman who developed adult-onset clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) presenting with hemiparesis and hemianesthesia secondary to adenovirus infection. The patient’s neurological symptoms and the lesion in the splenium resolved within 17 days without therapy. The radiographic features and clinical course observed in this case were consistent with a diagnosis of MERS; however, the only neurological symptoms were hemiparesis and hemianesthesia. This is the first reported case of MERS involving only hemiparesis and hemianesthesia at onset. This case suggests that a diagnosis of MERS should be suspected in patients with hemiparesis and hemianesthesia, especially when these conditions are preceded by infection.

Key words: clinically mild encephalitis/encephalopathy with a reversible splenial lesion, adenovirus, head MRI, hemiparesis, hemianesthesia

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Introduction

Recently, many aspects of the pathogenesis of acute encephalitis and acute encephalopathy have been clarified. For example, various viral infections have been reported to cause encephalitis/encephalopathy. However, many mechanisms remain to be elucidated. Clinically, mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) is a clinical entity first named and described by Takanashi et al. (1). The clinical symptoms of MERS include permanent consciousness disturbance, seizures, delirium and headaches (1, 2). The typical features of the acute phase of MERS on diffusion-weighted (DW) magnetic resonance (MR) images include high-intensity signals in the splenium of the corpus callosum; however, the high-intensity signals rarely expand to the whole corpus callosum or deep white matter (1, 2). The cause of these abnormalities, although not obvious, is thought to be intramyelinic axonal edema (related to hyponatremia) and/or local inflammatory cell infiltration (2-4). Interestingly, these abnormalities generally disappear within a few weeks, coinciding with the improvement of symptoms (2, 5). This finding is congruent with the results of several recent pediatric studies from Japan, which reported that MERS is associated with a good prognosis.

Previous studies have identified that MERS can be triggered by infection with either the influenza virus, rotavirus, mumps virus, varicella-zoster virus, Salmonella enteritidis, Escherichia coli O157, Mycoplasma pneumoniae or Legionella pneumophila. In addition to infection, MERS has also been reported to be associated with hypoglycemia and the administration of antiepileptic drugs. In this report, we describe the case of a patient with an atypical presentation of adult-onset MERS that occurred secondary to adenovirus infection.
Case Report

A previously healthy 24-year-old woman visited the emergency department with acute-onset weakness of the right upper extremity. Five days before admission, she exhibited a fever of 40°C and sore throat and was treated with cefcapene and clarithromycin. Two days before admission, she developed diarrhea and mild lower abdominal pain. On admission, her vital signs were within the normal ranges and her mental status was clear. A neurological examination revealed right-sided hemiparesis (manual muscle testing: 4/5) with decreased pain and temperature sensation that affected the face, arm, trunk and leg equally. An examination of the cranial nerves showed no abnormalities except for incomplete fifth and seventh cranial nerve palsies on the right side. Deep tendon reflexes showed no laterality, and no pathological Babinski, Chaddock or palmomental reflexes were observed. On the day of admission, brain DW imaging disclosed a high-intensity signal in the splenium of the corpus callosum (Figure A). A low apparent diffusion coefficient (ADC) was noted in the same area (Figure B). There were no abnormalities in the complete blood count, blood chemistry, urinalysis or a chest roentgenogram, except for an elevated C-reactive protein level (CRP: 12.21 mg/dL). A lumber puncture was not performed, and no specific therapy was administered. On post-admission day 2, the right-sided hemiparesis had worsened (manual muscle testing: 3/5); however, by day 3, the patient’s right-sided muscle weakness had fully recovered. On day 5, follow-up brain MR images demonstrated similar abnormal signal changes in the same area as that observed on the previous DW images (data not shown). On day 7, slightly decreased levels of pain and temperature sensation persisted; however, the patient was discharged. On day 17, the neurological findings were normal, and no abnormal signal changes were noted on DW or ADC images (Figure C, D).

Paired serum tests for adenovirus antibodies were performed on days 1 and 17. The titers of both complement fixation (CF) and neutralization (NT) for adenovirus type 1 in the convalescent phase showed a diagnostic increase of four times or more, from less than 4 (CF/NT) in the acute phase to 32 (CF) and 16 (NT), respectively, although the titers of adenovirus types 2-7 were not significantly increased.

Discussion

In the present case, transient hemiparesis, decreased sensations and a lesion in the splenium of the corpus callosum appeared after the development of a fever with upper respiratory and abdominal symptoms. Recently, many cases of MERS have been reported in Japan, primarily among pediatric patients. However, not all patients presenting with reversible splenial lesions during febrile illness (RESLEF) (6) exhibit neurological symptoms, such as delirious behavior. Among those with RESLEF, patients presenting with neurological symptoms are diagnosed with MERS (1). In the present case, the radiographic abnormalities, acute neurological symptoms and fever caused by the preceding infection were consistent with the features of MERS. We did not try to separate the virus; therefore, the presence of adenovirus infection was not directly confirmed. However, the preceding symptoms were consistent with adenovirus infection, and paired serum tests for adenovirus antibodies revealed significantly high titers, which together suggest that the MERS was caused by adenovirus type 1 infection.

Recently, a report of clarithromycin-induced neurotoxicity was published (7). In the present case, the patient received treatment with clarithromycin before admission; therefore, it cannot be completely ruled out that her clinical course was influenced by clarithromycin-induced neurotoxicity. However, since there are no reports showing that MERS or hemiparesis and/or hemianesthesia are associated with clarithromycin-induced neurotoxicity, it is not clear whether the clarithromycin treatment influenced the neurological symptoms observed in the present case.

Initially, the characteristic features of the present case included neurological symptoms at onset. While the patient’s mental state was unaltered and she did not have seizures, she did develop right-sided hemiparesis and hemianesthesia.
To the best of our knowledge, the present case is the first case of MERS presenting with symptoms of only hemiparesis and hemianesthesia at onset. The corpus callosum is a band of white matter connecting the left and right hemispheres, disorders of which usually present as callosal disconnection syndromes (8, 9). Hemiparesis is an atypical presentation of this syndrome (9). Hemiasomatognosia can be complicated by this syndrome and may mimic hemiparesis. However, we do not believe this occurred in the present case, as the patient’s chief complaint was right-sided muscle weakness, which demonstrated that she was aware of her own body. Furthermore, the presence of muscle weakness was confirmed by the patient’s awareness of her own right arm and leg.

Lesions causing hemiparesis and sensory defects are generally located within the pyramidal tract and sensory pathway. Therefore, the culprit lesion in the present case was estimated to be located above the midbrain based on the findings of the neurological examination. However, in the present case, no white matter lesions were detected on MR images obtained on either day 1 or day 5 after admission, although abnormalities of the splenium of the corpus callosum were detectable both times. Therefore, we have two hypotheses as to the cause of hemiparesis and hemianesthesia in this case. The first hypothesis, which we support, is that the culprit lesion was located within the deep white matter above the midbrain, although it was not detectable on MR imaging. This possibility concurs with the neuroanatomical localization of the lesions and the fact that MERS can involve regions of the deep white matter besides the splenium of the corpus callosum (10). The second hypothesis is related to the splenium of the corpus callosum lesion itself. Based on the neuroanatomical localization of the lesions, we believe the second option to be less likely. However, the corpus callosum body was described as being responsible for hemiparesis in a previous report (9). Therefore, the second hypothesis cannot be ruled out entirely. Further cases must be accumulated to identify the relationship between the presence of lesions in the splenium of the corpus callosum and the incidence of hemiparesis and/or hemianesthesia.

Another characteristic feature of the present case was the trigger of MERS, which was indirectly confirmed to be an adenovirus infection. Adult cases of MERS are only reported sporadically; therefore, there are limited data regarding its pathogenesis. Most reported cases of MERS involve pediatric patients and are the result of a nationwide surveillance study conducted from 2007 to 2010 on the epidemiology of acute encephalopathy in Japan (11). In that report, the preceding infections were most frequently caused by the influenza virus (34%), followed by the rotavirus (12%) and the mumps virus (4%). Adenovirus was very rare, accounting for only 1% of all pathogens. Compared to other viral infections, adenovirus infection often presents with an exceptionally high CRP level and is often treated with unnecessary antibiotics. The present case suggests that when MERS is associated with a high CRP level, it may be due to an adenovirus infection rather than a bacterial infection. Therefore, our report implies that if the clinical findings are consistent with an adenovirus infection and the results of the rapid test for adenovirus are positive, the administration of antibiotic therapy is not necessary in patients with MERS presenting with a high CRP level.

In conclusion, this report described a patient with adult-onset MERS who presented with hemiparesis and hemianesthesia secondary to adenovirus infection. Although MERS is rare, this case suggests that a diagnosis of MERS should be suspected in patients with hemiparesis and hemianesthesia, especially when these conditions develop after a preceding infection.

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

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References