Acute Disseminated Encephalomyelitis Developed after *Mycoplasma Pneumoniae* Infection Complicating Subclinical Measles Infection

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**Abstract**

A 26-year-old man developed acute disseminated encephalomyelitis (ADEM) after *Mycoplasma pneumoniae* infection, and was admitted after developing disturbed consciousness. Magnetic resonance images revealed lesions in the midbrain, bilateral internal capsules, left corona radiata, white matter of the left occipital lobe, and thoracic spinal cord. He was diagnosed with subclinical measles infection since no anthera was observed despite the fact that his serum and cerebrospinal fluid samples were positive for measles IgM antibodies. ADEM following mixed infection with measles and *M. pneumoniae* is rare, and it is not clear whether an additional infection with measles influenced the onset of ADEM after *M. pneumoniae* infection. Symptoms did not improve with steroid or immunoglobulin treatment, but improvement in symptoms was observed after plasmapheresis.

**Key words:** acute disseminated encephalomyelitis, *Mycoplasma pneumoniae*, measles, plasmapheresis

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**Introduction**

Acute disseminated encephalomyelitis (ADEM) is suspected when symptoms of acute encephalitis and myelitis are found to be associated with those of systemic inflammation. It often develops after infection or vaccination, and autoimmune mechanisms are considered to be the cause. Infections with viruses, *Campylobacter* spp, *Streptococcus* spp, *Leptospira* spp and *Mycoplasma pneumoniae* are known to precede ADEM. Here, we describe a patient with ADEM believed to be caused by *M. pneumoniae* infection complicating subclinical measles infection. Plasmapheresis was found to be an effective treatment for this patient.

**Case Report**

A 26-year-old man was admitted to our hospital for disturbed consciousness. In February 2004, he developed fever and cold symptoms, which did not improve after about 1 week. Following this, he was examined by a physician and hospitalized on being diagnosed with *M. pneumoniae* infection. After treatment with minocycline hydrochloride, the clinical symptoms showed improvement; however, 5 days after hospitalization, right hemiplegia and dysarthria developed, moreover, disturbed consciousness progressed, therefore he was transferred to our hospital. The patient had no particular history of any disease and had been vaccinated against measles at the age of 1 year, but had not been vaccinated recently. On admission, his blood pressure was 144/70 mmHg, pulse rate 120/minutes, body temperature 38.5°C, and level of consciousness 4 (Glasgow Coma Scale; E1V1 M2); bilateral pupils were 2 mm in diameter and the light reflex was sluggish. The deep tendon reflexes of the limbs were normal, and no pathological reflexes or meningeal irritation signs were evident. While the left upper extremity could be moved slightly, the right upper extremity and bilateral lower extremities were paralyzed.

Blood examination revealed elevated WBC (18,800/μL) and CRP (1.26 mg/dL) as well as impaired liver function (AST 63 IU/L, ALT 146 IU/L, and LDH 253 IU/L). Serum tested positive for IgG antibody (but negative for IgM anti-
Figure 1. Chest XR and CT confirmed an infiltrative shadow of the right lung, diagnosed as Mycoplasma pneumoniae-induced pneumonia.

Figure 2. MRI on Day 17 confirmed lesions, which were of high signal intensity on T2-weighted images in the midbrain, bilateral internal capsules, left corona radiata, and white matter of the left occipital lobe.

For EB virus, mumps virus, cytomegalovirus, rubella virus, and varicella zoster virus. It tested positive for measles virus IgG antibody (EIA 6.3(+) on Day 1 and 10.3(+) after 2 months) and IgM antibody (antibody index 10.74(+) on Day 1 and 2.36(+) after 2 months). Polymerase chain reaction (PCR) for measles virus RNA was negative. Cold agglutination and M. pneumoniae antibody titers were 4,096- and 1,280-fold, respectively, and the anti-galactocerebroside (GalCer) antibody had a low ELISA (OD) titer (0.158). Cerebrospinal fluid (CSF) examination demonstrated a total cell count of 71/mm³ (mononuclear cells, 27/mm³ and polymorphonuclear cells, 44/mm³), glucose 63 mg/dL, and protein 60 mg/dL, along with an increase in myelin basic protein (>2,000 pg/mL). It was negative for oligoclonal bands and positive for measles virus IgM antibody (antibody index 5.13(+)). The M. pneumoniae antibody titer in CSF was less than 40-fold and M. pneumoniae PCR was negative. Chest XR and chest CT revealed an infiltrative shadow in the right lung, confirming pneumonia (Fig. 1). Brain MRI revealed lesions of high signal intensity on T2-weighted images in the midbrain, bilateral internal capsules, left corona radiata, and white matter of the left occipital lobe (Fig. 2). Gd-
Figure 3. MRI of the thoracic spinal cord from Th 4 to 6 and Th 8 to 9 showed lesions of high signal intensity on T2-weighted images with swelling of spinal cord.

Figure 4. MRI from 2 months after onset of the disease showed that lesions had decreased and that mainly on the left side lesions had remained in bilateral internal capsules.

DTPA had no enhancing effect at the lesions. Brain MR angiography did not reveal any abnormalities. MRI of the thoracic spinal cord from Th 4 to 6 and Th 8 to 9 showed lesions of high signal intensity on T2-weighted images, with swelling of the spinal cord (Fig. 3).

Due to his severely disturbed consciousness and poor respiratory condition from the day of admission (Day 1), endotracheal intubation and artificial respiration were performed. Minocycline hydrochloride was continued, and on the same day, steroid therapy with methylprednisolone (1 g/day) was administered for 3 days; however, the symptoms did not improve. From Day 4, immunoglobulin therapy (25 g/day) was administered for 5 days, but no changes were seen in the symptoms. On Day 10, plasmapheresis was initiated and performed for 7 rounds until Day 48. From Day 14, his disturbed consciousness was improved, and spontaneous eye opening and eye movement were observed; from Day 40 the patient could move his head when instructed and paralysis of the left upper and lower extremities improved. MRI performed 2 months after onset of the disease showed that lesions had improved with decreased signal intensities (Fig. 4). On Day 75, he was transferred to a rehabilitation clinic, and after approximately 1 year, although the subsequent complications (dysarthria and right hemiplegia) remained, he recovered to a level at which independent gait was possible using a cane.

**Discussion**

ADEM is an acute inflammatory disease with a monophasic course that results in neurological symptoms due to disseminated white matter lesions in the cerebrospinal region.
It often develops after an infection and when it is associated with infection as a causal factor, it is considered to be an autoimmune reaction resulting from molecular homologies between antigens of the pathogen that caused the infection and those of the central nervous system (1).

The preceding *M. pneumoniae* infection in the case reported here was confirmed by increases in serum *M. pneumoniae* antibody and cold agglutination. Inflammatory findings, rapidly progressing neurological symptoms, findings from cerebrospinal images (mainly of white matter lesions), and a marked increase in myelin basic protein in CSF, suggesting demyelination, led to the diagnosis of ADEM following *M. pneumoniae* infection. *M. pneumoniae* infections are complicated by neurological disorders, resulting in severe encephalitis, myelitis, meningitis, and cerebrovascular disorders in the case of the central nervous system (2). Neurological symptoms of the central nervous system were found in 7% of patients who were hospitalized for *M. pneumoniae* infection (3). ADEM associated with *M. pneumoniae* infection has also been reported (4-6). In addition to the direct effects of invasion of *M. pneumoniae* (7), autoimmune mechanisms may be involved in the development of neurological disorders after *M. pneumoniae* infection; an association has been reported with the anti-GarCer antibody against the main components of myelin in central and peripheral nerves (8). Although the anti-GarCer antibody titer was low in the present case, we suspected the autoimmune reactions associated with *M. pneumoniae* to be the mechanism of onset rather than direct invasion. This is because neurological symptoms developed after pneumonia was treated with macrolide hydrochloride, and PCR for *M. pneumoniae* in CSF was negative.

Furthermore, while no antha or Koplik’s spots were observed during the course of the disease in the present case, the measles IgM antibody was found in serum and cerebrospinal fluid. There have been cases of secondary measles infections in individuals who were immunized against measles and who were positive for serum IgM antibody, even though no symptoms were observed (9). The patient reported here was infected with measles, although he underwent measles vaccination at the age of 1 year, and thus was immune to measles; the patient was considered to have subclinical measles infection. Measles infection and vaccination are associated with the development of encephalitis and ADEM after measles (10). However, ADEM after mixed infection with measles and *M. pneumoniae* is rare, and it is not clear whether mixed infection in subclinical measles influences the onset of ADEM after *M. pneumoniae* infection in our patient, although there is a report of adult respiratory distress syndrome likely due to measles and *M. pneumoniae* (11). It is also possible that mixed infection with measles and *M. pneumoniae* causes severe inflammation.

ADEM was treated with anti-inflammatory and immunosuppressive therapies in the present case, and although steroid treatment with intravenous methylprednisolone is generally the treatment of choice, immunoglobulin therapy (12) and plasmapheresis (13, 14) are also regarded as effective. Although no obvious effect was observed in the present case even after steroid and immunoglobulin therapy, the symptoms improved gradually after plasmapheresis. It has been reported that plasmapheresis is effective even for cases of ADEM in which steroid treatment and immunoglobulin therapy are not sufficiently effective (15-17), and we believe that plasmapheresis should be considered without hesitation for severe ADEM, which responds poorly to steroid treatment.

In conclusion, we report a rare case of ADEM following *M. pneumoniae* infection, complicated by subclinical measles infection.

References


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