A Case of Acute Hemorrhagic Encephalomyelitis associated with *Mycoplasma Pneumoniae* Infection

Acute hemorrhagic encephalomyelitis (AHEM) is a severe form of encephalitis characterized by fulminant clinical course and presence of hemorrhagic necrosis of the white matter. *Mycoplasma pneumoniae* (M. pneumoniae) have severe central nervous syndrome complication with encephalitis as that most common pediatric manifestations, but have been extremely rare report with AHME. A 10-year-old boy was referred to emergency room because of drowsy mental status, weakness of left side extremities and truncal ataxia. His deep tendon reflexes were hyperactive, neck stiffness sign and Babinski sign were both positive. Motor power were decreased on the both left upper and lower extremities. The sequences of T2-weighted and gradient recalled echo (GRE) showed hyper-intense lesions on multifocal white matter areas with hemorrhagic signal. Cerebrospinal fluid (CSF) analysis showed the pleocytosis with neutrophil dominant. The results of deoxyribonucleic acid (DNA) test and culture of *M. pneumoniae* were reported negative in CSF, but immunoglobulin M (IgM) was positive in blood. He received intravenous high dose corticosteroid and macrolide. After discharge, his neurologic function gradually returned to normal including sitting and standing without support. We reported the previously healthy boy with *M. pneumonia* related AHEM. The early diagnosis with brain MRI and the aggressive immunosuppressive treatment may be beneficial for recovery.

**Key Words:** Acute hemorrhagic encephalomyelitis (AHEM), Mycoplasma pneumoniae

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**Introduction**

Acute disseminated encephalomyelitis (ADEM) is a rare disease with severe central nervous system (CNS) complications, including damage to myelin and white matter\(^1,2\). Acute hemorrhagic encephalomyelitis (AHEM) is a fatal form of ADEM characterized by fulminant clinical course and hemorrhagic necrosis of the white matter\(^3\).

*Mycoplasma pneumoniae* causes 6%–20% of all community-acquired lower respiratory infections in older children and adults\(^5\). One of the most common extrapulmonary manifestations of such infections includes severe central nervous system complications, with meningitis, and encephalitis being the most
common pediatric manifestations\(^2\). Although some viral infections are linked to AHEM in children, *M. pneumoniae* has been rarely implicated\(^4\).

Herein, the authors report a case of AHEM with abnormalities of brain magnetic resonance imaging (MRI) and the aggressive immunosuppressive treatment in the early course of disease.

**Case report**

A previously healthy, 10–year–old boy presented to the emergency room at our hospital, with drowsiness, left side extremity weakness, and truncal ataxia. He had mild upper respiratory symptoms a week prior to presentation, including 2 days of fever (39°C). On the morning of admission, he became drowsy and was unable to stand, with truncal weakness causing him to fall to the left.

On examination, he was not speaking spontaneously, answering questions, or following commands. His fundoscopic examination showed normal. He had no lateralizing cranial nerve findings. Deep tendon reflexes were diffusely hyperactive (3+/3+), with positive neck stiffness and Babinski signs. We noted positive left ankle clonus; motor strength was reduced to 3/5th on the left upper and lower extremities. Touch, pain, temperature, and proprioceptive sensations were impaired bilaterally. Laboratory investigations revealed the following: hemoglobin, 12 g/dL (normal range, 11–16 g/dL); white blood cell count, 15,800 10\(^3\)/µL (normal range, 4,000–10,000 10\(^3\)/µL); erythrocyte sedimentation rate, 81 mm/h (normal range, 10–30 mm/h); C-reactive protein (CRP), 0.39 mg/dL (normal range, 0–0.5 mg/dL). Liver, and renal parameters and electrolytes levels were normal. Initial chest x-ray showed bilateral lung field infiltrates.

Brain magnetic resonance imaging (MRI) showed multifocal T2-weighted and fluid–attenuated inversion recovery hyper–intense lesions throughout the left frontal and right parieto–occipital subcortical white matter (Fig. 1A). Gradient recalled echo (GRE) T2–weighted images revealed a punctate dark signal extension to the splenium of the corpus callosum (Fig. 1B). Magnetic resonance angiography findings were normal. Cerebrospinal fluid (CSF) examination revealed the following: 880 nucleated cells (neutrophils, 92.8%; lymphocytes, 5.1%); protein levels, 106 mg/dL (normal range, 15–45 mg/dL); and glucose levels, 53 mg/dL (normal range, 40–70 mg/dL). CSF sample was sent for bacterial cultures and viral studies, and treatment with antibiotics and acyclovir was initiated for the patient.

He was admitted to the intensive care unit and received high-dose intravenous corticosteroids (methylprednisolone pulse therapy 250 mg every 6 hours) for 5 days. Few hours after the commencement of steroid therapy, CSF culture result of *M. pneumoniae* was reported negative but blood *M. pneumoniae* immunoglobulin M (IgM) level was 8.4 (normal range, 1). Consequently, we changed the antibiotic regimen to clarithromycin for 14 days and continued acyclovir for 7 days until the herpes simplex virus 1 and 2 viral polymerase chain reaction (PCR) and cultures were reported negative. On hospital day 2, he was awake and alert, but decreased motor strength and left–sided extremity weakness persisted. On hospital day 6, we switched him to oral steroids and began tapering. Other

![Fig. 1. WI /FLAIR and (A) Axial T2-weighted/fluid-attenuated inversion recovery and (B) T2 gradient-recalled echo images display multifocal hyperintensities of the right parieto–occipital and left frontal regions with parietal and occipital subcortical white matter extension to the splenium of the corpus callosum. Arrow indicates a dark punctate lesion in the right occipital lobe, suggestive of hemorrhage (B).](image-url)
evaluations for infection, and autoimmune disease are described in Table 1. *M. pneumoniae* PCR and culture were negative. Anti-nuclear antibody test result was initially positive, but negative on follow-up. His electroencephalogram showed slowing waves across all background activities, and no epileptic discharges.

His clinical condition improved, and he was transferred to the Department of Pediatric Physical Medicine and Rehabilitation on hospital day 17. Two weeks later, at discharge, his motor strength improved to 4/5th. His neurologic function, including sitting and standing without assistance, gradually returned to normal. He exhibited normal school performance and resumed his typical exercise at 6-month follow-up.

### Discussion

*M. pneumoniae* is a major cause of community-acquired pneumonia, accounting for approximately 40% of cases in children, especially those aged 5–14 years. It also leads to extrapulmonary manifestations including neurological, dermatological, cardiac, renal, and gastrointestinal disorders, with neurological disorders being the most frequent. *M. pneumoniae* associated encephalitis is the most common cause of encephalitis in children and is implicated in approximately 7% of patients with *M. pneumoniae* infection. Although there are some reports of *M. pneumoniae*–associated mild encephalitis, there are few articles describing severe form of encephalitis, including ADEM.

AHEM is an extremely rare and fatal form of ADEM that was first described by Hurst in 1941. It is characterized by a fulminant clinical course and hemorrhagic necrosis of the white matter. In contrast to ADEM, AHEM is more common in young adults and children. There are few reports of pediatric cases of viral infection–associated AHEM and only one report of a pediatric case of *M. pneumoniae* infection–associated AHEM.

Disturbances of consciousness and behavior, delirium, seizures, and ataxia are the common neurologic symptoms of *M. pneumoniae*–associated encephalitis. Although our patient did not have seizures, he exhibited severe neurologic complications such as a positive Babinski sign, ankle clonus, and deep tendon reflex (DTR). These neurologic symptoms can result from infection (particularly influenza and herpes simplex virus infection), autoimmune diseases, or vascular lesions. MRI is essential for diagnosing ADEM. Previous reports confirmed AHEM using biopsy, but recent advances in MRI technology, especially diffusion restriction and gradient-recalled echo imaging, permit non-invasive detection of hemorrhagic lesions.

Our patient presented with respiratory symptoms and fever. Chest x-ray showed bilateral lung infection. We detected *M. pneumoniae* IgM in the patient’s blood, but no *M. pneumoniae* DNA in his CSF. Qualitative measurement of IgM has moderate sensitivity (32%–77%), but it is widely used and suggested that patient’s encephalitis was likely immune-mediated following respiratory infection. A recent study reported that patient having *M. pneumoniae*–associated encephalitis with negative PCR for *M. pneumoniae* in CSF showed radiological signs of pneumonia more often than those with positive PCR in CSF. A few studies have reported that *M. pneumoniae* antibodies cross-react with galactocerebroside; this observation requires further study in pediatric patient with *M. pneumoniae*–associated encephalitis.

AHEM outcomes are generally poor, with death typically occurring within days or weeks of onset. However, there are a few reports that describe good recovery with immunosuppres-

### Table 1. Diagnostic Evaluation of Blood and Cerebrospinal Fluid (CSF)

<table>
<thead>
<tr>
<th>Infectious studies</th>
<th>Autoimmune studies</th>
<th>CSF studies</th>
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<tbody>
<tr>
<td>Blood</td>
<td>ANA: positive → negative</td>
<td>880 nucleated cells (neutrophils 92.8%, lymphocytes 5.1%)</td>
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<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>ANCA: negative</td>
<td></td>
</tr>
<tr>
<td>IgM: positive → negative</td>
<td>C3: normal</td>
<td>Protein: 106 mg/dL</td>
</tr>
<tr>
<td>CSF</td>
<td>C4: normal</td>
<td>Glucose: 53 mg/dL</td>
</tr>
<tr>
<td>HSV-1, 2 PCR &amp; culture: all negative</td>
<td>B2 Glycoprotein ab: negative</td>
<td>IgG index: 1.5</td>
</tr>
<tr>
<td>EBV/CMV/HHV-6,7: all negative</td>
<td>Anti-cardiolipin ab: negative</td>
<td></td>
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<tr>
<td>oligoclonal band: negative</td>
<td>Lupus Anticoagulant ab: negative</td>
<td>anti-cardiolipin antibody:</td>
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<tr>
<td><em>Mycoplasma pneumoniae</em></td>
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<tr>
<td>PCR &amp; culture: all negative</td>
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<tr>
<td>Bacterial culture: negative</td>
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<tr>
<td>Nasopharyngeal aspiration</td>
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<tr>
<td>Respiratory virus PCR: all negative</td>
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</tbody>
</table>

ANA, Anti-nuclear antibody; ANCA, Anti-neutrophil cytoplasmic antibody; CMV, Cytomegalovirus; CSF, Cerebrospinal fluid; EBV, Epstein-Barr virus; HHV, Human herpes virus; HSV, Herpes simplex virus; Ig, Immunoglobulin; NMO, Neuromyelitis optica (AQP4); PCR, Polymerase chain reaction.
sive therapies, similar to those used to treat ADEM. Our patient had disturbance of consciousness, truncal ataxia, and left-sided extremity weakness, but no seizures. He was initiated on early immunosuppressive treatment with high-dose steroids and recovered without severe neurologic sequelae or steroid-related side effects. Our use of antimicrobial agents for *M. pneumoniae*–associated encephalitis was somewhat controversial. Most macrolides do not transverse the blood-brain barrier, and doxycycline use is restricted in young children. Recent studies recommend intravenous immunoglobulin or steroid therapies in severe cases of *M. pneumoniae*–associated encephalitis.

In conclusion, AHEM is a very rare, severe form of encephalitis characterized by fulminant clinical course and presence of hemorrhagic necrosis of the white matter. The Brain MRI with GRE image is good for the detection of AHEM and the aggressive immunosuppressive treatment in the early course of disease may be contribute to better results of recovery.

**References**


요약

급성 출혈성 뇌척수염은 수초 및 백색질의 출혈성 괴사를 동반하는 드문 질환이다. 소아에서 바이러스 감염 후 급성 출혈성 뇌척수염이 동반된 증례는 몇몇 보고가 있었으나 *M. pneumoniae* 감염 후 급성 출혈성 뇌척수염이 발생한 경우는 매우 드물다. 이 증례의 환아는 의식저하, 좌측 사지 근력 저하 및 체간 운동 실조를 주소로 본원에 내원하였다. 혈액검사를 통해 마이코플라마의 감염을 확인하였고 경사회복에코 자기공명 영상에서 다발성 백색질 고음영 병변과 출혈 소견이 확인되었다. 환자는 발병 초기부터 적극적으로 면역억제 치료 및 고용량 스테로이드 촉발 요법을 시행 후 내원 당시 동반한 신경학적 증상은 후유증 없이 소실되었다. 이 증례를 통해 급성 출혈성 뇌척수염 진단에 있어 초기 경사회복에코 자기공명 영상이 매우 유용하며 공격적인 초기 면역억제 치료가 질병의 예후에 중요한 것으로 사료된다.