엔테로바이러스 뇌수막염 직후 발생한 급성 횡단성 척수염 1례

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A Case of Acute Transverse Myelitis Following Enteroviral Meningitis

Acute transverse myelitis is a rare acquired inflammatory disease of the spinal cord that presents with rapid onset of bilateral motor weakness, sensory alterations, and bladder or bowel dysfunction. Enteroviruses are the most common pathogens of aseptic meningitis, which is usually self-limited and recovers completely without complication. However, enteroviruses can also cause more severe neurological diseases such as encephalitis, Guillain-Barre syndrome, and myelopathy. A 6-year-old girl was admitted to our hospital because of weakness in both lower extremities, sensory alterations below the umbilicus, and bladder and bowel dysfunction. One day prior to admission, the patient experienced a fever, headache, and recurrent vomiting, and was diagnosed with enteroviral meningitis at our emergency department. Cerebrospinal fluid and stool samples collected from the patient revealed enterovirus-positivity via reverse transcription polymerase chain reaction. Magnetic resonance imaging revealed high signal intensity in the spinal cord at the level of C2-C7 and T3-T11 on sagittal T2-weighted images. Despite intravenous immunoglobulin, high-dose methylprednisolone, and physical therapy, the patient was still unable to walk and required intermittent nelaton catheterization for urination at 11 months after the disease onset. This report demonstrates that enteroviral meningitis, which is known to be a relatively benign condition, can progress to critical neurological disease such as acute transverse myelitis.

Key Words: Transverse myelitis, Enterovirus, Meningitis, Child

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Introduction

Acute transverse myelitis (ATM) is a rare acquired inflammatory disease of the spinal cord that can present with rapid onset of bilateral motor weakness, sensory alterations, and bladder or bowel dysfunction. ATM may be associated with an infection or a postinfectious immune-mediated process¹⁾. The inciting infection is usually viral in origin, although other microorganisms may be involved. Viral agents associated with ATM include cytomegalovirus, herpes simplex virus, Epstein-Barr virus, varicella-zoster virus, echovirus, coxsackievirus, and mumps, hepatitis, rubella, and measles viruses²⁾.

Enteroviruses are the most common pathogen of aseptic meningitis, accounting for 85-90% of all viral meningitis cases³⁾. Enteroviral meningitis is typically self-

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limited without neurological complications or sequelae. However, enteroviruses can cause more critical neurological diseases, such as encephalitis, acute cerebellar ataxia, Guillain-Barre syndrome, and myelopathy⁴⁾. Cases of ATM caused by enteroviruses have rarely been reported⁵⁾. To the best of our knowledge, this case report is the first to describe acute transverse myelitis following enteroviral meningitis.

Here we report the case of a 6-year-old patient who presented with typical ATM preceded by enteroviral meningitis.

Case Report

A 6-year-old girl was admitted to the emergency department at Ulsan University Hospital because of weakness in both lower extremities. Her symptoms developed abruptly on the morning of admission. Two days prior to admission, the patient experienced a fever, headache, and 3 episodes of emesis. One day prior to admission, she was referred to our emergency department by local pediatric clinic due to suspected meningitis. At that time, the only abnormality on neurological examination was neck stiffness. Cerebrospinal fluid (CSF) analysis revealed a white blood cell count of 4/mm³, red blood cell count of 0/mm³, protein level

of 26.3 mg/dL, glucose level of 49 mg/dL, and negative bacterial culture. She was discharged on the night of admission day. However, when the patient woke up the next morning, she could not move her lower extremities and complained of lower back pain. Prior to this, she had been healthy, and had no history of medication or trauma. She did not have history of infection within the previous 1 month, including that of upper respiratory infection. Her vaccinations were up to date. Upon the second admission to the emergency department, the patient had no fever, headache, or vomiting. The patient's parents were concerned that the patient's leg weakness resulted from the initial lumbar puncture. On neurologic examination, she was fully alert and oriented. All of her cranial nerves were intact. The patient had normal motor power in the upper extremities, but displayed no movement (grade 0 motor power) in the lower extremities. Muscle tone in the lower extremities was flaccid. She reported decreased sensation to pain and touch below the umbilicus. Knee and ankle jerks were absent, and Babinski sign was present bilaterally. The patient was not able to urinate or control her anal sphincter. Magnetic resonance imaging (MRI) of the spine revealed high signal intensity in the spinal cord at the level of C2-C7 and T3-T11 on sagittal T2-weighted images (Fig. 1A). Involvement of both gray matter and white matter were seen on axial images (Fig. 1B and

Fig. 1. Initial spine magnetic resonance imaging (MRI) findings. Sagittal T2-weighted MRI (A) showing high signal intensity in the spinal cord at the level of C2-C7 and T3-T11 (arrows). Axial T2-weighted MRI (B and C) showing high signal intensity in both of the gray and white matter of the spinal cord (arrowheads).

1C). MRI of the brain exhibited no obvious abnormality. MR angiography of the brain was not performed. Analysis of the CSF revealed absence of oligoclonal IgG bands, NMO (neuromyelitis optica) IgG antibody, and myelin basic protein. In addition, polymerase chain reaction for herpes simplex virus type 1 and 2 yielded negative results. CSF IgG index was 0.51. Serological tests for measles virus, varicella zoster virus, Epstein-Barr virus, cytomegalovirus, hepatitis A, B and C virus, and Mycoplasma pneumoniae were all negative. Tests for antinuclear antibody, anti-double stranded DNA antibody, anti-neutrophil cytoplasmic antibody and anticardiolipin antibody were negative. Her vitamin B12 level was 1,236 pg/mL (reference value, 180–914 pg/mL). CSF and stool samples collected from the patient at the first admission revealed enterovirus-positivity via reverse transcription polymerase chain reaction. However, the enterovirus genotype was undetermined. The patient was treated with intravenous methylprednisolone ($30 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$ for 5 days), intravenous immunoglobulin ($400 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$ for 5 days) and empirical antimicrobial therapy (acyclovir and cefotaxime). On the fifth day, she showed flickers of the feet in response to pain. On the seventh day, a follow-up CSF examination revealed a white blood cell count of $3/\text{mm}^3$, red blood cell count of $30/\text{mm}^3$, protein level of 163.1 mg/dL, and glucose level of 75 mg/dL. She was provided with physical therapy. On the eleventh day, she was able to move only the feet in response to pain without volitional movement. A follow-up MRI of the spine performed on this day showed a decrease in the extent of high signal lesions on T2-weighted images (C2–C7 and T6–T10 level). A second cycle of intravenous immunoglobulin ($500 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$ for 4 days) was administered. Subsequently, she was referred to the department of rehabilitation medicine for more aggressive rehabilitation. After 11 months, the patient was still unable to walk due to spasticity of the lower extremities. She required regular administration of enema for defecation and intermittent nelaton catheterization due to residual urine.

Discussion

Diverse etiologies of acute nontraumatic myelopathies have been documented, and at least three hypotheses have been proposed with respect to the pathogenesis: cell-mediated post-infectious autoimmune response, direct viral invasion into the spinal cord, and acute vascular occlusion⁶.

In this case, the patient presented with typical clinical features of meningitis and ATM 2 days apart. Enterovirus was isolated from the CSF sample, and the lesions on MRI were confined to

the spinal cord. There are two possibilities regarding the pathogenesis of the meningitis and ATM in this case. First, the enterovirus might have directly invaded the meninges and spinal cord in serial order. Second, the enterovirus might have caused meningitis initially. The ATM might have been induced by the post-infectious immune response of the patient.

Acute viral myelitis can be subdivided into acute flaccid paralysis (AFP) and ATM³. AFP is reminiscent of poliomyelitis and involves the gray matter of spinal cord, whereas ATM involves the partial or complete white matter with or without simultaneous gray matter involvement. Patients with virus-induced AFP usually develop signs of aseptic meningitis such as headache, fever, and vomiting³. Flaccid weakness of one or more extremities then becomes evident within a few days. Affected patients typically do not present with prominent bladder symptoms or overt sensory impairment. In contrast, patients with ATM caused by a viral infection of the spinal white matter may develop ascending sensory deficits and urinary retention over several days, along with progressive weakness caudal to the sensory level³. Both halves of the spinal cord are commonly involved to produce relatively symmetric deficits. In this case, acute myelitis was preceded by the typical signs of aseptic meningitis. However, the clinical and MRI findings were in accordance with those of typical ATM rather than AFP. Certain serotypes of enteroviruses such as poliovirus and enterovirus 71, sometimes involve the gray matter of the spinal cord, specifically the anterior horn cells, leading to AFP^{1,4}. However, it is rare that an enterovirus infection simultaneously involves the gray and white matter of the spinal cord, resulting in an ATM case, such as the one presented here.

In terms of long-term prognosis of childhood ATM, a large retrospective study of 47 children with ATM demonstrated that at a median age of 3.2 years after the acute illness, 43% were still unable to walk 30ft, 50% required bladder catheterization, and 54% had persistent dysesthesias⁷. A recent study of 95 children with idiopathic ATM demonstrated that 16 (17%) relapsed, with a diagnosis of multiple sclerosis in 13 (14%) and neuromyelitis optica in 3 (3%) children⁸. The report showed that factors associated with poor outcomes were female sex, severe scores on the ASIA (American Spinal Injury Association) scale at onset, gadolinium enhancement on spinal MRI, absence of pleocytosis, and absence of cervical or cervico-thoracic lesion on spinal MRI. In this case, the patient showed a significantly higher protein level (163.1 mg/dL) in the 7 days follow-up CSF analysis compared with the initial analysis (26.3 mg/dL). It is necessary to study whether this finding could help to predict poor outcome of patients with ATM, although a relationship between CSF protein level and the outcome of ATM has not been established.

Enteroviruses sometimes cause aseptic meningitis not accompanied by CSF pleocytosis in children, particularly infants, accounting for 14-44% of enteroviral meningitis cases^{9,10}. In this case, the patient revealed no apparent pleocytosis and normal protein levels in the initial CSF analysis despite apparent clinical manifestations of meningitis in conjunction with enterovirus isolation from the CSF samples. This indicates that if viral meningitis is clinically suspected, PCR for common pathogenic viruses including enterovirus is essential, and the possibility of viral central nervous system infection should not be excluded until the result of the PCR, even in patients with normal CSF profiles.

Epidemics of enteroviral meningitis occasionally occur in summer and early fall³. As enteroviral meningitis is usually self-limited and recovers completely without complication, physicians tend to reassure patients and caretakers about the disease. However, this case demonstrates that it could be followed by critical neurological disease such as ATM.

요약

급성 횡단성 척수염은 드물게 발생하는 척수의 후천적 염증성 질환으로, 급격히 발생하는 양측의 근력 저하, 감각 이상, 소변 혹은 대변 조절능력의 상실 증상으로 발현된다. 엔테로바이러스는 무균성 뇌수막염의 가장 흔한 원인 바이러스로, 대부분 특별한 치료 없이도 합병증 없이 완쾌된다. 하지만, 엔테로바이러스는 뇌염, 길랑 바레 증후군, 척수병증도 유발할 수 있는 것으로 알려져 있다. 저자들은 6세 여아에서 엔테로바이러스 뇌수막염 직후 발생한 전형적인 급성 횡단성 척수염 증례를 경험하였기에 보고하는 바이다. 환자는 내원 당일 갑작스럽게 발생한 양측 하지의 근력 저하, 배꼽 아래의 감각 이상, 소변과 대변 조절능력의 상실을 주소로 본원에 내원하였다. 내원 전일 환자는 발열, 두통, 반복되는 구토 증상으로 본원 응급실 내원하여 엔테로바이러스 뇌수막염을 진단받고 귀가 하였었다. 환자의 뇌척수액 및 분변에서 엔테로바이러스가 확인되었으며, 척수 자기공명영상에서는 T2 강조영상에서 C2-C7과 T3-T11 부위에 신호증강 소견을 보였다. 환자는 정맥내 면역글로불린, 고용량 스테로이드 치료와 함께 물리치

료를 시행 받았으나, 발병 11개월 후에도 아직 걸을 수 없는 상태이며, 소변 배출을 위해 간헐적인 단순도뇨가 필요한 상태이다. 엔테로바이러스 뇌수막염은 상대적으로 경한 질환으로 알려져 있지만, 본 증례는 엔테로바이러스 뇌수막염이 급성 횡단성 척수염과 같은 심각한 신경학적 질병으로 진행할 수 있음을 보여주었다.

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