MR Features in Patients with Residual Paralysis following Aseptic Meningitis

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Introduction

Polio-like paralysis can be caused by neurovirulent strains of nonpolio enteroviruses. Enterovirus 71 (EV 71) is documented as one of the potentially neurovirulent strains and a causative agent of some epidemics (1-7). The clinical manifestations associated with the EV 71 infection include aseptic meningitis, hand-food-mouth disease (HFMD), acute respiratory illness and gastrointestinal disease(6). Although rarely fatal, flaccid paralysis can be followed by EV 71 induced aseptic meningitis. Anterior horn cell necrosis was suggested on MR in two patients with residual paralysis(7). MR features, however, have not yet been described in detail. In this report we present three cases of patients with clinical evidence of EV 71 induced aseptic meningitis whose

Materials and Methods

During four months from April to August, 1990, 201 patients of aseptic meningitis were diagnosed as a aseptic meningitis in our hospital. Diagnosis of aseptic meningitis was based on clinical symptoms and signs, cerebrospinal fluid (CSF) findings, negative CSF and blood culture, negative CSF latex agglutinin test, negative CSF AFB and India ink staining. Among them acute onset of lower motor paralysis was developed in four patients. The paralysis involved the lower extremities in three and the upper in one. MR studies were performed in three patients with paralysis in the lower extremities. The titrations of neutralizing antibody against EV71 performed on sera in three including a patient with paralysis In the
upper extremities showed initial high titer or fourfold increase in antibody titer. The titrations for coxsackievirus A16 in three revealed antibody titers within normal range. Viral culture was not performed.

MR studies were performed on a 1.5T superconducting system (Signa, General Electric Medical System, Milwaukee). T1-weighted images, 500-600/20/2 (TR/TE/excitations), were obtained in axial, sagittal and/or coronal planes. T2-weighted images (1,800-2,500/30, 80/1) were obtained in axial planes in two patients and in sagittal plane in a patient. Sagittal gradient echo images (350/20/4) were obtained in a patient.

**Results**

**Case 1**

An 8 month-old boy presented with HFMD and developed left lower extremity paralysis 4 days after fever and rash. This was followed in a day by ascending paralysis, which eventually progressed to quadriplegia. His initial neurologic examination showed a weak motor response in the right leg and no motor response in the left leg. Deep tendon reflexes were diminished in both sides without sensory deficit. CSF examination showed 210 white blood cells (WBC)/mm³ with 88% mononuclear cells, and a protein and a glucose level of 27 and 68 mg/dl, respectively. He slowly regained the activity of his right leg 14 days after onset. MR performed 20 days after onset showed two small circular lesions within the spinal cord with signal intensities similar to CSF (Fig. 1). He was discharged on the 16th hospital day, at which time he was able to move his left big toe. Improvement continued and by five months after discharge he became to move his ankle but the weakness was still present at that time.

**Case 2**

A 10/12-year-old girl presented with a high fever, vomiting and weakness in the left lower leg preceded by mild fever and rash in hand, foot and mouth three days ago. The neurologic examination showed neck stiffness. The motor response was absent in the left leg. The deep tendon reflexes were decreased in left side. The pain responses were intact in both sides. Spinal fluid examination showed 360 WBC/mm³ with 32% mononuclear cells and a protein content of 45.6 mg/dl and a glucose level of 60 mg/dl. MR performed three weeks after onset revealed two small cavitory lesions at the area of anterior horn cells (Fig. 2).
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Fig. 2. Case 2: 10/12-year-old girl with residual paralysis.

a. A sagittal T1-weighted image shows mild swelling of the lower thoracic spinal cord. Note the low signal intensities at anterior one-third of the spinal cord.
b. An axial T1-weighted image demonstrates the small cavitary lesions.
c. Axial T2-weighted image shows the same lesions of high signal intensities, larger on the left. The paralysis was more severe in the left extremities.

weakness was slowly improved but still present two months after onset.

Case 3

A 4-year-old girl was admitted because of URI-like symptoms for four days and inability to bear weight on her legs for one day. On admission, she was afebrile, alert but irritable. Muscle power of both lower extremities were decreased. The pain sense was absent 2 cm below umbilicus. The deep tendon reflexes were diminished. There was a loss of bladder control. CSF examination showed 360 WBC/mm³ with 32% mononuclear cells, and a protein content of 45 mg/dl and a glucose level at 60 mg/dl. The result of electromyelography was consistent with polyno-neuropathy. MR performed 7 days after onset revealed a mild enlargement of conus medullaris (Fig. 3A). A central syrinx-like cavity was noted within the spinal cord on axial T1 and T2-weighted images (Fig. 3B) but regarded as a truncation artifact because the images were acquired with 128 matrix. Four month later, the follow-up MR demonstrated atrophic changes of spinal cord below T₁₀ level (Fig. 3C). The paralysis of lower extremities persisted after four month follow-up.

Discussion

The occurrence of two hundred and one patients of aseptic meningitis during short period of four
months can be regarded as an epidemic outbreak. Among the 201 patients with aseptic meningitis, four patients including a referred patient developed flaccid paralysis (2%). The paralysis mainly involved the lower extremities except one patient who showed weakness of upper extremities and did not have MR examination. Three of them revealed elevated titers against EV 71 in serologic test. Although viral culture was not done we assume that EV 71 is incriminated as the cause of the epidemic.

Since the first outbreak was reported in the United States, EV 71 has been associated with rare outbreaks in worldwide distribution as well as sporadic cases of flaccid paralysis (1-7). The spectrum of the illness observed in the outbreaks were variable (6). Rash is a common clinical findings in EV 71 infection. Maculopapular, generalized vesicular, and diffuse erythematous exanthems have been observed, but
the most frequently noted pattern of rash in all outbreaks was HFMD. The simultaneous occurrence of HFMD and CNS disease may suggest EV 71 infection as a common cause of HFMD. In our cases, HFMD was the initial symptomatic manifestation in three of four patients. Coxsackie A-16 is seldom associated with CNS disease and the serologic test for coxsackie A-16 was negative in three of four patients. The clinical pattern of the CNS disease associated with EV 71 includes aseptic meningitis, meningoencephalitis and myelitis causing motoparesis. The striking feature of our outbreak is the occurrence of paralytic disease, since paralysis was not common feature for reported outbreaks. However, the epidemic of EV 71 disease in Bulgaria (1975) differed considerably from epidemics in other country because of the high incidence of paralytic cases (2). A large portion of case had severe poliomyelitis-like paralytic disease with a bulbar form of poliomyelitis and encephalomyelitis. High mortality (64.7%) among the bulbar cases was noted. Except Bulgarian outbreaks, only ten cases of flaccid paralysis were reported to date: a case of infective polyneuritis in Australia (1972), two cases in Japan (1978), five cases in Philadelphia (1987).

MR findings were first reported in two of five cases in Philadelphia (7). A MR in a patient with weakness in upper extremities showed an enlarged cervical cord. Repeated MRI five months later revealed a circular hypointensity in the left ventral aspect of the cervical cord. A MR performed in another patient 7 month later was only described as two small hyperintensities on T2-weighted image in the ventral horns of the lower thoracic spinal cord, larger on the right, corresponding to side and distribution of residual weakness. In our cases, the cord lesions occupying the areas of anterior horn cells were well demonstrated on axial T1 and T2-weighted images. The small circular cavities of low signal intensities formed a configuration shaped like a pig nose on axial T1-weighted images. The size of the cavity corresponded to the severity of the residual paralysis. Swelling of conus medullaris was noted on sagittal T1 weighted image at acute phase. The involvement of anterior horn cells can be identified at anterior one third of swollen spinal cord as in case 2 (Fig. 2). Atrophic changes shown in case 3, to our knowledge, is not previously documented in other outbreaks. The clinical manifestation of the patient was also suggestive of transverse myelitis instead of poliomyelitis-like paralysis which characterizedly involved the anterior horn cells. In spite of the fourfold elevation of antibody titer for EV 71 in that patient, we can not completely exclude the possibility of aseptic meningitis induced by other viral infection.

The differential diagnosis of an acute onset of extremity weakness in children includes three important viral syndromes of the caudal central nervous system (9). Poliomyelitis refers to the primary involvement of the gray matter of the spinal cord and usually the anterior horn cell. Although poliovirus infections have been controlled by vaccine, poliomyelitis may be caused by neurovirulent strains of enterovirus. The lack of sensory involvement in two patients (case 1 and 2) and MRI defect in the ventral horns of the spinal cords with persistent weakness support the anterior horn cell as target of involvement. The second type is a transverse myelitis in which there is less predilection for cell type. The entire spinal cord at one level is usually involved as in case 3. Acute transverse myelitis has been described in association with mumps, measles, varicellar-zoster, infectious mononucleosis, enterovirus, and herpes simplex infections. The cord swelling in acute transverse myelitis is also reported in AIDS patients (10, 11). A third viral syndrome is polyradiculitis which is commonly associated with infectious mononucleosis but MR findings have not been described.

Identification of the lesion within the spinal cord is important for determination of the extent and prediction of the prognosis. MR is highly sensitive in depicting spinal cord lesion. Because the paralysis was noticed in three to five days after symptom onset. MR studies must be included in workups when the weakness is noted during the course of viral meningitis. MR images should be obtained in multiple planes. Axial T1 and T2-weighted images are necessary to find small cavitory lesions within the spinal cord. Sagittal T1 and T2-weighted or gradient echo images are also useful in evaluation of the cord swelling and the extent of the lesion involved. Truncation artifact can mimic a syrinx-like artifact as in case 3. By increasing the number of phase encoding
steps, decreasing the field of view, and switching phase-and frequency-encoding axes, syrinx-like artifact can be eliminated (8).

REFERENCES