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MR Features in Patients with Residual Paralysis Following Aseptic Meningitis

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Poliomyelitislike paralysis can be caused by neurovirulent strains of nonpolioenteroviruses. Enterovirus 71 (EV 71) has been documented as one of the potentially neurovirulent strains and a causative agent of some epidemics [1–7]. The clinical manifestations associated with EV 71 infection include aseptic meningitis, hand-foot-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 images in two patients with residual paralysis [7]. We present the findings in three patients with clinical evidence of EV 71–induced aseptic meningitis whose MR studies showed residual changes in the spinal cord.

Subjects and Methods

During the 4 months from April to August 1990, 201 patients in our hospital were diagnosed as having aseptic meningitis. The diagnoses were based on clinical symptoms and signs, CSF findings, negative CSF and blood culture, negative CSF latex agglutinin test, negative CSF acid-fast bacillus, and India ink staining. Acute motor paralysis developed in four patients, involving the lower extremities in three and the upper in one. MR studies were performed in the three patients with paralysis in the lower extremities. Serologic tests for titrations of neutralizing antibody for EV 71 showed initial high titers, or a fourfold increase in titers. Serologic tests for coxsackievirus A16 revealed titers within the normal range. Viral cultures were not performed.

MR studies were obtained on a 1.5-T superconducting system (Signa, General Electric Medical Systems, Milwaukee). T1-weighted images, 400–700/20–25/2 (TR/TE/excitations), were obtained in axial, sagittal, and/or coronal planes. T2-weighted images (1800–2500/30, 80/1–1.5) were obtained in the axial plane in two patients and in the sagittal plane in one patient. Sagittal gradient-echo images (350/20/4) were obtained in one patient.

Case Reports

Case 1

An 8-month-old boy presented with HFMD and developed left lower extremity paralysis 4 days after onset of a fever and rash. This was followed a day later by ascending paralysis, which eventually progressed to quadriparesis. 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 on both sides without sensory deficit. CSF examination showed 210 white blood cells (WBC)/mm^3 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 of paralysis. MR imaging 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 day after admission, at which time he was able to move his left big toe. Improvement continued and by 5 months after discharge he was able to move his ankle but the weakness was still present at that time.

Case 2

A 22-month-old girl presented with high fever, vomiting, and weakness in the left lower leg preceded by mild fever and a rash in the hand, foot, and mouth 3 days earlier. The neurologic examination showed neck stiffness and absent motor response in the left leg. The deep tendon reflexes were decreased on the left side. Pain responses were intact on both sides. CSF examination showed 360 WBC/mm^3 with 32% mononuclear cells and a protein content of 45 mg/dl and a glucose level of 60 mg/dl. MR imaging performed 3 weeks after onset revealed two small cavitary lesions in the area of the anterior horn cells (Fig. 2). The weakness slowly improved but was still present 2 months after onset.

Case 3

A 4-year-old girl was admitted because of symptoms of 4 days duration similar to those of an upper respiratory infection and an inability to bear weight on her legs for a period of 1 day. On admission, she was afebrile, alert, but irritable. Muscle power in both lower extremities was decreased. Pain sensation was absent 2 cm below the umbilicus. The deep tendon reflexes were diminished and there was a loss of bladder control. CSF examination showed 15 WBC/mm^3 and a protein content of 98 mg/dl and a glucose level of 64 mg/dl. Electromyography suggested polyradiculoneuropathy. MR imaging performed 7 days after onset revealed a mild enlargement of the conus medullaris (Fig. 3A). A central syrinxlike cavity was noted within the spinal cord on axial T1- and T2-weighted images (Fig. 3B).

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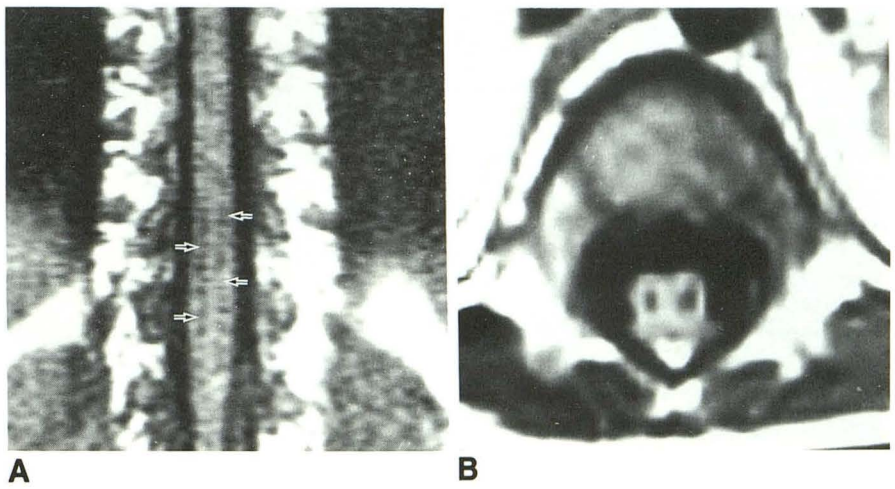

Fig. 1.—Case 1: 8-month-old boy with residual paralysis preceded by hand-foot-mouth disease and aseptic meningitis.
***A*, Coronal T1-weighted image (500/20/1) shows two parallel linear lesions of low signal intensity within lower thoracic spinal cord (*arrows*).**
***B*, Axial T1-weighted image (700/20/2) at T11 level reveals the circular cavities of low signal intensity forming a configuration like a "pig's nose."**

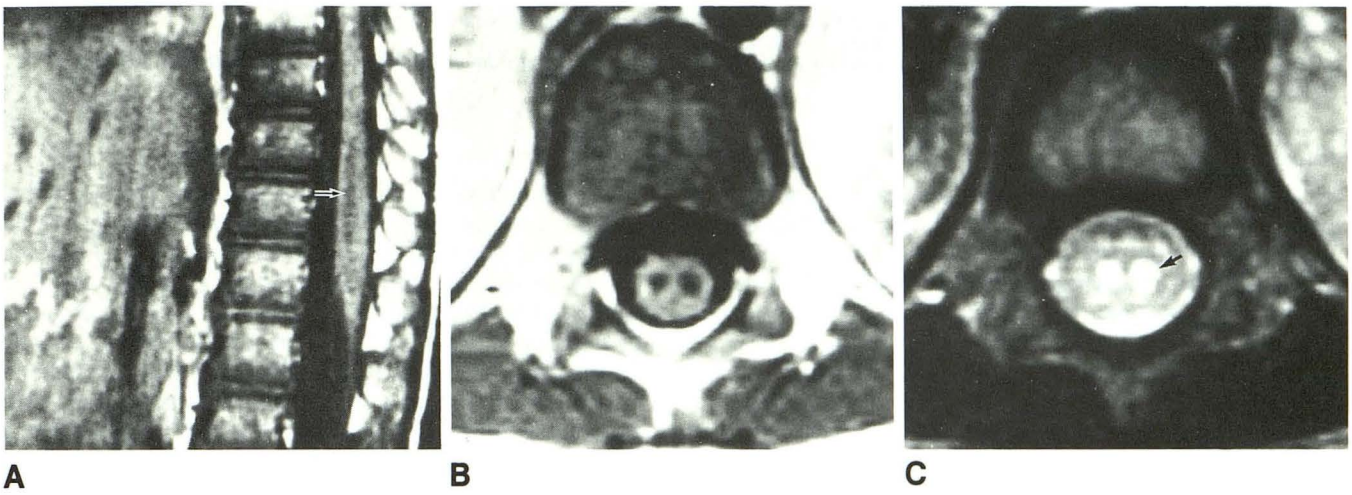

Fig. 2.—Case 2: 22-month-old girl with residual paralysis.
***A*, Sagittal T1-weighted image (600/25/2) shows mild swelling of lower thoracic spinal cord. Note low signal intensities in anterior one third of spinal cord (*arrow*).**
***B*, Axial T1-weighted image (500/20/2) shows small cavitary lesions.**
***C*, Axial T2-weighted image (2000/80/1.5) shows the same lesions to be of high signal intensity, larger on the left (*arrow*). Paralysis was more severe in left lower extremity.**

Four months later, a follow-up MR examination demonstrated atrophic changes of the spinal cord below the T10 level (Fig. 3C). The paralysis of the lower extremities was present at the 4-month follow-up examination.

Discussion

The occurrence of 201 cases of aseptic meningitis during a period of 4 months can be regarded as an epidemic outbreak. Among the 201 patients, four (2%) developed flaccid paralysis. The paralysis mainly involved the lower extremities except in one patient who showed weakness of the upper extremities. This individual did not have an MR examination. Three of the four patients had elevated titers against EV 71 on a serologic test. Although a viral culture was not done it was assumed that EV 71 was the cause of the epidemic.

Since the first outbreak was reported in the United States, EV 71 has been associated with rare worldwide outbreaks as well as with sporadic cases of flaccid paralysis [1–7]. The spectrum of the illness as observed during the outbreaks has been variable [6]. Rash is a common clinical finding in EV 71 infection, and maculopapular, generalized vesicular and diffuse erythematous exanthems have been observed. The most frequently noted pattern of rash in all outbreaks is 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 symptom 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 paresis. The striking feature of the outbreak we report was the occurrence of paralytic disease, since paralysis was not a common feature of previously reported outbreaks. However, the epidemic of EV 71 disease in Bulgaria (1975) differed considerably from epidem-

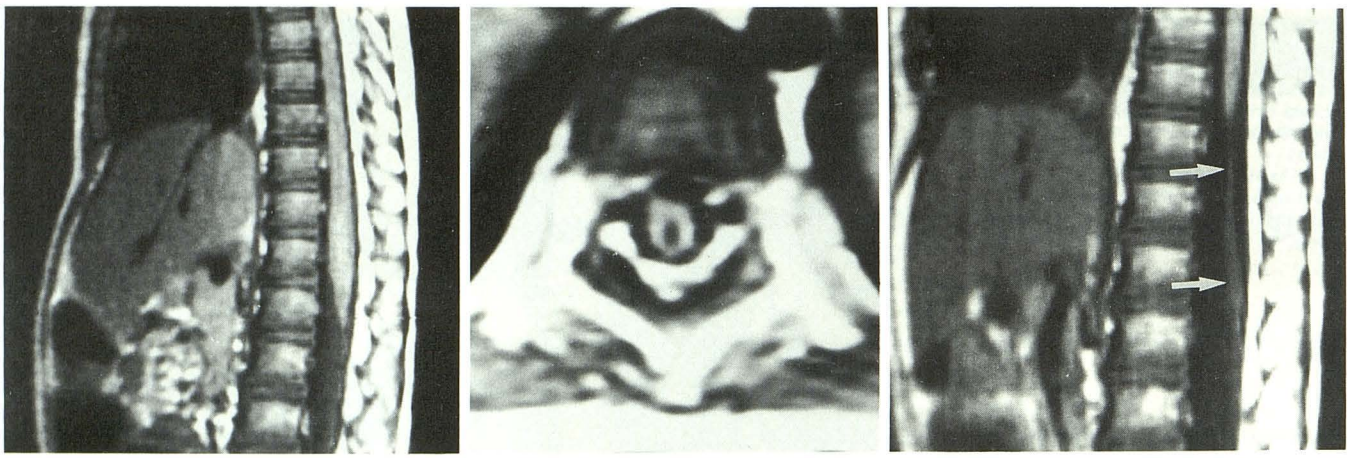

Fig. 3.—Case 3: 4-year-old girl with transverse myelitis.
***A*, MR performed 7 days after onset shows mild swelling of conus medullaris on sagittal T1-weighted image (500/20/2).**
***B*, Axial T1-weighted image (600/20/2) shows a central low signal intensity.**
***C*, MR performed 4 months later reveals atrophic changes (*arrows*) in lower thoracic spinal cord on sagittal T1-weighted image (400/20/2).**

ics in other countries in that there were a large number of paralytic cases [2]. A large portion of cases had severe poliomyelitislike paralytic disease with a bulbar form of poliomyelitis and encephalomyelitis. High mortality (64.7%) among the bulbar cases was noted. In addition to the Bulgarian outbreak, only 10 cases of flaccid paralysis have been reported: one case of infectious polyneuritis in Australia (1972) [8], two cases in New York (1977) [7], two cases in Japan (1978) [3], and five cases in Philadelphia (1987) [7].

MR findings were first reported in two of five cases in Philadelphia [7]. MR images in a patient with weakness in the upper extremities showed an enlarged cervical cord. A repeat MR examination 5 months later revealed a circular hypointensity in the left ventral aspect of the cervical cord. T2-weighted MR study in another patient 7 months later revealed two small hyperintensities in the ventral horns of the lower thoracic spinal cord, larger on the right, corresponding to the side and distribution of residual weakness. In our cases, the cord lesions occupying the areas of the anterior horn cells were well demonstrated on axial T1- and T2-weighted images. The cord with small circular cavities of low signal intensity formed a configuration shaped like a "pig's nose" on axial T1-weighted images. The size of the cavity corresponded to the severity of the residual paralysis. Swelling of the conus medullaris was noted on a sagittal T1-weighted image in the acute phase. Involvement of the anterior horn cells can be identified in the anterior one third of the swollen spinal cord, as in case 2 (Fig. 2). Atrophic changes of the cord are shown in case 3. The patient's clinical manifestations were also suggestive of transverse myelitis instead of a poliomyelitislike paralysis, which characteristically involves the anterior horn cells. In spite of the fourfold elevation of antibody titer for EV 71 in that patient, we cannot 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 CNS [9]. The first, 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 (cases 1 and 2) and a defect in the ventral horns of the spinal cords with persistent weakness support the theory of the anterior horn cell as the 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, varicella-zoster, infectious mononucleosis, enterovirus, and herpes simplex infections. The cord swelling in acute transverse myelitis also has been reported in AIDS patients [10, 11]. A third viral syndrome is polyradiculitis, which is commonly associated with infectious mononucleosis; however, MR findings have not been described.

Identification of the lesion within the spinal cord is important for determining the extent of paralysis and predicting its residual effects if a cavitary lesion remains within the spinal cord. MR is highly sensitive in depicting spinal cord lesions. And because paralysis is noticed within 3–5 days after symptom onset, MR studies should probably be included in workups when the weakness is first 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 cavitary lesions within the spinal cord; sagittal T1- and T2-weighted or gradient-echo images are useful in evaluating cord swelling and the extent of the lesion. Truncation artifacts can mimic syrinxlike artifacts; by increasing the number of phase-encoding steps, decreasing the field of view, and switching phase- and frequency-encoding axes, these artifacts can be eliminated [12].

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