Tohoku J. Exp. Med., 2000, **192**, 151-155

Case Report

Acute Disseminated Encephalomyelitis Developed after Acute Herpetic Gingivostomatitis

TADAHIKO ITO, ARATA WATANABE and JINZO AKABANE

Department of Pediatrics, Nakadori General Hospital, Akita 010-8577

ITO, T., WATANABE, A. and AKABANE, J. *Acute Disseminated Encephalomyelitis Developed after Acute Herpetic Gingivostomatitis.* Tohoku J. Exp. Med., 2000, **192** (2), 151-155 —— A child with acute disseminated encephalomyelitis (ADEM) developed after acute herpetic gingivostomatisis was described. Inspite of the improvement of his gingivostomatitis, his consciousness gradually deteriorated and he was admitted to Nakadori General Hospital. His consciousness level was drowsiness and increased bilateral patellar reflexes were shown. Because magnetic resonance imaging (MRI) T2-weighted scan showed areas of high signal intensity disseminated in superior portion of medulla oblongata, dorsal portion of pons, basal nuclei and thalamus, he was suspected as having ADEM. Anti-herpes simplex virus (HSV) 1 IgG and IgM antibodies elevated in both blood and cerebrospinal fluid. From these results, HSV1 infection was thought to be the preceding infection of ADEM. Methylprednisolone therapy (20 mg/kg daily) for 3 days, followed by prednisolone (2 mg/kg) was started, with an excellent response. In addition, administration of acyclovir was also continued, considering the complication of HSV encephalitis. MRI T2-weighted scan performed at 2 months later after the onset of ADEM revealed disappearance of the lesions. He was discharged without remaining disorders. It is difficult to distinguish between ADEM and HSV encephalitis because both of these diseases show various neurological symptoms. In our case, MRI was the most useful method for correct diagnosis of ADEM. We concluded that ADEM is important as a disease of central nervus system due to HSV1 infection, in addition to encephalitis. ———— acute disseminated encephalomyelitis; herpes simplex virus 1; herpes simplex encephalitis

Acute disseminated encephalomyelitis (ADEM) is an inflammatory demyelinating disease of central nervous system and often develops after viral infection (McAlpine 1931). ADEM developed after infection of herpes simplex virus (HSV) is relatively rare compared with other viral infections including measles, rubella, varicella and mumps. We report a child with ADEM after acute herpetic gingivostomatitis and discussed the differential diagnosis between ADEM

Received June 26, 2000; revision accepted for publication October 3, 2000.

Address for reprints: Tadahiko Ito, M.D., Department of Pediatrics, Nakadori General Hospital, 3-15 Misono-cho, Minami-dori, Akita 010-8577, Japan.

and HSV encephalitis.

Case Report

In August, 1998, a 3-year-old male with gingivostomatitis consulted to Nakadori General Hospital. Although his gingivostomatitis was improved by medication, his consciousness began to deteriorate 9 days later after the appearance of the gingivostomatitis. Because of disturbance of consciousness, he was admitted to the hospital 10 days later after the first consultation. On admission, his consciousness level was drowsiness. Neurological examination showed increased bilateral patellar reflexes and appearance of bilateral Babinski reflexes and ankle clonus. Although lumbar puncture showed normal counts of cells and normal values of protein and sugar of cerebrospinal fluid on admission, mild elevation of monocytes (42/mm^3) in cerebrospinal fluid was revealed on the eighth day after admission.

Electroencephalogram revealed the dominance of slow waves without spikes. Serum lactate dehydrogenase, creatine phosphokinase and others were all within normal limits in blood examination. Brain magnetic resonance imaging (MRI) T2-weighted scan performed on the second day after admission showed areas of high signal intensity disseminated in superior portion of medulla oblongata, dorsal portion of pons, basal nuclei and thalamus (Fig. 1). Based on these MRI findings, he was suspected as having ADEM. Blood anti-HSV1 IgG and IgM antibodies obtained by enzyme immuno-assay elevated to respectively 13.3 mg/100 ml and

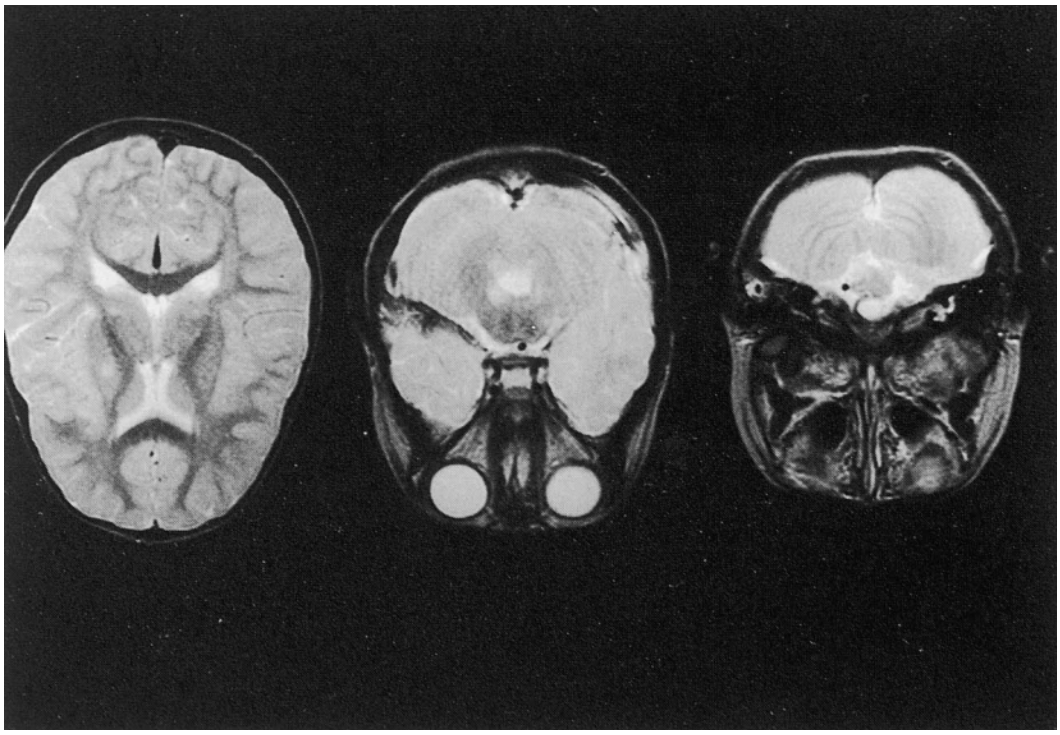

Fig. 1. Brain MRI T2-weighted scan performed on the second day after admission shows areas of high signal intensity disseminated in superior portion of medulla oblongata, dorsal portion of pons, basal nuclei and thalamus.

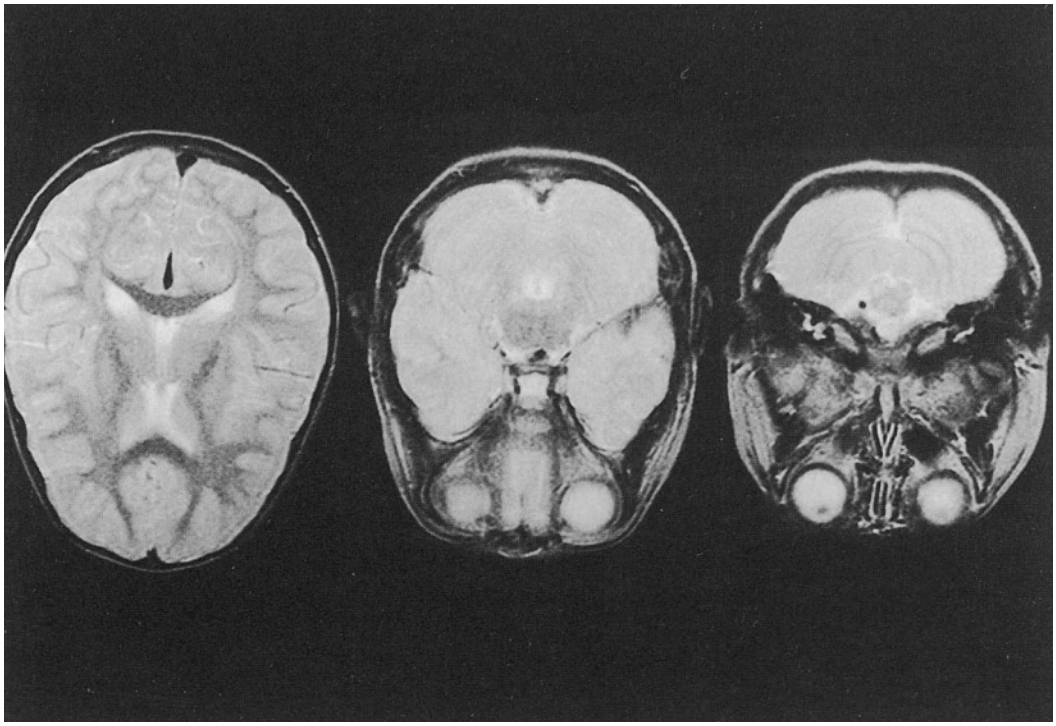

Fig. 2. Brain MRI T2-weighted scan performed at 2 months later since the onset of ADEM shows disappearance of the areas of high signal intensity.

13.32 mg/100 ml on the third day after admission, and three weeks later, HSV1 IgG and IgM were respectively 19.1 mg/100 ml and 11.24 mg/100 ml. Those antibodies in cerebrospinal fluid were also elevated (IgG; 0.813 mg/100 ml and IgM; 2.81 mg/100 ml) on the seventh day after admission. There were no significant elevations of antibodies against other virus such as Epstein-Barr virus and cytomegalovirus. HSV-DNA was not detected from cerebrospinal fluid by the PCR method. From these results, acute herpetic gingivostomatitis was thought to be the preceding infection of ADEM. Methylprednisolone therapy (20 mg/kg daily) for 3 days, followed by prednisolone (2 mg/kg) was started, with an excellent response. In addition, administration of acyclovir was also continued, considering the complication of HSV encephalitis. His consciousness level gradually improved and became clear on the 10th day after admission. Prednisolone was gradually reduced in dose and discontinued. MRI T2-weighted scan performed at 2 months later after the onset of ADEM revealed disappearance of the areas of high signal intensity (Fig. 2). He was discharged without remaining disorders. We had the correct diagnosis of ADEM differentiating from multiple sclerosis beause of the monophasic course of his clinical symptoms and the improvement of MRI findings.

Discussion

ADEM is an inflammatory demyelinating disease based on disseminated lesions of central nervous system, which often develops after infection or vaccination. Various viral infections, including measles, rubella, varicella and mumps

were reported as preceding infection. Encephalitis is common as a disease of central nervous system caused by HSV infection, and several patients with ADEM developed after HSV infection were reported (Kaji et al. 1996). However, child patient with ADEM caused by HSV infection like our case seems to be very rare. Differential diagnosis between HSV encephalitis and ADEM seems to be the most serious problem for planning the treatment. For the treatment of HSV encephalitis, early diagnosis and early administration of acyclovir are important because of high mortality and serious remaining neurological disorders. On the other hand, the administration of corticosteroids is effective for ADEM. In our case, it seemed to be very difficult to differentiate between encephalitis and ADEM from his clinical symptoms on admission, because both of these diseases show various neurological symptoms (McAlpine 1931; Whitley 1982). MRI seems to be very useful for the differential diagnosis. In ADEM, multiple and asymmetrical T2-weighted hyperintense are shown in the white matter and lesions are sometimes distributed in other regions including internal capsule, thalamus, basal nuclei, optic nerve and cerebellum (Anezaki et al. 1999; Murthy et al. 1999; Gomez-Gosalvez et al. 2000). In HSV encephalitis, hyperintensity of unilateral temporal and/or frontal lobes was shown on T2 weighted scan, and bilateral involvement is not rare (Neils et al. 1987; Schroth et al. 1987). Because of the multiple and asymmetrical T2-weighted hyperintense in medulla oblongata, pons, basal nuclei and tharamus in our patient, we suspected that he had ADEM developed after HSV infection with or without HSV encephalitis.

We administered corticosteroids and acyclovir to our patient. A case with disseminated hemorrhagic leukoencephalomyelitis with locarized herpes simplex brain stem encephalitis was reported. We think that, despite of the typical MRI findings indicating ADEM, both of corticosteroids and acyclovir should be administered considering the association with HSV encephalitis.

Atypical findings on MRI such as tumor-like demyelinating lesions were reported in patients who were clinically diagnosed as having ADEM (Kepes 1993). Therefore, we should consider the existence of patients with the history of HSV infection, who could not be made differential diagnosis between HSV encephalitis and ADEM by single examination using MRI. In case we have a patient diagnosed as having HSV encephalitis, but administration of acyclovir is not effective, we should repeatedly perform MRI considering the possibility of ADEM. We concluded that ADEM is important as a disease of central nervous system caused by HSV1 infection, in addition to encephalitis.

References

1) Anezaki, T., Aida, I., Inuzuka, T. & Tsuji, S. (1999) An early-onset case of acute disseminated encephalomyelitis with bilateral thalamic lesions on MRI. *Rinsho Shinkeigaku*, **39**, 821–824.
2) Gomez-Gosalvez, F.A., Smeyers, P., Menor, F., Morant, A., Carbonell, J. & Mulas, F.

(2000) Disseminated acute encephalomyelitis in children. A retrospective study of seven patients. *Rev. Neurol.*, **30**, 304-310.

3) Kaji, M., Kusuhara, T., Ayabe, M., Hino, H., Shoji, H. & Nagao, T. (1996) Survey of herpes simplex virus infections of the central nervous system, including acute disseminated encephalomyelitis, in the Kyushu and Okinawa regions of Japan. *Mult. Scler.*, **2**, 83-87.
4) Kepes, J.J. (1993) Large focal tumor-like demyelinating lesions of the brain: Intermediate entity between muliple sclerosis and acute disseminated encephalomyelitis ? A study of 31 patients. *Ann. Neurol.*, **33**, 18-27.
5) McAlpine, D. (1931) Acute disseminated encephalomyelitis: Its sequele and its relationship to disseminated sclerosis. *Lancet*, **1**, 846-852.
6) Murthy, J.M., Yangala, R., Meena, A.K. & Jaganmohan Reddy, J. (1999) Acute disseminated encephalomyelitis: clinical and MRI study from South India. *J. Neurol. Sci.*, **165**, 133-138.
7) Neils, E.W., Lukin, R., Tomsick, T.A. & Twe, J.M. (1987) Magnetic resonance imaging and computerized tomography scanning of herpes simplex encephalitis. Report of two cases. *J. Neurosurg.*, **67**, 592-594.
8) Schroth, G., Gawehn, J., Thron, A., Vallbracht, A. & Voigt, k. (1987) Early diagnosis herpes simplex encephalitis by MRI. *Neurology*, **37**, 179-183.
9) Whitley, R.J. (1982) Herpes simplex encephalitis. Clinical assessment. *JAMA*, **247**, 317-320.