Acute disseminated encephalomyelitis (ADEM) is an acute inflammatory demyelinating disorder of the central nervous system commonly seen in children and young adults (1). With modern imaging techniques ADEM is now readily and more commonly diagnosed. Magnetic resonance imaging (MRI) of cases with ADEM typically reveals asymmetrical, bilateral T2 hyperintense lesions in white matter and deep gray matter (2). Although the pathogenesis of ADEM is yet not well known, histologically and clinically, it resembles experimental autoimmune encephalomyelitis (3, 4). Therefore, it is possibly related to an inappropriate autoimmune reaction to myelin antigens of the host triggered by an exogenous antigen.

The disease is clinically characterized by the acute onset of neurological symptoms including alternation of consciousness, paresis, ataxia, seizures, behavioral changes, and urinary incontinence after an infection or immunization (1, 5, 6). Although various viral and bacterial pathogens have been associated with ADEM, the preceding infection cannot be identified frequently (1, 5, 6), and ADEM after Epstein-Barr virus infection has only rarely been reported in English literature (7-11). In this report, we present a girl with ADEM associated with Epstein-Barr virus infection.

Case Report

A 4-year-old girl was admitted to our hospital with a 7-day history of fever, sore throat, headache, and drowsiness noticed in last 2 days. She was well until three days prior to admission when her complaints had appeared abruptly. She had no recent history of vaccination. She was...
examined by her pediatrician in the first day of her disease, during this visit, the diagnosis of exudative tonsillitis was established and the treatment of cefuroxime axetil was initiated without throat culture or rapid antigen detection for group A streptococcus. Despite excellent compliance to the treatment, her complaints persisted until her admission.

On the admission, the child was conscious, body temperature was 38.3°C. Pharyngeal examination revealed severe inflammation, swelling and exudate in tonsillar area. Enlarged, tender lymph nodes were noted in cervical, and inguinal regions. The liver and spleen were palpable 2 and 3 cm below the costal margins, respectively. Neurological examination was completely normal.

Laboratory examinations included hemoglobin level of 12.5 g/dl, leukocyte count of 25,100/mm³ (24% neutrophils, 50% lymphocytes, 24% atypical lymphocytes, and %2 monocytes), and platelet count of 623,000/mm³. Sedimentation rate was 70 mm/h and C-reactive protein level was 0.26 mg/dl. Blood chemistry and anti-streptolysin O titer were within normal limits. Cranial computed tomography scan was normal. Cerebrospinal fluid (CSF) examination was normal except for slightly lymphocytic pleocytosis (40 lymphocytes/mm³). There was no serologic evidence of acute infection by measles, rubella, mumps, cytomegalovirus, human immunodeficiency virus, herpes simplex virus type I and II, varicella-zoster, hepatitis A, B, and C viruses, Toxoplasma gondii, or Mycoplasma pneumoniae, while Epstein-Barr virus viral capsid antigen IgM and IgG were positive. The diagnosis of infectious mononucleosis was established, cefuroxime treatment was discontinued, and patient was followed symptomatically.

Patient’s fever returned to normal at the second day of hospitalization. Tonsillitis, enlarged lymph nodes, and hepatosplenomegaly were also begun to regress spontaneously. On the fourth day of hospitalization, however, the patient was not able to walk and she had expressive dysphasia. The physical examination revealed hyperactive deep tendon reflexes, generalized muscle rigidity, bilaterally positive Achilles’ clonus and Babinsky’s sign. Repeated CSF examination was completely normal, and CSF oligoclonal band was negative. Cranial MR imaging revealed increased signal intensity in areas of lentiform nucleus, caudate nucleus, and frontal, parietal, and temporal subcortical white matter (Figure 1). The lesions were hypo- or isointense on T1-weighted images and did not show any contrast enhancement after intravenous gadolinium injection.

According to the findings on MRI, the diagnosis of ADEM was established, and the treatment with methylprednisolone (20 mg/kg/day, intravenously for three days, then 2 mg/kg/day, orally for ten days) was initiated. Her abnormal neurological findings were improved on the second day, and completely resolved at the end of the treatment. Control MRI performed on the seventh day of the treatment revealed significant regression of the ADEM lesions, and patient was discharged after the discontinuation of methylprednisolone therapy.

Control MR examination after 3 months demonstrated complete resolution of the lesions (Figure 2). No recurrence was observed during 18 months of follow-up.
ADEM is thought to be an autoimmune disease precipitated by infectious agents, which trigger an autoimmune reaction against neural constituents with cross-reactive molecular structures (5, 6). Histologically, multifocal perivenous infiltrations with lymphocytes and plasma cells are seen with edema and demyelination (5, 6). The triggering factors for ADEM include viral illnesses such as measles, rubella, mumps, herpes simplex, chickenpox, cytomegalovirus, and coxsackie B, vaccines such as rabies, pertussis, diphtheria, tetanus, smallpox, influenza, Japanese B encephalitis, mumps/measles/rubella, group A and C meningococcus, bacteria such as Streptococcus pyogenes, Mycoplasma pneumoniae and Salmonella, and drugs such as sulphonamides and para-aminosalicylic acid (5, 6).

Our patient did not have any recent immunization history, and we could not demonstrate evidence of acute viral or bacterial infection other than Epstein-Barr virus infection. She had clinical findings consistent with infectious mononucleosis and acute Epstein-Barr virus infection was confirmed by specific antibodies. Many uncommon and unusual conditions including aseptic meningitis, encephalitis, transverse myelitis, cranial nerve paralyses, ataxia, seizures, Alice in Wonderland syndrome, and Guillain-Barré syndrome have been reported to be associated with Epstein-Barr virus infection (7, 12), however, ADEM has only rarely been reported (7-11).

After an infection or vaccination, ADEM presents as an acute or subacute illness. Fever, headache, and meningeal irritation sings are the most common initial symptoms and findings followed by neurological findings such as seizures, focal neurological deficits, and altered consciousness. CSF abnormalities in patients with ADEM often include a modestly elevated protein level, and occasionally some degree of pleocytosis. CSF oligoclonal bands may be seen on presentation but do not persist later (5, 6). The electroencephalography usually shows slow wave activity. The cranial computed tomography (CT) is usually normal. MRI is usually required to establish the diagnosis (5, 6). The cranial CT of our patient was normal, while MRI revealed brain involvement typical for ADEM. She also had some vague symptoms such as headache and drowsiness possibly associated with ADEM at the time of cranial CT examination performed on admission. Although the CT scan and MRI were not performed simultaneously, this observation supports the opinion that MRI is required for the diagnosis of ADEM.

ADEM is mostly confused with multiple sclerosis. On the contrary of multiple sclerosis, ADEM follows a monophasic clinical course, and generally occurs in children (5, 6). We have not observed a recurrence during 18 months of follow-up in our patient.

Treatment of ADEM has not been systematically studied, and spontaneous improvement has been noted. Except for its fulminant form, the acute hemorrhagic necrotizing encephalomyelitis (Hurst syndrome), the prognosis of ADEM has been uniformly reported as favorable (5, 6). Treatment of patients with ADEM has focused on a presumed autoimmune etiology. The use of corticosteroids in the treatment of ADEM is based on their efficacy in preventing or modifying the course of experimental allergic encephalomyelitis and their use in treating MS (5, 6). Oral and IV steroids are often effective, and represent the most widely
used treatment (5, 6), although they have been reported to be successful in most patients with ADEM, relapses have also been reported (13). We obtained excellent response with high-dose intravenous methyl-prednisolone therapy, and continued oral therapy for another 10 days. Intravenous immunoglobulin, plasmapheresis, and cytostatic drugs are alternative treatment options in patients who do not respond to steroid therapy (14-16).
REFERENCES


ACUTE DISSEMINATED ENCEPHALOMYELITIS ASSOCIATED WITH EPSTEIN-BARR VIRUS INFECTION