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Original Article

Acute Disseminated Encephalomyelitis in Childhood; Epidemiologic, Clinical, and Laboratory Features

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Abstract

Background: Acute disseminated encephalomyelitis **(**ADEM), which occurs spontaneously or after systemic viral infection and vaccination mostly affects children. This study aims at describing the epidemiologic, clinical, neuroimaging, laboratory features, treatment and outcome in children who diagnosed as having ADEM and admitted in a referral center in Tehran.

Methods: This descriptive prospective study was conducted on patients with a diagnosis of ADEM over a period of 30 months, between Sep 2003 and Mar 2006, admitted to the neurology ward of Mofid Pediatric Hospital. All these patients were visited in regular follow-up every 6 months for two years.

Results: Eighteen patients with the mean age of 6 years (range 5 months - 12 years) were studied. No sex predominance was noted. Sixty-one percent had prodromal illness, and two patients had been vaccinated before the illness. Thirteen (72%) patients presented in fall or winter. Motor deficits and cranial nerve palsy were the most common features, which had occurred in 13 (72%) patients. Abnormal findings in cerebrospinal fluid evaluation were detected in 33% of the patients. Brain computed tomography was normal in all but one patient. Electroencephalograms done in nine patients were normal in 54%. Magnetic resonance imaging showed lesions were most commonly in the subcortical and periventricular areas (76%). Nine (50%) patients were treated with corticosteroids and intravenous immunoglobulin. The mortality rate was 5.5%, and the relapse occurred only in one case. In two-thirds of the patients, prognosis for complete recovery was excellent.

Conclusion: Childhood ADEM is a benign condition, affecting both sexes equally. Recurrent infections have been its common cause in our center.
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Keywords ● Acute disseminated encephalomyelitis ● demyelination ● children

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Introduction

Acute disseminated encephalomyelitis (ADEM) is an inflammatory demyelinating disease of the central nervous system, characterized by acute or subacute

onset of neurologic signs and symptoms along with the evidence of multifocal lesions of demyelination on neuroimaging.[1] ADEM occurs most commonly in children and young adults after viral infection or vaccination.[1,2]

The aim of the present study was to review the epidemiology of the disease as well as its clinical features, neuroimaging, treatment, and outcomes in patients referred to a single institution in Tehran.

Materials and Methods

In this descriptive and prospective study from September 2003 to March 2006, of all the patients admitted at Mofid Children Hospital -a tertiary center for pediatric neurology disorders affiliated to Shahid Beheshti University of Medical Sciences in Tehran- those with acute or subacute onset of polysymptomatic presentation, affecting focal or multifocal areas of CNS were enrolled. Patients were followed-up for two years in every 6 months intervals.

The patients had no history of neurological symptoms suggestive of an earlier demyelinating episode. The inclusion criterion was white matter changes on brain-spinal imaging, without radiologic evidence of a previous destructive white matter process. All the patients were evaluated at 3, 6, 12, and 24 months after the onset of the disease.

We gathered and analyzed the data related to gender, age at onset, preceding infection or immunization, season of onset, neurological symptoms at of the time of presentation, the findings on neuroimaging and cerebrospinal fluid evaluations, clinical course, and final neurologic outcomes.

Results

Eighteen patients with a mean age of 6 years (age range 5 months to 12 years) were included in this study.Male to female ratio was 0.9:1. Thirteen (72%) patients presented in fall or winter.

The preceding events in the eighteen patients are shown in table 1. Seven patients (39%) had no documented previous illness and were considered to have spontaneous or cryptogenic ADEM.

Table 1: Precedent events in children with acute disseminated encephalomyelitis.

Precedent event	Patients No (%)
non specific URI	5 (28)
vaccination	2 (11)
gastroenteritis	1 (5.5)
non-specific febrile illness	2 (11)
hepatitis	1 (5.5)
no defined prodrome	7 (39)
Total	18 (100)

The frequency of presenting features is shown in table 2. The polysymptomatic presentation was a combination of multifocal deficits. Motor deficits and cranial nerve palsies were the most frequent initial findings each were detected in 13 (72%) patients.

Table 2: Frequency of presenting features in children with acute disseminated encephalomyelitis.

Presenting feature	Patients No (%)
Motor deficit	13 (72)
Cranial nerve palsy	13 (72)
Fever	7 (38)
Consciousness impairment	7 (38)
Seizure	6 (33)
Visual complains	5 (27)
Vomiting	4 (22)
Headache	2 (11)
Dysarthria	2 (11)
Vertigo	1 (5.5)

In six (33%) patients, evaluation of cerebrospinal fluid (CSF) showed abnormal findings such as lymphocyte pleocytosis (cells from 3 up to 210/mm3) or mildly elevated protein (up to 84 mg/dl). Because of limited laboratory facilities, no serologic and microbiologic studies were done on CSF and blood samples. Elevated sedimentation rate, was seen in 50% of our patients. Oligoclonal antibodies, which were only checked in one patient because of symptom recurrence, were negative. Elevated sedimentation rate was detected in nine patients (50%).

Electroencephalography (EEG), done in half the patients, with seizure as a disease manifestation, yielded normal findings in 54% and non-specific findings in 46%.

Brain computed tomography was performed in 10 patients, which was normal in all but one patient with brain edema. For all the patients, magnetic resonance imaging (MRI) was requested and the images were reviewed by a single radiologist. MRI of the brain showed multifocal white matter damage, as the hallmark of the disease in 89% of the patients. In two (%11) patients the lesion was single. Focal or multifocal areas of increased signal intensity were noted on T2-weighted images of white matter, basal ganglia, brain stem, cerebellum, or spinal cord. White matter changes were observed in 13 (76%) patients, mostly in occipital region (71%). Involvement of the gray matter (thalamus and basal ganglia) was noted in four patients (22%) and of the brain stem in two (11%). Changes of the spinal cord and cerebellum were observed in three (17%) and five patients (28%) respectively.

All the patients received supportive care and treatment for the symptoms during the acute stage of the disease. A short course of high dose corticosteroid (intravenous methylprednisolone, 20-30 mg/kg/day) was administered to

eight (44%) patients for five consecutive days. One patient received intravenous immunoglobulin (IVIG) and the remaining nine patients received combined IVIG and methylprednisolone.

Twelve out of the 18 (66%) patients had complete neurological recovery confirmed by normal results of neurological examinations. Three (17%) patients had mild neurological sequelae without disability. One (5.5%) patient had two relapses that responded to steroids. Mortality rate was 5.5% and two patients were lost to follow-up. Marked resolution of demyelinating lesions was noted in five patients who had a second cranial MRI at the end of the clinical course.

Discussion

Mean age of the patients in our study was 6 years, with no sex predominance. Kalra et al. reported a mean age of 7.8 years with no sex predominance.[3] Tenembaum et al. reported a mean age of 5.3±3.9 years with a significant male predominance (M/F:1.8:1).[4] Lee et al. reported a mean age of 8.6 years,[5] and Anlar et al. reported the mean age of 8 years with a M/F ratio of 1.7:1.[6]

Admission policy of the Mofid hospital prohibits admission of patients over the age of 14 years; consequently the mean age of cases in our study was less than that of other studies. Our youngest patient was a 5-month old, while in the other studies the lowest ages were 3, 4, 6, and 8 months.[7-10]

In our study most of the patients presented in fall or winter (71%), a finding similar to that of the other studies done by Bennetto et al. and Murthy et al.[11,12]

Preceding events were noted in 61% of our patients (either viral infection or vaccination). Murthy reported that 72% of their cases had had recent upper respiratory tract illness.[12] Hyson et al. reported that 71% of their study group had a prodromal illness.[13] History of preceding viral infection or vaccination was also reported by Kalra et al. in 52% of their patients, and by Thomas et al. in 50% of theirs.[3,8]

The most common presenting signs and symptoms in our study group were motor deficit and cranial nerve palsy. Murthy et al. reported that their patients presented most often primarily with motor deficits (77%). The second most common condition in their study was altered level of consciousness (45%).[12] Similar findings were also reported by Anlar et al.[6]

Ataxia, a common feature in the study done by Hynson et al. was not seen in our study.[13] Unilateral or bilateral long tract signs and acute hemiparesis (85% and 76% respectively), were presenting findings in the Tenembaum et al. study.[4]

Although visual problems were not a common finding in other studies, visual deficits were reported by Karla and Tenembaum, at 42.1% and 23% respectively.[3,4]

The results of CSF examination and electroencephalographic studies were not significant in our patients, a finding similar to that of the other studies.[3,4] Brain computed tomography, specifically at the onset of the disease, may be normal, and hence is not often helpful in establishing the diagnosis.[1]

Elevated sedimentation rate, rarely indicated in other studies,[4] was seen in 50% of our patients. MRI findings varied in different studies. We found occipital white matter involvement in 71% of our patients at the beginning of the illness, whereas Karla reported white matter changes mostly in the frontoparietal (84.2%) and occipital (52.6%) areas. Hynson noted that lesions found by MRI were most commonly seen in the frontal and parietal lobes.[13] Murthy reported those lesions were located in the frontal (48%), followed by the parietal (22%), the temporal (7%), and the occipital (6%) regions.[12] Occipital lesions found by MRI could cause the patients' visual problems. Neurological outcomes in our patients were favorable, which were similar to the other studies.[1,13,14]

Conclusions

Acute disseminated encephalomyelitis is an acute yet treatable inflammatory and demyelinating disease with varying clinical presentations. It seems more frequent than previously reported. Childhood ADEM is a benign condition, affecting both sexes equally. Recurrent infections have been its common cause in our center.

Computed tomography is not a sensitive diagnostic tool, but MRI can be helpful. Patients with acute onset of unexplained encephalopathy or focal neurological deficit should hence be considered for brain-spine MRI at the early stage of the disease. It appears that ADEM is a benign disease that responds well to immunomodulating therapy and the clinical outcome, overall is favorable.

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