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

N. Khosroshahi, K. Kamrani, F. Mahvelati, M. Ghofrani

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.

Keywords ● Acute disseminated encephalomyelitis ● demyelination ● children

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 de-
myelination 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 insti-
tution in Tehran.

Materials and Methods

In this descriptive and prospective study from
September 2003 to March 2006, of all the pa-
tients 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 presen-
tation, 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 demyelinat-
ing episode. The inclusion criterion was white
matter changes on brain-spinal imaging, with-
out radiologic evidence of a previous destruc-
tive 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 neu-
rologic 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. Thir-
ten (72%) patients presented in fall or winter.

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

<table>
<thead>
<tr>
<th>Precedent event</th>
<th>Patients No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>non specific URI</td>
<td>5 (28)</td>
</tr>
<tr>
<td>vaccination</td>
<td>2 (11)</td>
</tr>
<tr>
<td>gastroenteritis</td>
<td>1 (5.5)</td>
</tr>
<tr>
<td>non-specific febrile illness</td>
<td>2 (11)</td>
</tr>
<tr>
<td>hepatitis</td>
<td>1 (5.5)</td>
</tr>
<tr>
<td>no defined prodrome</td>
<td>7 (39)</td>
</tr>
<tr>
<td>Total</td>
<td>18 (100)</td>
</tr>
</tbody>
</table>

The frequency of presenting features is
shown in table 2. The polysymptomatic presen-
tation 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>
<thead>
<tr>
<th>Presenting feature</th>
<th>Patients No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor deficit</td>
<td>13 (72)</td>
</tr>
<tr>
<td>Cranial nerve palsy</td>
<td>13 (72)</td>
</tr>
<tr>
<td>Fever</td>
<td>7 (38)</td>
</tr>
<tr>
<td>Consciousness impairment</td>
<td>7 (38)</td>
</tr>
<tr>
<td>Seizure</td>
<td>6 (33)</td>
</tr>
<tr>
<td>Visual complains</td>
<td>5 (27)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4 (22)</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (11)</td>
</tr>
<tr>
<td>Dysarthria</td>
<td>2 (11)</td>
</tr>
<tr>
<td>Vertigo</td>
<td>1 (5.5)</td>
</tr>
</tbody>
</table>

In six (33%) patients, evaluation of cerebro-
spinal 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 pa-
tients. Oligoclonal antibodies, which were only
checked in one patient because of symptom
recurrence, were negative. Elevated sedimenta-
tion 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 re-
quested and the images were reviewed by a
single radiologist. MRI of the brain showed
multifocal white matter damage, as the hall-
mark 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 cere-
bellum 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 methylpredni-
solone, 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. Tenembaum et al. reported a mean age of 5.3±3.9 years with a significant male predominance (M/F:1.8:1). Lee et al. reported a mean age of 8.6 years, and Anlar et al. reported the mean age of 8 years with a M/F ratio of 1.7:1.

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.

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.

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. Hyson et al. reported that 71% of their study group had a prodromal illness.

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.

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%). Similar findings were also reported by Anlar et al.

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

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

Elevated sedimentation rate, rarely indicated in other studies, 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. Murthy reported those lesions were located in the frontal (48%), followed by the parietal (22%), the temporal (7%), and the occipital (6%) regions. 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.

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.

Acknowledgments

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References

1 Stonehouse M, Gupte G, Wassmer E, Whitehouse WP. Acute disseminated encephalomyelitis: recognition in the hands