Outcome of children with acute disseminated encephalomyelitis in a tertiary care center in India

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Acute disseminated encephalomyelitis (ADEM) is an immune-mediated disease of the brain that follows viral infection or vaccination, or even appears spontaneously. The objective of the study was to evaluate the clinical, neuroimaging and laboratory profiles of children with ADEM. Seventeen children admitted to the Pediatric Department of Dayanand Medical College and Hospital, Ludhiana, whose cases were consistent with the diagnosis of ADEM, were included. Their clinical and neuroimaging profiles and outcomes were studied. The most common presenting features were fever (71%), altered sensorium (59%) and headache and convulsions (41%). Brain MRI identified lesions in subcortical white matter (75%) and periventricular white matter (38%). Most patients were treated with corticosteroids. A favorable outcome was seen in 88% of patients. Although 59% of patients had neurologic sequelae at discharge, only one patient had a major neurological deficit at follow-up. Prognosis for survival and outcome was good in the majority of patients. Neurological sequelae at discharge do not predict poor outcome.

Key words: acute disseminated encephalomyelitis, ADEM, encephalitis.

Acute disseminated encephalomyelitis (ADEM) is an uncommon inflammatory demyelinating disease of the central nervous system (CNS) and can strictly be defined as scattered focal or multifocal (disseminated) inflammation of brain and/or spinal cord[1]. The present study was conducted to describe the clinical profile, neuroimaging findings and outcome of children with acute disseminated encephalomyelitis (ADEM) in a tertiary center in North India.

Material and Methods

The study was carried out in the Department of Pediatrics of Dayanand Medical College and Hospital, Ludhiana, a tertiary care teaching hospital. Seventeen ADEM patients admitted during a five-year period (2008-2012) were included in the study. The diagnosis of ADEM was based on the acute onset of neurologic signs and symptoms together with typical magnetic resonance imaging (MRI) findings. CNS infections, vasculitis and other autoimmune disorders were excluded, where suspected. The study had Institutional Ethics Committee approval, and consent was obtained from all patients.

Detailed histories, demographic profiles, clinical examinations and relevant investigations were obtained from inpatient case records and documented on the pro forma. Brain MRI was performed on all the patients on the Magnetom Avanto 1.5 T (Siemens, Germany). Non-contrast enhanced spin-echo MRI was used to take axial, coronal and sagittal T1- and T2-weighted spin-echo images with a slice thickness of 5 mm. When feasible, contrast-enhanced images were also obtained. MRI images were read independently by the radiologist.

Patients were treated with methyl prednisolone (30 mg/kg) daily for three days. Subsequently, prednisolone (1 mg/kg orally) was started and tapered over four weeks. Seizures were managed accordingly. Patients were followed up for a minimum of six months. Brain MRI was not repeated due to financial constraints.

Results

The mean age of patients in our study was 7.96 years (range 1-18 years), with 57% between 6 and 10 years of age. Males were more affected (M:F ratio: 1.4:1). Clustering of cases between the months of January and May (59%) was seen.

Common presenting features were fever (71%), altered sensorium (59%) and headache and convulsions (41%). Two patients had respiratory failure. Upper motor neuron signs were seen in 59% of cases. Cranial nerve palsy was seen in 53% of cases, with the facial nerve most commonly affected. Optic neuritis was seen in one case. No patient had papilledema or bladder/bowel involvement (Table I).

Leukocytosis was seen in 23% of cases (mean 12.1 x 10^9/L, range 4-21.3 x 10^9/L). Elevated ESR was seen in 35% of cases. Fifty-three percent of the patients had CSF pleocytosis with lymphocytic predominance (mean 10 cell/mm^3, range 2-30 cells/mm^3). CSF protein was elevated in 29% of cases (mean 37.3 mg/dl, range 15-114 mg/dl). CSF hypoglycorrhachia was seen in 17% (mean 70.2 mg/dl, range 35-112 mg/dl). Virology studies and oligoclonal bands could not be performed. One patient had dengue serology, with a positive ELISA Ig M antibody test.

Brain MRI was done on all of the children. Cortical lesions (the most common temporal region) were seen in 31% cases (Table II).

All patients were treated with steroids, with the exception of one who showed spontaneous improvement. An antiviral (acyclovir) was given in 53% of cases. Nine cases required anticonvulsants. Out of 17 cases, 15 had a favorable outcome. One case expired due to sepsis secondary to ventilator-associated pneumonia, and one case with respiratory failure did not continue treatment. Neurological deficit was seen at discharge in ten cases (59%), in the form of tone abnormality (59%), gait disturbance (53%), altered sensorium (18%) and cranial nerve palsy (18%). At follow-up after one year, one patient had a major neurological deficit, in the form of cranial nerve palsy. Two cases showed minor neurological deficits, in the form of sensory deficit[1] and cognitive deficit[1] (Table III).

Discussion

ADEM is a monophasic immune-mediated demyelinating disorder of the CNS that can follow infection or immunization[2]. The diagnosis of ADEM is based on the acute onset of neurological signs and symptoms along with evidence of multifocal lesions of demyelination on neuroimaging[3].

Seventeen cases of childhood ADEM were reviewed during the study period. The youngest patient in the study was 1 year old, though most of the cases were between 6 and 10 years of age. There was no sex predilection noted. Most cases were accompanied or followed by acute febrile illness. Fever was a common feature, noted in 67% cases in the study.

ADEM typically begins within 6 days to 6 weeks following an antigenic challenge. Approximately 70% of patients report a precipitating event, e.g., a viral or bacterial infection or vaccination. A

Table I. Signs and Symptoms of Cases with ADEM

Symptoms	N=17 (%)	Signs	N=17 (%)
Fever	12 (71%)	Low GCS	
Motor weakness	4 (24%)	< 11	4 (24%)
Headache	7 (41%)	Neck stiffness	1 (6%)
Vomiting	5 (29%)	Hypertonia	4 (24%)
Altered sensorium	10 (59%)	Hypereflexia	7 (41%)
Convulsions	7 (41%)	Cranial nerve palsy	5 (29%)
Gait disturbances	6 (35%)	Optic neuritis	1 (6%)
Respiratory failure	2 (12%)	Ophthalmoplegia	1 (6%)

GCS: Glasgow Coma Scale

Table II. Brain MRI Findings in ADEM Patients

Brain MRI findings	n=17	Percent (%)
Cortical lesions	5	31%
Subcortical lesions	12	75%
Periventricular lesions	6	38%
Thalamic lesions	0	0%
Midbrain lesions	0	0%
Brain stem lesions	2	13%
Cerebellum lesions	1	6%
Cervical spine	1	6%

number of infectious agents, such as influenza, measles, mumps, rubella, varicella, herpes simplex virus, hepatitis virus, EBV, Coxsackie, mycoplasma, campylobacter, streptococcus, legionella and rickettsia have been implicated in ADEM[4]. Positive dengue serology was found in the study. Seasonal clustering was also seen, as in other studies[2,5,6]. In the study by Madan et al.[7], DPT and measles vaccinations were the triggering factors for ADEM.

In the study by Jayakrishnan et al.[3], presenting features seen were motor deficit (71%), cranial nerve palsy (36%) and seizures and altered sensorium (21%). The clinical features of ADEM were comparable to those reported in previous studies[2,5,6]. Cranial neuropathy (53%) and seizures (41%) were more frequently noted. Optic neuritis was seen in one case; it persisted to the one-year follow-up and then resolved.

Several clinical characteristics differ between ADEM and multiple sclerosis (MS) at first presentation; encephalopathy, when present, strongly suggests the diagnosis of ADEM[8]. The diagnosis of multiphasic ADEM, in contrast to MS, is supported by: florid polysymptomatic presentation; lack of oligoclonal bands in CSF; predominance of MRI lesions in the subcortical region with relative sparing of the periventricular areas but with possible involvement of deep gray matter; complete or partial resolution of MRI lesions during convalescence; and recurrence within six months of a previous episode[9]. According to current diagnostic criteria, the presence of new lesions on MRI repeated three months after the attack is predictive of MS[10]. No relapse was noted in our patients during the follow-up period. All ADEM patents need to be monitored over their future course.

Brain MRI is an essential diagnostic investigation in ADEM. ADEM is not purely a disease of white matter; bilateral involvement of deep gray matter, including the basal ganglia and thalamus, is well recognized[11]. Tosun et al.[12]

Table III. Neurological Status of ADEM Cases at Discharge and at One Year Follow-Up

Neurological status	At discharge N=15(%)	At one year follow-up N=15(%)
Abnormal tone	10(59%)	0(0%)
Gait disturbance	8(47%)	0(0%)
Altered sensorium	3(18%)	0(0%)
Cranial nerve palsy	3(18%)	1(6%)
Optic neuritis	1(6%)	0(0%)
Sensory deficit	1(6%)	1(6%)
Cognitive deficit	1(6%)	1(6%)
Seizures	1(6%)	0(0%)
Cases with deficit	10(59%)	3(18%)

reported hyperintense signal changes, mainly in the basal ganglia and thalamus (58%) and cortical and subcortical areas (33%) in T2-weighted images of 12 children with ADEM. Myelitis was also seen in two cases. Surprisingly, involvement of deep gray matter was not a feature in the present study. One of our patients had cervical spine involvement with associated quadriparesis and prolonged respiratory failure, with poor outcome.

Language disturbances are more common in pediatric patients with ADEM. The presence of impaired consciousness, and possibly seizures, predict poor functional outcome at hospital discharge[13].

Although 59% of cases had neurological deficit on discharge, outcome was good, with 88% survival, as in other studies[2,5,6]. At follow-up, these children should be monitored for the minor cognitive dysfunction known to occur in such cases.

Brain MRI is the modality of choice to diagnose ADEM, on the basis of asymmetric demyelination in the cortical and subcortical white matter of the brain. Prognosis for survival and outcome is good in the majority of patients with ADEM. Neurological sequelae at discharge do not necessarily predict poor outcome.

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