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Original Research Article

A Hospital-Based Study to Assess Acute Disseminated Encephalomylitis in Children: An Observational Study

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Abstract

Aim: The aim of the present study was to assess acute disseminated encephalomyelitis in children.

Methods: This was a prospective hospital based clinical study conducted by the Department of Pediatrics, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar, India over a period of one year. Total 50 patients were included in the study.

Results: Age distribution of study sample has been analyzed. It showed maximum prevalence in 5- 9-year age group (50%) with 30% in 0-4 year & 20 % in 10-14 years age group. Male predominates in the study 60% with female being 40%. Seizures were documented to occur in highest number of cases (66%). Next fever (60%) & altered sensorium (58%) followed. Encephalopathy was observed in 86%, followed by motor deficit in 68% & autonomic involvement in 40%. T1 hypointensity/isointensity was observed in 52%, T2 hyper intensity in 76%, FLAIRS changes in 72% cases. It was observed that the cases with severe presentation had lower proportion of recovery & higher proportion of mortality which was found to be statistically significant.

Conclusion: ADEM is a rare autoimmune demyelinating disorder that mainly affects the CNS and is characterized by an acute inflammatory response targeting the myelin sheath surrounding fibers in the brain and spinal cord. The early recognition and accurate diagnosis of ADEM facilitate timely management and minimize neurological damage.

Keywords: Encephalomyelitis, Demyelinating Diseases, Magnetic Resonance Imaging.

Introduction

Acute disseminated encephalomyelitis (ADEM) is a demyelinating disorder of the central nervous system (CNS). It is common in children and is usually regarded as a monophasic illness often heralded by infection. It is characterized by acute onset polyfocal neurologic deficits and encephalopathy clinically. Radiologically, fluffy demyelinating lesions in the white-matter of the brain and or spinal cord with or without involvement of deep gray matter are seen. The widely followed diagnostic criteria for ADEM were initially delineated by the International Pediatric Multiple Sclerosis Society Group in 2007 and revised in 2013. [1,2]

Acute disseminated encephalomyelitis (ADEM) is an acute demyelinating disorder of central nervous system characterized by scattered focal / multifocal inflammation of brain & spinal cord that usually follows an apparently benign infection in otherwise healthy children & young adults. It represents 30% of all childhood encephalitic illnesses. [3] It is considered as an autoimmune disorder that is triggered by environment stimulus in genetically susceptible individuals. It is usually presenting as a monophasic disorder associated with multifocal neurological symptoms & encephalopathy. In the past, ADEM commonly followed common childhood infection like measles, chickenpox & smallpox. Because of significant advances in infectious disease control & extensive immunisation coverage, nonspecific upper respiratory illness are the most common triggering event in developing countries, but the exact etiological agent still remain unknown. But in developing countries, the high frequency of vaccination & exanthematous fever account for frequent occurrences of post infectious demyelinating diseases. [4]

There are no specific biomarkers available currently to diagnose ADEM; hence, diagnosis is

made after excluding clinical and laboratory findings and suggestive neuroradiological features of other diseases. [5] Prompt initiation of immunomodulatory treatments with a multidisciplinary approach involving the expertise of neurologists, neuropsychologists, and physiatrists, among other clinicians, is necessary for a good functional recovery. [6] At present, magnetic resonance imaging (MRI) plays a vital role in diagnosing ADEM, revealing characteristic demyelinating brain lesions. It helps distinguish ADEM from other neurological conditions, guiding treatment decisions for better patient outcomes. [5]

The aim of the present study was to assess acute disseminated encephalomyelitis in children.

Materials and Methods

This was a prospective hospital based clinical study conducted in the Department of Pediatrics, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar, India over a period of one year. Total 50 patients were included in the study.

Inclusion Criteria:

1. Study group consisted of hospitalised children < 15 years of age admitted to the indoors of Indira Gandhi Institute of Medical Sciences (IGIMS), Patna with the diagnosis of ADEM as per the defined criteria i.e.,1 Acute / sub-acute onset of polysymptomatic² neurological presentation with prominence of cortical signs (changes in mental status, seizures, acute behavioural changes etc) preferably with a preceding history of infectious illness or vaccination.
2. Monophasic time course of illness.
3. Signs & symptoms cannot be explained by other known aetiologies.
4. MRI evidence of ADEM (bilateral asymmetric, multifocal, hyper intense lesions on FLAIR or T2 weighted images predominantly involving white matter with or without involvement of grey matter, thalamus & basal ganglia without previous white matter changes) was considered corroborative.

Exclusion Criteria:

1. Recurrence of neurological signs & symptoms beyond 3 months of Initial illness.
2. Acute onset of flaccid paralysis of limbs or isolated optic neuritis or isolated transverse myelitis.
3. Presence of a significant preceding neurological abnormality or features suggestive of neurodegenerative disorder.
4. Signs & symptoms attributable to any systemic involvement.

All these patients selected were first stabilized. Detailed history and clinical examination special reference to central nervous system was done. The level of consciousness was assessed using Glassgow coma scale. Motor or sensory deficits were classified as partial or complete. The presence of aphasia, hemiparesis and visual defect was evaluated whenever possible according to child's age. All associated symptoms like seizure, headache, fever, altered level of consciousness were recorded.

Relevant investigations were performed to exclude infective or inflammatory aetiologies which included complete blood count and measurement of serum electrolytes, erythrocyte sedimentation rate and Cerebrospinal fluid analysis (CSF). All patients had serological testing for mycoplasma and various implicated virus as well as nasopharyngeal & rectal culture. ELISA (enzyme-linked immunosorbent assay), real time Polymerase chain reaction (PCR), conventional PCR were done to isolate the organism. A viral pathogen was regarded as etiologic if one of the following criteria was met: 1.CSF &/or serum contained virus specific IgM by ELISA.2. Raising IgG specific antibody levels or relatively high single IgG specific antibody level.3. Positive PCR result. Routine Lumbar puncture was done, taking into consideration cardio-respiratory stability and after examining the fundus. CSF analysis was done in term of cytological, biochemical, culture& sensitivity, ADA (adenosine deaminase) assay and PCR study for isolating implicated viruses. Neuroimaging was done in all patient after initial stabilisation. MRI (Magnetic Resonance Imaging) was the imaging modality of choice. A 1.5-T seimens machine was used for the brain MRI study. T1, T2, fluid attenuated inversion recovery (FLAIR) and diffusion weighted images were obtained in the axial, sagittal and coronal plane. When feasible, contrast enhanced images were obtained using gadopentetate dimeglumine (0.1mmol/kg). CT (Computed Tomography) was done in third generation scanner and contrast enhanced images were obtained in the selected few cases. Scans were reviewed by neurologist who was blinded to the clinical findings. The images were assessed for lesion site, size, number, distribution, symmetry, any midline shift, haemorrhage and pattern of contrast enhancement. Standard 30-minute interictal surface electroencephalogram (EEG) was recorded in patients with impaired consciousness or seizures. These differential levels of investigations are the standard protocol in the diagnostic work up of patient with a neurological catastrophe and do not influence the etiologic diagnosis. The incidence was defined as number of new cases of ADEM admitted to the hospital which came into existence within certain period of time per 1000 patients admitted to the hospital. All those cases then segregated as per age and gender. The mean age at onset is calculated and sex predilection determined.

The incidence of prodermal period and history of recent vaccination was assessed. After neuroimaging study, the incidence of abnormal findings on MRI/CT was calculated. Mode of onset mode of presentation i.e. the type of deficit, cranial nerve involvement, and level of consciousness, seizures, headache, and all the features then correlated with the immediate outcome. Thorough history and a formal neurological examination to evaluate the outcome in terms of full recovery, motor deficit, cognitive defect, visual field defect, recurrent seizure, learning disorder, personality changes, psychiatric manifestations, death etc.. Repeat brain imaging was arranged if there was suggestion of progression or recurrence of neurological deficits. After ADEM was diagnosed, all cases were treated with high dose intravenous corticosteroids, either methyl prednisolone (10-30mg/kg) or dexamethasone (1mg/kg) daily for 3-5days. Subsequently prednisolone (1mg/kg orally) was started and continued for six weeks with gradual tapper. Plasma exchange, intravenous immunoglobulin (IVIG) (2mg/kg divided dose over 5days) or repeat high dose intravenous methyl prednisolone were given for patient who continued to detoriate. Data thus computed were analyzed and inferences drawn.

Analysis of data:

Results were expressed as mean ± standard deviation for continuous variables and as number (%) for categorical data. Since all data were normally distributed, the parametric tests were used for statistical analyses. The data was analyzed by SPSS version 21 software along with below mentioned appropriate statistical tests at 5% level of significance. p value is calculated using Chi-Square Test given by the formula where Oi is Observed frequency and Ei is Expected frequency. Significance was interpreted as: $0.05<p<0.10$ Suggestive of significance, $0.01<p<0.05$ moderately significant, $p<0.01$ strongly significant.

Results

Table 1: Age& Sex distribution of study subjects

Age groups	Sex		Total
	Male	Female	
0-4 years	10	5	15
5-9 years	15	10	25
10-14 years	5	5	10
Total	30	20	50

Age distribution of study sample has been analyzed. It showed maximum prevalence in 5- 9 year age group (50%) with 30% in 0-4 year& 20 % in 10-14years age group. Male predominates in the study 60% with female being 40%.

Table 2: Presenting Symptoms

Symptoms	N	%
Convulsion	33	66
Fever	30	60
Altered sensorium	29	58
Paralysis	22	44
Vomiting	12	24
Headache	8	16
Speech abnormality	8	16
Bowel & bladder changes	5	10
Abnormal movements	4	8
Blurring of vision	3	6
Rash	3	6
Double vision	2	4
Dysphagia	2	4
Neck retraction	2	4
Dizziness	2	4

Seizures were documented to occur in highest number of cases (66%). Next fever (60%) & altered sensorium (58%) followed.

Table 3: Pattern of neurological involvement

Neurological involvement	N	%
Motor deficit	34	68
Encephalopathy	43	86
Autonomic involvement	20	40
Cranial nerve involvement	13	26

Cerebellar sign	10	20
Aphasia	8	16
Meningeal sign	6	12
Involuntary movement	4	8

Encephalopathy was observed in 86%, followed by motor deficit in 68% & autonomic involvement in 40%.

Table 4: Pattern of MRI abnormality

MRI abnormality	N	%
T1 hypointensity/isointensity	26	52
T2 hyperintensity	38	76
FLAIR hyperintensity	36	72
DWI restriction	24	48
Temporal shrinkage	8	16
Contrast enhancement	3	6
Gyral thickening	3	6
Sinusitis	3	6
Perifocal edema/mass effect	2	4
T2hyperintensity of spinal cord	4	8
Normal	2	4

T1 hypointensity/isointensity was observed in 52%, T2 hyperintensity in 76% , FLAIRS changes in 72% cases.

Table 5: Association of severity of presentation with outcome at discharge

Outcome at discharge	Glasgow coma score			Total (%)
	Mild	Moderate	Severe	
Complete recovery	8	6	2	16 (32)
Partial recovery	6	12	8	26 (52)
Death	0	0	8	8 (16)
Total	14	18	18	50 (100)

It was observed that the cases with severe presentation had lower proportion of recovery & higher proportion of mortality which was found to be statistically significant.

Discussion

Acute disseminated encephalomy-elitis (ADEM) is a complex immune-mediated disorder characterized by demyelination of the central nervous system (CNS) with a higher prevalence observed in the pediatric population. ADEM involves a multifactorial interplay of immunological processes, molecular mimicry, and inflammatory responses, leading to diverse clinical presentation and diagnostic challenges. It is typically a monophasic illness presenting with encephalopathy and multifocal brain and spinal cord lesions. Humoral and cell-mediated immunity activation due to the molecular mimicry between microbial epitopes and myelin antigens, especially myelin oligodendrocyte glycoprotein (MOG), is considered the most important mechanism causing immune-mediated injury. [7]

Age distribution of study sample has been analyzed. It showed maximum prevalence in 5- 9 year age group (50%) with 30% in 0-4 year& 20 % in 10-14years age group. Male predominates in the study 60% with female being 40%. Seizures were documented to occur in highest number of cases (66%). Next fever (60%) & altered sensorium (58%) followed. Encephalopathy was observed in 86%, followed by motor deficit in 68% & autonomic involvement in 40%. T1 hypointensity / isointensity was observed in 52%, T2 hyperintensity in 76%, FLAIRS changes in 72% cases. MRI is of central importance in the diagnosis of acute CNS white matter disorder. CT is frequently normal in ADEM (Dunn et al 1986, caldemeyer et al 1994). [8,9]

The pathogen causing ADEM is unknown. Prodromal manifestations of ADEM may mimic the flu with symptoms such as fever, headache, and body aches. In addition, patients may experience respiratory or gastrointestinal issues prior to the onset of neurological symptoms. ADEM shows a seasonal peak in winter and spring. Exanthematous diseases are commonly observed preceding pediatric ADEM while common viruses such as Epstein-Barr, measles, mumps, rubella and coxsackie B are frequently associated with postinfectious ADEM. Bacterial infections such as Borrelia burgdorferi, Mycoplasma pneumoniae, and Legionella pneumophila are rarely reported. [10]

ADEM clinically presents as a prodrome of fever, headache and nausea preceded by a latent period of approximately 12 days followed by the onset of neurological symptoms. The most common neurological manifestations include

encephalopathy, pyramidal signs, cerebellar signs, and cranial nerve deficits [5]. In our case the child presented with abnormal speech, difficulty walking, and decreased power in the right side of the body with bilateral exaggerated deep tendon reflexes. In order to diagnose this condition, clinical presentation and distinct imaging findings are required. Patient outcomes are improved, and potential complications are minimized when intervention occurs in a timely manner. The diagnosis of ADEM is usually one of the exclusions and is largely dependent on clinical and imaging findings. CSF analysis may show nonspecific changes; the use of cell counts, cultures, and viral polymerase chain reactions is predominantly aimed at excluding the possibility of infectious etiologies. [11]

It was observed that the cases with severe presentation had lower proportion of recovery & higher proportion of mortality which was found to be statistically significant. In patient who had complete recovery, the recovery period ranged from 8 days to maximum 3 months, recovery may continue from weeks to months as per previous studies. [12] The T2-FLAIR sequences have been observed to exhibit the pathology most effectively, showing multiple patchy white matter hyperintensities with the involvement of the cerebellum and brainstem. It is more frequently observed that the pediatric population exhibits a higher incidence of cerebellar and brainstem involvement. While white matter is primarily affected, gray matter involvement, specifically in the basal ganglia, thalamus, and brainstem, can be seen. Few MRI lesions may enhance after gadolinium administration, but it was not so in our case. Thalamic involvement and sparing of the corpus callosum are indicative of a higher likelihood of an ADEM diagnosis while simultaneously ruling out MS as a potential diagnosis. ADEM most commonly present as a polysymptomatic encephalopathy and initially diagnosis may not be clear. [13] Clinical evaluation, MRI & CSF studies are most useful to establish the diagnosis and rule out important differential diagnosis. There is presence of antecedent illness in case of severe presentation. The age, gender, predisposing factor do not influence the outcome, but the severity of presentation influence the outcome at discharge. Early institution of therapy with immunosuppressive drugs hasten recovery and reduces morbidity as evidence by the study done by Rust RS et al [14], Francis GS et al [15], Ravaglia S. [16]

Conclusion

ADEM is a rare autoimmune demyelinating disorder that mainly affects the CNS and is characterized by an acute inflammatory response targeting the myelin sheath surrounding fibers in the brain and spinal cord. The early recognition and accurate diagnosis of ADEM facilitate timely management and minimize neurological damage. Prompt initiation of appropriate treatment is important to promote favorable outcomes in affected individuals. A multidisciplinary approach involving neurologists, neuroradiologists, and other healthcare professionals is necessary for comprehensive care and optimal functional recovery.

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