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Original Research Article

A Retrospective Assessment of the Acute Disseminated Encephalomyelitis 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.

Material & Methods: A retrospectively evaluated 20 consecutive children with ADEM and adolescents at the Department of Paediatrics for the duration of 12 months. All children had been diagnosed using reliable clinical, laboratory, and neuroimaging techniques according to the International Pediatric Multiple Sclerosis (MS) Study Group criteria.

Results: There were 20 children admitted with the diagnosis of ADEM during the study period. They included 16 (80%) girls and 4 (20%) boys. 4 children were below the age of three years, 8 children in the 3-6 year age group and 8 children in the 6-12 year age group. The youngest was a six-month-old infant. All of them had first episode of the illness. The common presenting symptoms were fever, vomiting, headache, gait disturbance and generalized seizures. Neurological manifestations included altered sensorium, multiple cranial nerve involvement, quadriplegia and paraplegia, dystonia and choreiform movements, nystagmus, bladder involvement (both incontinence and retention), speech defect and double vision. Facial nerve was the most common cranial nerve involved. Both LMN and UMN facial palsy occurred. Psychological manifestations included aggressive behavior, emotional liability, and irritable, elated or depressed mood. Magnetic resonance imaging (MRI) was done in all children. The area involved in the majority of children was the parietal lobe. Lesions were noted in the subcortical white matter, mid brain, pons, corpus callosum, basal ganglia, medulla and cerebellum. One third of children had spinal cord involvement.

Conclusion: Despite the serious neuropsychiatric manifestations, ADEM in children generally has a good outcome. Children with ADEM need long-term follow up for cognitive impairments and emotional problems. Clinical presentation of ADEM in the present sample is comparable to previous studies except for the female preponderance. Further studies are required to analyze the reason for this female preponderance.

Keywords: Alzheimer's disease, acute disseminated encephalomyelitis, multiple sclerosis, children, adolescents

Introduction

Acute disseminated encephalomyelitis (ADEM) is an acute demyelinating inflammatory disorder of the central nervous system. It is characterized by encephalopathy, multifocal neurological deficits, and typical magnetic resonance imaging findings of widespread demyelinating lesions, predominantly involving the white matter of the brain and spinal cord. [1] It is a first clinical event with a presumed inflammatory or demyelinating cause, with acute or subacute onset that affects multifocal areas of the brain and spinal cord. Numerous causative pathogens have been identified to date. Viruses that have been implicated include coronavirus, coxsackie virus, cytomegalovirus, Epstein-Barr virus, herpes simplex virus, hepatitis A virus, human immunodeficiency virus, influenza virus, measles virus, rubella virus, varicella zoster virus, and West Nile virus. Other organisms associated include Borrelia burgdorferi, Chlamydia, Leptospira, Mycoplasma pneumoniae, Rickettsia, and beta-hemolytic Streptococcus. [2]

ADEM can occur at any age, but predominantly develops in childhood and adolescence. Its annual incidence is estimated to be 0.3 to 0.6 cases per 100,000 children with a mean age of 5 to 8 years at presentation. [3] The clinical presentation must be

polysymptomatic and must include encephalopathy in the form of alteration in consciousness or behavioral change. Systemic symptoms, such as fever, malaise, myalgia, headache, nausea, and vomiting, are common precursors to the neurologic symptoms. [4,5] The etiology and pathophysiology of ADEM are not fully understood, but ADEM usually follows an infection of the upper respiratory tract or immunization in children and young adults. An autoimmune response to myelin basic protein, triggered by infection or immunization, is considered among the most likely etiologic factors [6,7,8] ADEM is considered an autoimmune disorder that is triggered by an environmental stimulus in genetically susceptible individuals.

The diagnosis of ADEM is based on clinical and radiological features. Deep and subcortical white-matter lesions and gray-matter lesions such as thalami and basal ganglia on magnetic resonance imaging (MRI) are associated with ADEM. [9] Sequential MRI is required to confirm the diagnosis of ADEM, as relapses with the appearance of new lesions on MRI may suggest either multiphasic ADEM or multiple sclerosis (MS). Actually, ADEM treatment is based on nonspecific immunotherapy, in accordance with the supposed pathogenesis of the syndrome itself and the analogy with multiple sclerosis (MS). [10]

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

Material & Methods

A retrospectively evaluated 20 consecutive children with ADEM and adolescents at the Department of Paediatrics, ANMMCH , Gaya, Bihar,for the duration of 12 Months. All children had been diagnosed using reliable clinical, laboratory, and neuroimaging techniques according to the International Pediatric Multiple Sclerosis (MS) Study Group criteria. Patients presenting with a clinically isolated demyelinating syndrome (e.g., optic neuritis or transverse myelitis) or with clinical or radiologic evidence for dissemination in time and space suggesting MS were excluded 2,5. Extensive workup for bacterial and viral infections was performed for all patients. Immunologic investigations were simultaneously performed in cerebrospinal fluid (CSF) and serum samples.At the time of diagnosis, C-reactive protein, erythrocyte sedimentation rate, complete blood count, CSF analyses (cell counts and phenotypes, protein and glucose content, serum serologic tests for bacterial (salmonella, brucella, and mycoplasma pneumoniae) and viral infections (cytomegalovirus, Epstein-Barr virus, and herpes simplex virus), All physical and neurologic examinations performed in the hospital and during outpatient follow-up were performed by the same pediatric (IE).

Brain computed tomography (CT) was performed as part of the initial examination in some patients and brain MRIs were acquired in all patients. Brain MRI scans were performed in all patients using a 1.5-T MR scanner (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany). Imaging studies included axial contrast-enhanced T1- weighted spin echo with fat suppression images, axial and sagittal precontrast spin echo T1-weighted images, T2-weighted coronal and axial turbo spin echo image, axial fluid-attenuated inversion recovery images, and T1-weighted axial, sagittal, and coronal contrast-enhanced spin echo images. Spinal MRIs were acquired in cases where there was a clinical suspicion of spinal cord involvement. All patients underwent follow-up MRI several weeks after their neurologic symptoms resolved. All children were treated with a standard protocol consisting of 3 to 5 days' treatment with intravenous methylprednisolone 30 mg/kg followed by oral prednisolone 1 mg/kg for 2 weeks and then tapering over the next 2 weeks along with symptomatic treatment. Intravenous immunoglobulin (2 gm/kg divided over 2 days) was given for patients who continued to deteriorate. Seizures were managed with intravenous phenytoin. Antiviral and antibiotic therapy was given according to the patients' clinical status at admission. All of the patients were regularly followed at the outpatient clinic at 4 weeks after discharge and every 3 to 6 months thereafter until preparation of this article, depending on clinical conditions.

Statistical Analyses

Statistical analyses were performed using SPSS for Windows version 14.0 (Statistical Package for Social Sciences, SPSS Inc, Chicago, IL). Descriptive statistics regarding age, sex, symptoms, neurologic findings, results of neuroimaging, history of prodromal infection at the time of diagnosis, and prognosis were calculated.

Results

Table 1: Demographic data

Gender	**N%**
Boy	4 (20)
Girl	16 (80)
Age in years	
Below the age of 3 years	4 (20)
3-6 years	8 (40)
6-12 years	8 (40)

There were 20 children admitted with the diagnosis of ADEM during the study period. They included 16 (80%) girls and 4 (20%) boys. 4 children were below the age of three years, 8 children in the 3-6 year age group and 8 children in the 6-12 year age group. The youngest was a six-month-old infant. All of them had first episode of the illness.

Table 2: Clinical presentation of ADEM

Clinical presentation	**N%**
Fever at onset	13 (65)
Vomiting	9 (45)
Headache	6 (30)
Neurological manifestations	
Generalized seizures	4 (20)
Speech defect	6 (30)
Altered sensorium	4 (20)
Double vision	1 (5)
Aphasia	1 (5)
+Motor deficits	14 (70)
++Cranial nerve	7 (35)
Nystagmus	4 (20)
Abnormal movements	4 (20)
Urinary incontinence/ retention	4 (20)
Psychiatric manifestations	
Aggressive behavior	1 (5)
Acute psychosis	1 (5)
Mood changes	10 (50)

The common presenting symptoms were fever, vomiting, headache, gait disturbance and generalized seizures. Neurological manifestations included altered sensorium, multiple cranial nerve involvement, quadriplegia and paraplegia, dystonia and choreiform movements, nystagmus, bladder involvement (both incontinence and retention), speech defect and double vision. Facial nerve was the most common cranial nerve involved. Both LMN and UMN facial palsy occurred. Psychological manifestations included aggressive behavior, emotional liability, and irritable, elated or depressed mood.

Table 3: Site of lesion in MR imaging

Site of lesion in MR imaging	**N%**
Frontal lobe	7 (35)
Parietal lobe	11 (55)
Temporal lobe	6 (30)
Occipital lobe	3 (15)
Cortical grey matter	3 (15)
Subcortical white matter	9 (45)
Periventricular white matter	1 (5)
Internal capsule	1 (5)
Thalamus	1 (5)
Basal ganglia	4 (20)
Pons	6 (30)
Mid brain	6 (30)
Medulla	1 (5)
Corpus callosum	6 (30)
Cerebellum	1 (5)
Cerebellar peduncle	3 (15)
Cervical cord	4 (20)
Thoracic cord	7 (35)
Lumbosacral	1 (5)
Centrum semiovale	3 (15)
Corona radiata	3 (15)
Peritrigonal area	1 (5)

Magnetic resonance imaging (MRI) was done in all children. The area involved in the majority of children was the parietal lobe. Lesions were noted in the subcortical white matter, mid brain, pons, corpus callosum, basal ganglia, medulla and cerebellum. One third of children had spinal cord involvement.

Discussion

Acute disseminated encephalomyelitis (ADEM) is a monophasic, immune-mediated demyelinating disorder of the central nervous system that can follow infections or immunizations. [11] The diagnosis of ADEM is based on the acute onset of neurologic signs and symptoms along with evidence of multifocal lesions of demyelination on neuroimaging. [7,11] The typical neuroradiologic findings of ADEM are subcortical and central white matter lesions and lesions at the cortical grayewhite matter junction of both cerebral hemispheres, the cerebellum, the brainstem, and the spinal cord. Periventricular white matter and gray matter of the cortex, thalamus, and basal ganglia may also be involved. [12]

There were 20 children admitted with the diagnosis of ADEM during the study period. They included 16 (80%) girls and 4 (20%) boys. Studies from India and abroad have reported that ADEM is more common in boys [7,9,13,14] while multiple sclerosis, the other demyelinating disorder with many similarities, is more common in women. [15,16] 4 children were below the age of three years, 8 children in the 3-6 year age group and 8 children in the 6-12 year age group. The youngest was a six-month-old infant. All of them had first episode of the illness. The common presenting symptoms were fever, vomiting, headache, gait disturbance and generalized seizures. Neurological manifestations included altered sensorium, multiple cranial nerve involvement, quadriplegia and paraplegia, dystonia and choreiform movements, nystagmus, bladder involvement (both incontinence and retention), speech defect and double vision. Facial nerve was the most common cranial nerve involved. Both LMN and UMN facial palsy occurred. ADEM is classically considered an acute monophasic illness, although not all symptoms and deficits occur contemporaneously. New deficits within 3 months of onset are considered to be part of the same acute episode. Additional ADEM episodes occur rarely and happen in two main contexts: recurrent ADEM and multiphasic ADEM.

Psychological manifestations included aggressive behavior, emotional lability, and irritable, elated or depressed mood. Magnetic resonance imaging (MRI) was done in all children. The area involved in the majority of children was the parietal lobe. Lesions were noted in the subcortical white matter, mid brain, pons, corpus callosum, basal ganglia, medulla and cerebellum. One third of children had spinal cord involvement. Tenembaum et al [17] divided ADEM MRI findings into four groups: small lesions (<5 mm), large confluent white matter lesions, symmetric bilateral lesions with thalamic involvement, and large demyelinating acute hemorrhagic encephalomyelitis. [18] Liao et al[18] suggested that ADEM is a broad spectrum disease and that patients showing bilateral large confluent lesions, focal demyelination lesions, or pure bilateral basal ganglia or bilateral thalamic lesions on MRI have classic ADEM and have a lower probability of progression to MS compared with patients with multiple small ovoid lesions. By this definition, all of the patients in the current study should be considered classic ADEM cases.

Conclusion

Despite the serious neuropsychiatric manifestations, ADEM in children generally has a good outcome. Children with ADEM need long-term follow up for cognitive impairments and emotional problems. Clinical presentation of ADEM in the present sample is comparable to previous studies except for the female preponderance. Further studies are required to analyze the reason for this female preponderance.

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