Acute Disseminated Encephalomyelitis in Children

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ABSTRACT. *Objective.* **To describe the epidemiologic, clinical, neuroimaging, and laboratory features; treatment; and outcome in a cohort of children with acute disseminated encephalomyelitis (ADEM).**

Methods. **A 6-year retrospective chart review of children with the diagnosis of ADEM was conducted.**

Results. **Eighteen cases were identified. Sixteen patients (88%) presented in either winter or spring. Thirteen children (72%) had a recent upper respiratory tract illness. Patients presented most often with motor deficits (77%) and secondly with altered consciousness (45%). Spinal fluid abnormalities occurred in 70%. Despite rigorous microbiologic testing, a definite microbiologic diagnosis was established only in 1 child with Epstein-Barr virus disease and probable or possible diagnoses in 3 children with *Bartonella henselae*, *Mycoplasma pneumoniae*, or rotavirus disease. Brain magnetic resonance imaging identified lesions in the cerebral cortex in 80%, in subcortical white matter in 93%, in periventricular white matter in 60%, in deep gray matter in 47%, and in brainstem in 47% of patients. Eleven patients (61%) were treated with corticosteroids, and 2 were treated with intravenous immunoglobulins. All patients survived. Three patients (17%) had long-term neurologic sequelae.**

Conclusions. **Epidemiologic evidence from this study suggests an infectious cause for ADEM. The agent is most likely a difficult-to-diagnose winter/spring respiratory virus. Magnetic resonance imaging was the neuroimaging study of choice for establishing the diagnosis and for following the course of the disease. Prognosis for survival and outcome was excellent. Recurrent episodes of ADEM must be differentiated from multiple sclerosis.** *Pediatrics* **2002;110:e0–e0. URL: www.pediatrics.org/cgi/doi/10.1542/peds.;** ***acute disseminated encephalomyelitis, ADEM, encephalitis, postinfectious encephalitis, encephalomyelitis.***

ABBREVIATIONS. ADEM, acute disseminated encephalomyelitis; CNS, central nervous system; MRI, magnetic resonance imaging; FLAIR, fluid-attenuated inversion recovery; PCR, polymerase chain reaction; EBV, Epstein-Barr virus; Ig, immunoglobulin; TR, repetition time; TE, echo time; NSA, number of signal averages; FOV, field of view; CT, computerized tomography; WBC, white blood cell; CSF, cerebrospinal fluid; IVIG, intravenous gammaglobulin; MS, multiple sclerosis.

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Acute disseminated encephalomyelitis (ADEM) is considered a monophasic acute demyelinating disorder of the central nervous system (CNS) characterized by diffuse neurologic signs and symptoms coupled with evidence of multifocal lesions of demyelination on neuroimaging. The epidemiology of ADEM has changed since its original description by Lucas[1] in the early 18th century. At that time, ADEM commonly followed common childhood infections such as measles, smallpox, and chickenpox and was associated with significant mortality and morbidity. In a series of case reports in 1931 in *The Lancet*, McAlpine[2] described 3 sets of patients with ADEM: 1) postvaccination, 2) after infectious fevers such as in measles, and 3) spontaneous. Those with spontaneous and postvaccination ADEM did well despite the lack of antibiotics, steroids, and intensive care facilities, whereas those with an infectious cause fared poorly. A number of recent reports of ADEM in children have confirmed the observations of McAlpine.[3,4] Several articles suggested that improved outcome of ADEM was attributable mainly to the use of steroids; however, evidence for this was mainly anecdotal.[5,6]

The purpose of the present study was to review ADEM from a single institution with an emphasis on the relationship of clinical features, microbiology, neuroimaging, and treatment to clinical outcome. Eighteen patients with ADEM were identified. Respiratory infections preceded the neurologic presentation in the vast majority. Although in most cases a specific cause could not be identified, the outcome was good regardless of treatment.

METHODS

The inpatient database of Children's Hospital of Buffalo was broadly searched for patients with the diagnosis of ADEM, viral encephalitis, postinfectious encephalitis, encephalomyelitis, and transverse myelitis. Sixty-seven cases that occurred between January 1995 and March 2001 were identified. The diagnosis of ADEM was based on the acute onset of neurologic signs and symptoms together with magnetic resonance imaging (MRI) evidence of multifocal, hyperintense lesions on fluid-attenuated inversion recovery (FLAIR) and T2-weighted images. Of the 67 patients, 18 patients fulfilled the diagnostic criteria for ADEM.

Clinical information was obtained from the inpatient case records. Microbiologic data were extracted from laboratory reports and progress notes in the individual charts. Records maintained in the microbiology laboratories were reviewed for any tests performed beginning 1 month before admission to the hospital and ending 1 month after discharge. The specific tests reviewed included cultures for bacteria, viruses, and fungi; fluorescent antibody tests for respiratory viruses; polymerase chain reaction (PCR) tests for enteroviruses, herpes simplex virus, Epstein-Barr virus (EBV), and *Mycoplasma pneumoniae*; enzyme-linked immunosorbent assay for rotavirus; and immunoglobulin

G (IgG) and IgM antibody tests for viruses and *M pneumoniae*. To ascertain the clinical relevance of the microbiologic test results, we interpreted them in relation to the history of the present illness, the medical history, and the physical examination. In the case of antibody titers, IgM-specific antibody levels, rising IgG-specific antibody levels, or relatively high single IgG-specific antibody levels were considered significant. An infectious diagnosis was classified as definite, probable, possible, or not diagnostic on the basis of the interpretation of the microbiologic test results.

All head MRI scans were performed with a uniform protocol on an inpatient 1.5-T unit (Philips Gyroscan ACS-NT, Best, the Netherlands). The protocol included axial conventional spin-echo T1-weighted images before and after a single dose (0.1 mmol/kg) of gadolinium contrast (repetition time/echo time [TR/TE]: 450/20, 5-mm thickness, 0.5-mm gaps, 205 × 256 matrix size, number of signal averages [NSA] 1, field of view [FOV] 23 cm, scanning time 2:59), axial fast spin-echo T2-weighted images (TR/TE: 5000/100, 6-mm, 0.6-mm gaps, 245 × 256, NSA 3, FOV 23 cm, 15 echoes, scanning time 3:20), and axial fast spin-echo FLAIR images (TR/TE/TI: 8000/120/2300, 5-mm, 1.0-mm gaps, 140 256, NSA 2, FOV 23 cm, 21 echoes, scanning time 3:12). Sagittal and coronal T1 and FLAIR images were also performed. Diffusion-weighted imaging and magnetization transfer imaging were not performed. Spinal MRI of the cervical and thoracic cord included T1- and T2-weighted axial and sagittal and postcontrast T1 imaging. The hard copies of brain and spine MRI and brain computerized tomography (CT) scans of all patients were obtained and reread by an experienced neuroimager without knowledge of clinical involvement (R.B.). All studies were available for review except for MRI of the head of 2 patients and of the spine of 1 patient. The imaging assessment included quantification of T2/FLAIR lesions and their size and location and the presence of mass effect and enhancement. Spinal MRI scans available for 5 patients were also reviewed. Follow-up scans were reviewed for degree of improvement, new lesions, and enhancement. Detailed neuroimaging features with extensive illustration are being prepared for a separate publication.

Clinical follow-up information was obtained from outpatient records maintained in the neurology department. Data of patients not seen in follow-up in the neurology clinics were obtained by telephone interviews.

RESULTS

Clinical Information

The records of all 18 patients were reviewed. The patients ranged in age from 2.5 years to 22 years with a mean of 7.5 years and a median of 7 years. There were 11 male and 7 female patients. The cases occurred in a seasonal distribution with 88% (16 of 18) presenting in winter and spring (December to May; Fig 1). Only 1 case (6%) occurred in summer and 2 (12%) in late fall. Clustering of cases occurred in 1997 and 2000. No cases occurred in 1996 or 1998.

Seventy-two percent of patients (13 of 18) had a history of upper respiratory tract illness 2 days to 4 weeks before presentation. An average of 10 days occurred between the upper respiratory tract illness and the appearance of neurologic symptoms. None of the patients had vaccinations in the 3 months before presentation. Details of the clinical presentation are presented in Table 1. Nonspecific signs or symptoms of systemic illness, such as fever, headache, nausea, and vomiting, occurred in 74% of patients (14 of 18). Motor deficits, the most common presenting signs/symptoms, included ataxia, paraparesis, hemiparesis, and monoparesis. Altered consciousness was the second most common neurologic sign/symptom. Five patients had urinary symptoms, which included retention of urine in 4 and incontinence in 1. Paraparesis, sensory deficits, and urinary symptoms occurred predominantly in patients with spinal cord disease as seen on MRI images.

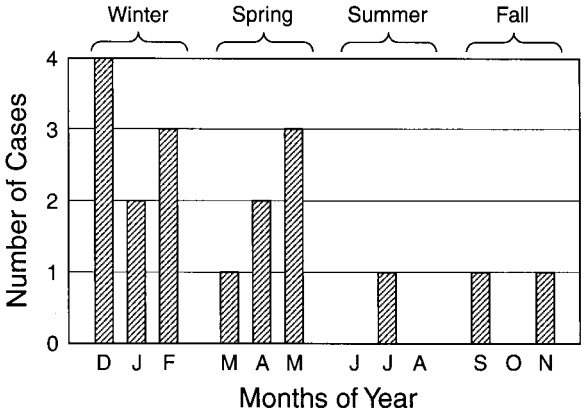

Fig 1. Seasonal distribution of 18 cases of ADEM.

TABLE 1. Clinical Features of ADEM in 18 Patients

	n (%)
Systemic signs and symptoms	
Fever	7 (38.5)
Nausea and/or vomiting	5 (27.5)
Headache	4 (22.5)
Stiff neck	1 (5.5)
Neurological signs and symptoms	
Motor deficits*	14 (77)
Altered consciousness	8 (44.5)
Sensory deficits	5 (27.5)
Urinary symptoms	5 (27.5)
Cranial neuropathy†	4 (22.5)
Seizures	3 (16.5)
Nystagmus	2 (11)
Internuclear ophthalmoplegia	2 (11)
Aphasia	1 (5.5)

* Ataxia (7), paraparesis (4), hemiparesis (2), and monoparesis (1).
† Optic, oculomotor, abducens, and facial nerves.

Laboratory Studies

The white blood cell (WBC) count ranged between 3200 and 25 100/mm^3 with a mean of 11 300 cells/mm^3. Seven patients (38.9%) had significant increases in WBC counts. Erythrocyte sedimentation rates were elevated in 5 of 12 patients (41.7%). Cerebrospinal fluid (CSF) was analyzed in 17. The CSF was not obtained in 1 patient because of the presence of a mass effect on CT scan. CSF evidence of inflammation (either pleocytosis or elevated protein) was present in 12 patients (70%). The CSF WBC count ranged between 0 and 137 with a mean of 40.8 cells/mm^3. WBC count was elevated in 7 (39%). The CSF protein ranged between 45 mg/dL and 120 mg/dL with a mean of 73.9 mg/dL. The CSF protein was elevated in 10 patients (55%). CSF glucose concentrations were normal in all patients. Oligoclonal bands were identified in the CSF of 1 of 8 patients. Electroencephalograms were performed in 7 patients; 4 showed generalized slowing, and 1 showed focal discharges.

None of the bacterial or fungal cultures was positive. Table 2 lists the other microbiologic studies obtained. Viruses were not identified in any of the 34 cultures and in only 1 of the 38 PCR studies. Three respiratory secretions were obtained for fluorescent

TABLE 2. Results of Microbiologic Studies

Studies	Specimens Tested	Number Positive
Virus culture		
Throat/nasopharynx	11	0
Stool	9	0
CSF	14	0
PCR		
Throat/nasopharynx		
Enterovirus	6	0
Mycoplasma	2	0
Epstein-Barr virus	1	1
Stool		
Enterovirus	5	0
CSF		
Enterovirus	9	0
Herpes simplex virus	15	0
Antibody		
EBV VCA IgG	11	5
EBV VCA IgM	10	1
M pneumoniae IgG	5	2
M pneumoniae IgM	1	0
Influenza	3	3
B henselae IgG	1	1
B henselae IgM	1	1
ELISA		
Rotavirus	2	2

VCA indicates viral capsid antigen; ELISA, enzyme-linked immunosorbent assay.

antibody testing, and none was positive. Virus-specific antibody was detected in 16 of 38 tests. A definite microbiologic diagnosis of EBV was established in 1 patient. This patient presented with 5 days of severe pharyngitis. Serologic studies demonstrated IgG-specific seroconversion and the presence of IgM-specific EBV antibody. In addition, EBV DNA was detected in pharyngeal secretions by PCR. A probable diagnosis of cat scratch disease was established in a patient with a history of cat contact and IgM and IgG *Bartonella henselae* antibodies. A possible diagnosis of *M pneumoniae* disease was made in 1 patient with a history of a cough, wheezing, and pharyngitis with IgG-specific mycoplasmal antibody. A second possible diagnosis of rotavirus disease was established in 1 patient with vomiting and diarrhea. Fourteen patients did not have microbiologic diagnoses.

Neuroimaging

All patients had head CT scans, which revealed lesions in only 2 patients. One of these patients had multiple supratentorial lesions with mild hypodensity in the subcortical white matter and no associated mass effect. These lesions were bilateral and asymmetric, measuring <1 cm in diameter. Another patient had mild unilateral brain swelling with mild associated mass effect and midline shift; no distinct parenchymal foci of hypodensity were seen. This patient was treated initially as having herpes encephalitis. However, brain MRI subsequently showed multiple supratentorial lesions in the subcortical white matter of the left hemisphere with additional lesions in the brainstem, suggesting multifocal involvement. MRI was performed in all but 1 patient, for whom the study was contraindicated because of the presence of a cardiac pacemaker. This patient was identified above with multiple bilateral subcortical lesions on the CT scan.

Seventeen patients had T1, T2, FLAIR, and gadolinium-enhanced T1 images. MRI findings are summarized in Table 3. Information on the localization of lesions shown in detail in Table 4 and summarized below is from the 15 patients for whom MRI films were available for direct rereview. A representative patient MRI scan is shown in Fig 2. All patients had multiple hyperintense brain lesions on T2/FLAIR

TABLE 3. Comparison of 3 Pediatric ADEM Studies

Parameters	Present	Dale[7]	Hynson[8]
Demographics			
Study type	Retrospective	Retrospective	Retrospective
Geographical area	USA	UK	Australia
Number of patients	18	28	31
Age (y; range, mean)	2–22, 8	3–15, 7	2–16, 6
Seasonal clustering	Yes	Yes	Not known
Preceding infection (%)	72	74	77
Clinical findings (%)			
Motor signs	77	71	23
Altered consciousness	45	69	68
Fever	39	43	52
Cranial neuropathy	23	51	45
Seizures	17	17	13
Laboratory findings (%)			
Leucocytosis	39	64	62
CSF pleocytosis	69	64	62
Elevated CSF protein	55	60	45
MRI findings (%)			
White matter lesions	93	91	90
Thalamic lesions	27	41	32
Periventricuar lesions	60	44	29
Patients with follow-up MRI	81	30	25
Normal follow-up MRI	7	37	25
Treatment and outcome (%)			
High-dose steroids	21	87	74
Survival	100	100	100
Residual deficits	17	43	19
Relapses	0	25	12

TABLE 4. Initial T2/FLAIR MRI Findings in 15 Patients With ADEM*

Location of Hyperintense Lesions on T2/FLAIR	No. of Patients (%)	No. of Lesions Per Patient (Mean [Range])	Total No. of Lesions in All Patients (%)
Frontal lobe	15 (100%)	8.0 (1–30)	120 (48%)
Parietal lobe	14 (93%)	3.7 (0–18)	55 (22%)
Temporal lobe	8 (53%)	1.2 (0–5)	18 (7%)
Occipital lobe	6 (40%)	1.0 (0–6)	15 (6%)
Cortical gray matter	12 (80%)	4.9 (0–28)	73 (29%)
Subcortical white matter	14 (93%)	6.0 (0–44)	90 (36%)
Periventricular white matter	9 (60%)	2.5 (0–16)	37 (15%)
Internal capsule	1 (7%)	0.1 (0–2)	2 (0.8%)
Thalamus	4 (27%)	0.3 (0–2)	5 (2%)
Basal ganglia	3 (20%)	0.3 (02)	4 (1.6%)
Brainstem	7 (47%)	1.1 (0–6)	16 (6%)
Cerebellum	2 (13%)	0.1 (0–1)	2 (0.8%)
Corpus callosum (Splenium)	1 (7%)	0.1 (0–2)	1 (0.4%)
Total brain lesions	15 (100%)	16.8 (4–56)	252 (100%)

* Data are from 15 patients for whom MRI films were available for detailed rereading.

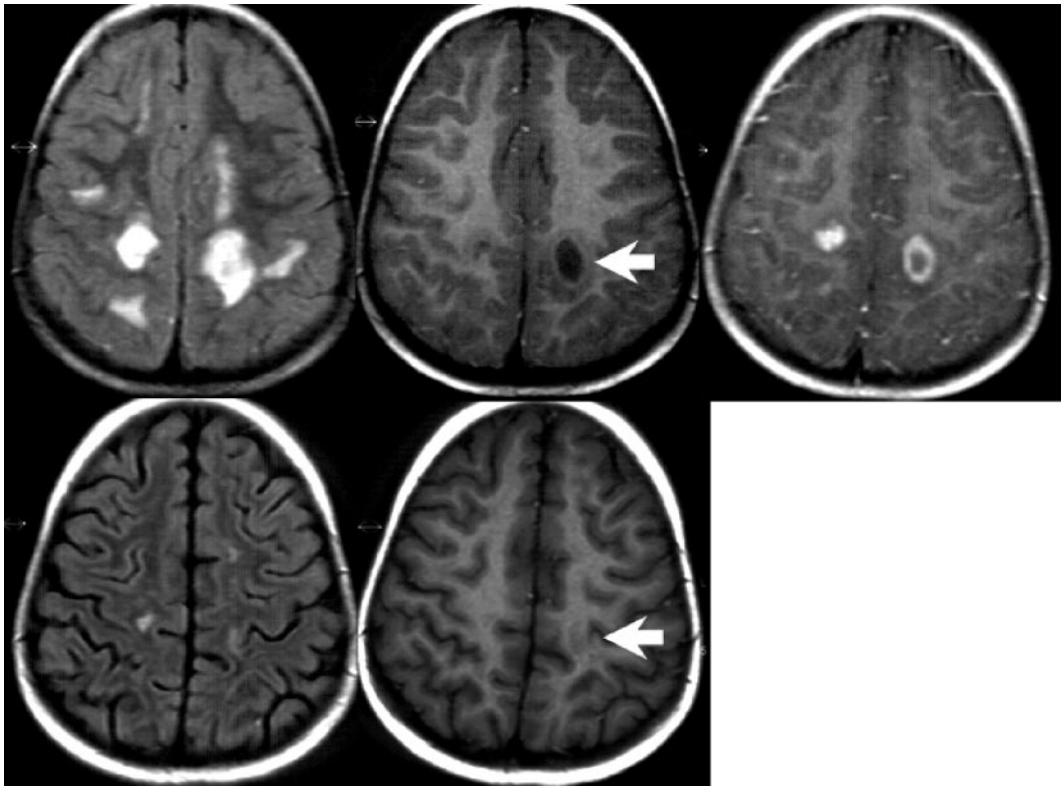

Fig 2. MRI findings in 1 case demonstrating typical asymmetric supratentorial lesions (top row, initial study; bottom row, 8 weeks later). Lesions are bilateral cortical and subcortical, hyperintense on FLAIR (left) and mildly hypointense on noncontrast T1 (middle, arrow) with no mass effect. Postcontrast imaging (right) shows a variable enhancement pattern including homogeneous enhancement of 1 lesion and ring enhancement of another. Eight weeks later, the lesions are nearly resolved on noncontrast studies (bottom row); enhancement was no longer seen (not shown).

images, with a mean of 16.8 lesions per patient (range: 4–56). Sixteen (94%) of 17 patients had cortical and/or subcortical white matter lesions. The lesions were asymmetric in location and size. In 2 patients, predominantly unilateral involvement of the cortical gray and subcortical white matter was noted. A total of 252 lesions were seen in the brain (mean: 16.8 per patient; range: 4–56; Table 4). Most lesions were 1 × 1 cm in diameter or slightly less but in some cases were up to 5 cm in diameter. All patients had supratentorial involvement. Regarding lobar location, 48% of these were frontal, followed by parietal (22%), temporal (7%), and occipital (6%; Table 4). Lesions were detected in the cerebral cortex in 80%, in subcortical white matter in 93%, in periventricular white matter in 60%, in deep gray matter (basal ganglia or thalamus) in 47%, and in brainstem in 47% of patients. The internal capsule, cerebellum, and corpus callosum were only rarely involved (Table 4). On noncontrast T1-weighted images, only 2 lesions were hypointense; all others were isointense. There was no heterogeneous signal, T1 shortening, or T2 shortening in the lesions to suggest acute or subacute hemorrhage. Mild mass effect was present

in only 2 cases but absent in all other cases. Gadolinium-enhanced studies were performed in 15 of 17 patients and enhancement was present in brain lesions of 4 patients. The enhancement patterns in the brain ranged from homogeneous to heterogeneous or ring-like patterns (Fig 2). T1 enhancement was present in 7 patients, 5 of which occurred in the spinal cord. Spinal cord involvement was typically multisegmental with patchy enhancement. Follow-up MRI was performed in 14 patients from 2 weeks to 1.5 years after discharge from the hospital. Ten of the 14 follow-up MRI scans were done at 3 months or less from the initial MRI. In only 1 of 14 patients did the MRI return to normal. In 8 patients, the findings were improved both in number and in size of lesions. In 3 patients, the lesions were unchanged. In 2 patients, new lesions were identified in follow-up scans before 8 weeks despite clinical recovery from the illness. These lesions were considered part of the initial illness.

Spinal cord MRI generally revealed large confluent intramedullary lesions extending over multiple segments of the spinal cord with variable enhancement. Cervical and thoracic spinal cord MRI was performed in 8 patients, and 7 studies were available for rereview. Two patients had normal spinal MRI. Five patients had intramedullary lesions that were hyperintense on T2-weighted images and isointense on noncontrast T1-weighted images. One patient had 5 lesions distributed throughout the cervical and thoracic cord and conus medullaris, with faint linear and patchy enhancement. Another patient had large confluent lesions with cord swelling at C2 to C7 with no enhancement; 1 week later, the lesions and swelling were nearly resolved. A third patient had contiguous cord lesions extending from C4 to the conus medullaris with patchy enhancement but no cord swelling. A fourth patient had a large confluent lesion from T2 to the conus with cord swelling but no enhancement; 3 months later, only a residual conus lesion remained. The fifth patient had contiguous lesions in the cord from C6 to the conus with heterogeneous and ring enhancement and swelling of the conus.

One patient had recurrence of gait symptoms and urinary retention at 9 months from the initial presentation. A repeat MRI showed complete disappearance of previous lesions, but new lesions appeared in different locations. This patient had no evidence of further recurrence in the past 4 years. Another patient had a repeat MRI at 18 months because of continuing seizures. This patient had new lesions in the subcortical white matter of the contralateral side with atrophy of the previously involved hemisphere. The new lesions were asymptomatic. However, a putative diagnosis of multiple sclerosis (MS) remains a consideration in both of the patients.

Hospital Course

Duration of hospitalization ranged from 2 days to 94 days with a mean of 14.5 days and a median of 6 days. Twelve patients had maximum deficits at admission. Six patients had deterioration in their neurologic status during the first week of hospitalization and none beyond 1 week. Five patients were ventilated because of respiratory failure. Duration of ventilation ranged from 1 to 20 days. One patient progressed to a "locked-in syndrome" and remained in that state for nearly 2 weeks. He subsequently made a near total recovery except for minor gait difficulties and urinary incontinence.

Treatment

Eleven patients (61%) were treated with steroids. Eight patients received prednisone at 2 mg/kg/d or dexamethasone at 0.5 mg/kg/d for 5 to 7 days and tapered over 1 to 2 weeks. Three patients received high-dose intravenous methylprednisolone of 20 mg/kg/d within the first week of hospitalization for 5 days and tapered over 4 to 6 weeks. None of the patients on either steroid regimen experienced any adverse effects from steroids. Two patients also received intravenous immunoglobulin (IVIG) at 400 mg/kg/d for 5 days. One of these patients received a second course of IVIG because he remained comatose and quadriplegic 3 weeks into the illness. Seven patients did not receive steroids or IVIG. Antibiotics were given to 15 patients, and acyclovir was given to 13 patients. One patient received ganciclovir for EBV infection. Treatment was continued until the throat secretions were negative for EBV by PCR. Anticonvulsants were administered to 3 patients who had seizures during the course of their illnesses; 1 of them required long-term anticonvulsant medication.

Outcome

Deficits at Discharge

All of the patients had clear sensorium at discharge. Fifteen patients had neurologic deficits at discharge. Eight patients had gait disturbances. Four patients had paraparesis and/or urinary problems, and 1 patient had quadriparesis with urinary problems. One patient had resolving hemiparesis. One patient had fatigue and headache. Three patients did not have any deficits at the time of discharge from the hospital.

Deficits at Follow-up

All 18 patients had been seen at follow-up. The duration of follow-up ranged between 2 months and 60 months with a mean of 22 months. Thirteen patients who had deficits at discharge were functioning normally without any deficits at the 3-month follow-up. Of the remaining 5 patients who had deficits at the 3-month follow-up, 2 improved and only 3 patients had continuing deficits. Two of these patients had residual urinary symptoms and gait problems. Both of these patients had severe spinal cord disease at presentation. Another patient had recurrence of symptoms 9 months after initial hospitalization. He had new hyperintense lesions on T2/FLAIR at recurrence. The initial lesions had completely resolved. He had returned to his baseline function before this recurrence. Although he improved with repeat high-dose methylprednisolone treatment, he continued to have mild gait difficulties and urinary symptoms. No further recurrences occurred for 4 years. The

third patient had continuing seizures and needed anticonvulsant medication. This patient had predominantly unilateral lesions on the initial MRI. Repeat MRI 18 months after the initial diagnosis showed atrophy and encephalomalacia in the left temporal lobe and new hyperintense lesions on T2 FLAIR in the cortical gray and subcortical white matter on the contralateral side. However, she did not have any new neurologic symptoms, and the new lesions were asymptomatic.

DISCUSSION

Eighteen cases of ADEM were identified during a 6-year period in a single children's hospital. The results are consistent with findings in 2 other, similar reviews from the United Kingdom and Australia.[7,8] In all 3 studies, a nonspecific infectious disease preceded the onset of ADEM in >70% of cases (Table 3).[7,8] Two of the 3 studies documented a seasonal distribution of cases, further suggesting an infectious cause. Although a number of infectious agents, such as influenza, measles, mumps, rubella, varicella, herpes simplex virus, hepatitis viruses, EBV, coxsackieviruses, mycoplasma, Campylobacter, streptococcus, legionella, and rickettsia, have been implicated in ADEM, only influenza is associated with the winter/spring respiratory illness pattern observed in the present report.[9–19] Despite vigorous attempts to identify microbial pathogens in the present study, only 1 patient with EBV disease was classified with a definite microbiologic ADEM cause. Of the 2 patients with rotavirus disease, 1 was classified as possibly associated with ADEM. Rotavirus typically occurs during winter/spring but produces gastrointestinal rather than respiratory illness. A recent report, however, described encephalopathy in 2 children with rotavirus diarrhea, and MRI findings in 1 of the children was consistent with ADEM.[20]

The vast majority of patients in the present study had no microbiologic diagnosis despite numerous laboratory investigations. The failure to identify a viral agent suggests that the inciting agent or agents are unusual or cannot be recovered by standard laboratory procedures. The list of potential winter/spring respiratory pathogens includes influenza, respiratory syncytial virus, and coronavirus. Coronavirus is the most difficult to detect in standard hospital-based virus laboratories. It has not been associated with neurologic disease in humans. However, coronavirus has the ability to induce CNS demyelination in an animal model.[21] These findings deserve additional epidemiologic study in humans.

Two patients in the present study were considered to have possible MS because of clinical and/or radiologic recurrence. ADEM by definition is a monophasic illness; any recurrences beyond the first few months of the initial illness should be considered MS. A minority of children initially presenting with clinical and neuroimaging features of ADEM may subsequently be considered as having MS as in the cases illustrated. Distinction between these 2 conditions at initial presentation cannot be made with certainty, although some of the clinical and radiologic features may point toward one or the other diagnosis.[7,22] A second attack of MS occurs over a period of months to several years in children; therefore, establishing a diagnosis of MS may require prolonged follow-up.[23] In the absence of clinical recurrence, new MRI lesions that appear beyond the first few months after ADEM may help in the early diagnosis of MS.[23] This is important, as the early treatment of MS has been shown to prevent the progression of the disease.[24]

The present study also confirmed the overall good outcome observed in the British and Australian reports. One hundred percent of children survived ADEM in the 3 studies, and >80% of children were neurologically normal at the conclusion of follow-up in 2 studies (Table 3). In addition, relapses occurred in only 0% to 25% of patients. Most of the reported relapses occurred after the rapid weaning of high-dose steroids. Although high-dose steroid therapy was used in only 21% of the children in the present report, 74% and 88% of children received high-dose steroids in the British and Australian studies, respectively. Despite these differences in treatment, neurologic outcome, relapse rates, and MRI findings at follow-up were similar. It is difficult to assess the actual benefits of steroid therapy in ADEM because none of the 3 studies was prospective or designed to evaluate therapy.

CONCLUSION

The present study demonstrated that ADEM in children occurs in winter/spring and closely follows an upper respiratory tract illness. MRI studies demonstrate asymmetric lesions in the cortical and subcortical white matter of the brain. Initial lesions may persist and new lesions may appear during the immediate recovery period. Clinical outcome, in general, is favorable regardless of therapy. A minority of patients may subsequently be shown to have MS because of clinical and/or radiologic recurrence.

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