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Original Research Article

A Prospective Clinical Study to Evaluate Children with Acute Disseminated Encephalomyelitis

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Abstract

Aim: The aim of this study to study on acute disseminated encephalomyelitis in children. **Methods:** The present Prospective study was conducted in the Department of Paediatrics Vardhman Institute of Medical Science, Pawapuri Nalanda, Bihar, India for 1 year. Study group consisted of hospitalized children < 15 years of age admitted to our hospital with the diagnosis of ADEM were included in this study. **Results:** Maximum prevalence in 5- 9-year age group (58%) with 28% in 0-4 year& 14 % in 10-14years age group. Male predominates in the study 64% with female being 36%. 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%. Out of 50 cases, MRI was done in 43cases, CT scan was done in 2 cases, 5 could not be done. T1 hypo intensity was observed in 52%, T2 hypo intensity in 76%, FLAIRS changes in 72% cases. Frontal lobe was involved in maximum number of cases (56%). CSF was done in 47 out of 50 cases, pleocytosis was observed in 42% cases, elevated protein in 70% cases & low sugar in 30% cases. Steroid were given in only 43 number of patients, steroid plus IVIG were given in 2 patient, only supportive treatment were given in 5 out of 50 patients. Out of 26 children with sequelae, epilepsy was predominantly seen 50% of cases. Motor deficit is seen in 50% of cases. **Conclusion:** ADEM most commonly present as a polysymptomatic encephalopathy and initially diagnosis may not be clear. Clinical evaluation, MRI & CSF studies are most useful to establish the diagnosis and rule out important differential diagnosis.

Keywords: Disseminated Encephalomyelitis, Children, MRI

Introduction

Acute disseminated encephalomyelitis (ADEM) is an immune driven illness of the central nervous system (CNS) that causes numerous inflammatory lesions in the brain and spinal cord, particularly in the white matter. ADEM should be differentiated from other central inflammatory demyelinating diseases of children, including multiple sclerosis (MS) and clinically isolated syndromes that include optic neuritis, transverse myelitis, and neuromyelitis optica (Devic's disease). Most of these diseases are believed to be caused by immune system dysregulation induced by an infectious or other environmental agent in a genetically vulnerable host.

ADEM is frequently preceded by a viral or bacterial illness, generally in the form of a generic upper respiratory infection. In 3 prior investigations, an antecedent infection was found in 72 to 77 percent of ADEM patients [1-3]. In typically, individuals will come within 1 month after this first sickness. Numerous causal pathogens have been discovered 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 [4-11]. Other organisms linked include Borrelia burgdorferi, Chlamydia, Leptospira, Mycoplasma pneumoniae, Rickettsia, and beta-hemolyticStreptococcus [4, 12].

Less than 5 percent of all ADEM cases follow vaccination. Postvaccinal ADEM has been linked with vaccination for rabies, hepatitis B, influenza, Japanese B encephalitis, diphtheria/ pertussis/tetanus, measles, mumps, rubella, pneumococcus, polio, smallpox, and varicella. 12 No infectious agent is identified in most instances. Currently, measles, mumps, and rubella immunization are most frequently linked with post-vaccination ADEM. It is essential to note the substantial difference between the incidence of ADEM linked with the live measles vaccine (1 to 2 per million) and the incidence of ADEM previously related with the measles virus infection (1 in 1,000). (1 in 1,000) [13]. The pathophysiology of ADEM is incompletely known. The hypothesised mechanism of ADEM is that myelin autoantigens, such as myelin basic protein, proteolipid protein, and myelin oligodendrocyte protein, share antigenic determinants with those of an invading pathogen [12]. This hypothesis is confirmed by investigations of lymphocytes in children with ADEM. In 1 study, the frequency of T cell reactivity to myelin basic protein was 10 times greater in individuals with ADEM than in those with encephalitis or normal controls [5].

Material and methods

The current prospective research was carried out at the Department of Paediatrics at the Vardhman Institute of Medical Science in Pawapuri Nalanda, Bihar, India, for 1 year with the permission of the protocol review committee and the institutional ethics committee, respectively.

Criteria for inclusion

Patients in the study group were all hospitalised children under the age of 15 who had been diagnosed with ADEM according to the defined criteria, which were as follows: Acute or sub-acute onset of polysymptomatic, neurological presentation with prominence of cortical signs (changes in mental status, seizures, acute behavioural changes, etc.) in the absence of prior history of infectious illness or vaccination. The disease progressed in a single phase. Other recognized etiologies are unable to explain the observed signs and symptoms. When gadopentetate dimeglumine (0.1mmol/kg) was used, 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, and basal ganglia without previous white matter changes) was considered conclusive. Using a third-generation scanner, CT (Computerized Tomography) pictures were acquired in a small number of instances, with contrast enhancement in the remaining cases. The scans were examined by a neurologist who was not aware of the clinical results at the time.

The pictures were evaluated for the location of the lesion, its size, number, distribution, symmetry, any midline shift, haemorrhage, and the pattern of contrast

enhancement on the images. Patients with altered awareness or seizures were subjected to a standard 30-minute interictal surface electroencephalogram (EEG), which was recorded on their scalps. In the diagnostic workup of a patient with a neurological disaster, these differential levels of examinations are normal practise, and they have no effect on the etiologic diagnosis. The prevalence of the prodermal phase as well as the history of recent immunisation was investigated. Following a neuroimaging investigation, the incidence of aberrant findings on MRI/CT scans was determined and reported.

It was found that the kind of deficiency, the involvement of cranial nerves, the degree of awareness, seizures, headache, and all the other characteristics were associated with the immediate result in patients with Mode of Onset and Mode of Presentation, i.e. in-depth medical history and a formal neurological examination are performed to determine the outcome, which may include full recovery, motor deficits, cognitive deficits, visual field defects, recurrent seizures, learning disorders, personality changes, psychiatric manifestations, death, and other outcomes. If there was any indication of progression or return of neurological impairments, a second brain MRI session would be scheduled. 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.

Following that, prednisolone (1mg/kg orally) was administered for six weeks, with tapering occurring gradually over time. 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. The data obtained as a result of this computation was examined, and conclusions were made.

Criteria for exclusion

- Recurrence of neurological signs and symptoms more than 3 months after the onset of the first disease.
- Acute onset of flaccid paralysis of limbs or isolated optic neuritis or isolated transverse myelitis.
- Presence of a significant preceding neurological abnormality or features suggestive of neurodegenerative disorder.
- Signs and symptoms associated with 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, hemi paresis 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 patients 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.

Statistical analysis

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 22 software.

Table 1: Age & Sex distribution of study subjects

Age in year	Sex		Total
	Male	Female	
0-4Years	8	6	14
5-9years	19	10	29
10-14years	5	2	7
Total	32	18	50

Age distribution of study sample has been analyzed. It shows maximum prevalence in 5- 9 year age group (58%) with 28% in 0-4 year& 14 % in 10-14years age group. Male predominates in the study 64% with female being 36%.

Table 2: Presenting Symptoms (n=50)

Symptoms	Number	Percentage
Convulsion	33	66
Fever	30	60
Altered sensorium	29	58
Paralysis	20	40
Vomiting	13	26
Headache	8	16
Speech abnormality	8	16
Bowel & bladderchanges	5	10
Abnormal movement	4	8
Blurring of vision	3	6
Rash	3	6
Double vision	2	4
Dysphagia	2	4
Neck retraction	2	4
Dizziness	2	4

The variety of symptoms presented by the study sample at the onset was analyzed here. Seizures were documented to occur in highest number of cases (66%). Next fever (60%) & altered sensorium (58%) followed.

Table-3: Pattern of neurological involvement.

Sign	Number	Percentage
Motor deficit	34	68
Encephalopathy	43	86
Autonomic involvement	20	40
Cranial nerve involvement	14	28
Cerebellar sign	10	20
Aphasia	8	16
Meningeal sign	12	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	Number	Percentage
T1 hypo intensity	26	52
T2 hypo intensity	38	76
FLAIR hyper intensity	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	5	10
Normal	1	2

Out of 50 cases, MRI was done in 43cases, CT scan was done in 2 cases, 5 could not be done. T1 hypo intensity was observed in 52%, T2 hypo intensity in 76%, FLAIRS changes in 72% cases. Frontal lobe was involved in maximum number of cases (56%).

CSF was done in 47 out of 50 cases, pleocytosis was observed in 42% cases, elevated protein in 70% cases & low sugar in 30% cases.

Steroid were given in only 43 number of patients, steroid plus IVIG were given in 2 patient, only supportive treatment was given in 5 out of 50 patients. Out of 26 children with sequelae, epilepsy was predominantly seen 50% of cases. Motor deficit is seen in 50% of cases.

Predisposing factors [Respiratory infection (40%), Nonspecific fever (20%), GI infection (10%), UTI (10%), CNS infection (10%), Measles (4%), Mumps (4%), appendicitis (4%)].

Although the prevalence of predisposing factor seems to be higher in 0-4years age group, it is not confirmed statistically. It seems that 0-4 years had mostly moderate to severe presentation and 5–9-year age group had mostly severe presentation. Statistically significant association could not be established. There is not statistically significance as seen with outcome at discharge.

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

Outcome at discharge	Glassgow coma score						Total	
	Mild		Moderate		Severe			
	No	%	No	%	No	%	No	%
Complete recovery	6	60	6	30	4	20	16	32
Partial or no recovery	4	40	14	70	9	45	27	54
Death	0	0	0	0	7	35	7	14
Total	10	100	20	100	20	100	50	100

Chi square =12.54, p=0.023

It was observed that the cases with severe presentation had lower proportion of recovery (20%) & higher proportion of mortality (45%) which was found to be statistically significant.

Discussion

50 children with signs of CNS demylination were included in the research; 36 of them met the criteria for a first episode of ADEM and two were diagnosed with multiple sclerosis, according to the findings. ADEM accounted for 0.42 percent of all indoor admissions over the time period, out of 12000 total admissions.

ADEM was detected in all age groups of children, with a preponderance in the early childhood years. In this group, the youngest was a 45-day-old baby and the oldest was fourteen years old. The highest incidence was found in the 5–9-year-old age group, with the mean age of presentation being 5.4 years and 3.54 months on average. Previous studies have revealed results that are similar to this one [14-16].

Males accounted for 64 percent of the participants in the research, with females accounting for 36 percent. Multiple sclerosis is more frequent in females than in boys, according to studies conducted in India and elsewhere. ADEM is more common in boys than in girls [15,17]. The clinical characteristics of ADEM in the current study were similar to those reported in earlier studies. Seizures were found to occur in the greatest number of instances, according to the data (66%). Fever (60%) and altered sensorium (58%) were the next symptoms to appear. Encephalopathy was found in 86 percent of the participants, followed by motor impairment in 68 percent and autonomic involvement in 40 percent. The use of magnetic resonance imaging (MRI) is critical in the diagnosis of acute CNS white matter dysfunction. When it comes to ADEM, CT scans are often normal (Dunn et al 198618, caldemeyer 1994) [19]. In our research, CT scans were performed on about 2 individuals, with 1 patient having characteristics indicative of demyelination on the scan.

Adults with multiple sclerosis have been found to exhibit brain MRI abnormalities that are indicative of the onset of the disease. O'Riordan and colleagues (1998) found that in clinically isolated syndromes, an abnormal MRI brain on presentation was linked with development of multiple sclerosis in 83 percent of patients over the course of the final ten years of follow-up [20].

A normal magnetic resonance imaging (MRI) scan was linked with the development of multiple sclerosis in our single patient throughout the research period. Out of 50 instances, an MRI was performed in 43 cases, a CT scan was performed in two cases, and a fifth case could not be performed. T1 hypo intensity was found in 52 percent of the patients, T2 hypo intensity in 76 percent of the cases, and FLAIRS alterations were observed in 72 percent of the cases.

Temporal atrophy was seen in 8 patients (16 percent), contrast enhancement in 3 patients (6 percent), and gyral thickening in 3 patients (all of whom were female) (6 percent) The lobes of the brain were the most often affected areas, with the fontal lobe being the most frequently affected (56 percent). T2 hyper intensity of the spinal cord was seen in four of our patients who had a screening MRI spine; the whole cord was implicated in one, the cervical region in one, and the medulla was involved in one. Multiple sclerosis in children has been studied extensively in the past, and the findings have shown a preponderance of periventricular lesions (near universality), especially at the trig one and the body of the lateral ventricle (Alper G et al 2009) [21]. The presence of cortical grey lesions was uncommon.

It was also discovered that ADEM included deep grey matter in 30 percent of the patients in our research. This is believed to be the sole imaging discovery in ADEM (Baum et al 1994, Kimura et al 1996) [22, 23]. In the case of white matter lesions, the asymmetry seen is a hallmark of an acquired demyelinating disease. The presence of symmetrical white matter anomalies should raise the possibility of leucodystrophy. Deep grey matter anomalies in ADEM, on the other hand, are often symmetrical in nature. According to earlier research [19, 24], thalamic involvement was seen in 20% of instances, although it may be as high as 40% in certain situations. The CSF was taken in 47 out of 50 cases, pleocytosis was found in 42 percent of cases, high protein in 70 percent of cases, and low sugar in 30 percent of cases, all of which were reported in 28-65 percent of ADEM patients examined [25]. In nearly all instances, with the exception of a few, the CSF opening pressure was normal. The number of cells was somewhat increased, with a mean cell count of 14/cumm ranging from 0-100/cumm, and they were mainly mononuclear in composition.

When infective encephalitis has been ruled out and acute post infectious demyelination is suspected, current consensus recommends the use of intravenous methyl prednisolone followed by oral prednisolone treatment. Notably, some children seem to heal completely without the need for therapeutic care, but in reality, recovery is typically just partial [26, 27]. In our research, no therapy (just supportive treatment) was administered to seven individuals, some of whom presented with a fulminant presentation that left little time for intervention. Just 43 patients received steroid therapy, two patients had steroid plus IVIG treatment, and five patients received only supportive care out of a total of 50 patients. Although the treatment intervention was chosen at random, prior research has shown the effectiveness of different therapeutic modalities in particular areas of engagement [28].

The following risk factors have been identified: respiratory infection (40 percent), nonspecific fever (20 percent), gastrointestinal infection (10 percent), UTI (10 percent), central nervous system infection (ten percent), Measles (4 percent), Mumps (4 percent), appendicitis (4 percent) in previous studies [29, 30]. The prevalence of antecedent illness was highest in children under 10 years of age (80%), with the youngest age group accounting for the majority of cases (0-4 years). Although the association was not statistically significant ($p=0.074$), this study requires a larger sample size before it can make a definitive conclusion. In earlier research, it was shown that >30 percent of teenage patients did not have any signs of illness [19]. In the case of multiple sclerosis, the incidence of previous disease is often less well documented (R C Dale et al 2000) [17]. The relationship between age and severity of presentation does not have statistical significance; thus, a larger sample size is required. The result at discharge, on the other hand, does not have statistical significance.

Patients with severe presentation had a lower percentage of recovery (20%) and a greater percentage of death (45%) than those with less severe presentation, and this was shown to be statistically significant. In a similar vein, patients with moderate degrees of presentation had a lower percentage of full recovery (28 percent) than those with mild degrees of presentation (56 percent), indicating that the severity of presentation was inversely related to the likelihood of complete recovery at discharge. The chi-square test of association, which yielded a p value of 0.023, demonstrated that it was statistically significant.

Conclusion

ADEM is most frequently manifested as a polysymptomatic encephalopathy, and the diagnosis may be difficult to establish at first. Clinical examination, magnetic resonance imaging (MRI), and cerebrospinal fluid (CSF) tests are the most helpful in establishing the diagnosis and ruling out significant differential diagnoses. When there is a severe presentation, it is likely that there was an underlying disease. When it comes to the result, the age, gender, and predisposing factor have no effect, but the intensity of the presentation has an impact on the outcome at discharge.

References

1. Dale RC, de Sousa C, Chong WK, Cox TC, Harding B, Neville BG. Acute disseminated encephalomyelitis, multiphasic disseminated encephalomyelitis and multiple sclerosis in children. Brain 2000;123 Pt 12:2407-22.
2. Hynson JL, Kornberg AJ, Coleman LT, Shield L, Harvey AS, Kean MJ. Clinical and neuroradiologic features of acute disseminated encephalomyelitis in children. Neurology 2001; 56:1308-12.
3. Tenembaum S, Chamoles N, Fejerman N. Acute disseminated encephalomyelitis: a long-term follow-up study of 84 pediatric patients. Neurology 2002; 59:1224-31.
4. Tenembaum S, Chitnis T, Ness J, Hahn JS; International Pediatric MS Study Group. Acute disseminated encephalomyelitis. Neurology 2007;68(16 Suppl 2):S23-36.
5. Pohl-Koppe A, Burchett SK, Thiele EA, Hafler DA. Myelin basic protein reactive Th2 T cells are found in acute disseminated encephalomyelitis. J Neuroimmunol 1998; 91:19-27.
6. Stüve O, Zamvil SS. Pathogenesis, diagnosis, and treatment of acute disseminated encephalomyelitis. Curr Opin Neurol 1999; 12:395-401.
7. Caldemeyer KS, Smith RR, Harris TM, Edwards MK. MRI in acute disseminated encephalomyelitis. Neuroradiology 1994; 36:216-20.
8. Kim SC, Jang HJ, Han DJ. Acute disseminated encephalomyelitis after renal transplantation in patients with positive Epstein-Barr virus antibody. Transplant Proc 1998; 30:3139.
9. Apak RA, Köse G, Anlar B, Turanli G, Topaloğlu H, Ozdirim E. Acute disseminated encephalomyelitis in childhood: report of 10 cases. J Child Neurol 1999; 14:198-201.
10. Huber S, Kappos L, Fuhr P, Wetzel S, Steck AJ. Combined acute disseminated encephalomyelitis and acute motor axonal neuropathy after vaccination for hepatitis A and infection with Campylobacter jejuni. J Neurol 1999; 246:1204-6.
11. Murthy JM. MRI in acute disseminated encephalomyelitis following Semple antirabies vaccine. Neuroradiology 1998; 40:420-3.
12. Stonehouse M, Gupte G, Wassmer E, Whitehouse WP. Acute dis- seminated encephalomyelitis: recognition in the hands of general paediatricians. Arch Dis Child 2003; 88:122-4.
13. Fenichel GM. Neurological complications of immunization. Ann Neurol 1982; 12:119-28.

14. Hynson JL, Kornberg AJ, Coleman LT, et al. Clinical and neuroradiologic features of acute disseminated encephalomyelitis in children. Neurology. 2001 May 22;56(10):1308-12.
15. Tenembaum S, Chamoles N, Fejerman N. Acute disseminated encephalomyelitis: a long-term follow-up study of 84 pediatric patients. Neurology. 2002 Oct 22;59(8):1224-31.
16. Anlar B, Basaran C, Kose G, Guven A, Haspolat S, Yakut A, et al. Acute disseminated Encephalomyelitis in Children: Outcome and Prognosis. Neuropediatrics. 2003; 34:194–9
17. R. C. Dale C. de Sousa W. K. Chong T. C. S. Cox B. Harding B. G. R. Neville. Acute disseminated encephalomyelitis, multiphasic disseminated encephalo-myelitis and multiple sclerosis in children. Brain, 2000;123:2407–2422
18. Dun V, Bale JF Jr, Zimmerman RA, et al. MRI in children with postinfectious disseminated encephalomyelitis. Magn Reson Imaging. 1986; 4 (1): 25-32.
19. Caldemeyer, K.S., Smith, R.R., Harris, T.M. et al. Neuroradiology (1994) 36: 216.
20. O'Riordan JI, Gomez-Anson B, Moseley IF, et al. long-term MRI follow-up of patients with post infectious encephalomyelitis: evidence for a monophasic disease. J Neurol Sci. 1999 Aug 15;167(2): 132-6.
21. Alper G. Acute disseminated encephalomyelitis. J Child Neurol. 2012 Nov;27(11):1408-25.
22. Baum PA, Barkovich AJ, Koch TK, Berg BO. Deep gray matter involvement in children with acute disseminated encephalomyelitis. Am J Neuroradiol. 1994; 15:1275–83.
23. Kimura S, Nezu A, Ohtsuki N, et al. Serial magnetic resonance imaging in children with postinfectious encephalitis. Brain Dev. 1996 Nov-Dec; 18 (6): 461-5.
24. Schwarz S, Mohr A, Knauth M, et al. Acute disseminated encephalomyelitis: a follow-up study of 40 adult patients. Neurology. 2001 May 22;56(10): 1313-8.
25. Shahar E, Andraus J, Savitzki D, et al. Outcome of severe encephalomyelitis in children: effect of high- dose methylprednisolone and immunoglobulins. J Child Neurol. 2002 Nov;17(11):810-4.
26. Rust RS, Dodson W, Prensky A. Classification and outcome of acute disseminated encephalomyelitis. Ann Neurol. 1997; 42:491.
27. Francis GS, Deguette P, Antel JP. Inflammatory demyelinating disease of the central nervous system. In: Bradely WG, Daroff RB, Fenichel GM, editors. Neurol Clin Prac. 3rd ed. Vol. 2. Boston: Butter worth Heinemann; 1995. pp. 1307–1343.
28. Ravaglia S, Piccolo G, Ceroni M, et al. Severe steroid-resistant post-infectious encephalomyelitis: general features and effects of IVIg. J Neurol. 2007 Nov; 254(11):1518-23.
29. Menge T, Hemmer B, Nessler S, et al. Acute disseminated encephalomyelitis: an update. Arch Neurol. 2005 Nov;62(11):1673-80.
30. Rust RS. Multiple sclerosis, acute disseminated encephalomyelitis, and related conditions. Semin Pediatr Neurol. 2000 Jun;7(2):66-90.