A Clinical profile of Acute Disseminated Encephalomyelitis

PROJECT REPORT

DR. BOBY VARKEY M.

RESIDENT IN NEUROLOGY 1999-2001

SREE CHITRA TIRUNAL INSTITUTE OF MEDICAL SCIENCES & TECHNOLOGY,
THIRUVANANTHAPURAM.

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Title of the Project: A Clinical profile of Acute disseminated encephalomyelitis(ADEM)

Name: Dr. Boby Varkey M.

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CERTIFICATE

I, Dr.Boby Varkey M, hereby declare that I have actually carried out the project –

A Clinical profile of Acute Disseminated Encephalomyelitis.

Signature:

Name: **Dr.Boby Varkey. M**

Thiruvanthapuram
16.11.2001

Forwarded

He has carried out the above mentioned project in the department of Neurology , SCTIMST, Thiruvanthapuram

Signature

Prof.K.Radhakrishnan
Head of the Department
Dept of Neurology
SCTIMST, Thiruvanthapuram

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Dr. Boby Varkey M.

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INTRODUCTION

Introduction

Acute disseminated encephalomyelitis (ADEM) is an acute inflammatory disease of the central nervous system[1,11,14,34]. It occurs secondary to systemic viral infections (post infectious encephalomyelitis) , following the administration of vaccines (post vaccinial encephalomyelitis), in association with rheumatic fever or without any recognized antecedents[1,40]. . Typically, it is antedated by an infectious illness, most commonly measles, mumps, influenza A or B, Rocky Mountain spotted fever, or hepatitis A or B, or infection with herpes simplex, human herpesvirus 6, varicella, rubella, vaccinia, Epstein–Barr virus, cytomegalovirus, *Mycoplasma pneumoniae, Chlamydia, Legionella, Campylobacter,* or *Streptococci* [47]. ADEM can also follow immunizations: rabies, diphtheria–tetanus–pertussis, smallpox, measles, Japanese B encephalitis, and hog Various other terminologies have been used interchangeably in the literature including disseminated vasculomyelinopathy, microglial encephalitis, perivenous encephalitis, perivenous allergic encephalopathy, allergic neuroloencephalopathies, para or post infectious encephalomyelitis , post vaccinial encephalomyelitis , acute encephalo-myeloradiculitis and acute Multiple sclerosis[1,6]. Unlike Multiple Sclerosis, ADEM is usually a monophasic disease with acute onset focal or multifocal neurological dysfunction. Like Multiple Sclerosis, ADEM is an inflammatory demyelinating disease ,however ADEM is monophasic whereas MS is multi-phasic and results in stepwise or steadily progressive deterioration in neurological function. There are no generally accepted diagnostic criteria for ADEM; thus, distinguishing ADEM from the first episode of MS is often difficult[46].

AIM OF STUDY

Aim of study

To study the clinical presentation and outcomes of patients who presented with Acute disseminated encephalomyelitis (ADEM) in our institute

REVIEW OF LITERATURE

Early History of ADEM

'An unmarried woman , aged 23 yrs was seized with a fever , July 21st, 1790. On the 23rd , in the evening , the measles began to appear and on the 28th ,the eruption seemed to be gradually declining. On the 29th , in the evening , she perceived that she was deprived of the use of her lower limbs.....the following morning she could not pass any urine'.

James Lucas (1790)

This was one of the first descriptions of an entity called Acute Disseminated Encephalomyelitis . Initially , most reports were of this entity following vaccinations.In 1885, Pasteur developed a treatment for rabies , by injecting a suspension of rabbit spinal cords inoculated with fixed rabies virus[8] . In 1889 Barrregi reported 5 fatal cases of neuroparalytic accidents following this rabies vaccination. Subsequently a large number of reports ensued. In 1932 , Hurst first attributed these accidents to an immune reaction to the nervous tissue in these vaccines[9]. Recognising this, Suckling mouse brain (SMB) vaccine , developed in Chile, to reduce the number of neuroparalytic accidents seen with the earlier vaccine , still continued to produce cases of post vaccinial encephalomyelitis , though at a reduced rate of 1/7865 vaccinations[8]. Reports of neurologic complications related to duck embryo rabies vaccine and 2 cases following human diploid cell vaccine have also been reported. Subsequently the association of ADEM with other infections was also recognized.

Epidemiology of ADEM;

Post infectious encephalomyelitis

ADEM most commonly occurs in temporal relation to either systemic viral infections or following vaccination . Post infectious encephalomyelitis is most frequent after measles and occurs with a frequency of 1:1000 in children above two years of age. ADEM is the most common neurological complication of measles[2]. It is rare in children under two years of age, but complicates infections in older children. The mortality rate is 10- 20% and the majority of survivors have neurological complications. Post infectious

measles encephalomyelitis is distinct from two rare neurological complications of measles- Subacute inclusion body encephalitis (SIBE) occurring in immuno-deficient patients and subacute sclerosing panencephalitis (SSPE) in immunocompetent patients [2].

Varicella is also a common cause (1:10,000). The incidence of ADEM after rubella is noted to be 1:20,000[3] . Other notable causes of ADEM include herpes zoster, herpes simplex [2] ,mumps, influenza, coxsackie B virus [27], infectious mononucleosis and non-specific acute febrile illnesses.

A case report of ADEM associated with chronic Epstein Barr virus infection with multifocal abnormalities on MRI , 1 year after the acute infection has also been published[2]. Herpes simplex type 2 may be associated with dysuria and features of ADEM..

Bacterial infections are not generally complicated by ADEM[42]. However case reports have been reported with mycoplasma infections, pseudomonas and other gram negative organisms. Most of the latter cases were associated with endotoxic shock and suffered from hypotension and renal failure. Salmonella typhi has been associated commonly with post infectious cerebellar ataxia[35,41]. Campylobacter jejuni has been associated with a post infectious encephalopathy in a 4 yr old child 10 days following a diarrhoeal illness[5].. C jejuni has been implicated in other autoimmune syndromes involving the nervous system , most notably Guillain-Barre syndrome and Miller fisher syndrome. In these conditions infection usually precedes the neurological illness by 1-3 weeks. ADEM complicating Legionella cincinnatiensis has been reported[2] .

Encephalomyelitis complicating streptococcal infection has been described recently[6]. Jorens et al described a 3 year old Caucasian boy with a preceding history of otitis media caused by S.pyogenes . There was clonal expansion of myelin reactive T cells in this child , presumably caused by exposure to S.pyogenes exotoxins.

Cerebral malaria has been associated with disseminated vasculomyelinopathy in the tropics[7]. A form of hyperergic reaction of the CNS occurs in response to the antigenic challenge of Plasmodium falciparum. The manifestations depend on the immune status of the host. Paradoxically ADEM is more common in previously healthy individuals as

compared to children with Kwashiorkor or marasmus .. Presumably the feeble immune response in the latter individuals protects them from the consequences of a hyperimmune response.

Basic characteristics of patients in Schwartz's series [46]

Characteristics	ADEM (n = 26)
Prior infection, n (%)	12 (46)
Prior immunization, n (%)	0

Post vaccinial encephalomyelitis

Post vaccinial encephalomyelitis was classically recognized after rabies vaccination. Neuroparalytic accidents after Pasteur's postexposure rabies immunization was recognized as far back as 1889. These vaccines contained a suspension of rabbit spinal cords inoculated with fixed rabies virus[ii]. Barregi (1889) reported 5 fatal cases of neuroparalytic accidents following vaccination with this preparation. . Subsequently Remlinger (1928) found an incidence of 1 case per 3538 vaccinations . He described a symptom complex with a short incubation period , fever , transverse myelitis , facial neuritis and was associated with a mortality rate of 30%. He termed it "Landry's Paralysis" . Hurst attributed these neuroparalytic disorders to an immune response to the nervous tissue in these vaccines[16]. The evaluation of this hypothesis lead to the discovery of Experimental allergic encephalomyelitis (EAE) , which formed the basis of pathologic definition of the syndromes of immune demyelinating diseases[iii].

Semple type vaccine contained phenol killed virus grown in rabbit brain. This vaccine was given once daily for 14-21 consecutive days , in the periumbilical region , depending upon the severity and location of the wound.. In 1983, the Pasteur institute in Bangkok , Thailand reported an incidence of post vaccinial encephalomyelitis following administration of this vaccine ranging from 1:220 to 1:400[9].

Suckling mouse brain vaccine was developed by Fuenzelida and Palacios in Chile (1955). Neuroparalytic accidents were expected to decline in incidence as this vaccine contained very little myelin. Held and lopez reported 32 cases of neurological complications with this vaccine , of the order of 1 / 7,865 vaccinations ,with a fatality rate of 21.9%[6].

The rate of neurological complications with duck embryo rabies vaccine was around 1/25,000 vaccinees. This preparation also contained minimal amounts of neural tissue. In India , previously mainly Beta-propionolactone and phenolized vaccines were used for post exposure prophylaxis[8]. Accurate figures are not available for these 2 vaccine related complications. Human diploid cell vaccine, which is a non neural tissue vaccine was introduced in 1976 .Few cases of neurological complications have been reported with the introduction of this vaccine[17].

Other vaccines have also been associated with ADEM . Currently ADEM is more common following measles, mumps or rubella vaccination than following antirabies vaccination . Measles vaccination is associated with an incidence of 1-2 per million which is significantly lower than that of post infectious encephalomyelitis following measles itself[2]. Infact the risk of developing ADEM after vaccination is nearly 20 times lower than the risk after a natural virus infection.

Live attenuated varicella vaccine administration may produce a mild chicken pox infection followed by acute cerebellar ataxia. Recovery is usually complete, like that of ataxia complicating wild type chicken pox infection . Pertussis vaccines have been associated with the development of an encephalopathic syndrome in less than one in a million cases. ADEM may follow administration of diphtheria vaccine. A single case report of acute cerebellar ataxia following administration of plasma derived Hepatitis B vaccine has been reported.. Meningococcal A and C vaccine has been associated with ADEM in a 25 year old woman [24].Other vaccines implicated include Japanese B Vaccine [26].Generally vaccinations have an excellent track record and the risk benefit ratio is quite

small. The cause and effect relationship of many of the vaccines with single case reports is still in doubt[iv]

Less common associations with ADEM

Other conditions associated with ADEM include common variable immunodeficiency (CVID)[37]. CVID is thought to predispose to a variety of autoimmune diseases and a case report of ADEM as the initial presentation of CVID has been published recently. This patient had good clinical recovery with intravenous immunoglobulins and corticosteroids. 2 recent case reports of ADEM in post transplant patients have also emerged [3]. In one of these cases , Epstein Barr virus was identified as the pathogen.

Clinical features

ADEM may have protean clinical manifestations which may be difficult to distinguish from acute viral encephalitis or acute multiple sclerosis[11] .It also lacks characteristic laboratory abnormalities . As a result , the diagnosis is usually made in retrospect and by exclusion . No definite diagnostic criteria have been published. Thajeb et al [1] used the following criteria for the diagnosis of ADEM . These include

(1) a monophasic illness
(2) the presence of symptomatology pertaining to the cerebrum with or without spinal cord or peripheral nervous system involvement
(3) fever if present is transient and low grade
(4) CSF profiles showing a normal glucose level , normal or mildly increased protein level and normal or mild lymphocytic pleocytosis
(5) EEG not showing lateralized abnormalities

The following criteria have also been used for the initial diagnosis of ADEM in a recent study [46]:

- *Clinical examination* Acute neurological symptoms without a history of previous, unexplained neurological symptoms. Generally patients with transverse myelitis or unilateral optic nerve neuritis as the only neurological deficit were excluded from this study.
- *Cranial MRI*—One or multiple supra- or infratentorial demyelinating lesions. Absence of "black holes" on T1-weighted MRI as a sign of a previous destructive inflammatory–demyelinating process. Because MRI abnormalities in ADEM are highly variable, more specific radiologic criteria are not available.
- *Lumbar puncture*—Exclusion of CNS infection, vasculitis, or other autoimmune disease with CSF analysis, including additional serologic and microbiologic tests.

Typically ADEM is preceded by an infection or vaccination. ADEM most commonly occurs in infants and young children [3]. The interval prior to the onset of neurological dysfunction varies , most often being 5 days to 2 weeks[34]. Most often the cerebrum bears the brunt of ADEM and symptoms of headache, mild fever and drowsiness progressing to stupor and coma within a few days predominate[11,42]. Seizures may occur. Focal abnormalities indicating multiple lesions of the cerebrum, cerebellum, brainstem, spinal cord and optic nerves set in (Hemiplegia, paraplegia, quadriplegia, monoplegias, cranial nerve palsies , ataxia, sensory disturbances). The most frequent clinical signs in the series of Schwartz et al [46] were motor deficit (80%), followed by sensory deficits, brainstem signs, and ataxia. Many patients (62%) with ADEM presented with brainstem signs, the most frequent of which were ocular motor deficits, which were seen in 27% patients, followed by dysarthria (19%) and various other brainstem signs. Fever and meningeal signs may be present, however the fever is usually transient and low grade [1,10] and meningeal signs are uncommon [11]. The incidence of fever, loss of consciousness, and meningism is low; however, and these symptoms are uniformly restricted to patients with ADEM as compared to MS [46]. Bilateral optic neuritis is common[v]. In Multiple sclerosis , the optic neuritis is more commonly unilateral by contrast [13]. Myelopathy in ADEM is frequently complete and associated with areflexia, unlike in Multiple sclerosis where it is partial. Ascending myelitis progressing to respiratory failure [28] and micturitional disturbances at the onset[29] (UMN as well as LMN bladder) have been seen. Occasionally

the peripheral nervous system is also involved [10,11]. Myeloradiculopathies and polyradiculopathies are particularly common in post vaccinial cases [7]. Peripheral neuropathy may be seen [8]. Demyelinating peripheral neuropathy occurring along with central demyelination has been described by various authors[30,31,32].

In general, patients with ADEM tend to present with a more acute, widespread CNS disturbance, causing loss of consciousness and multifocal neurological signs [46]. Characteristic clinical features include sudden onset of multifocal neurological disturbances such as bilateral optic neuritis, visual field defects, aphasia, motor and sensory deficits, ataxia, movement disorders, and signs of an acute meningoencephalopathy with meningismus, a depressed level of consciousness, focal or generalized seizures, and psychosis. Maximal deficits are reached within several days and remission may be similarly rapid. More often, however, resolution is partial and takes weeks or months[47].

A comparison of 3 recent studies on ADEM was published in 2001. This has compared the various clinical manifestations of ADEM at presentation across 3 relatively large populations of ADEM patients[47].

Table 1. ***ADEM: Comparison of three series***

Characteristic of symptoms at onset, %	Hynson et al., 2001	Dale et al., 2000	Schwarz et al., 2001
Headache	45	58	Not given
Fever	52	43	15
Meningism	26	31	15
Disturbed consciousness	68	69	19
ON	13	29	Not given
Cranial nerve abnormalities	45	51	Not given
Pyramidal motor signs	23	71	77
Sensory deficits	3	17	65

Ataxia	65	49	38
Brainstem	Not given	Not given	62
Spinal	Not given	23	15
Aphasia	26	0	8
Seizure	13	0	4
Extra pyramidal	0	2	0

Unusual presentations have included presentation with signs of raised intracranial pressure[33], alternating hemiplegia [15], acute psychosis [36].

When the disease follows specific viral infection or vaccination in a child, the distinction from Multiple sclerosis can be made with confidence. Rarely it may be confused with an encephalopathic form of MS. In an adult however the distinction may be difficult [11].

The response to treatment has again varied. In their series Hemachuda et al [9] found complete recovery by the 8th day of treatment in 70% of cases. Ninety-five percent of all patients improved during the acute phase of the disease itself in the series of Schwartz [46].

Sequalae are frequent in ADEM . About 50% of the survivors may be left with significant disabilities (blindness, paraplegia and ataxia etc)[42]. Mortality figures have varied from study to study. ADEM following measles may have a mortality rate of around 25 % with major neurological sequalae in 25-40% of survivors [3]. High mortality rates (up to 20%) were frequent in the past, particularly when ADEM followed measles. However, with the introduction of effective vaccination strategies and the decline of measles, death is rare. In the encephalomyelitis complicating rubella and varicella zoster the rate of major sequalae is much lower.

Swamy et al [8] found a mortality rate of 18.4 % in their post vaccinial encephalomyelitis cases. Other studies have found between 0-57 %.

Post-viral encephalomyelitis

Post infectious encephalomyelitis most commonly complicates viral infections than bacterial infections.

Measles infections are still quite common in India. Approximately 18 million cases of measles occur annually in India. ADEM complicates about 1:1000 infections, leading to about 18,000 cases. Older children and adults are disproportionately involved compared to children below the age of 2 years. Characteristically ADEM supervenes when the measles rash is fading and the child is recovering from primary measles[1]. Most often ADEM sets in 2-7 days after the onset of rash, with the rare case occurring before the rash or several weeks after the rash. There is abrupt recrudescence of fever associated with multifocal neurological signs. The abruptness of neurological symptomatology is cited in favor of ADEM rather than viral encephalomyelitis , which usually has a more gradual onset. Alteration in sensorium, seizures, cranial nerve deficits, focal neurological signs (pyramidal weakness, sensory signs, ataxia) and movement disorders may occur. Alteration in sensorium ranging from mild obtundation to profound coma with decerebrate rigidity has been described. A high rate of seizures was noted in a series of 19 cases, occurring in 9/19 cases [2]. Focal or generalized seizures could occur. Meningeal signs were noted in 3 of these 19 cases. ADEM does not correlate with the severity of the exanthem. Miller et al reported figures of seizures in 47%, abnormal movements in 18%, acute hemiplegia in 10% and pure myelitis in 2% of their post measles encephalomyelitis cases[vi].

Following varicella ADEM is seen with a frequency of 1 in 10,000 infections. The commonest complication is acute cerebellar ataxia at an average of 21 days after the rash and has a good outcome. Boudewijn Peters et al [13] have however described two cases of varicella associated cerebellar ataxia in which varicella antigens in CSF cell were demonstrated by an indirect immunofluorescence test. Hence the possibility of direct viral invasion of the CNS cannot be ruled out. The florid clinical features of ADEM are seen rarely. When they do set in , it is usually a week after the rash ,as in measles. Other

exanthems associated with ADEM include rubella, mumps , influenza , Epstein barr virus etc. A variety of presentations have been described including transverse myelopathy, optic neuritis and polyradiculopathy.

The delay of the myelitis after a preceding infection is not significantly different in infectious and post infectious myelitis. The interval was 9+/-6 days in parainfectious myelitis , 5 days in mumps myelitis , 10 days in in mycoplasma myelitis and 12 days in zoster myelitis[39] .In the latter 3 instances , direct infection of the spinal cord has been demonstrated by viral isolation from the CSF. As a result the differentiation between infectious and post infectious myelitis now will require viral isolation in addition. Other viruses associated with infectious myelitis now include Echovirus type 11, Coxsackie , Mumps , herpes simplex[39].

Relapsing ADEM has been described with chronic EBV infection , occurring 1 year after the first episode. Chronicity of the infection was established by finding persistently elevated Early antigen , diffuse or restricted (EA DV)in the patient[2].

ADEM following bacterial infections

The manifestations of ADEM following bacterial infections does not differ significantly from the post viral or post vaccinial cases. Following S .typhi infection and typhoid fever, cerebellar ataxia has been found to be the most common form of post infectious neurological deficit[35,41]. Other bacterial infections associated with ADEM have included C jejuni , S.pyogenes , L cincinnatiensis [2,5,6]

Post vaccinial ADEM

Neuroparalytic complications have been described with all types of vaccines, though classically with the anti rabies vaccine (ARV). A preponderance of males has been cited , probably because men are more frequently exposed to dog bites and consequent vaccination than women. The interval between the administration of ARV and the time to onset of ADEM has been found to vary from 2 days to 64 days [7,8]. The mean interval seen

was 12.2 +/- 8.4 days [7]. The number of doses of the vaccine has not been found to related to the severity of the disease.[7,8]

The neurological manifestations seen have included meningo encephalomyelitis , meningoencephalitis, encephalitis , myelitis , meningitis and .Guillain barre syndrome Various authors have emphasized the frequency of involvement of the peripheral nervous system in post vaccinial ADEM . The frequency of PNS involvement has ranged from 8.7-68.1% in various series[7,8]. In some cases Subclinical ENMG changes were seen without peripheral nervous system involvement on clinical examination. The course has been found to be monophasic, progressive or rarely relapsing. There may also be chronic symptoms. Mortality ranged from 0- 18.4%.

Recurrence of ADEM and the distinction from multiple sclerosis

ADEM is classically a monophasic illness , occurring once and departing with sequalae. This feature is considered one of the defining features for differentiation of ADEM from multiple sclerosis. Features suggesting ADEM rather than multiple sclerosis include widespread CNS disturbance with coma, drowsiness , seizures and multifocal neurological signs implicating the brain , spinal cord and optic nerves[14]. The optic neuritis in ADEM is commonly bilateral unlike multiple sclerosis where it is unilateral . Myelopathy in ADEM is usually complete and associated with areflexia , whereas in MS it is frequently partial .Furthermore ADEM is typically preceded by an infection or vaccination.

Nevertheless clinical criteria have so far been established to make a certain distinction between the first attack of multiple sclerosis or ADEM . Although ADEM is more common in children and young adults, it has been reported in middle aged and elderly adults[25]. Conversely multiple sclerosis usually occurs in the third and fourth decades, but has been reported in children[22,23]. Features considered more in favour of ADEM such as encephalopathy, bilateral optic neuritis and complete transverse myelitis have all been reported in MS[11,21].Hasse et al have suggested that good clinical outcome from postinfectious , monophasic episode, correlating with regressive demyelinating lesions on MRI ,after more than 2 years differentiate best between ADEM and multiple sclerosis [38].

However, criteria for the differentiation between recurrent ADEM and multiple episodes of MS have not yet been developed.

Evolution of ADEM however may occur over several weeks and rare episodes may recur for upto 8 months in children and adults in the same setting . Several cases of children and young adults with relapses have been described [18,19,20]. Affected individuals developed previous episodes consistent with ADEM . After a period of stabilization or improvement , these patients developed recurrent symptoms , which were indistinguishable from relapsing remitting MS [2]. To qualify as a relapse of ADEM , Kesselring et al suggested a period of 6 months between episodes[vii]. Other authors have suggested that ADEM be followed up for a maximum duration of 2 years before reclassifying it as MS[38]. However isolated case reports with pathologically proven ADEM have been documented with relapses occurring after a period of 3 years[15].

Stuve et al [2] have suggested the term "relapsing disseminated encephalomyelitis" for these episodes, rather than relapsing acute disseminated encephalomyelitis . A classification of recurrent disseminated encephalomyelitis has also been proposed by Poser et al. Two types are recognized. An initial episode of ADEM with complete or partial recovery is followed by stereotyped recurrences- that is the symptoms are the same , though the complete syndrome may not be present . This is called Recurrent disseminated encephalomyelitis (RDEM). This type may be confused with pseudorecurrences seen in patients with steroid dependent ADEM when treatment is stopped. The differentiation may be difficult[viii].

The second type is characterised by two or more separate acute episodes that differ in clinical manifestations and is termed Multiphasic disseminated encephalomyelitis (MDEM). This subtype would be difficult to distinguish from Multiple sclerosis on purely clinical grounds , though it would be important from a prognostic point of view as ADEM has a better prognosis. Also patients with ADEM have been reported to develop multiple sclerosis [11,46].

Stuve et al [2] suggest that two issues should be addressed in a patient who has developed a recurrence after an initial diagnosis of ADEM . The development of new symptoms as opposed to recurrence of the same symptoms experienced during the initial illness , should favour the diagnosis of multiple sclerosis . Also the appearance of new CNS demyelinating lesions over time on neuroimaging studies support the diagnosis of relapsing remitting multiple sclerosis . When Schwartz et al studied a population of 40 adults, they found that 35% of all patients initially diagnosed with ADEM developed clinically definite MS over a mean observation period of 38 months. . Patients with the final diagnosis of ADEM were older, and more often had a preceding infection, clinical signs of brainstem involvement, a higher CSF albumin fraction, and infratentorial lesions[46] . The authors found no useful diagnostic criteria for the differentiation of a first episode of MS from monophasic ADEM and even go so far as to suggest that the term ADEM may still be employed as a description of a clinical syndrome, but should not be used as a distinct entity until reliable diagnostic criteria have been developed.

Laboratory findings in ADEM

No specific findings have been described in ADEM. Cerebrospinal fluid often shows a mild lymphocytic pleocytosis and protein elevation[3]. Cell counts may be normal in one-third of cases [42]. A mixed polymorphonuclear and lymphocytic or predominantly mononuclear pleocytosis may be seen [11]. Johnson et al [2] found a lymphocytic pleocytosis in 13 of their 18 patients. 4 out of 31 counts exceeded 100 cell per cubic millimeter and in these cases the sample was obtained within the first 2 days of disease. Thajeb et al [1] found a pleocytosis of upto 262 cells. Hemachuda et al [9] noted a cell range from 36 to 700/mm^3. Cell counts may be greatly elevated in cases of acute hemorrhagic leukoencephalitis. A case report describing WBC counts of 880 cells and RBC counts of 2700 per cubic mm in a patient with ADEM progressing to acute hemorrhagic leukoencephalitis has also come out [45]. RBC's have been frequently seen in ADEM with counts of upto 950 cells per cubic mm[44]. Cells have been seen to persist in the CSF , without the recurrence of symptoms[9]. CSF findings were highly variable when analysed in the series of Schwartz et al [46]; normal results were present in 20% of patients. Oligoclonal bands were positive in

65% of patients.Elevation of protein is also variable upto 191 mg/dl[44]. The CSF protein was found to be elevated in postvaccinial cases with means of 76 mg% [9]. Even large amounts of protein upto 2.68 g/l have been described [46].

CSF finding in the series of Schwartz et al [46]

Characteristics	ADEM
Leukocytes/μL, median (range)	52 (3–472)
Normal CSF findings, (%)	19 %
Plasma cells present, (%)	65 %
Protein, g/L, median (range)	0.63 (0.25–2.68)

CSf IgG would be expected to increase in an inflammatory demyelinating disease, however in their 12 samples of CSF tested for an IgG index , only 1 of 12 samples had a disproportionate increase of this index[2]. CSF oligoclonal bands are also of not much significance. However their persistence may help to differentiate multiple sclerosis from ADEM , as they tend to persist in the former. In ADEM , oligoclonal bands tend to disappear on repeated CSF examinations over several months[43]. Oligoclonal bands were positive in 65% of patients in one series [46]. However, the presence of oligoclonal bands of IgG did not discriminate ADEM from MS in this study.

No correlation has been found between the severity of disease and the CSF protein levels or pleocytosis[2]. Even post vaccinial cases have not demonstrated any correlation between the severity of disease and CSF parameters[9].

Some authors have suggested that it may not be possible to differentiate between ADEM and MS on the basis of a single CSF examination as similar findings may be obtained in both conditions

Neuroimaging findings in ADEM

Neuroimaging has established itself as a cornerstone of diagnostic techniques in ADEM . Both computed tomography and Magnetic resonance imaging have been widely used in the

diagnosis of patients suspected of having ADEM . Though MRI is a superior technique , occasionally lesions may appear only after a delay of 5-14 days[3].

Computed tomography (CT) generally shows a low attenuation lesion in the subcortical white matter . Lesions may be seen in the basal ganglia and brainstem also[51]. Mass effect due to the large lesions may be present[1]. Contrast enhancement and intracerebral calcifications have also been reported[50,51]. CT lesions may follow the onset of clinical symptoms by 5-14 days[51]. CT findings may also be normal. Clinical improvement was correlated with an improvement in CT abnormalities in one study. There is usually a combination of decreased density in the subcortical white matter and patchy or confluent contrast enhancing lesions. Gyral enhancement may be noticed[1]. However the CT picture is not specific or pathognomic of ADEM .

MRI findings in ADEM have been the subject of several studies [34,40,43,46,48,49]. MRI reveals multifocal areas of increased signal intensity on T2-weighted sequences that commonly enhance synchronously with contrast medium. Proton density and fluid attenuated inversion recovery sequences (FLAIR) also show high intensity lesions[3]. Intense perifocal edema may be seen. White matter involvement predominates but gray matter can also be affected, particularly basal ganglia, thalami, and brainstem. This deep gray involvement is only rarely seen in MS and is more specific for ADEM[52]. Gyriform involvement of the cortical gray matter , usually with underlying involvement of the subcortical white matter has been described[5]. Lesions may also be restricted to the brainstem or cerebellum.

A single case report of acute disseminated encephalomyelitis presenting as a solitary brainstem mass lesion mimicking a glioma has been published[53]. Large lesions may extend into the callosum ; but primary callosum involvement appears to be rare[48]. Some patients show simultaneous involvement of the brain and spinal cord. Single large lesions or multiple lesions at the same or multiple levels may be found. Rarely spinal hemorrhage and long segmental involvement may also be seen. Spinal cord lesions have a high specificity for demyelination as nonspecific pathologies do not lead to high intensity lesions on T2 weighted scans in the cord , as opposed to the cerebral white matter.

Kesselring et al[14] found extensive and relatively symmetrical lesions in the cerebral and cerebellar white matter in ADEM in contrast to MS, where the lesions were more asymmetric and multifocal. Tumor-like lesions also occur , with mass effect [3,47] . Large lobar lesions are virtually never seen in MS[15]. On T1 weighted images , iso- to low signal intensity lesions are seen in the white matter and gray matter. On T1 weighted images the cortical ribbon is usually spared[48]. Hemorrhage appears to be relatively rare.

Various "typical" signs for ADEM have been advocated, including the involvement of the basal ganglia and thalamus,' presence of cortical lesions, and predominant brainstem involvement. However in the large study of Schwartz et al [46], none of the MRI findings had a high specificity for either disease, and the authors felt that in the individual patient, the MRI pattern may be indistinguishable and cannot predict the further course. Cortical involvement or lesions in the basal ganglia were exclusively present in patients with the final diagnosis of ADEM; however, these findings were uncommon as compared to MS patients[46]. Generally ADEM lesions are large and symmetrical in contrast to MS[3,14]. However diffuse confluent bilaterally symmetrical lesions and multiple unilateral lesions have also been seen [48].The morphology of lesions may vary from small and round to large , irregualar and amorphous. Occasionally a 'fried egg appearance' with a central rounded hyperintensity on T2 weighted images , corresponding to the egg yolk is seen.

Demyelinating lesions in ADEM evolve over a short period of time. It has been speculated that after administration of gadolinium, "all lesions should enhance since all lesions should be active."[34]. This assumption has been based on the fact that in ADEM all the lesions would appear at the same time and be active , in contrast to MS , where they would be of varying ages[14]. However, this hypothesis has been contradicted by newer studies, which demonstrated that lesions in ADEM may evolve over several weeks. Kesselring et al [14] found that new lesions could continue to appear upto 8 months after the onset of illness. Also the lesions could persist for upto 18 months. Commonly the lesions dramatically regress after a short course of corticosteroid therapy or immunoglobulin / plasma exchange treatment [48]. The decrease in the number and signal intensity of lesions generally parallels clinical improvement. Complete lesion resolution and steroid induced

reversible cortical atrophy may be seen. This reversible corticosteroid induced cerebral shrinkage may be confused with a permanent cerebral atrophic process[49]. There may be enhancement of some of the lesions without enhancement of others, or there may also be no enhancement at all.[46,48,49]. Enhancement patterns may also vary , from spotty , nodular, diffuse nodular, amorphous, gyral or incomplete or complete rings of enhancement [48].

The situation becomes more complicated with the recently described entities multiphasic and recurrent disseminated encephalomyelitis (MDEM & RDEM)[15]. In MDEM , new lesions may appear with relapses and lesions tend to be of varying age. This can be shown by contrast enhancement of some lesions whereas other lesions appear inactive and are seen only as high signal intensities on T2 weighted images. The differentiation between RDEM and MDEM is that new lesions are not seen in RDEM ,where patients tend to have relapses that are stereotyped- that is the symptoms are always the same. With conventional MRI techniques, the age of nonenhancing lesions cannot be determined with certainity except for "black holes" on T1-weighted images, indicating a previous destructive inflammatory–demyelinating process. New MRI techniques may allow determination of the age of demyelinating lesions with greater reliability; thus, previously clinically silent episodes of CNS demyelination may be detected in patients presenting with a first clinical episode[46]

Electroneuromyography and evoked potentials

Peripheral nerve involvement has been reported in various series with incidences ranging from 9% (Appelbaum et al[54]), 11% (Hemachuda et al[9]) to 50% (Swamy et al[8]). Pure motor and sensory motor neuropathies have been reported. Out of 25 patients in Swamy's series [8] , motor conduction studies were abnormal in 60%, sensory conduction studies were abnormal in 16% and the remainder showed normal NCV studies. Visual evoked potentials were abnormal only in 2 out of 11 patients in Swamy's series[8]. In both cases the P100 latencies were prolonged.

MATERIALS AND METHODS

Materials and Methods

Between 1995 and 2001 , a total of 42 patients diagnosed as ADEM were seen at our institute – the Sree Chitra Tirunal Institute of Medical sciences and Technology, Trivandrum, Kerala. The study was based on retrospective chart review from 1995-1999. From the period of 1999- 2001 , patients were directly examined by the author. Follow up was conducted by chart review as well as by direct examination .

Criteria for the diagnosis of ADEM

We used the following criteria for the diagnosis of ADEM . These include

(1)A monophasic illness

(2)The presence of symptomatology pertaining to the cerebrum with or without spinal cord or peripheral nervous system involvement

(3)Fever if present is transient and low grade

(4)EEG not showing lateralized abnormalities

An acute neurologic illness without a history of previous unexplained neurologic symptoms was taken as an operational criteria for the initial diagnosis of ADEM . Neuroimaging evidence of single or multiple supra- or infra-tentorial demyelinating lesions was considered corroborative. As MRI abnormalities in ADEM are variable and not well defined, more specific criteria were not available. Lumbar puncture excluded other CNS infective or autoimmune causes.

Clinical evaluation at presentation-

The findings at initial presentation were collected by chart review. All patients with a diagnosis of ADEM were admitted and worked up as inpatients. The following information was gathered – the age, gender, history of antecedent illness particularly history of recent immunizations ,vaccinations or recent infections, duration of current illness and initial symptomatology including the presence of fever, behavioural alteration, seizures and headache . From the examination , the following information was obtained- cognitive impairment, cranial nerve involvement , motor, sensory, extrapyramidal , cerebellar impairment and meningism. Neurologic examination at discharge and any

worsening during the course of hospital stay including complications related to treatment or to the primary disease was also documented. The length of hospital stay and the outcome including the presence of any relapses at follow up were noted . The time to onset of improvement of deficits was looked at. At follow up patients were assessed for improvement of residual deficits, occurrence of new deficits and relapses if any – minor or major .The final outcome at discharge and follow up were also assessed to estimate the burden of the disease process.

Neuroradiologic examination

Out of the study population of 42 patients, 37 were examined with cranial and or spinal Magnetic resonance imaging (MRI) as dictated by the disease presentation. As our center is a tertiary referral center and our study was conducted over a period of 6 years, 13 patients had already undergone CT (Computed Tomography) from outside, as part of investigation. These were also included in our analysis. Of the 5 patients who had not undergone MRI scanning, 2 underwent CT scanning of the brain as part of evaluation. Contrast administration was undertaken for CT scanning also.

Standard MRI examination consisted of T1, T2 and proton density weighted examinations on a GE 0.5 Tesla MRI scanner . In all patients who showed abnormalities on the above sequences, IV injection of gadolinium –diethylenetriaminepentaacetic acid (DTPA) was administered to look for contrast enhancement.The following items were scored from the MRI and CT scan images- the number of lesions, appearance , contrast enhancement with gadolinium DTPA, pattern of enhancement and sites of lesions . Specific sites looked for included the cortex, subcortical periventricular white matter, thalamus, basal ganglia, brainstem , cerebellum and spinal cord. The pattern of spinal cord involvement was graded according to Pradhans classification of spinal cord involvement in transverse myelitis into segmental, diffuse , ascending and restricted conus involvement. Only 2 patients underwent a repeat MRI .– 1 patient had presented with a relapse and another patient was a young child.

Electroneuromyography

Where clinically indicated , ENMG and visual evoked potentials were carried out . ENMG was carried out on a Nicolet apparatus. The results of nerve conduction studies were graded as normal , axonal, demyelinating or mixed processes.

CSF examination-

Lumbar puncture was performed at or immediately after admission in 40 patients . CSF analysis included leukocyte counts, cytology, determination of protein, glucose and IgG levels. CSF was cultured to rule out infectious causes and Polymerase chain reaction for Mycobacterium tuberculosis was done where clinical suspicion of a chronic meningitis was present.

Treatment

Patients were treated with a standard protocol of Intravenous Methylprednisolone 1 gram daily for 3-5 days depending upon the clinical response. Oral steroids were continued (Prednisolone 1mg/kg/day) for a period of 15-21 days in some patients. A few patients who did not improve with IV methylprednisolone, received Plasma Exchange (small volume 100 ml/kg total dose) or Immunoglobulin 0.4 mg/Kg/day x 5 days.

Follow up examination

At follow up examination , patients were assessed clinically for resolution of prior deficits , documented at discharge and for the presence of new symptoms or signs pertaining to the central nervous system.

RESULTS

Results

A total of 42 patients , 14 females and 28 males ,with a mean age of 30.74 yrs (2 to 68 yrs) entered the study. Most patients were adults (83.3%) , only 7 patients below the age of 10 yrs were seen (16.6%) . Patients above the age of 50 yrs were also uncommon ,only 8 were seen (19%). At initial presentation , all our patients fulfilled our criteria for ADEM .Antecedent infections were seen in 18 patients with a mean preceding interval of 13.3 days (2-60 days). Of these non-specific febrile illnesses were seen in 22 patients (52%), preceding diarrhoeal illness in 1, vaccination with Antirabies vaccine in 1 patient . Other preceding factors like parotitis, tooth extraction and herpes zoster ophthalmicus were seen in 3 patients . The mean duration of symptoms prior to admission was 20 days (1-120 days). 2 patients came in for evaluation 1year and 2 years after the onset of symptoms . These significantly skewed the results and were not considered for analysis. If these were also taken into consideration, then the mean duration increased to 44.92 days.

Table 1. General Characteristics of the subjects

Characteristics	Values
Age, yrs , median (range)	30.74 (2-68)
Gender – Male, n (%) Female,n (%)	28 (66.6%) 14(33.3%)
Antecedent infections,n (%)	18 (42.86 %)
Duration of symptoms prior to admission,days, median (range)	20.97 (1-120)
Length of hospital stay , days, median (range)	11.8 (2-65)
Duration of follow up from initial presentation to follow up, years (range)	2.35(0.75-5)

The mean length of hospital stay was 11.80 days (2-65 days). The duration of follow up from initial presentation to follow up was approximately 2.35 yrs (0.75-5 yrs).

Clinical presentation

The most common symptoms were motor weakness and cranial nerve complaints, of which visual blurring and diplopia accounted for approximately 31 %. Headache was uncommon at the onset. Only 2 patients presented with fever at onset , which was low grade and remitted within 2 days of admission. Sensorial alteration was seen in 28.5% of patients and ranged from a confusional state to stupor. Seizures were again uncommon , present at onset in about 12% of patients and tended to be generalized seizures. Sensory and bladder complaints were seen in about $1/3^{rd}$ of patients and were prominent features at the onset. Gait ataxia and limb incoordination were seen in about 15% of patients.The most common presenting symptoms are displayed in table 2.

Table 2- Presenting symptoms

Symptoms	Values (percentage)
Headache & vomiting	2 (4.76%)
Fever	2 (4.76%)
Sensorial alteration	12 (28.57%)
Seizures	5 (11.9%)
Aphasia	1 (2.38%)
Vertigo	2 (4.76%)
Cranial nerve symptoms	20 (47.6%)
Visual symptoms-blurring	9 (21.42%)
Diplopia	4 (9.52%)
Motor weakness	27 (64.3 %)
Sensory complaints	14 (33.3 %)
Bladder symptoms	16 (38.09%)

Ataxia	6 (14.28%)
Others-respiratory failure	1 (2.38%)

Pyramidal signs were the most common findings, being present in almost 71% of patients , more often bilateral than unilateral. Cerebellar signs and sensory findings (more often posterior column findings) were present in 35 and 30 % respectively being the next most common findings. Facial weakness and oculomotor weakness was found in about 26-28% of patients. Ocular motor involvement affected the VIth nerve predominantly . Partial or complete III rd nerve involvement was also seen . Optic nerve involvement was also common with bilateral optic neuritis more often found than unilateral (16.66% versus 2.38%). The severity of visual loss ranged from mild to complete visual loss (7.14%). Trigeminal sensory impairment and lower cranial nerve deficits were noticed in 16-21% of patients. Deafness was also noticed in 2 patients (unilaterally). No extrapyramidal involvement was noticed. Meningism was also absent.

Table 3-Signs at presentation

Signs	Number	Percentage
Optic neuritis	8	19.04%
Unilateral	1	2.38%
Bilateral	7	16.66%
Oculomotor involvement	11	26.19%
III n involvement	2	4.76%
VI n involvement	5	11.9%
Nystagmus	4	9.52%
Trigeminal involvement	7	16.66%
Sensory signs	6	14.28%
Motor weakness	2	4.76
Facial weakness	12	28.57%
Upper motor neuron type	6	14.28%
Lower motor neuron type	6	14.28
Other cranial nerve involvement	9	21.42%

VIII nerve	2	4.76%
IX, X	6	14.28%
XI	3	7.14%
XII	3	7.14%
Pyramidal involvement	30	71.42%
Unilateral	9	21.42%
Bilateral	21	50%
Cerebellar signs	15	35.71%
Sensory signs	13	30.95%

Outcome of ADEM and relapses.

The duration of follow up from initial presentation to follow up was approximately 2.35 yrs (0.75-5 yrs). The majority of patients had a good outcome and only 2 mortalities (4.76%) were observed. Most patients achieved a good functional outcome and were able to ambulate without support and perform activities of daily living independently. 6 patients (14.2%) were financially occupied, 15 patients (35%) were independently walking , but at home. About 9 % of patients were able to carry out their activities of daily living but with residual deficits. 11 patients (26%) were severely disabled and dependent for all activities of daily living. Only 2 patients had relapses , one had a relapse within 4 months with symptoms and signs suggesting involvement of the CNS at different sites as compared to his previous episode. On neuroimaging he demonstrated lesions at different sites as compared to his earlier imaging findings. On follow up he was left with severe disability but did not go onto develop any further episodes during the rest of the follow up period (14 months). According to criteria proposed by Kesselring et al [14], this would qualify as a part of the initial episode and would not be considered a relapse. The other patient went on to develop a 2nd episode after a period of 1 1/2 years.½ Due to the similar nature of illness as compared to the earlier episode, he was not neuroimaged again. This patient could be characterized as having a recurrent disseminated encephalomyelitis (RDEM). Both patients were not on long term steroids. Most patients demonstrated transient reappearance of earlier symptomatology during other concurrent illnesses. However only the 2 patients

described above showed severe and longer lasting worsening. During follow up, patients continued to improve in their functional outcome.

Neuroimaging findings

Of the 37 patients examined with an MRI of the cranium and or spinal cord, the following patterns were seen . 90 % of patients demonstrated abnormal MRI findings. 27 patients (74%) had multiple lesions on MRI (2 or more lesions) . T2 weighted MRI scans demonstrated the lesions better than the T1 weighted scans. The most common findings seen were T2WI hyperintense lesions seen in the subcortex and periventricular white matter (50.54%). In 8 patients , cord involvement was also seen (21.62%). In patients showing cord involvement , there was concurrent evidence of intracranial lesions. The cord showed diffuse involvement in 1 patient, segmental involvement in 5 and an ascending pattern in 2 patients. Brainstem lesions were less frequent (28.91%). Though lesions were seen in the cerebellar peduncles , no lesions were demonstrated in the cerebellar white matter or cortex . Thalamic and basal ganglionic lesions were seen in 5 patients (18.51%). Lesions involving the cortex were also relatively infrequent (13.51%). On T1WI , lesions were seen as mildly hypointense lesions. T1WI enhancement was uncommon, with only 6 patients (16.21%) demonstrating only patchy enhancement . Ring or nodular enhancements were seen only in one case. None of the lesions showed surrounding edema. MRI was normal in 9 patients (24.32%).

Table 4-Lesion locations

Sites	Preponderance
Cortex	13.5%
Subcortex and periventricular white matter	50.5%
Thalamus,Basal ganglia	18.5%
Brainstem	28.9%
Spinal cord	21.62%

CT scan of the brain was done in 13 patients which included 2 patients who had not undergone an MRI evaluation. These 2 patients had normal studies. In all only 7 CT scans (53.84%) were abnormal and did not pick up any additional lesions (Table 5).The lesion number in these scans was less than in the MRI scans , picking up multiple lesions only in 2 cases (15.38%). The imaging appearance was characterized by hypodensities on plain CT scans. None of the lesions exhibited contrast enhancement. The sites of lesions corresponded to the sites on MRI, including the subcortical and periventricular white matter. Posterior fossa lesions and brainstem lesions were not picked up by CT scanning. Overall MRI showed a higher number of lesions and had a higher pick up rate of lesions in ADEM.(Table 6)

Table 5- Comparison of MRI and CT Scans In our ADEM patients

Neuroimaging procedure (no; of pts)	Normal	Abnormal
MRI (37)	9 (24.32%)	33 (90%)
CT Scan (13)	6 (46.15%)	4 (10%)

Table 6-Number of lesions picked up by MRI /CT

Lesion number	MRI	CT Scan
Single	10 (26 %)	5 (38.46%)
Multiple	27 (74 %)	2 (15.38%)

Electrophysiological studies

Only 15 patients underwent ENMG studies. Of these 6 patients (14.3%) had a demyelinating neuropathy with mild prolongation of F waves , slowing of conduction velocities and prolongation of distal latencies. No conduction blocks were seen in any of

these patients. 4 patients (13.3%) had an axonal neuropathy . 15 patients (11.9%) showed normal ENMG studies.

CSF Examination

Lumbar puncture was performed at or immediately after admission in 40 patients after a mean of 15 days from the onset of illness. The CSF was drained at normal pressure. Cells showed a lymphocytic predominance in all patients. The cell count ranged from 2-450 cells (mean 141 cells). The highest cell count recorded was 450 cells , however only 4 patients showed CSF pleocytosis over 100 cells. 25 patients (62.5%) had a CSF cell count below 5 cells/cmm^3. The CSF protein ranged from 21-800 mg % (mean 73 mg %) , again in 72.5% the protein level was below 50 mg%. The CSF glucose values were normal in all patients. CSF IgG values were also normal.

Complications related to disease or hospital stay

Only 6 complications were detected during initial evaluation or hospital stay. 4 patients developed respiratory failure and had to be intubated and mechanically ventilated. All these patients had spinal cord lesions on MR imaging. In addition , one patient developed pneumonia and needed assisted ventilation. Other complications noticed in hospital were mild and resolved on follow up – including erectile dysfunction, mild dysautonomia etc. A total of 31 patients required treatment. 29 of these patients were treated with Intravenous Methylprednisolone.

DISCUSSION

Discussion

(1). Until now there have been only single case reports or small case series in ADEM , the large series have been confined to the pediatric age group. Of these there have no long term follow up either. Only recently has there been a large follow up study of adult patients with ADEM[46]. ADEM has been most commonly reported in children[3]. In this study we found that a significant proportion of patients were adults accounting for almost 83% and children formed only a small group. Of the adults the representation of the above 50 age group was also small , forming only 19 % of the total group. The predominant group was formed by young adults (64%).

(2). Antecedent infections were seen in 42% , this compares well with figures published by other studies [46]. Of these non specific febrile illnesses accounted for 52 %.

(3).Our patients presented later after the onset of illness –after a mean interval of 20 days as compared to western patients who presented earlier (mean of 4 days)[46].

(4). The most common presenting symptoms were weakness of limbs (64%) and cranial nerve symptomatology (47%). Sensory ,bladder complaints and sensorial alteration were found in a 3rd of patients. Other series published in literature also describe similar proportions of patients with motor and cranial nerve complaints.

(5). The most common signs were pyramidal signs (71%) , cerebellar (35%) and sensory findings (30%). Cranial nerve involvement was seen in a 3rd of patients. All cranial nerves were involved , but deafness was uncommon , being present only in about 5%. These figures also compare well with the figures of Schwarz et al[46].

(6). The majority of patients had a good outcome with respect to improvement of deficits. However only 14% were able to return to their prior occupations. The mortality rate was 4.7% and severe disability was seen in 26%. The remainder were left with minor deficits, not interfering with activities of daily living.

(7). Relapses were rare, being seen only in 2 patients (4.7%). Of these one had a relapse at different sites, though it occurred within a short time frame after the initial episode. The other had a relapse similar to the first episode after a period of 1 ½ years.

(8). Only 90 % of patients showed abnormalities on neuroimaging. This may have been due to the fact that lesions may take upto 5-14 days to evolve and be visualized on MRI[3,51]. Lesions may also disappear with resolution of clinical symptoms and signs[1,3,51]. In our study , some of the patients underwent neuroimaging at a delayed interval after the onset of symptoms (mean 20 days). This may have been the reason for negative neuroimaging. Lesions were multiple in most patients (74%), and better visualized on T2 Weighted images. The most common locations were in the subcortex and periventricular white matter. Lesions were also seen in all other locations , including the spinal cord. T1 Weighted images were not as sensitive as T2 weighted images. Unlike prior studies, where contrast enhancement was as high as 95% of patients , in this study it was seen only in 16%.

(9). Of the 15 patients who underwent ENMG studies , 27% had abnormalities showing either demyelinating (14%) or axonal neuropathies (13%). In literature also , the frequency of abnormalities on ENMG studies has varied from 9-50%[8,54].

(10).Cerebrospinal fluid showed lymphocytic predominance in all cases. The majority of patients had a CSF cell count below 100 cells (90%), with 62.5% of patients having a cell count below 5 cells/cmm^3. The CSF protein was again normal in the majority (72.5%).The CSF glucose values were normal in all patients.

(11). The incidence of major complications was rare with only about 10% requiring intensive care management with assisted ventilation. The vast majority had minor complications which resolved on follow up.

CONCLUSIONS

Conclusions

ADEM is seen commonly in young adult patients in our series. The most common symptoms were related to motor weaknes and cranial nerve symptomatology and reflected in the signs elicited. Generally patients have a noncomplicated hospital stay. Though mortality and severe disability rates were low, ADEM leaves patients with deficits sufficient to impair their capacity to return to their previous occupations. The incidence of relapses in ADEM is rare. Neuroimaging with MRI is the diagnostic modality of choice and picks up most lesions if performed in an appropriate time interval. Other contributory investigations may include CSF which rules out infectious and other pathology and electroneuromyography which may demonstrate coexistent peripheral nervous system involvement .

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