Spinal form of ADEM

Rajaguru M1, Sangamithra Gandra2, Ganesh Vellampalli3

1Professor & Head, 2, 3Postgraduate Students, Department of Neurology, Narayana Medical College & Hospital Nellore - 524003, Andhra Pradesh, India.

Corresponding Author: Dr. M. Rajaguru, Email ID: drmrajaguru@gmail.com

ABSTRACT

Acute disseminated encephalomyelitis (ADEM), or acute demyelinating encephalomyelitis, is a rare autoimmune disease marked by a sudden, widespread attack of inflammation in the brain and spinal cord. Along with inflammation of the brain and spinal cord, ADEM also attacks the nerves of the central nervous system and damages their myelin insulation, which, as a result, destroys the white matter. It is often triggered after the patient had a viral infection or, perhaps exceedingly rarely specific non-routine vaccinations.[1][2][3]

We report a case of a 29 yr old male who presented with symptoms of sudden onset paraparesis which was suggestive of transverse myelitis but upon detailed evaluation, he was found to have ADEM which presented as spinal form which is a rare presentation of ADEM. Although ADEM is most commonly reported in children, rarely it can also occur in adults as in our case.

Keywords: ADEM, brain, spinal cord, white matter, Multiple sclerosis

Introduction:

Acute disseminated encephalomyelitis (ADEM) is traditionally considered a monophasic inflammatory demyelinating disorder with pleiotropic clinical manifestations, which usually include encephalopathy, but variably include other focal or multifocal syndromes suggestive of a central nervous system (CNS) inflammatory demyelinating disorder, including optic neuritis (ON) and myelitis. Consequently, ADEM is often considered in the differential diagnosis of a clinically isolated (demyelinating) syndrome (CIS). However, most CISs, especially in adults, are harbingers of multiple sclerosis and, therefore, of future relapses. The hallmark of ADEM is its monophasic course. Therefore, most physicians treat ADEM with short-term treatments rather than long-term disease-modifying therapies. However, early and accurate distinction between ADEM and other inflammatory demyelinating disorders, especially multiple sclerosis (MS) and neuromyelitis optica (NMO), is important for prognosis and treatment because many patients with MS or NMO, particularly those with aggressive fulminant disease, may benefit from

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early disease-modifying therapy to suppress ongoing and future relapses. The incidence is about 8 per 1,000,000 people per year.[4] Although it occurs in all ages, most reported cases are in children and adolescents, with the average age around 5 to 8 years old.[5][6][7] The disease affects males and females almost equally. [5][6][7] The mortality rate may be as high as 5%; however, full recovery is seen in 50 to 75% of cases with increase in survival rates up to 70 to 90% with figures including minor residual disability as well. The average time to recover from ADEM flare-ups is one to six months.

Nonmonophasic ADEM

A small but important subset of patients with ADEM will subsequently be diagnosed with relapsing disorders, including neuromyelitis optica spectrum disorders (NMOSD) and multiple sclerosis (MS). We currently have insufficient diagnostic technologies to reliably distinguish this subset from the majority of patients with ADEM for whom the disease course is monophasic (Table 1).

Case report

A 29 years old male patient came to the hospital with complaints of pain in right thigh, difficulty in walking due to swaying of 1 week duration.

This patient who was apparently healthy a week ago had fever for 1 week. He developed weakness of lower limbs and numbness in both lower limbs up to the level of groin. He developed urinary retention. He had no weakness of upper limbs. He had no symptoms suggestive of any cranial nerve lesion. No h/o headache, behavioural disturbances. He had fever of 1 week duration with cough.

Examination revealed a well oriented, clearly communicative patient with normal

<table>
<thead>
<tr>
<th>Table 1</th>
<th>ADEM and its convergence with relapsing demyelinating disorders</th>
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<tbody>
<tr>
<td>Diagnosis</td>
<td>Clinical criteria</td>
</tr>
<tr>
<td>ADEM, monophasic</td>
<td>Single polyfocal CNS event with encephalopathy and presumed inflammatory demyelination and no new disease activity (clinical or MRI) &gt;3 months after onset</td>
</tr>
<tr>
<td>ADEM, multiphasic</td>
<td>ADEM followed at &gt;3 months by second ADEM episode, but no further ADEM or non-ADEM demyelinating events</td>
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| ADEM-MS | ADEM followed at >3 months by non-ADEM demyelinating relapse and new MRI lesions meeting criteria for dissemination in space
| ADEM-NMOSD | ADEM followed at >3 months by events including optic neuritis, longitudinally extensive transverse myelitis, or area postrema syndrome, meeting MRI requirements according to revised NMOSD criteria |
| ADEM-ON | ADEM, MDEM, or multiple ADEM attacks followed by optic neuritis |

Abbreviations: ADEM = acute disseminated encephalomyelitis; MDEM = multiphasic disseminated encephalomyelitis; MS = multiple sclerosis; NMOSD = neuromyelitis optica spectrum disorder; ON = optic neuritis.
behaviour having horizontal gaze evoked nystagmus with impaired finger nose test and heel knee test. Tandem gait was impaired. Spastic paraplegia was noted and loss of all modalities of sensation below T8 level with brisk lower limb reflexes and plantars extensor.

His upper limbs were normal in all aspects except finger nose incoordination.

Fundus was normal, peripheral nerves normal, no meningeal signs. CVS, RS, GIT were normal.

This case based on the history and findings was diagnosed as Demyelinating Disease of cerebellum & spinal cord and MRI Brain & Spinal cord were taken which showed hyperintense lesions in the spinal cord extending from D8 to L1 and multiple patches of hyperintense lesions both in the cerebellum & cerebral cortex in the cortical & subcortical region of grey, white matter junction (Images 1,& 2). No lesion was seen in the peri ventricular region ruling out Multiple sclerosis. Visual evoked potentials (VEP) were normal. LP & CSF analysis revealed 2cells, all lymphocytes, protein 31mg/dl (5-45mg/dl) and glucose 57mg/dl (75-115mg/dl). CSF study was negative for oligoclonal bands.

The case was diagnosed as spinal form of ADEM and treated with Inj. Methylprednisolone for 5 days & the patient improved well.

Discussion
Recent retrospective and prospective series suggest clinical, neuroimaging, and laboratory characteristics of ADEM that may be helpful in distinguishing ADEM from MS.8-13 Collectively, this literature suggests ADEM should be considered when one or more of the following are present: multifocal,
polysymptomatic initial presentation; age younger than 10 years; signs and symptoms of meningoencephalitis; encephalopathy; bilateral ON; cerebrospinal fluid (CSF) pleocytosis without oligoclonal bands; magnetic resonance imaging (MRI)-detected lesions involving structures not typically affected in MS such as the deep gray matter or cortex; and MRI-detected lesions that are large and exhibit indistinct borders and enhancement following gadolinium administration.24 The presentation of ADEM is usually polysymptomatic with encephalopathy, headache, meningismus, seizures and optic neuritis being the most common presentations. Myelopathy as the initial presentation of ADEM as in the present case has been reported very rarely.

Clinical definitions of acute disseminated encephalomyelitis

There are no accepted, prospective, or pathologically verified clinical diagnostic criteria for ADEM. Early retrospective studies suffered from broad inclusion criteria, which almost certainly included cases of probable first presentations of MS14and NMO.15 Building on clinicopathological and retrospective studies of ADEM, Mikaeloff et al have applied the most restricted definition of ADEM to date in a prospective study of children: The occurrence in a previously healthy child of acute symptoms associating the following at onset: more than one neurological deficit ("polysymptomatic" onset); change in mental state; and any combination of alterations seen on MRI, providing that these included white matter lesions.16 Although the Mikaeloff et al criteria predicted a monophasic course in most patients over a mean duration of follow-up of 5.5±3.6 years, 18% of patients still went on to have a relapse at a different CNS site than the first attack and appeared to have a clinical course consistent with MS.16 The first set of consensus diagnostic criteria for ADEM were recently proposed by the International Pediatric MS Study Group (IPMSSG), a group of adult and pediatric neurologists and experts in genetics, epidemiology, neuropsychology, nursing, and immunology organized by the National Multiple Sclerosis Society.17,18 These criteria are similar to those used by Mikaeloff et al and are outlined in Table 1. The IPMSSG does not propose these criteria as final and emphasizes the need for prospective validation over the next 10 to 20 years. These consensus criteria were developed for children (< 10 years). It is unclear whether any clinical diagnostic criteria for ADEM should be different in adult patients.

Pathological definitions

The pathological hallmark of ADEM is perivenular inflammation with limited "sleeves of demyelination."19,20 In some cases, larger areas of demyelination occur secondary to coalescence of many perivenous demyelinating lesions. Although perivascular inflammation is also a feature of MS pathology, the patterns of demyelination in ADEM stand in contrast to the confluent sheets of macrophage infiltration admixed with reactive astrocytes in completely demyelinated regions that are typical of an MS plaque.21 Acute hemorrhagic leukoencephalitis (AHLE) is pathologically similar to ADEM but
additionally exhibits petechial hemorrhage and venular necrosis.19

Table 2 International Pediatric MS Study Group-Consensus Definitions

**Younger age at presentation**

ADEM is more frequent in children. In one study of children with ADEM living in San Diego County, California, the incidence was estimated to be at least 0.4/100,000/y.13 The incidence of ADEM in adult patients has not been evaluated. Pediatric patients meeting Mikaeloff et al criteria for ADEM presented at a mean age of 7.1 years versus a mean of 12.0 years for MS.22 Five percent of MS patients present at an age younger than 16 years, but MS patients have been reported to present as young as 1 year of age. However, as the spectrum of pediatric MS has expanded, some evidence suggests that an "ADEM-like" presentation in pediatric MS may be underrecognized.23 Although patients presenting with demyelinating disease before age 10 years may be more likely to have ADEM than MS,22 considerable overlap in age of presentation limits the utility of using age as a discriminating factor.

**Spinal fluid pleocytosis without oligoclonal bands**

Before diagnosing ADEM, infection must be excluded by CSF analysis and culture. The CSF may be normal in ADEM or reveal a lymphocytic pleocytosis, in contrast to cases of MS, which rarely have a pleocytosis. Detection of oligoclonal bands (OCBs) may be helpful in predicting a subsequent diagnosis of MS, but the true utility is unknown because as many as 58% of adult and 29% of pediatric cases with ADEM have OCBs. Anecdotally, the bands should resolve in ADEM but are more likely to persist in MS. This was true in a series of nine ADEM patients who
initially had OCBs, which resolved when analysis was repeated 6 days to 6 months later.23 The presence of OCBs on initial presentation is not specific for MS; however, if OCBs persist, then a diagnosis of MS is more likely.

**FIG 1: Clinical and investigation differences between ADEM and MS (trends only).** *MR lesions other than white matter.*

**Magnetic Resonance Imaging**

Although MRI neuroimaging is useful for the diagnosis of ADEM and exclusion of other diagnoses, the consensus ADEM criteria emphasize clinical criteria and underplay the role of MRI to establish a diagnosis. In clinically defined cases of ADEM, the MRI will often demonstrate multifocal areas of increased T2-weighted (T2W) signal abnormalities in the CNS white matter, with or without gray matter involvement. Some authors have proposed that ADEM lesions are indistinct and lack sharply defined borders characteristic of MS lesions. Although ADEM lesions (of similar age) should all hypothetically enhance with gadolinium, this finding is rarely seen, and gadolinium enhancement may even be absent.24,25 Early MRI series identified overlap in lesion location and distribution between ADEM and MS, but also highlighted features of ADEM that are unusual in MS, such as symmetric bilateral disease, relative sparing of the periventricular white
matter, or deep gray matter involvement. Absolute and relative periventricular sparing on MRI is typical of ADEM, and was present in 78% of patients with ADEM reported by Dale et al.1

**Table 3 MRI characteristics in ADEM vs MS**

<table>
<thead>
<tr>
<th>MRI characteristics</th>
<th>ADEM: Typical</th>
<th>MS: Typical</th>
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<tbody>
<tr>
<td>Deep gray matter and cortical involvement</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Bilateral diffuse lesions</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Poorly marginated lesions</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Large globular lesions</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Periventricular pattern of lesions</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Lesions perpendicular to long axis of corpus callosum</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Ovoid lesions</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Lesions confined to corpus callosum</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Sole presence of well-defined lesions</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Black holes (on T1 sequence)</td>
<td>No</td>
<td>Yes</td>
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Abbreviations: ADEM = acute disseminated encephalomyelitis; MS = multiple sclerosis.

**Treatment**

Despite the lack of conclusive evidence, high-dose corticosteroids are currently widely accepted as first-line therapy for ADEM.26 A typical treatment regimen consists of IV methylprednisolone at a dose of 30mg/kg/d (maximally 1,000 mg/d) for 5 days, followed by an oral taper over 4-6 weeks with a starting dose of prednisone of 1-2 mg/kg/d. IV immunoglobulin treatment has been described in case reports and small case series, mostly in combination with corticosteroids or as a second-line treatment in steroid-unresponsive ADEM. The usual total dose is 2 g/kg, administered over 2-5 days. Plasma exchange is recommended for therapy-refractory patients with fulminant disease, e.g., using 7 exchanges every other day. Whereas for Multiple sclerosis (MS) along with steroids, disease-modifying therapy to suppress ongoing and future relapses is recommended.

**Conclusion**

Various studies have been done on pediatric patients with ADEM but our case report is of a 29 year old man who presented with complaints mainly related to the spinal form of ADEM and features of encephalopathy were not present. The spinal form of ADEM is a rare presentation. As ADEM and MS have common features we tried to exclude MS by checking CSF for OCBs which
were negative and the MRI of brain and spine were also not suggestive of MS. Hence, we report a case of spinal form of ADEM in an adult.

References:


