Acute Disseminated Encephalomyelitis (ADEM) versus Multiple Sclerosis (MS)- A Diagnostic Challenge in an Adult

Swapnil Lahole[1], Sourya Acharya[2], Sanket Bakshi[3], Samarth Shukla[4], Vidyashree Hulkoti[5]

[1]Department of Medicine, DMIMS (Deemed to be University), J. N. Medical College, Sawangi, Meghe, Wardha, Maharashtra, India. [2] Department of Medicine, DMIMS (Deemed to be University), J. N. Medical College, Sawangi, Meghe, Wardha, Maharashtra, India. [3]Department of Medicine, DMIMS (Deemed to be University), J. N. Medical College, Sawangi, Meghe, Wardha, Maharashtra, India. [4]Department of Pathology, DMIMS (Deemed to be University), J. N. Medical College, Sawangi, Meghe, Wardha, Maharashtra, India. [5]Department of Medicine, DMIMS (Deemed to be University), J. N. Medical College, Sawangi, Meghe, Wardha, Maharashtra, India.

INTRODUCTION

Acute Disseminated Encephalomyelitis (ADEM) is a demyelinating disease of Central Nervous System (CNS). It usually is followed by infection and vaccinations. It commonly occurs in the paediatric age group. Its occurrence in adults is rare. When present in adults, a diagnostic dilemma always occurs between ADEM and Multiple Sclerosis (MS), because of overlapping clinical, and neuroimaging features. We present a case of a 46 year old female who presented to us with variable neurologic manifestations and later was diagnosed with ADEM. This case tries to embark on arguments so as to differentiate ADEM from MS while dealing with such cases.

Acute Disseminated Encephalomyelitis (ADEM) and Multiple Sclerosis (MS) are both considered as immune mediated inflammatory demyelinating diseases of the central nervous system.[1,2] Although considered as different conditions, the clinical presentation of both these conditions may overlap. The only gold standard differentiation is pathologically determined. Perivenous demyelination is a feature of ADEM and discrete confluent demyelination (plaque) is signature of MS. Still hybrid cases showing pathological features of both ADEM and MS may co-exist.

ADEM, typically though not always is preceded by some infection or vaccination. The course of ADEM is usually monophasic and prognosis is better than MS which commonly presents with a relapsing and remitting course. Each exacerbating event worsens the clinical course in MS. Different clinical and/or radiological criteria to differentiate between the two spectrums of diseases have been proposed, but none of those unequivocally differentiate them.

Hartung and Grossmann hypothesized that ADEM may be a part of the MS spectrum, rather than a different entity.[3] The characteristic demyelination in ADEM is perivenous as opposed to MS where the demyelination is confluent. [4]

Acute Disseminated Encephalomyelitis (ADEM) is a demyelinating disease associated with inflammation and demyelination of the Central Nervous System (CNS) in a monophasic pattern. ADEM occurs commonly in paediatric age group often following viral infections, bacterial infections, or vaccinations.[5,6] The clinical characteristics include a sub-acute development of focal neurologic deficits, accompanied by encephalopathy. [5,6] It can rarely occur in middle-aged or elderly adults. The course is usually fulminant, but typically there is recovery in 50–75% of cases, with progression to multiple sclerosis in up to 20% of cases.[5,6]

Corresponding Author:
Sourya Acharya,
Professor,
Department of Medicine,
DMIMS (Deemed to be University),
J. N. Medical College, Sawangi, Meghe,
Wardha, Maharashtra, India.
E-mail: souryaacharya74@gmail.com

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PRESENTATION OF CASE

A 46-year old female presented to us with history of on and off headache since 20 days, abnormal behaviour in form of intermittent rage reactions and abusiveness since 15 days, gradually progressive weakness of the right side of the body since 10 days and 4 episodes of generalized tonic clonic seizures (GTCS) over the last 2 days. There was no history of vomiting, diplopia, blurring of vision, urinary incontinence, dysphagia, nasal twang to voice, nasal regurgitation of food, or sensory symptoms.

On asking leading questions, the patient admitted of having fever before the onset of headaches. The fever was intermittent and was associated with running nose, myalgia, headaches which lasted for 4 to 5 days. The patient visited private practitioner and received treatment and got relieved in 2 days. Then after 4 to 5 days the symptoms started.

On examinations vitals were normal and other general physical examination was within normal limits. CNS examination: higher function: patient was conscious and oriented but was intermittently having mood swings, abnormal smiling. She had dysarthria speech, comprehension and expression was normal.

There was no paraphrasia. Cranial nerve examination revealed right supranuclear 7th nerve palsy. Motor system examination revealed right brachio-crural hemiparesis. Bilateral plantars were extensor, with positive crossed extensor responses which suggested diffuse disease. DTR in all 4 limbs were exaggerated with sustained ankle clonus in right side. There were no signs of meningeal irritation.

Investigations

Magnetic Resonance Imaging (MRI) revealed, bilateral symmetrical white matter altered signal intensity noted in bilateral parietal region appearing hyper intense on T2WI/FLAIR, isointense on T1WI, showing mild restriction on DWI, no blooming on GRE s/o demyelinating disease. (Figure-1) There is e/o subtle T2WI/FLAIR hyper intensity noted in bilateral hippocampal region. (Figure-2) Features suggestive of ADEM. There were no intracranial masses and MRI of the spine was normal.

A diagnostic lumbar puncture showed opening pressure of 7.0 cm of H2O. CSF cell counts were 10 cells all lymphocytes, glucose-78 mg/dl, protein-22 mg/dl, oligoclonal bands were negative. CSF cryptococcal Ag was negative, Toxoplasma Ig G/M was negative, Quantiferon TB Gold was negative. CSF ADA was 14 Units. ELISA for HIV 1, 2 was negative in serum. Serum ANA, ds DNA, ACE, C3, C4 complements were within normal ranges.

The patient began treatment with methylprednisolone 1 gram intravenously (IV) daily, for a total of five days, IV anti-epileptic. After 5 days there was significant recovery in weakness, dysarthria and emotional lability.

The patient was shifted to oral prednisolone starting from 50 mg/day with a gradually tapering dose for the next month. A possibility of first attack of MS was still entertained and patient was advised to be in recurrent follow ups.

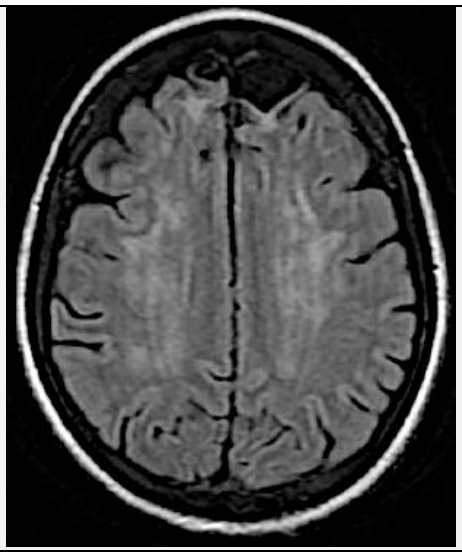

Figure 1. MRI Brain Showing Bilateral Symmetrical White Matter Altered Signal Intensity in Bilateral Parietal Region Appearing as Hyperintense Regions on T2WI/FLAIR

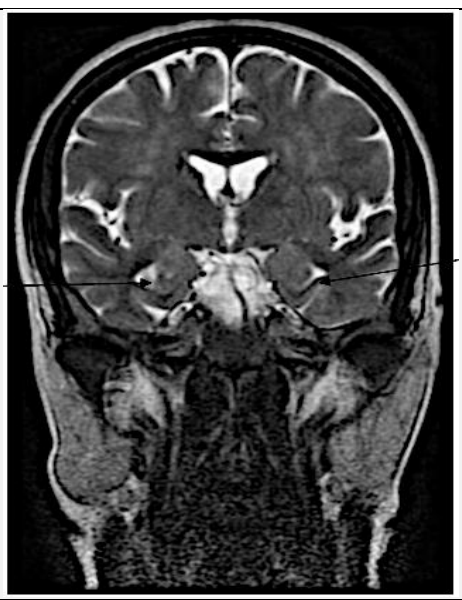

Figure 2. MRI Brain Coronal View Showing Subtle T2WI/FLAIR Hyperintensity, Noted in Bilateral Hippocampal Region (Black Arrows)

DISCUSSION

ADEM is commonly occurs on children. The diagnosis of ADEM in adults remains a challenge as there are no established diagnostic criteria available.[5]

As per Pediatric clinical guidelines the presence of encephalopathy is mandatory, but, for adults, encephalopathy is an unclear diagnostic feature.[6,7] The presenting clinical features in ADEM ranges from; hemiparesis, cranial nerve palsies, par paresis, meningism, ataxia, movement disorders, and in some extreme cases, seizures can occur.

ADEM is usually diagnosed clinically. The clinical features overlap with MS making it a diagnostic challenge in adults. MRI features that can help distinguish between the two are; better demarcation of the lesions favours MS and indistinct demarcation of lesions suggests ADEM. On T 1 weighted image a characteristic hypo intense "black hole sign" indicates white

matter destruction, axonal loss and favours MS with poor prognostic outcome.[8]

Brain MRI in ADEM shows patchy increased signal intensity on T2-weighted imaging and on fluid-attenuated inversion recovery (FLAIR) MRI. This case had similar imaging features. In ADEM, the white matter is more frequently involved like hippocampus in this case as compared to grey matter.

The revised McDonald Criteria (2017) provided useful criteria that might help to distinguish between MS and ADEM.[9] The diagnosis of MS requires clinical or imaging support for the dissemination of lesions of the CNS in time and space,[9] while ADEM remains chiefly monophasic, with clinically significant encephalopathy and a self-limiting course.[10–13]

CSF examination in patients with ADEM is usually normal, though rarely lymphocytic pleocytosis may be evident. CSF glucose is always normal. Oligoclonal bands in the CSF favours MS.[14,15] Treatment with methylprednisolone and supportive management remain the mainstay of treatment for ADEM and more than half of cases recover completely after treatment.[16,17]

The most favoured distinguishing approach is brain biopsy and histopathological examination.[18] A perivenous demyelination is commonly encountered in ADEM and diffuse confluent demyelination is a feature of MS.

CONCLUSIONS

ADEM and MS are two clinical disorders with overlapping features. However, cases of the first clinical episode of CNS demyelination showing both features of ADEM and MS do exist, suggesting that CNS pathology of ADEM may share common pathologic mechanism(s) with certain subgroups of MS.

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