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Case report

Recurrent disseminated encephalomyelitis: A case report and literature review

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ABSTRACT

Background: Acute disseminated encephalomyelitis has been understood as a monophasic, often post-infectious illness that predominantly affects the pediatric population. Though that describes the majority of cases, exceptions do exist. In this case report, we present an adult case of recurrent disseminated encephalomyelitis (DEM) and review the available literature on this clinical entity.

Methods: PubMed search performed using the terms "MDEM" and "Recurrent ADEM" in April 2018. A total of 23 items resulted for the first search and another 142 for the second. We selected articles that described cases of recurrent ADEM with a preference for those publications describing adult cases and those written in English language.

Conclusion: Recurrent disseminated encephalomyelitis is a distinct clinical entity that has features which overlap with multiple sclerosis, making it imperative to distinguish the two. Our case presentation and accompanying literature review highlights the limited scope of data available on recurrent DEM and the need for further study.

1. Introduction

Historically, acute disseminated encephalomyelitis has been understood as a monophasic, often post-infectious illness that predominantly affects the pediatric population. Though that describes the majority of cases, exceptions do exist. In this case report, we present an adult case of recurrent disseminated encephalomyelitis (DEM). We also performed a literature review in PubMed using the terms “MDEM” and “Recurrent ADEM” in April 2018. A total of 23 items resulted for the first search and another 142 for the second; the timing of these publications spanned from October 1996 to November 2017 and July 1971 to February 2018, respectively. We selected articles that describe cases of recurrent ADEM with a preference for those publications describing adult cases and those written in English language.

2. Case report

A 51-year-old woman was brought to the emergency department by her family for evaluation of bizarre behavior over the preceding two days. She carried diagnoses of diabetes and hypertension and her family history was notable for multiple sclerosis in her mother. Her family denied a history of alcohol or illicit drug use. She had developed symptoms of an upper respiratory infection and had become less interactive over several days. Her exam was notable for orientation to person only and an inability to follow commands. She was spontaneously moving all four extremities and tracking her eyes in all directions. Reflexes were 2 + and symmetric with flexor plantar response. Initial CT brain showed patchy parenchymal hypodensities in periventricular and subcortical distribution concerning for demyelination. Subsequent MRI brain (Fig. 1) revealed numerous enhancing lesions throughout bilateral supratentorial periventricular and subcortical white matter. Cerebrospinal fluid (CSF) and serologic testing results are in Table 1. CT chest, abdomen and pelvis obtained to evaluate for malignancy showed 6 cm cystic lesion in right adnexa and less than 2 mm pulmonary nodule in left lung. The adnexal mass was biopsied and found to be benign. She was diagnosed with acute disseminated encephalomyelitis (ADEM) and initially treated with IV methylprednisolone 250 mg every 6 h for 5 days. She improved modestly but was still not at baseline, prompting further treatment with IVIg at 1 g/kg for two days. At a six-month clinic follow up with a neuroimmunologist, she had returned to baseline.

Ten years later, she was again brought to the emergency department for evaluation of five days of gradually progressive left sided weakness, headache, dizziness and vertigo complicated by one fall. She had minimal cognitive or personality changes. MRI brain revealed multiple enhancing bilateral white matter lesions, similar in distribution to prior

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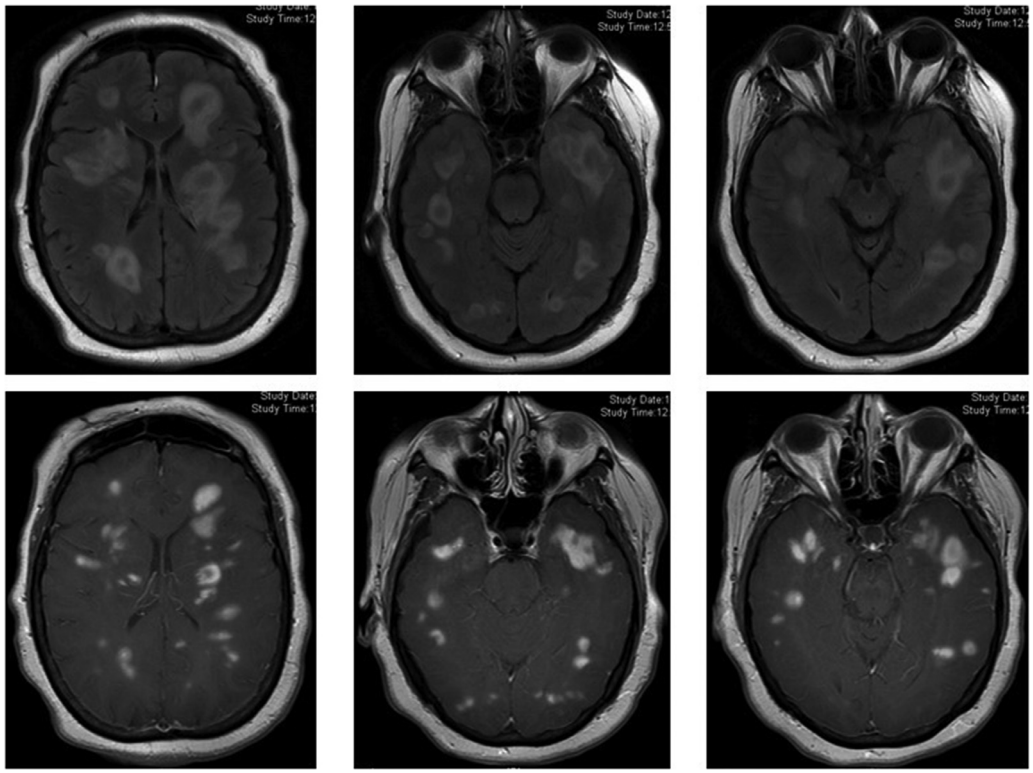

Fig. 1. MRI Brain FLAIR sequences (top row) and images after administration of contrast (bottom row) during initial presentation with encephalopathy. Evidence of numerous enhancing T1 hypointense lesions with surrounding edema in the bilateral supratentorial, periventricular, and subcortical white matter.

Table 1
Serum and cerebrospinal fluid study results.

	Initial presentation, 2008		Recurrent presentation, 2018	
Serum/Urine studies				
Urine toxicology screen	+benzodiazepine, THC, cocaine		Negative	
Serum toxicology screen	Negative		Negative	
Ammonia (16–50 umol/L)	27			
TSH (0.34–5.66 uIU/mL)	1.83		1.39	
HIV	Negative		Negative	
RPR	Non-reactive		Non-reactive	
ANA	1:160- Low titer positive		–	
ANCA	Negative		–	
Anti-SM, RNP, Ro, La	Negative		–	
ESR (0–15 mm/h)	22		7	
C- reactive protein (< = 0.60 mg/dL)	–		0.47	
Serum ACE (7–46 U/L)	3		–	
Lyme IgG	Negative		–	
Paraneoplastic Autoantibody Evaluation	Negative		–	
HHV-6 PCR	Negative		–	
JC Virus PCR	–		Negative	
Vitamin B12 (123–730 pg/mL)	–		274	
CSF studies				
	Tube 1	Tube 4	Tube 1	Tube 4
WBC	11	9	0	1
Neutrophils (%)	92	3		
Lymphocytes (%)	5	81		
Monocytes (%)		10		
Macrophages (%)	3	3		
Variant lymphocytes (%)		3		
RBC	29	11	1450	568
Protein (15–50 mg/dL)	63		82	
Glucose (mg/dL)	71		115	
Bacterial culture	Negative		Negative	
Meningitis panel	–		Negative	
Oligoclonal Band, IgG index	1		2	
IgG Index	0.45			
Paraneoplastic panel	No autoantibodies detected			
Cytology/Flow	Negative for malignancy		Negative for malignancy	
ACE (0.0–2.5 U/L)	<4.0		1.0	

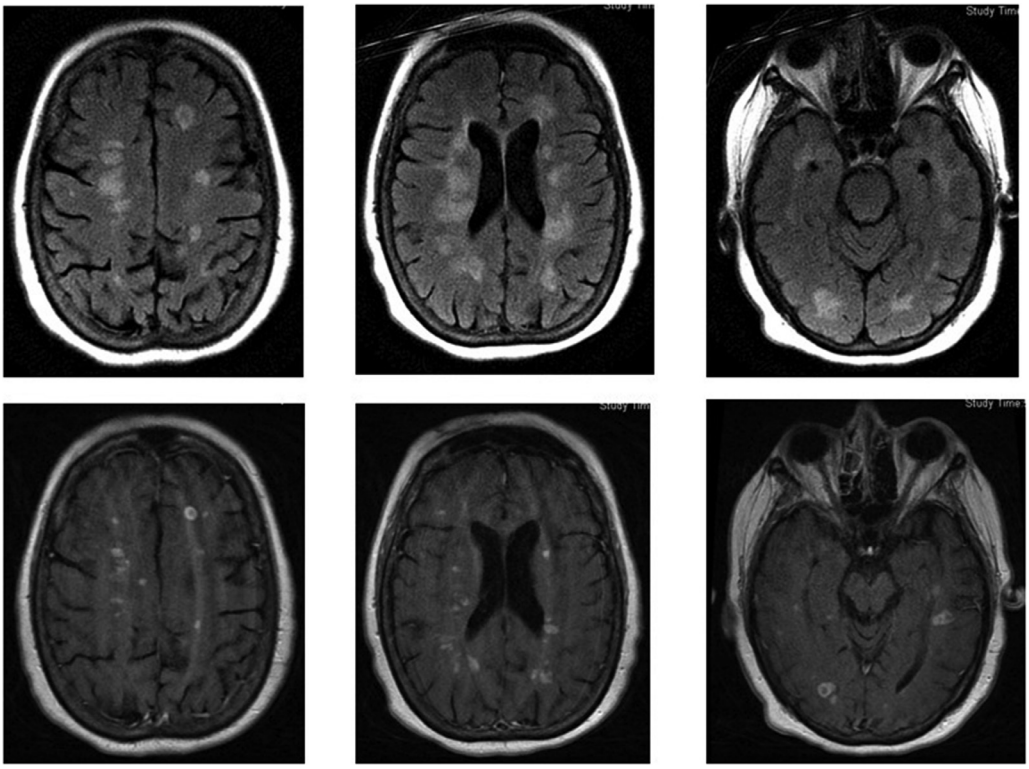

Fig. 2. Top row: MRI Brain FLAIR sequences from second presentation, ten years later. Bottom row: corresponding MRI brain postcontrast imaging with multiple enhancing white matter lesions in both cerebral hemispheres involving the deep and subcortical white matter. The white matter abnormalities have worsened since the previous exam and contrast enhancement is new.

presentation (Fig. 2). MRI of the cervical spine did not reveal any cord lesions or abnormal enhancement. She was initially treated with IVIg 0.4 g/kg/day for 4 days without notable improvement. Decision was made to then treat with IV methylprednisolone 1000 mg every 24 h for five days. She had some improvement in her weakness and was discharged to an acute rehabilitation facility. Prior to discharge, she was diagnosed with multiple sclerosis and referred to the neuroimmunology clinic for further management and consideration of disease modifying therapy. At follow-up two weeks later, she had no gross memory or cognitive findings on examination and had fairly symmetric normal strength throughout her extremities, mildly decreased sensation in right lower extremity to pinprick and 2 + reflexes except 1 + at ankles. She was able to ambulate with short steps and without assistance. Anti-MOG antibody testing (tested by cell-based flow cytometry assay at Mayo Clinic Laboratories) was checked at this visit and resulted negative.

3. Discussion

The distinction between acute disseminated encephalomyelitis (ADEM), recurrent DEM (RDEM), multiphasic DEM (MDEM), or MS has been previously explored with no satisfactory consensus (Brinar, 2004; Pohl et al., 2016). Historically, ADEM was defined as the initial presentation of disseminated encephalomyelitis, RDEM as the relapse of prior symptoms, and MDEM as the occurrence of new symptoms in the setting of a history of ADEM. In 2013, the International Pediatric Multiple Sclerosis Study Group (IPMSSG) published criteria defining ADEM in the pediatric population. Citing low frequency of occurrence, the category of RDEM was eliminated and replaced by multiphasic DEM (MDEM). The hallmark of this new category was the occurrence of two clinicoradiographic episodes of disseminated encephalomyelitis separated by at least three months. The clinical findings were defined as being new *or* a re-emergence of prior symptoms. If the patient sustained three or more episodes, he/she was classified as having a chronic inflammatory demyelinating disorder (Krupp et al., 2013).

Conversely in adults, the occurrence of recurrent neuroradiologic symptoms in patients with prior ADEM can be as high as 35% (Schwarz et al., 2001; de Seze et al., 2007; Cohen et al., 2001). Interestingly, all 5 patients presenting with recurrent DEM in one series presented with hemiparesis, as with our patient (Cohen et al., 2001). The studies of recurrent DEM in adults are limited by small sample sizes and by adhering to outdated diagnostic criteria for MS, often subjecting these patients to unnecessary treatment with disease modifying therapies for MS that may exacerbate DEM (Chen et al., 2013). It is clear that not all that is disseminated in space and time is multiple sclerosis. Presentation with fever, the absence/paucity of oligoclonal bands, presence of bilateral optic neuritis, peripheral nervous system involvement, and cognitive involvement have been identified as features that can help distinguish recurrent demyelinating syndromes from MS (Brinar and Poser, 2008; Marchioni et al., 2008). We propose that the multifocal radiographic nature of DEM also be considered when contemplating the two diagnoses.

Our patient's presentation poses the diagnostic challenge of disseminated clinical and neuroimaging findings ten years apart with no clinical symptoms in the interim. This is a uniquecase of ADEM initially presenting in adulthood and recurring after an extended (10-year) symptom-free period. Though it has been suggested that the overwhelming majority of relapses occur in the spinal cord, our patient did not follow this pattern (Marchioni et al., 2008). There is a recent report of a patient presenting with anti-MOG associated, steroid-responsive clinicoradiographic relapse 33 years after initial ADEM diagnosis at age 4 (Numa et al., 2016). Given the extended periods of time between relapses, it is challenging to prospectively study these patients with adequate follow-up. Though our patient was negative for the anti-MOG antibody, caution has to be taken when interpreting these results as the patient had received therapies for acute attack just two weeks prior. Additionally, testing for anti-MOG antibody may have a role in diagnostic evaluation and directing further management, particularly in the pediatric population (Numa et al., 2016).

There is persistent uncertainty regarding the diagnosis and management of recurrent episodes of DEM. We view this as an opportunity for improved investigation of this patient population and the eventual

characterization of recurrent DEM as a distinct clinical entity, potentially having its own antibody association.

Disclosure

Dr. S Shah reports no disclosures. Dr. D Shah reports no disclosures. Dr. Skeen reports no relevant disclosures. He has received honoraria from Biogen, Novartis, Celgene, and Mallinckrodt.

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