

Case Report

New onset seizures as a sole clinical presentation of multiple sclerosis

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Abstract

Background and objectives: Epileptic seizures frequently occur in people with multiple sclerosis (MS) and are thought to represent a manifestation of cortical pathology. However, at present, seizures are not considered to be a typical clinical presentation of demyelination.

Methods and results: In this case series, we identified four people, who presented with seizures as a sole presenting feature, with demyelinating imaging abnormalities that satisfy current diagnostic criteria for a clinically isolated syndrome (CIS) or early MS.

Conclusion: Based on this case series, we propose that people presenting with de novo seizures, with concurrent radiological abnormalities suggestive of demyelination could potentially be considered to have a CIS.

Keywords: Multiple sclerosis, epilepsy, cortical lesions, electroencephalogram, temporal lobe

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Introduction

Cortical lesions are widespread in the multiple sclerosis (MS)¹ brain. While such abnormalities may be readily appreciated at post mortem in progressive MS, recent evidence suggests that cortical abnormalities may be seen in clinically isolated syndrome (CIS) or early MS.^{2,3}

It has been reported that epileptic seizures occur frequently in people with MS, and indeed, an increased number of cortical lesions detected radiologically, may correlate with an increase in seizure frequency.⁴ The temporal lobe has been implicated as a potential epileptogenic focus in MS, and this appears to correlate with extensive pathological abnormalities in this region.^{1,5}

While epileptic seizures are a well-documented phenomenon in MS, seizures are not presently considered to be a typical presentation of a demyelinating syndrome.⁶ Herein, we outline a case series of people with CIS or early MS, who presented with epileptic seizures as a sole clinical manifestation.

Case series

We identified three people in whom a retrospective diagnosis of MS was made, and one case of MS. The demographics and seizure semiologies are summarized in Table 1. In each case, a workup was performed to investigate for other causes of demyelination and included a panel of bloods for infectious, neuroinflammatory, or systemic autoimmune diseases. In addition, we obtained cerebrospinal fluid in each person and identified unmatched oligoclonal bands, not present in serum. Following this workup, when “no better explanation” could be ascertained, a diagnosis of demyelination was made in each instance (either CIS or early MS), based on a clinical presentation of seizures (due to presumed cortical demyelination) with imaging abnormalities consistent with MS.

Case 1

A 29-year-old right-handed female presented acutely with paresthesia in her left foot radiating up her left lower limb, associated with nausea. This event was followed by tonic posturing of her arm and recurred in

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Table 1. Demographics, and MRI abnormalities suggestive of demyelination as well as EEG reports in a cohort of people with CIS presenting with epileptic seizures.

Gender	Age	Presenting feature	MRI		MRI lesions	EEG findings	Disease modifying therapy
			DIT	DIS			
Female	29	Simple partial seizures	No	Yes	Periventricular Infratentorial	None	Dimethyl fumarate
Female	19	Focal complex seizure with secondary generalization	Yes	Yes	Periventricular Infratentorial	Irregular slowing in the delta frequency over the frontal regions bilaterally	Fingolimod
Female	21	Two generalized tonic-clonic seizures	No	Yes	Periventricular Juxtacortical Infratentorial	None	None
Female	31	Complex partial seizures of temporal origin	No	Yes	Periventricular Juxtacortical	Video EEG Sharp waves captured over right mid-temporal regions with rare left temporal sharp waves—temporal lobe epilepsy	None

MRI: magnetic resonance imaging; CIS: clinically isolated syndrome; EEG: electroencephalogram; DIS: dissemination in space; DIT: dissemination in time.

a stereotypical fashion lasting approximately 30 seconds, with spontaneous resolution. Neurological exam was normal; magnetic resonance imaging (MRI) brain and cervical spine were compatible with demyelination and fulfilled current diagnostic criteria for dissemination in space (DIS) but not dissemination in time (DIT).⁶ An electroencephalogram (EEG) was performed within days of her initial presentation where no definite epileptiform discharges were noted. We made a diagnosis of a CIS with partial seizure presentation and commenced treatment with eslicarbazepine, at 800 mg, with control of further seizures and dimethyl fumarate, no disease activity was identified at 6-month follow-up.

Case 2

A 19-year-old woman presented emergently with a number of episodes of eye rolling associated with aphasia, followed by collapse and tonic clonic convulsions. MRI brain showed large white matter lesions perpendicular to the corpus callosum on sagittal imaging, and in a periventricular distribution compatible with demyelination on axial views. In addition, we identified an infratentorial lesion on T2-weighted imaging, thereby satisfying criteria for DIS. EEG showed runs of irregular slowing in the delta frequency over the frontal regions bilaterally. She has remained seizure-free at 2 years since commencing lamotrigine. Following the initial presentation of a CIS, manifesting

as convulsive seizures, we commenced treatment with fingolimod, and the patient has remained free of clinical relapses or new radiological activity in the subsequent 2-year follow-up.

Case 3

A 21-year-old female presented following a witnessed convulsive seizure, characterized by tonic clonic limb movements, tongue biting, and post-ictal confusion. She had a prior episode of collapse, precipitated by sleep deprivation, which was not investigated, and 1 year prior to presentation with a convulsive seizure. She had experienced an episode of right-sided numbness, in the absence of infection or other illnesses. We identified MRI abnormalities consistent with demyelination: periventricular, juxtacortical, and infratentorial lesions were present on T2-weighted imaging. EEG was normal. She has remained seizure-free for 5 months since commencing levetiracetam. We diagnosed a CIS, and based on the patient's wishes, we deferred initiation of a disease modifying treatment.

Case 4

A 31-year-old right-handed female who presented 10 years prior with recurrent episodes of déjà vu, in a stereotyped fashion, with concurrent loss of awareness. Each event lasted approximately 60 seconds, at this time point MRI of her brain was normal. She

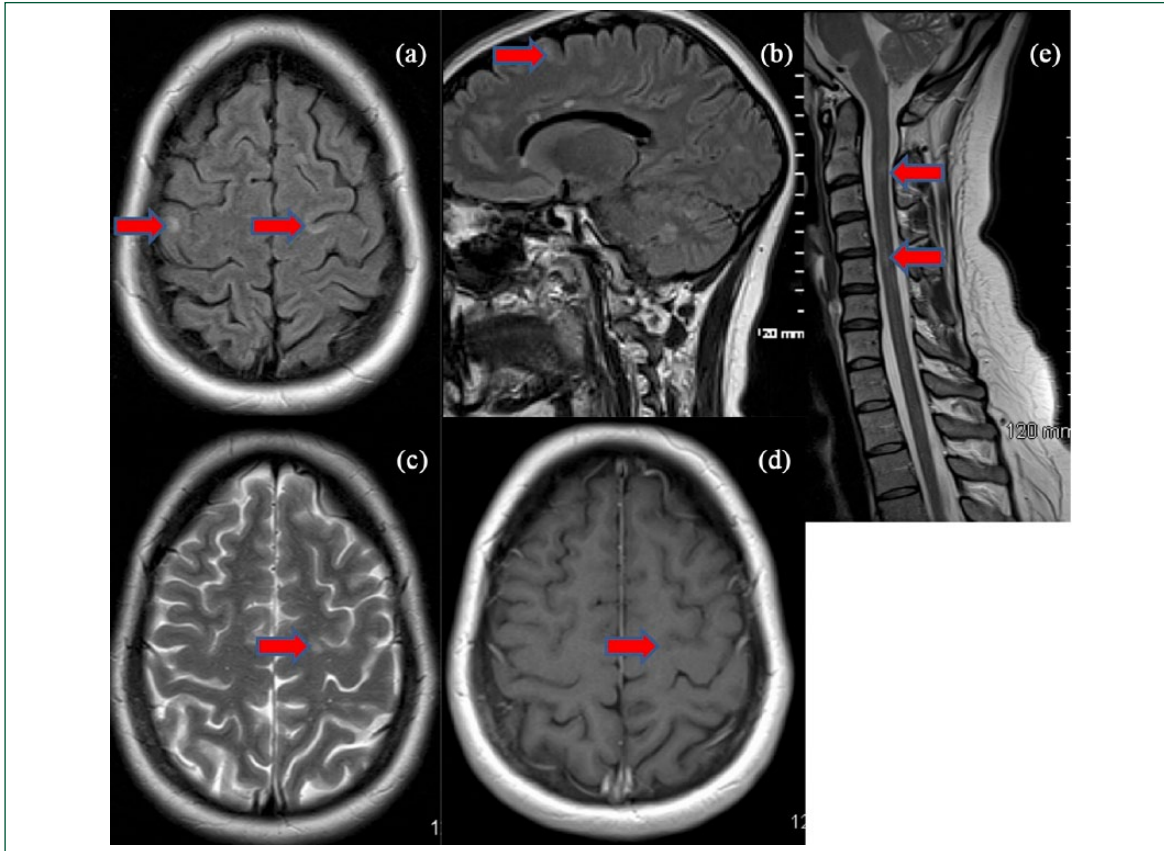


Figure 1. Axial FLAIR brain scan (a) and sagittal FLAIR brain scan (b), axial T2-weighted brain scan (c), and T1-weighted post gadolinium brain scan (d). The axial images shown demonstrate high signal abnormalities with lesions located in a periventricular, juxtacortical, and infratentorial abnormalities. T2-weighted spinal cord lesions are shown in (e).

remained seizure-free for 8 years while taking slow-release carbamazepine. Following the birth of her second child, her seizures began to occur at a much greater frequency. She subsequently presented for investigation and her repeat brain MRI, was compatible with demyelination with T2-weighted lesions identifiable in a periventricular and juxtacortical distribution. Video EEG monitoring demonstrated complex partial seizures of temporal lobe etiology. She has been commenced on levetiracetam monotherapy at 1000 mg bd.

Discussion

This case series demonstrates that epileptic seizures could potentially be considered to be a presentation of a CIS. The cortex in MS has been shown pathologically to contain numerous cortical lesions.² We propose that the epileptic seizures seen in this series are symptomatic localization-related seizures as a consequence of cortical pathology, and as such may be considered to be a clinical manifestation of demyelination.

While cortical abnormalities are not typically visualized on conventional MRI sequences in routine clinical practice, cortical lesions may be visualized using double inversion recovery (DIR) or phase sensitive inversion recovery sequences.⁵⁻⁷ It has been proposed that cortical lesions on DIR could be incorporated into the current diagnostic criteria for MS.⁸ Given the acceptance that cortical abnormalities are widespread in MS, and may be seen *in vivo*, we propose that symptoms arising from cortical demyelination (i.e. seizures) may be considered to be a CIS.

While MRI is limited in its utility in routine clinical practice for the detection of cortical lesions, EEG may be used to detect electrophysiological cortical abnormalities, thereby providing supportive evidence of cortical abnormalities. In our case series, two people had EEG abnormalities in a fronto-temporal distribution, where extensive subpial demyelination and cortical lesions may be seen *ex vivo* (Figure 1).

In conclusion, this case series highlights that epileptic seizures, in the context of imaging abnormalities

compatible with demyelination, may be a sole clinical manifestation of a demyelinating syndrome.

Declaration of Conflicting Interests

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