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Case Report

Electroencephalographic and fluorodeoxyglucose-positron emission tomography correlates in anti-*N*-methyl-D-aspartate receptor autoimmune encephalitis

John C. Probasco [a,*], David R. Benavides [a], Anthony Ciarallo [b], Beatriz Wills Sanin [c], Angela Wabulya [a], Gregory K. Bergey [a], Peter W. Kaplan [a,d]

[a] Department of Neurology, The Johns Hopkins University School of Medicine, Baltimore, MD, USA
[b] Division of Nuclear Medicine, The Russell H. Morgan Department of Radiology and Radiological Sciences, The Johns Hopkins University School of Medicine, Baltimore, MD, USA
[c] Department of Neurology, Los Andes University, Bogota, Colombia
[d] Department of Neurology, The Johns Hopkins Bayview Medical Center, Baltimore, MD, USA

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ABSTRACT

Importance: Anti-*N*-methyl-D-aspartate receptor (anti-NMDAR) autoimmune encephalitis is an increasingly recognized cause of limbic encephalitis (LE). Prolonged LE and limbic status epilepticus (LSE) share many features. The ability to distinguish between the two is crucial in directing appropriate therapy because of the potential iatrogenesis associated with immunosuppression and anesthetic-induced coma.

Observations: A 34-year-old woman with recurrent LE developed behavioral changes, global aphasia, and repetitive focal and generalized tonic–clonic seizures. Because asymmetric rhythmic delta patterns recurred on electroencephalography (EEG) despite treatment with nonsedating antiepileptic drugs followed by anesthetic-induced coma, an investigation to distinguish LSE from LE was undertaken. Implanted limbic/temporal lobe depth electrodes revealed no epileptiform activity. Brain single-photon emission computerized tomography (SPECT) showed no hyperperfusion, and brain fluorodeoxyglucose-positron emission tomography (FDG-PET) showed hypermetabolism in the left frontal, temporal, and parietal cortices. Anti-*N*-methyl-D-aspartate receptor autoimmune encephalitis was diagnosed based detection of anti-NMDAR antibody in the cerebrospinal fluid (CSF). With chronic immunosuppression, the resolution of brain FDG-PET abnormalities paralleled clinical improvement.

Conclusions and relevance: This case of anti-NMDAR autoimmune encephalitis illustrates the challenges of distinguishing prolonged LE from LSE. We discuss the parallels between these two conditions and propose a management paradigm to optimize evaluation and treatment.

1. Introduction

Limbic encephalitis (LE) is considered in patients with short-term memory loss, confusion, behavioral changes with irritability, depression, sleep disturbance, hallucinations, orofacial dyskinesias, and seizures involving the medial temporal lobes and amygdala [1,2]. Encephalitis with anti-*N*-methyl-D-aspartate receptor (anti-NMDAR) antibodies is an autoimmune, and often paraneoplastic, form of LE with prodromal viral-like illness, prominent impaired consciousness, abnormal movements, and autonomic instability [3]. Prolonged states of behavioral changes, orofacial movements, and partial seizures in LE suggest underlying limbic status epilepticus (LSE) [4]. When facing the diagnostic dilemma of autoimmune LE and LSE, antiepileptic and immunosuppressive treatment is often initiated while awaiting confirmatory antibody titers. However, patients may develop refractory or malignant features with diagnostically ambiguous rhythmic activity on electroencephalography (EEG). The clinician must weigh the morbidity of ongoing limbic seizures against the morbidity of anesthetic-induced coma in an effort to overcome suspected LSE. Here, we present a case where this conundrum was explored using surface and depth electrode EEG. We propose a paradigm for distinguishing LE from LSE.

2. Report of a case

A 34-year-old woman with a history of two episodes of LE in the prior nine years developed gradual onset difficulty with concentration, mild headaches, and hemibody paresthesias that progressed to include orofacial dyskinesias, hemiparesis, global aphasia, and repetitive focal and generalized tonic–clonic seizures. Her previous episodes of LE, from

* Corresponding author at: Department of Neurology, The Johns Hopkins University School of Medicine, 600 North Wolfe Street, Meyer 6-113, Baltimore, MD 21205, USA. Tel.: +1 410 955 8174; fax: +1 410 955 0672.
E-mail address: jprobas1@jhmi.edu (J.C. Probasco).

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which she made a complete recovery, were characterized by behavioral changes, aphasia, and focal and generalized tonic–clonic seizures. She had a family history of autoimmunity, with a mother with Sjögren's disease and a maternal aunt with systemic lupus erythematosus. Her initial evaluation revealed a cerebrospinal fluid (CSF) lymphocytic pleocytosis (46 leukocytes/mm^3) and elevated protein (95 mg/dL), with negative anti-NMDAR serologies. Fluorodeoxyglucose-positron emission tomography (FDG-PET) performed during the first clinical episode demonstrated multiple FDG-avid hypermetabolic areas involving the right frontal, temporal, and parietal lobes. She was treated with high-dose intravenous (IV) corticosteroids, intravenous immunoglobulin (IVIg), and oral corticosteroid taper. A corticomeningeal biopsy was nondiagnostic. The brain FDG-PET abnormality resolved prior to the second clinical episode. She was subsequently treated with a regimen of lamotrigine, carbamazepine, and oral prednisone.

Five years after her second clinical episode, she experienced trouble concentrating at work with intermittent headaches and presented to her neurologist for evaluation. Outpatient brain magnetic resonance imaging (MRI) revealed a T2 hyperintensity in the left parietal lobe that prompted hospitalization and CSF analysis showing a lymphocytic pleocytosis (103 leukocytes/mm^3) and normal protein (42 mg/dL). By report, EEG demonstrated intermittent irregular slowing over the left temporal region, without epileptiform discharges. Following high-dose IV corticosteroids, she was discharged on oral corticosteroid taper, carbamazepine, and lamotrigine. She continued to have language deficits, right arm weakness, and difficulty with feeding and dressing herself. A follow-up outpatient brain MRI was normal. Within weeks, she developed episodic right face twitching, right hemibody paresthesias with hemiparesis, and generalized tonic–clonic seizures. She was readmitted, given IV antiepileptic drugs, and reinitiated on high-dose IV corticosteroids. Per report, repeat CSF studies and EEG were unchanged from prior studies, showing lymphocytic pleocytosis (76 leukocytes/mm^3) with normal protein (36 mg/dL) and focal left temporal slowing. Following prolonged right facial twitching and generalized abnormal movements, IVIg was initiated, and she was transferred to our hospital for further evaluation and management.

On admission, she was alert and nonverbal with global aphasia. Intermittent right facial twitches and right arm movements were noted. Motor examination showed antigravity strength in the left hemibody and right leg. No purposeful movements of the right arm were noted. Electrographic seizures with clinical correlates were captured on EEG, so her antiepileptic regimen was escalated. On subsequent continuous EEG monitoring, intermittent rhythmic left temporal delta activity was seen (Fig. 1A), without sharps or epileptiform waveforms. Repeat CSF analysis showed persistent lymphocytic pleocytosis (53 leukocytes/mm^3), and serologic inflammatory and rheumatologic markers were normal. A brain single-photon emission computerized tomography (SPECT) study showed no abnormal perfusion (data not shown). Clinically, she had fluctuating worsening of her aphasia and right arm weakness that correlated with temporal delta activity that would progress and evolve asymmetrically and rhythmically in bursts of 10 s. Levetiracetam, fosphenytoin, valproic acid, lacosamide,

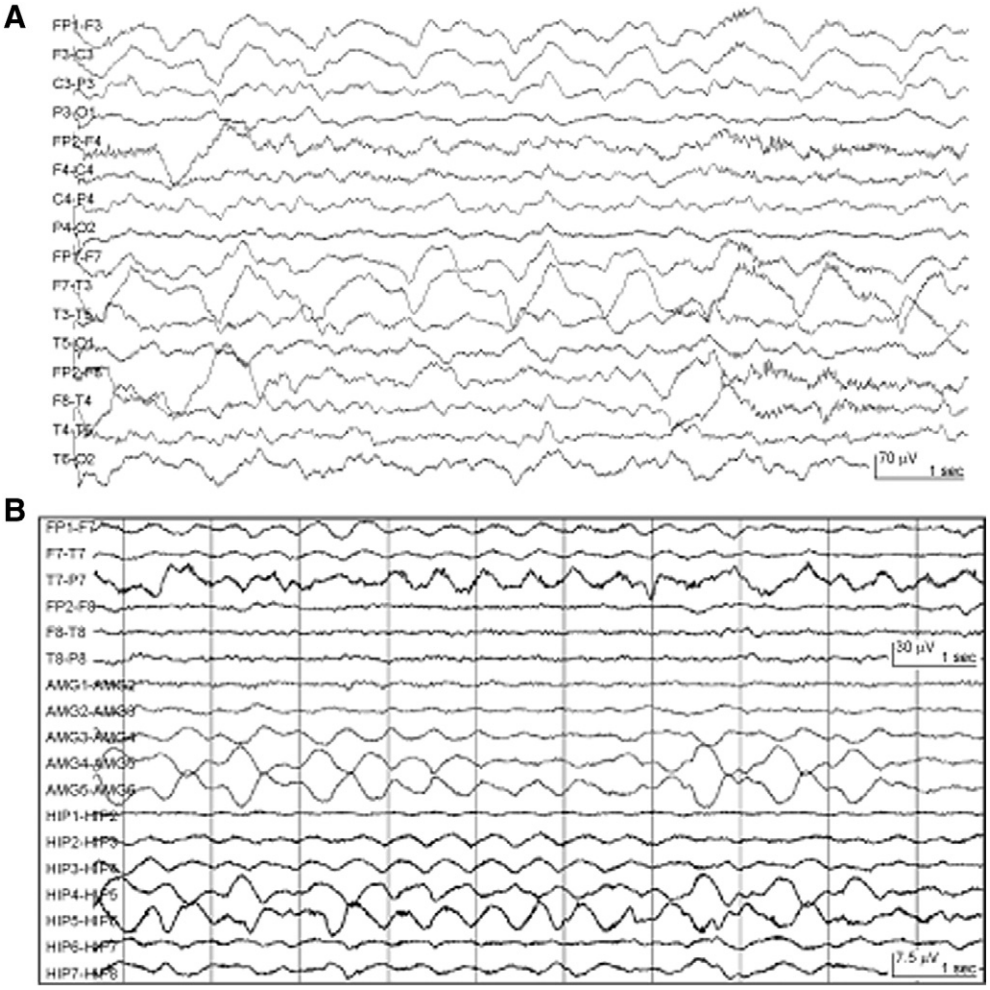

Fig. 1. Continuous surface and depth electrode electroencephalographic monitoring in anti-NMDAR autoimmune encephalitis. (A) Scalp EEG monitoring demonstrated delta slowing that was maximal over the left temporal area. (B) Surgically implanted depth electrodes targeting the left amygdala (AMG) and left hippocampus (HIP) showed nearly continuous semirhythmic to rhythmic delta activity that correlated with surface EEG slowing.