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Ictal Rhythmic Alpha Sinusoidal Waves in 3 Cases of Anti-NMDAR Encephalitis

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Abstract

Previous studies have shown that extreme delta brush and high beta/delta power ratio on electroencephalogram are suggestive of anti–*N*-methyl-D-aspartate receptor (anti-NMDAR) encephalitis. Here we report 3 anti-NMDAR encephalitis patients with ictal rhythmic alpha sinusoidal waves in temporal regions, which suggested electrographic seizures in anti-NMDAR encephalitis and indicated potential for seizure occurrence in the future. Rhythmic alpha sinusoidal waves may be an electrographic feature and helpful in distinguishing anti-NMDAR encephalitis. In addition, extreme delta brush was also observed at 47-50 days after morbidity in 2 of 3 patients.

Keywords

anti-NMDA receptor encephalitis, alpha sinusoidal waves, extreme delta brush

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Introduction

Anti–*N*-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is an autoimmune disease associated with positive anti-NMDAR antibody IgG in the cerebrospinal fluid (CSF) with or without combined positive anti-NMDAR antibody IgG in their serum. It is characterized by mental disorder, cognitive impairment, language impairment, disturbance of consciousness, epilepsy, involuntary movement, and autonomic nervous system dysfunction.[1] Extreme delta brush (EDB) on electroencephalogram (EEG) has been proposed to be useful for diagnosing anti-NMDAR encephalitis.[2] However, only 30.4% of anti-NMDAR encephalitis patients in the study showed EDB on EEG.[2] Foff et al[3] recently reported that an electrographic characteristic, namely the beta/delta power ratio (BDPR), is significantly higher for anti-NMDAR encephalitis patients than for non-NMDAR encephalitis patients on presenting EEG, which may be helpful in distinguishing anti-NMDAR encephalitis from non-NMDAR encephalitis.

It is unknown whether there are other electrographic features besides EDB and BDPR in patients with anti-NMDAR encephalitis. Here, we report an ictal electrographic pattern the "rhythmic alpha sinusoidal wave" (RASW) in 3 patients.

Case Report

Case 1

A 32-year-old man experiencing psychosis, agitation, incoherent speech, and seizures for 40 days was admitted. Results of indirect immune fluorescence technique (IIFT) revealed NMDAR antibody titers of 1:100 in his blood. Diffusion-weighted imaging (DWI) and T2 indicated hyperintensity in the right temporal lobe (Figure 1). On day 7, a 24-hour video-electroencephalogram (VEEG) showed EDB in the right frontal pole regions (Figure 1A, red line). After 10 seconds, EDB gradually attenuated and RASW mingled with a few sharp waves were observed in the right temporal lobe (Figure 1B and C). During RASW, the patient stayed in bed and no other clinical symptoms were observed. Subsequently, rhythmic alpha waves diminished while EDB became enhanced (Figure 1D). The patient received immunotherapy (glucocorticoid and immunoglobulin) and antiepileptic drugs. After 3 months, seizures were controlled. However, memory was impaired. The case had modified Rankin scale (mRS) score of 2.

Case 2

A 19-year-old woman undergoing verbal reduction, mutism, and seizures for 45 days was admitted. IIFT results revealed NMDAR antibody titers of 1:1 in the CSF and 1:10 in the blood. Magnetic resonance imaging (MRI) results showed hyperintensity in the DWI image and high blood flow on arterial spin labeling (ASL) of the left temporal region (Figure 2). On day 2, the first 24-hour VEEG showed RASW of the left

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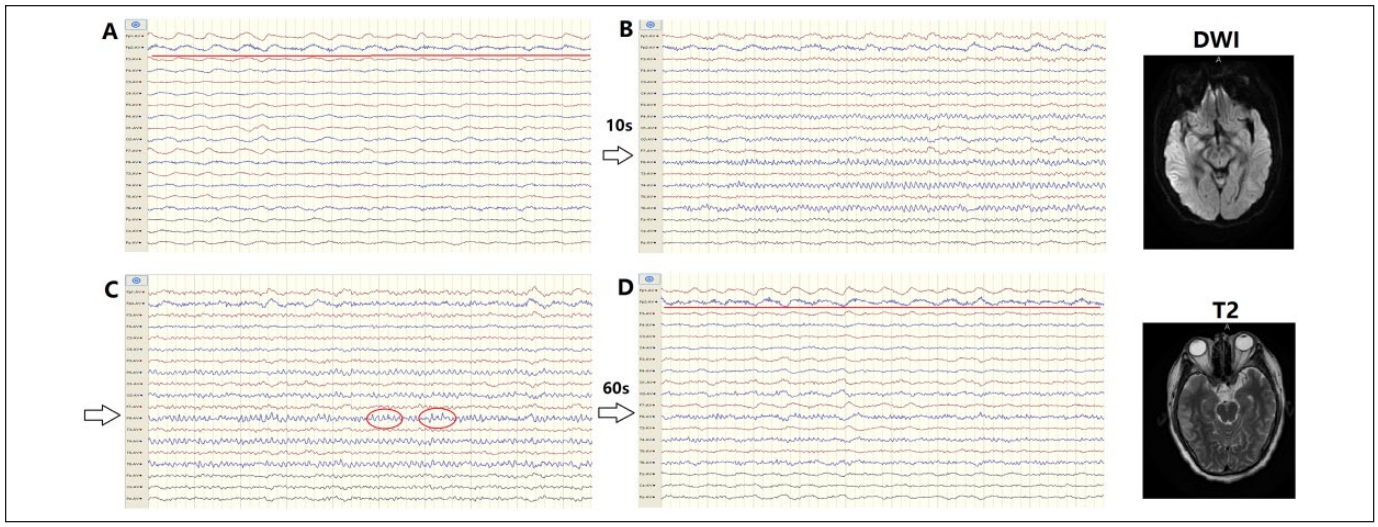

Figure 1. Extreme delta brush (EDB) in the right frontal pole regions (A, red line). After 10 seconds, EDB was gradually attenuated. Rhythmic alpha sinusoidal waves mixed with a few sharp (red circle) waves lasted up to 80 seconds in the right temporal lobe (B, C). Subsequently, rhythmic alpha waves weakened but EDB became enhanced (D). Diffusion-weighted and T2-weighted imaging indicated lesion in the right temporal lobe. Recording parameters were as follows: sensitivity 10 μV/mm, high-pass filter 1 Hz, low-pass filter 40 Hz.

temporal regions with evolution in frequency, amplitude, morphology, or field (Figure 2A-D). During RASW, the patient stayed in bed (Figure 2), and no other clinical symptoms were observed. After 10 days, left frontal and central epileptic discharges in second VEEG, instead of alpha waves, resulted in right facial seizures (focal status epilepticus). The patient also received immunotherapy (glucocorticoid and immunoglobulin) and antiepileptic drugs. After 6 months, the patient had mRS scores of 1, and seizures were controlled. The third VEEG showed mild 7 Hz waves in frontal regions and no epileptic discharges were observed.

Case 3

A 50-year-old woman suffering from psychosis and agitation for 10 days was admitted. IIFT results revealed NMDAR antibody titers of 1:10 and 1:100 in the CSF and the blood, respectively. MRI examinations were normal. Routine EEG on day 2 after admission showed RASW lasting to 6 seconds (Figure 2E). No other clinical symptoms were observed during RASW. On day 3 in the hospital, the patient experienced seizures. Although the patient received immunotherapy (glucocorticoid and immunoglobulin) and antiepileptic drugs, the illness did not improve, and constant chewing was observed. After 33 days, the second VEEG showed continue EDB in bilateral frontotemporal regions (Figure 2F) and intermittent chewing artifacts (Figure 2G and H). During chewing (video), synchronous EEG showed no epileptic discharges. EDB was constant during the whole EEG. However, chewing was intermittent. After 5 months, the patient had mRS scores of 3. Chewing and seizures were controlled. However, the patient suffered from impaired memory.

Discussion

EEG abnormalities are common in patients with anti-NMDAR encephalitis. EDB has received clinical attention since Schmitt et al[2] showed that this pattern might be a characteristic EEG change in patients with anti-NMDAR encephalitis. The EDB pattern without electrographic evolution or response to benzodiazepine suggests that EDB itself is an interictal, not an ictal pattern.[2] Furthermore, the patient's recovery without antiepileptic drugs also suggests that EDB is unlikely to be ictal in nature.[2] EDB is more likely to represent cortical dysfunction rather than seizure. EDB itself continues to be a useful marker of disease activity and a tool to monitor treatment response and relapses because of its resolution in parallel with clinical improvement.[2] Patients with EDB tend to have severe diseases but normal MRI, suggesting a more aggressive phenotype.[2] Schmitt et al[2] showed that EDB was most often symmetric and synchronous, typically seen broadly across all head regions. Our brush pattern was detected in unilateral or bilateral frontotemporal region at 47 to 50 days after morbidity. However, EDB on EEG were observed in only 30.4% of anti-NMDAR encephalitis patients.[2] BDPR may be another electrographic feature helpful in distinguishing anti-NMDAR encephalitis from non-NMDAR encephalitis, since BDPR is significantly higher in anti-NMDAR encephalitis patients than in non-NMDAR encephalitis patients on presenting EEG.[3] Constant chewing (video) was unlikely to be due to temporal or frontal seizures as no epileptic discharges were observed in the EEG recordings, and antiepileptic drugs were ineffective. EDB in case 3 was constant during the whole EEG. However, chewing was intermittent. In addition, previous studies have shown that chewing is an involuntary movement.[1,2] Constant chewing may be a useful marker of disease peak period.

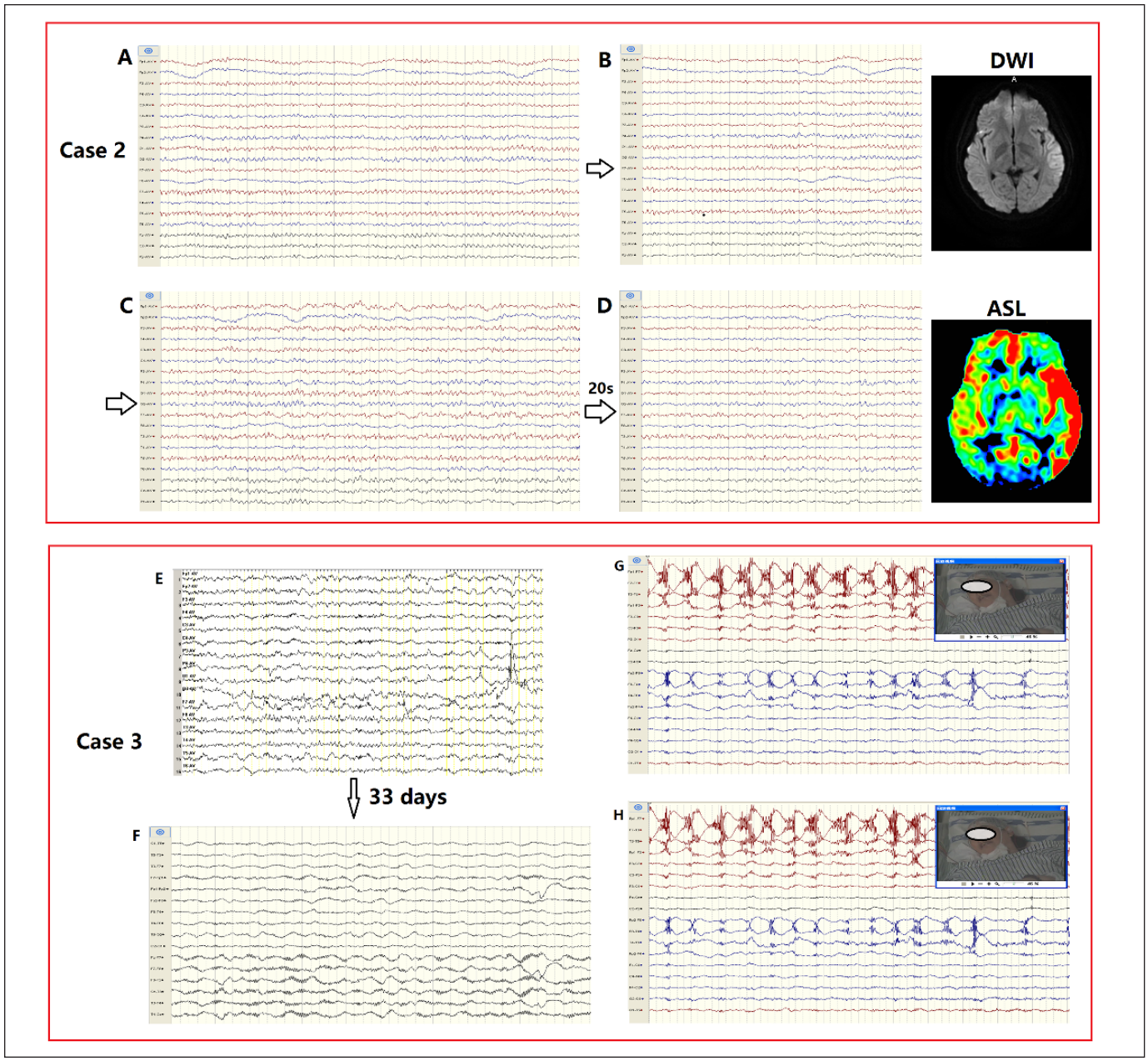

Figure 2. Alpha sinusoidal waves from case 2 in the left temporal lobe lasted 60 seconds (A-D). Diffusion-weighted imaging showed hyperintensity and arterial spin labeling (ASL) presented high blood flow in the left temporal regions. Alpha sinusoidal waves from case 3 in the right temporal lobe (E). extreme delta brush (EDB) in the bilateral frontotemporal regions (F). During chewing, the synchronous EEG showed no epileptic discharges. Only chewing artifacts were observed in EEG (G and H) (video). Recording parameters were as follows: sensitivity 10 μV/mm, high-pass filter 1 Hz, low-pass filter, 40 Hz.

RASW, an ictal pattern, lasted up to 2 minute with evolution in frequency, amplitude, morphology, or field, and mingled with a few sharp waves. During RASW, no clinical symptoms were observed from 3 cases. Subclinical seizures are electrographic discharges with frequency or spatial evolution and length of ≥10 seconds and lack clinical seizure signs, behavioral alteration, or subjective symptoms. EDB is an interictal, not an ictal, pattern.[2] In contrast to EDB, ictal RASW in cases 1 and 2 represented subclinical seizure. In addition, all patients in the current study presented seizures, suggesting that RASW are associated with seizures. In a previous study,[4] brief ictal rhythmic discharges (BIRDs) (<10 seconds) was defined as rhythmic activity with frequency greater than 4 Hz. The typical frequency for BIRDs was in the theta and alpha ranges. BIRDS in critically ill patients are associated with high prevalence (75%) of electrographic seizures and might serve as early predictor of seizures. Thus, if an EEG recording shows an ictal rhythmic alpha pattern, treatment with antiepileptic drugs is reasonable.

A previous study reported that subclinical seizures occurred in 60.1% of patients with anti-NMDAR encephalitis.[2] However, the electrographic features of subclinical seizures were not elucidated.[2] In the present study, subclinical seizures were characterized by ictal RASW. The electrographic features of subclinical seizure in patients with anti-NMDAR encephalitis might be different from those of temporal lobe epilepsy (TLE) in the hippocampus. Ictal rhythms of TLE presented background attenuation, start-stop-start phenomenon, irregular 2 to 5 Hz lateralized activity, and rhythmic delta activity (TIRDA) or repetitive epileptiform discharges.[5] TIRDA was the leading rhythm and was observed in up to 90% of patients with TLE.[5] Frequent rhythmic alpha waves were observed in the 2 patients with large lesions in the temporal lobe. The frequency of lesion rhythms during scalp EEG resulting from anti-NMDAR encephalitis ranged from 9 to 12 Hz.

RASW might be an electrographic pattern in patients with anti-NMDAR encephalitis and indicate a potential for seizures.

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Author Contributions

Ailiang Miao: drafting/revising the manuscript and acquisition of EEG. Xiaoshan Wang: study concept or design and study supervision. Hedong Lu: acquisition of EEG. In addtion, thanks for clinical work from Jianqing Ge, Lingling Wang, Chuanyong Yu, Yingxin Wang, Caiyun Wu, Yuan Gao and Qi Shi. Their contributions helped us to acquire clinical data successfully.

Declaration of Conflicting Interests

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