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Serial EEG Monitoring in a Patient With Anti-NMDA Receptor Encephalitis

Yanfang Shi[1]

Abstract

Electroencephalogram (EEG) abnormalities are very common in anti-*N*-methyl-D-aspartate receptor (anti-NMDAR) encephalitis. Extreme delta brush (EDB) is a distinctive EEG pattern that is can be suggestive of the diagnosis; however, the etiology of the EDB remains unclear. Furthermore, there is question with regard to its ictal or interictal nature. We report a 20-year-old woman with anti-NMDAR encephalitis whose serial video-EEG monitoring was obtained at 2, 2.5, 4, and 6 months after admission. There was a long-standing EDB lasting up to several hours, with no evolution in frequency, amplitude, or morphology, and without clear association her frequent orofacial dyskinesia. Intravenous benzodiazepine administrations did not change the EDB pattern. As her clinical symptoms improved, the EDB gradually became less prominent and less frequent, with complete resolution at 6 months after admission. These findings suggest that EDB is more likely a marker of the severity of the disease in contrast to an epileptic seizure and is useful for diagnosis and monitoring of treatment response in conjunction with clinical improvement.

Keywords

extreme delta brush, anti-NMDA receptor encephalitis, ictal pattern, nonconvulsive status epilepticus, continuous video-EEG monitoring

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Introduction

Autoimmune encephalitis associated with anti-*N*-methyl-D-aspartate receptor (anti-NMDAR) is increasingly recognized since its original description in 2007.[1] Clinical presentations are varied, including psychiatric symptoms, decreased responsiveness, abnormal movements, autonomic instability, and seizures. Magnetic resonance imaging (MRI) has been reported as normal in about 50% of the patients. The nonspecific clinical findings and often normal imaging pose a challenge in the recognition and diagnosis of anti-NMDAR encephalitis. Electroencephalogram (EEG) abnormalities are very common in anti-NMDAR encephalitis, and can be useful for diagnosis, in addition to seizure detection and status epilepticus (SE) monitoring. A distinctive EEG pattern, called "extreme delta brush" (EDB), has been observed in patients with anti-NMDAR encephalitis[2]; however, its etiology and significance between ictal and interictal nature remain unclear. Here, we report a patient with anti-NMDAR encephalitis with EEG showing EDB that showed no response to benzodiazepine, and resolved in parallel with clinical improvement.

Case Report

The patient is a 20-year-old woman who initially presented to the emergency department with suicidal attempt at an outside institution. She was also reported to have bilateral lower extremities weakness and agitation during the preceding week. After admission, she had decreased level of consciousness and would not verbalize or answer questions, along with psychosis and frequent orofacial movements. Imaging studies showed normal MRI brain, along with normal MRI pelvis, which was performed to assess for possible neoplasms. Her EEGs were reported as normal or showed generalized slowing. Cerebrospinal fluid (CSF) was tested positive for anti-NMDAR at 1:40, while other paraneoplastic antibodies and extensive viral studies were negative. The diagnosis of anti-NMDAR encephalitis was confirmed and she received treatments, which included 5 rounds of plasma exchanges, immunoglobulin, and rituximab. There was no clear clinical improvement after 2 months of admission, and the patient was transferred to our institution. On arrival, the CSF anti-NMDAR testing was repeated, which showed a reduction in titer to 1:20, and continuous EEG monitoring (cEEG) was performed for seizure monitoring.

[1]EEG Monitoring Unit, Neurology, Barnes Jewish Hospital, St Louis, MO, USA

Corresponding Author:
Yanfang Shi, 620 Westwood Drive, Apartment 2s, St Louis, MO 63105, USA.
Email: yxs9943@gmail.com

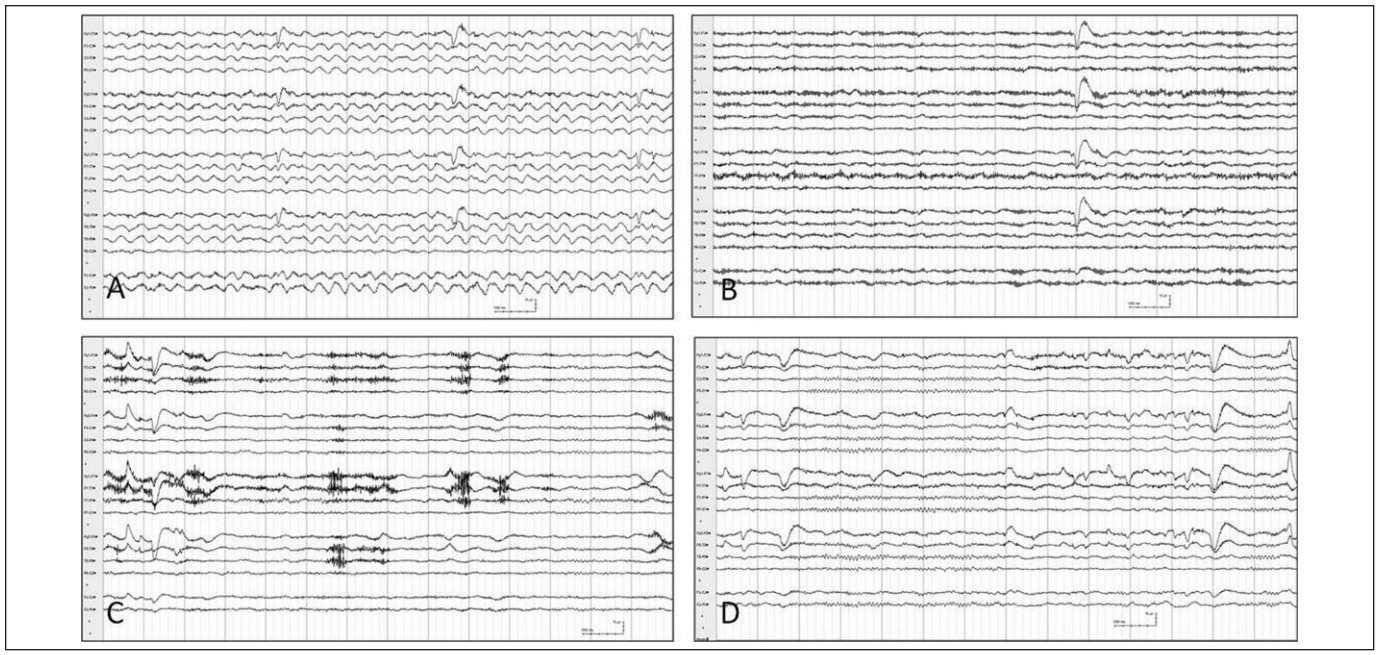

Figure 1. Serial EEGs recorded at the time of 2 months (A), 2.5 months (B), 4 months (C), and 6 months (D) after admission, which showed extreme delta brush (EDB) gradually resolved and return of normal background. Parameters were as follows: sensitivity 7 μV/mm, high-frequency filter 70 Hz, time constant 0.1 seconds.

Initial cEEG, performed at 2 months after clinical onset (Figure 1A), was of 4-day duration and showed EDB, characterized by prolonged periods of generalized 1- to 2-Hz monomorphic delta activity with superimposed bursts of symmetric and synchronous rhythmic beta activity, without variability or reactivity. The EDB occupied more than 50% of the recording and lasted up to several hours, and showed no evolution in frequency, amplitude, or morphology, and did not correlate with frequent orafacial dyskinesia. During the monitoring period, multiple dosages of intravenous midazolam were administered for agitation, without changes in the EDB pattern. No other antiepileptic medications or sedations were prescribed.

Her prednisone was gradually tapered during hospitalization, and the patient showed slow but steady improvement. However, while she showed increased wakefulness and orientation, she continued to have episodes of agitations and autonomic instability, with tachycardia reaching 170 beats/min at 2.5 months. A repeat cEEG of 2-day duration was performed at that time (Figure 1B), which showed intermittent diffuse background slowing and decreased EDB.

Significant clinical improvement was noted at 4 months, during which she was described as interactive; she was also able to read, but occasional hallucinations and delusions were still reported. A repeat cEEG study of 24-hour duration showed mild generalized background slowing without typical EDB (Figure 1C). The patient's clinical conditions continued to improve during the ensuing months. At 6 months, her medications were discontinued and she resumed normal daily living, but with occasional mood disturbances. An EEG of 1-hour duration was again performed at 6 months, which was normal (Figure 1D).

Discussion

EEG abnormalities are very common in anti-NMDAR encephalitis, with EDB being a distinct electrographic finding. While EDB continued to contribute to the diagnosis of anti-NMDAR encephalitis, its significance between ictal and interictal nature remained unclear.

Several distinctions can be made with regard to EDB pattern in this patient. Electrographically, EDB lasted up to several hours without evolution in frequency, amplitude, morphology, or field. Clinically, although the patient had frequent orofacial movements during the monitoring, these events showed no association with EDB. The EDB also showed no changes with midazolam administration. Finally, the EDB showed gradual resolution corresponding to clinical improvement, without antiepileptic treatment.

The EDB pattern in this patient, without electrographic evolution, correlation with clinical paroxysms, or response to benzodiazepine, is supportive that EDB itself is an interictal in contrast to an ictal pattern. Furthermore, the patient's recovery without usage of antiepileptics also suggests that EDB is unlikely to be ictal in nature. EDB itself continues to be useful marker of disease activity and a tool to monitor treatment response and relapses due to its resolution in parallel with clinical improvement.

This case is supportive of prior reports which suggest that EDB is more likely to represent cortical dysfunction rather than a seizure.[2-4] Schmitt et al[2] reported EDB in 30% of patients with anti-NMDAR encephalitis. The patients with EDB tend to have severe disease and with normal MRI, suggesting a more aggressive phenotype. EDB also does not show clinical

or electrographic response to either benzodiazepine or other antiepileptic medications. At least 2 patients demonstrated gradual improvement of EDB over the course of hospitalization. Other authors rule out their ictal nature based on the absence of voltage or field evolution or lack of response to antiepileptic medications. Intracranial pressure (ICP) and surface EEG monitoring, performed by Chanson et al,[5] revealed no increased ICP during EDB, which argues against its ictal nature.

Other cases described EDB or generalized rhythmic delta activity (GRDA) as a nonconvulsive status epilepticus. Kirkpatrick et al[6] described GRDA as a nonconvulsive status epilepticus due to the clear EEG activity that evolved in frequency, voltage, and field but there was no evidence of EDB. Veciana et al[7] reported EDB either following definitive seizures or admixed with the evolving delta activity, but without the clearly defined evolution of EDB itself.

The main strength of this case is the long-term follow-up (up to 6 months after clinical onset) along with the analysis of serial EEG recordings performed at different disease stage, which indicates EDB is a marker of disease activity. Also, our patient did not receive any antiepileptic medications except several doses of midazolam, which enhanced interictal nature of EDB.

EEG is widely available can be a useful diagnostic tool for anti-NMDAR encephalitis. Although EEGs can be abnormal, there are many patterns of indeterminate significance and it is important to avoid over interpretation. The EDB pattern, in particular, should not be considered as ictal unless in conjunction with other compelling evidence.

Declaration of Conflicting Interests

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