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Case Report

Extreme delta brush evolving into status epilepticus in a patient with anti-NMDA encephalitis

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ABSTRACT

Extreme delta brush (EDB) is an EEG pattern unique to anti-NMDA encephalitis. It is correlated with seizures and status epilepticus in patients who have a prolonged course of illness. The etiology of the underlying association between EDB and seizures is not understood. We present a patient with anti-NMDA encephalitis who developed status epilepticus evolving from the high frequency activity of the extreme delta brush. This case demonstrates that EDB is not only a marker for a greater propensity for seizures but also directly implicated in seizure generation.

Introduction

Anti-NMDA encephalitis is an autoimmune disease targeting extracellular epitopes of the NMDAR NR1-NR2 heteromers [1]. This syndrome is characterized initially by headache and psychiatric symptoms followed by encephalopathy, dyskinesias, autonomic instability, and hypoventilation in addition to seizures. It commonly develops in young women who have ovarian teratomas [2].

Patients with anti-NMDA encephalitis have different patterns on their EEG including diffuse rhythmic delta activity, generalized slowing, and EDB. Hirsch et al. observed the EDB pattern in 30% of patients with anti-NMDA encephalitis [3]. Its presence is associated with more severe and prolonged illness and seizures [3]. The etiology of the association of EDB with a propensity to seizures is not understood.

Case report

A 25-year-old right-handed woman without past medical history presented to an outside hospital emergency room with one-week history of headache, photophobia, nausea, and vomiting. Her family reported behavioral changes and that she had become hyperreligious. At the time of her presentation, she had two generalized tonic–clonic seizures. She was admitted to the hospital for evaluation. On day 1 of her admission, her neurological examination revealed mild encephalopathy. Her routine EEG (Fig. 1) and MRI brain with and without contrast were both normal (Fig. 2).

The patient rapidly deteriorated becoming psychotic and developed severe dysautonomia. On day 5, she was placed on continuous EEG (cEEG) that showed emergence of EDB pattern triggering anti-NMDA encephalitis workup (Fig. 1). Subsequently, she went into status epilepticus necessitating addition of antiseizure drugs (ASDs) as well as intubation and sedation. Her seizures arose from the 12- to 16-Hz high frequency activity that was overriding the 1.5- to 3-Hz delta waves seen within the EDB. Her initial LP results were significant for lymphocytic pleocytosis. Initial serum and CSF anti-NMDA titers were negative. Her repeat MRI brain with and without contrast was unremarkable (Fig. 2). She was started on high dose pulse steroids and received a 5-day course of IVIG while performing an extensive paraneoplastic workup that revealed a right ovarian cyst. On day 10, she was taken emergently for oophorectomy, and the pathology revealed ovarian teratoma with mature cortical tissue (Fig. 3). A repeat LP showed persistent lymphocytosis with repeat CSF anti-NMDA positivity and negative serum antibodies.

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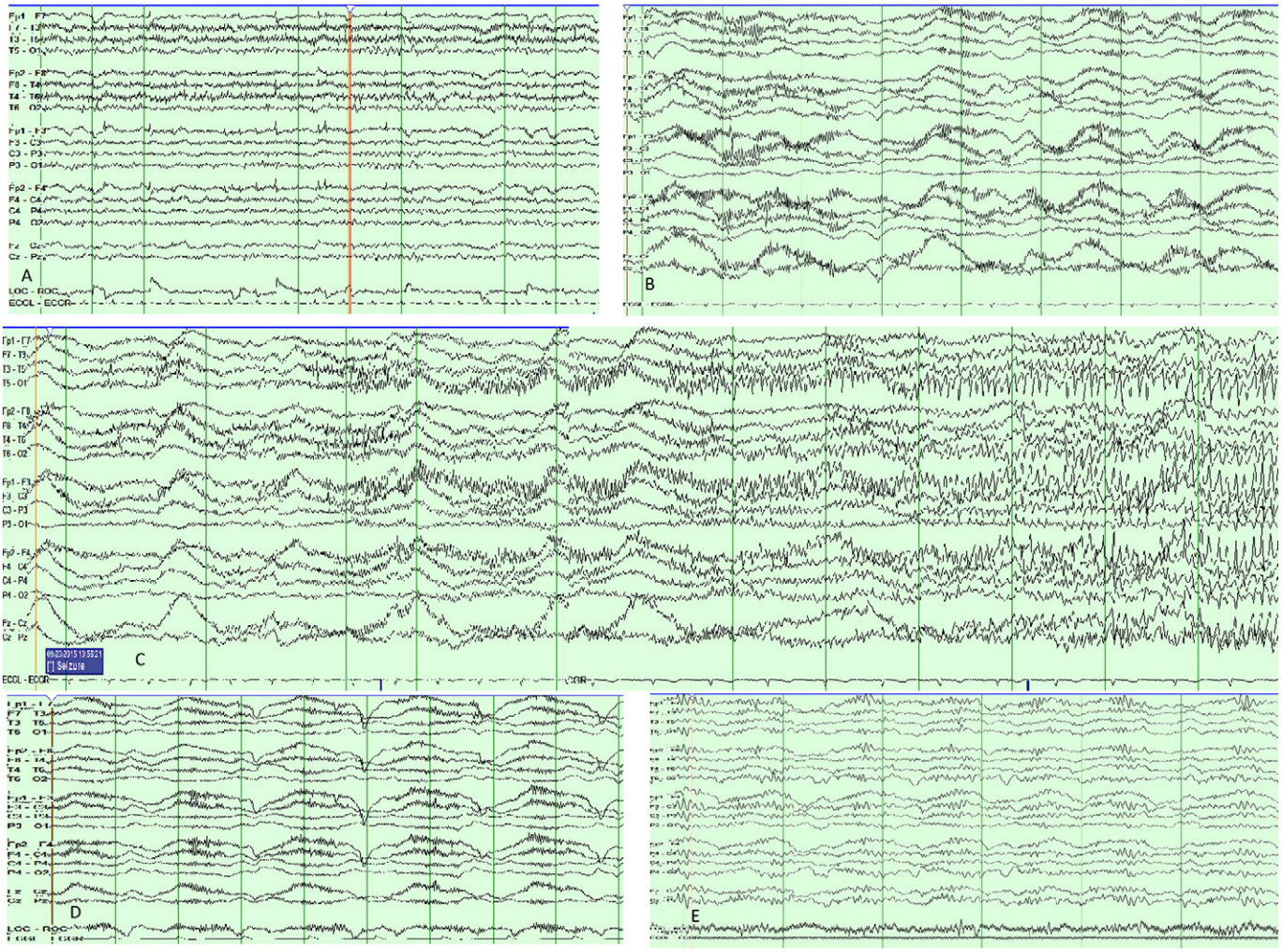

Fig. 1. Serial EEGs performed during hospitalization. A) Day 1: EEG shows a normal background at 9 Hz. Use an arrow/circle to identify the 9 Hz normal background. B) Day 5: there is emergence of EDB pattern with diffuse delta slowing at 1.5–3 Hz with overriding, high frequency activity. Use an arrow to definite the site where the seizure emerges from the EDB. C) Ictal recording showed ictal onset from the high frequency activity overriding the delta activity and generalizes. D) Day 44: EEG recorded choreoathetoid movements that did not have electrographic correlates. E) Day 66: persistent EDB pattern.

Her seizures were controlled on ASDs, but she developed choreoathetoid movements and was severely encephalopathic. Her dysautonomia was worsening too. On day 12, she was started on rituximab. For her dysautonomia, she was started on benzodiazepines and barbiturates. On day 16, repeat cEEG showed persistent EDB without electrographic correlates seen prior, during, and after the

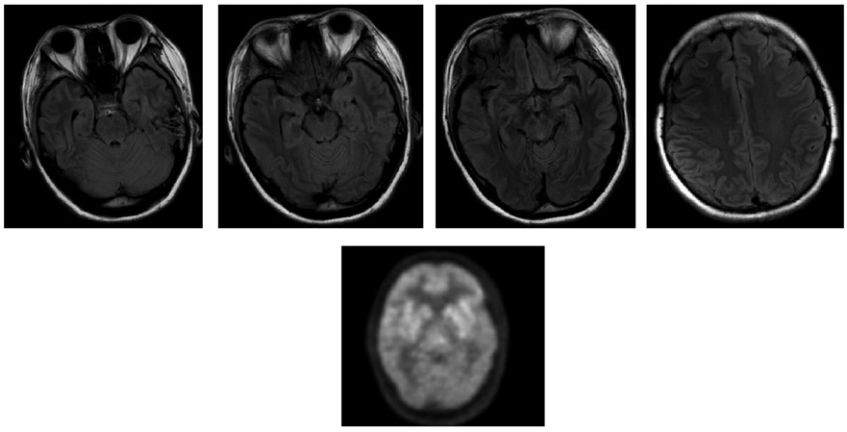

Fig. 2. A) MRI brain with and without contrast that was unremarkable. B) PET scan performed after the resolution of the status epilepticus while having persistent EDB pattern that showed hypometabolism in the bilateral parietal and occipital areas. Pace arrows at the parietal-occipital regions of maximal hypometabolism.

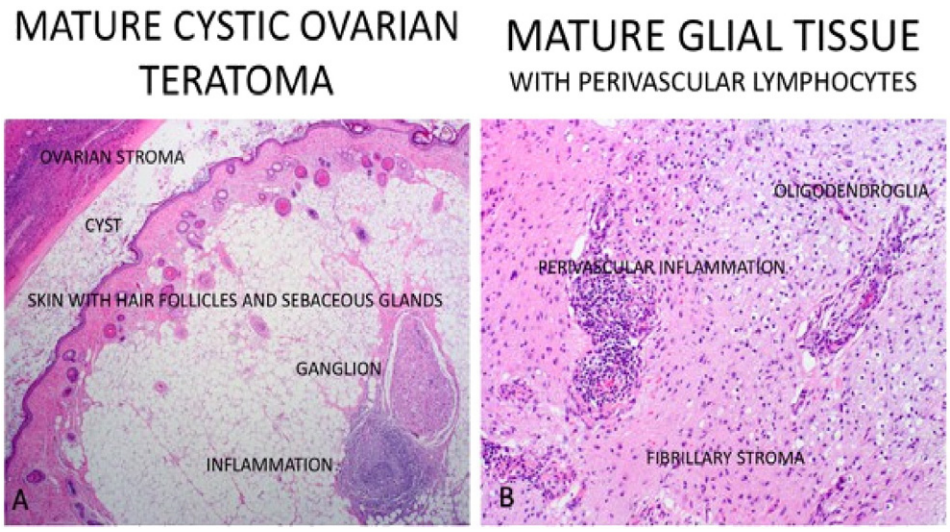

Fig. 3. A) A photomicrographic section of the right ovary that reveals microscopic evidence of the teratoma including B) a single focus of mature brain tissue which is associated with perivascular chronic inflammation and an adjacent prominent inflammatory infiltrate in the stroma of the 3.5-cm mature cystic teratoma.

choreoathetoid movements. On day 20, repeat PET scan showed hypometabolism in bilateral parietal and occipital areas (Fig. 2) as well as normal MRI brain with and without contrast (Fig. 2).

She did not improve clinically and had PEG placement as well as tracheostomy. On day 40, she was started on cyclophosphamide, and as of day 55, she received 5 sessions of plasmapheresis. Her AEDs were titrated down and was kept on two AEDs. On day 66, her EEG showed a persistent EDB pattern. Despite her CSF titers trending down, her clinical status did not improve.

Discussion

Extreme delta brush is a unique pattern described in patients with anti-NMDA encephalitis [3]. The clinical significance of this pattern and its epileptogenic potential is yet to be fully determined. In 2006, Ikeda et al. reported a patient with anti-NMDA antibodies positive in the serum and CSF who had seizures and a pattern on the EEG which they described as "burst and slow complexes". They considered this pattern as "intensive epileptic activities arising from hyperexitability of the cerebral cortex" mostly due to the clinical association [4]. In their series, Schmitt et al. reported 23 patients with anti-NMDA encephalitis out of which 78.3% had seizures [3]. Thirty percent of these 23 patients had EDB, 48% had generalized rhythmic delta activity, and 52% had diffuse excess beta frequency activity attributed to medications. Sixty-one percent of patients had electrographic seizures, and 35% had nonconvulsive seizures. The percentage of those who had EDB as well as seizures was not reported. However, they thought that this pattern could fall on the ictal–interictal continuum but did not consider it consistent with status epilepticus as it does not meet the criteria proposed by Young et al. [5]. VanHaerents et al. reported a patient with anti-NMDA encephalitis and seizures with EDB pattern. However, the seizures captured arose independently from left and right hemispheres [6]. Johnson et al. reported a patient with anti-NMDA encephalitis and nonconvulsive status who had on scalp EEG had rhythmic diffuse sharp and slow wave discharges that were consistent with ictal pattern. There was no EDB pattern observed [7]. Kirkpatrick et al. reported another patient with anti-NMDA encephalitis and generalized rhythmic activity on EEG consistent with nonconvulsive status [8].

In our patient, the seizures arose from the high frequency activity overriding the delta waves of the EDB. The seizures were controlled on multiple ASDs, but the EDB pattern on EEG persisted through numerous ASDs and immunotherapy trials. This case provides evidence of the ictal potential of fast frequencies overriding the delta slowing in an EDB during anti-NMDA encephalitis. A similar phenomenon has been described in periodic discharges associated with fast rhythmic activity add reference and citation. In these cases, the faster frequencies can evolve into discrete seizures. The clear association between this pattern and seizures, documented in this case, confirms that EDB belongs within the spectrum of the ictal–interictal continuum. The implications for management are less certain, as remains the case for many patterns within the ictal–interictal continuum in general.

Conflicts of interest

There are no conflicts of interest to disclose.

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