Original article

Spike persistence and normalization in benign epilepsy with centrotemporal spikes – Implications for management

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Abstract

Purpose: This study was performed 1) to determine the timing of spike normalization in patients with benign epilepsy with centrotemporal spikes (BECTS); 2) to identify relationships between age of seizure onset, age of spike normalization, years of spike persistence and treatment; and 3) to assess final outcomes between groups of patients with or without spikes at the time of medication tapering.

Methods: Retrospective analysis of BECTS patients confirmed by clinical data, including age of onset, seizure semiology and serial electroencephalography (EEG) from diagnosis to remission. Age at spike normalization, years of spike persistence, and time of treatment onset to spike normalization were assessed. Final seizure and EEG outcome were compared between the groups with or without spikes at the time of AED tapering.

Results: One hundred and thirty-four patients were included. Mean age at seizure onset was 7.52 ± 2.11 years. Mean age at spike normalization was 11.89 ± 2.11 (range: 6.3–16.8) years. Mean time of treatment onset to spike normalization was 4.11 ± 2.13 (range: 0.24–10.08) years. Younger age of seizure onset was correlated with longer duration of spike persistence ($r = -0.41$, $p < 0.001$). In treated patients, spikes persisted for 4.1 ± 1.95 years, compared with 2.9 ± 1.97 years in untreated patients. No patients had recurrent seizures after AED was discontinued, regardless of the presence/absence of spikes at time of AED tapering.

Conclusion: Years of spike persistence was longer in early onset BECTS patients. Treatment with AEDs did not shorten years of spike persistence. Persistence of spikes at time of treatment withdrawal was not associated with seizure recurrence.

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Keywords: Epilepsy; BECTS; Electroencephalography (EEG); Spike

1. Introduction

Benign epilepsy with centrotemporal spikes (BECTS) is the most common idiopathic focal epilepsy in childhood and the most prevalent epilepsy syndrome in school-aged children [1]. Its self-limited nature is well

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characterized by spontaneous remission before adulthood [2–6]. Due to its self-limited course and potential side effects of anti-epilepsy drugs (AEDs), treatment with AEDs is often not recommended. However, emerging data on neuropsychological problems in patients with BECTS suggests that the syndrome is not entirely benign [7–11].

Even though the number of untreated patients is increasing, BECTS was usually treated in South Korea due to the unique social and cultural environment and parental concerns of having recurrent seizures. We have observed that some BECTS patients with early seizure onset show very late normalization of spike discharges compared to late onset patients. Centrotemporal spikes are known to disappear by age of 18 years or adulthood [3,12] but there are no specific details of spike normalization that would be helpful for counseling and treating patients. There are few reports that compared long-term prognosis in patients with EEG abnormalities at the time of anticonvulsant withdrawal [13].

The clinical questions addressed in this study are: 1) When do the centrotemporal spikes resolve? 2) Is there an association between age of seizure onset and age of spike normalization? 3) Does treatment have any effect on spike normalization? 4) When do the spikes disappear after treatment? 5) Is there any difference in seizure recurrence between groups with and without spikes at time of AED tapering? To answer these questions we conducted a retrospective cohort study with analysis of serial EEGs from onset to remission in BECTS patients with confirmed remission of seizures based on long-term follow-up data.

2. Methods

2.1. Patient selection

We searched for the patients who had the diagnosis of BECTS using the Clinical Data Warehouse (CDW) system from Seoul National University Children's Hospital and Seoul National University Bundang Hospital. We also performed retrospective medical record review to confirm the diagnosis of BECTS according to ILAE criteria [14]. Patients not meeting ILAE criteria, showing an atypical progression [15,16], with short follow-up duration or lost to follow-up were excluded. Only patients with serial routine (sleep with or without waking) EEGs from onset to remission and sufficient data to confirm the typical self-limited nature were included.

2.2. Data collection

Demographic and clinical characteristics regarding gender, age of seizure onset, follow-up duration, and treatments were retrieved after reviewing electronic

medical records. The first recognized typical clinical Rolandic seizure was used as age of seizure onset. Data regarding treatment such as the age of treatment initiation, tapering, and complete withdrawal were also reviewed. Age at additional reported seizures was calculated based on medical records. Serial EEG findings from onset to remission were reviewed for presence or absence of centrotemporal spikes. Only the EEGs with sleep recording of at least 20 min were included for the data collection.

2.3. Analyses

We defined the age of spike normalization as the patient's age at which spike disappearance was first noted and persisted from serial EEG examinations. Distribution of age of spike normalization was also analyzed. Since the age of seizure onset and age at BECTS diagnosis varied widely, we defined and measured years of spike persistence as years from BECTS diagnosis to age of spike normalization. We further analyzed the data to identify whether years of spike persistence was associated with age of seizure onset. To exclude the possible confounding effect of treatment, we selected only a subgroup of untreated patients and analyzed the association between age of seizure onset and years of spike persistence. We compared years of spike persistence of treated and untreated patient groups to find any effects of treatment on spike normalization. Seizure recurrence during and after tapering were compared between the groups with or without spikes at the time of AED tapering.

2.4. Statistical analyses

The Shapiro–Wilk test was used to check normal distribution of variables. Either the student's *t*-test or the Mann–Whitney *U* test was used accordingly. Correlation between continuous variables was assessed by prediction model using linear regression. Statistical significance was defined as $p < 0.05$.

3. Results

3.1. Patients

Among 170 patients with confirmed BECTS diagnosis, 134 patients with sufficient follow-up information to confirm a typical benign course were included. The reasons for exclusion were lost to follow-up (23 patients), and atypical progression (13 patients.) There was prominent male predominance (male:female = 1.73:1). Average follow-up duration was 4.79 (range: 2.5–10.4) years and 6.1 (range: 3–11) serial EEGs were reviewed on average (Table 1). Anticonvulsants used in this cohort were mostly oxcarbazepine (87%), lamotrigine,