Original article

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Benign childhood epilepsy with centro-temporal spikes (BCECTS): early onset of seizures is associated with poorer response to initial treatment

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ABSTRACT – *Aim.* Benign childhood epilepsy with centro-temporal spikes (BCECTS) is the most common idiopathic partial epilepsy in children. Treatment attitudes remain a controversial issue. We examine features that could suggest refractoriness at onset. *Methods.* We retrospectively reviewed the medical records of 144 children with BCECTS diagnosed at the Division of Pediatric Neurology, Asan Medical Center, from March 1, 1995, to April 30, 2002 and treated with AEDs. The patients were subdivided into two groups according to the number of antiepileptic drugs used for effective seizure control. *Results.* Of the 144 patients, 75 were male and 69 were female, with a mean age at seizure-onset of 7.2 ± 2.3 years (range, 2.1-14.3 years); 119 children were taking one antiepileptic drug (AED) (Group A), and 25 were taking more than one (Group B). There were no significant group differences in female-to-male ratio, prescribed AEDs, number of seizures before the start of treatment, interval between seizure-onset and start of treatment, presence of secondarily generalized seizures, or presence of bilateral EEG abnormalities. The groups differed however, in mean age at seizure onset (7.6 ± 2.2 years *versus* 5.1 ± 1.9 years, $p < 0.05$) and percentage of patients with seizure-onset before 3 years ($p < 0.05$). *Conclusions.* When treated with AEDs, children with BCECTS usually respond well. However, an earlier onset of seizures is associated with more frequent seizures and initial refractoriness to medical treatment.

Key words: benign childhood epilepsy with centro-temporal spikes (BCECTS), refractory rolandic epilepsy, treatment, idiopathic epilepsy

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According to the ILAE classification benign childhood epilepsy with centro-temporal spikes (BCECTS) is a form of idiopathic partial epilepsy characterized by typical, brief, unilateral motor seizures preferentially involving the face and the oropharyngeal musculature. Secondary ge-

Table 1. Dermographic data of 144 patients with BCECTS.

		Group A	Group B
Number		119	25
Male/female		64/55	11/14
Age at seizure-onset (years)		7.6 ± 2.2	5.1 ± 1.9
Duration of follow-up (years)		4.5 ± 3.2	4.8 ± 2.1
Family history of epilepsy or febrile seizure	Epilepsy	2	0
	Febrile seizures	6	0
Past history of seizures or febrile seizures	Neonatal seizures	3	0
	Febrile seizures	6	1
Antiepileptic drugs	Carbamazepine	40	13
	Oxcarbazepine	72	8
	Valproate	3	4
	Lamotrigine	2	0
	Topiramate	2	0

neralization is observed in almost 20% of the patients. Interictal EEG findings include slow, diphasic, high voltage, centro-temporal spikes that are activated by sleep. The seizures, which usually appear in the first decade of life and disappear during the second, typically occur in otherwise healthy children who show no evidence of cerebral lesions. BCECTS is considered as having a genetic etiology, although to date no genes have been identified. The EEG marker is probably inherited as an autosomal dominant trait with age-related penetrance, although only about 10% of children inheriting this trait actually have recognized seizures (Kramer *et al.* 2002). Thus, whether or not a child develops BCECTS depends on various other factors, some of which may be inherited.

A minority of affected children however, present with atypical features (Aicardi 2000, Hahn 2000, Saint-Martin *et al.* 2001, Verrotti *et al.* 2002). Among the atypical features, frequent seizure recurrence (Kramer *et al.* 2002), refractoriness to medical treatment (Ong HT and Wyllie E, 2000, Deonna *et al.* 1986, AL-Twajri and Shevell 2002, Blom *et al.* 1982), cognitive decline (Yung *et al.* 2000, Welgage *et al.* 1997, Baglietto *et al.* 2001, Staden *et al.* 1998), and episodes of status epilepticus (Fejerman and Di Blasi 1987) have been reported. These features appear to occur in children with an earlier age-at-onset of seizures.

Most children have only rare seizures and, when treated, the response to antiepileptic drugs is good, indicating a low epileptogenicity of the focus which remains clinically silent in over 90% of cases (Arzimanoglou *et al.* 2004, Dalla Bernardina *et al.* 2005). However, in a poorly identified subset of children with BCECTS, more than one AED is required for an effective control of seizures. Only a few studies are available on factors associated with initial poor response to AEDs (Kramer *et al.* 2002). We therefore compared two groups of children with BCECTS, one group using one AED and a second group that required more than one AED, in an effort to determine the factors associated with the use of multiple AEDs for seizure control.

Methods

Patients were selected by reviewing all EEG reports in the Division of Pediatric Neurology, Asan Medical Center (a tertiary care referral epilepsy center), between March 1, 1995, and April 30, 2002.

Patients were included in the study when: 1) they presented with typical EEG features containing either spikes in one or both centro-temporal regions or spikes with typical rolandic morphology; 2) they had more than two attacks of seizures with typical BCECTS semiology; 3) they had been followed up at least every three months and had at least one EEG every year, for a minimum of two years. Other AEDs were added when secondarily generalized seizures were refractory to initial AED treatment. Patients with any simultaneous features suggesting another epilepsy syndrome were excluded. Patients were divided into two groups according to the number of AEDs used for effective seizure control. In Group A we included children that received only one AED, and in Group B patients that have been administered more than one AED (*table 1*).

The Mann-Whitney U test was used to compare the two groups with respect to mean age-at-seizure onset, number of seizures experienced before treatment, and interval between seizure-onset and initiation of AED.

Chi-square analysis was used to compare the two groups with respect to sex; type of AED initially used; unilateral or bilateral EEG abnormalities; occurrence of secondarily generalized seizures; and family history or past history of epilepsy or febrile seizure. Statistical significance was assumed for $p < 0,05$.

Table 2. Age-at-onset of seizures in Group A and Group B.

Age at seizure-onset (years)	Group A	Group B
< 3	1	3
≥ 3	118	22

Group A: group taking one AED for effective seizure control.
Group B: group taking more than one AED for effective seizure control.

Data processing and analysis were performed by SPSS 13.0 version.

Results

The entire study cohort consisted of 144 patients with BCECTS, 75 males and 69 females, with mean age at disease onset of 7.2 ± 2.3 years (range, 2.1-14.3 years). Of the 144 patients, 119 were taking one AED (Group A), and 25 were taking more than one AED (Group B). There were no significant differences between the two groups with regard to the female-to-male ratio; prescribed AEDs; number of seizures before treatment onset; interval between seizure-onset and start of treatment, the presence of secondarily generalized seizures, the presence of bilateral epileptiform activity or the duration of follow-up. The two groups differed, however, as regards the mean age of onset, which was 7.6 ± 2.2 years in Group A and 5.1 ± 1.9 years in Group B ($p < 0.05$). The two groups also differed in the percentage of patients with seizure-onset below three years old ($p < 0.05$, *table 2*), and the distribution of seizure-onset age (*table 3*).

Discussion

The long-term prognosis for children with BCECTS is usually excellent, in that, when treated, they respond well to AEDs, even those who initially experience frequent and troublesome seizures, with almost all patients achieving long-term remission by mid-adolescence.

In our study, we considered as atypical an evolution that necessitated the use of more than one AED for the control of seizures, a marker of initial medical refractoriness. Of the 144 children studied, 25 (17.4%) were taking more than one AED. There was a significant difference in mean age-at-onset between this group and the group of 119 children taking one AED. There was also a significant difference in the percentage of children in each group with age at seizure-onset below 3 years old, suggesting an association between earlier seizure-onset and medical refractoriness, a finding confirming previous results (Al-Twajri and Shevell 2002, Loiseau *et al.* 1988). Our findings suggest that, although BCECTS is an age-related epilepsy syndrome, following its own evolution and tending to disappear at a certain age regardless of age at onset, children who experience earlier seizure-onset are likely to be more refractory to initial medication whereas those who experience later seizure-onset are likely to be controlled by initial medication.

These features may be partially explained by the multifactorial pathogenesis of BCECTS (Doose and Baier 1989, and Doose *et al.* 1996). Thus, the complexity of causal factors may account for a wide spectrum of epileptic and non-epileptic conditions, ranging from mild, selective performance deficits to complex psychomental retardation, and from simple BCECTS to severe epilepsies with minor seizure and bioelectrical status. These conditions are not strictly syndromes, but sets of variably weighted symptoms of a complex pathogenetic background. In addition, these features may be explained by genetically different

Table 3. Age distribution of seizure-onset.

Seizure-onset age (years)	Group A	Group B
2 ≤ 3	1	3
3 ≤ 4	4	2
4 ≤ 5	10	5
5 ≤ 6	14	8
6 ≤ 7	16	4
8 ≤ 9	21	1
9 ≤ 10	25	0
10 ≤ 11	8	2
≤ 12	20	0

Group A: group taking one AED for effective seizure control.
Group B: group taking more than one AED for effective seizure control.

mechanisms between early-onset BCECTS and late-onset BCECTS.

This being a retrospective study, based on an EEG data selection of the patients, some limitations need to be underscored. Our data on seizure frequency were based on patients' reports, and we cannot exclude that seizures with secondary generalization were more systematically reported as compared to a minor, sensorimotor event. Patients with a very benign evolution may have been lost from follow-up and consequently not included. A control group of patients with BCECTS that did not receive any treatment would be of value. A future prospective study addressing refractoriness of BCECTS, should take into consideration these remarks.

Although BCECTS with early seizure-onset may prove to be refractory to initial medical treatment, the long-term prognosis for BCECTS is excellent, with almost all patients achieving long-term remission by mid-adolescence. However, minor atypical clinical and electrographic features are not uncommon. Thus, in children with early-onset of rolandic seizures, the physician should inform the patient and the family that a relatively refractory course may be observed, which should not necessarily be interpreted as a reason to question the diagnosis of BCECTS and the overall satisfactory evolution. □

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