

# Evolution de l'épilepsie bénigne à pointes centro temporelle: étude à propos de 24 cas

## Outcome of benign childhood epilepsy with centro temporal spikes: A study of 24 cases

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### RÉSUMÉ

**Introduction :** L'épilepsie bénigne à pointes centro temporelle (EPCT) est l'épilepsie focale la plus fréquente chez l'enfant. Le but de notre travail était de décrire les particularités épidémiologiques et évolutifs de l'épilepsie à pointes centro temporelles (EPCT) chez nos patients.

**Patients et méthodes :** Nous avons mené une étude rétrospective de tous les cas d'EPCT colligés dans notre service entre 2010-2017. Les critères d'inclusion : absence d'antécédents médicaux personnels ; début entre 2 et 16 ans ; crises focales avec ou sans généralisation secondaire ; anomalies EEG intercritiques à type de pointes focalisées sur les régions centro temporelles et activées par le sommeil.

**Résultats :** Nous avons colligés 24 cas d'EPCT. Tous nos patients étaient âgés entre 3 et 11 ans. Les crises étaient focales dans tous les cas avec perte de l'état de conscience dans 16 cas/24, (66%). Une généralisation secondaire a été notée dans 6 cas (25%). Un traitement anti épileptique a été prescrit chez 22 patients. Le recul moyen était de 4 ans. Au cours de l'évolution, 2 patients (8.3%) avaient une crise isolée, 16 (66%) 2 à 5 crises et 5 (20%) 6 à 10 crises. Cinq patients (20.8%) ont présenté des troubles de l'attention et de concentration et une baisse des performances scolaires.

**Conclusion :** Notre travail illustre que l'EPCT est loin d'être une épilepsie bénigne. Des complications neuro-psychologiques à type de trouble de l'attention et du comportement sont fréquentes.

### ABSTRACT

**Introduction :** Benign childhood epilepsy with centrotemporal spikes (BECTS) is the most common form of benign childhood focal epilepsy. We conducted this study in order to describe the specific clinical characteristics and outcomes of BECTS in our area.

**Patients and methods :** We conducted a retrospective study of all cases of BECTS treated by our department from January 2010 to December 2017. During this period, 24 children aged 2 to 16 years of age were diagnosed with BECTS and enrolled for long-term follow-up. The diagnosis was based on characteristic seizure manifestations and the typical EEG pattern of spikes or sharp waves in the centrotemporal area.

**Results :** All patients had their first seizure between the ages of 3 and 11 years. Most patients presented with simple partial seizures (16/24, 66%), while 6 patients (25%) developed secondary generalized seizures. Twenty-two patients received anti-epileptic drugs to control recurrent seizures. The mean duration of follow-up was 4 years. Two patients (8.3%) experienced only a single seizure, 16 patients (66%) had 2 to 5 seizures over the course of the disease, and 5 patients (20%) had 6 to 10 seizures. Five patients (20.8%) exhibited major behavioral problems at school and deficits in concentration.

**Conclusion :** BECTS is a benign childhood epilepsy with generally favorable prognosis. However, a fraction of patients show learning disabilities and behavioral disturbances, particularly during the most active phase, and may require additional or continued therapy.

**Mots clés :** enfant, épilepsie, pointes centro-temporelles

**Keywords :** child, epilepsy, centrotemporal spikes

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## INTRODUCTION :

Benign childhood epilepsy with centrotemporal spikes (BECTS) is the most common form of benign childhood focal epilepsy, with an incidence of approximately 21/100,000 [1] and accounting for 20–25% of all childhood epilepsies [2]. It is classified as an idiopathic localization-related epilepsy [3]. BECTS has a characteristic age at onset, seizure pattern, neurodevelopmental profile, neuroimaging and electroencephalographic pattern, and higher prevalence during sleep [3].

Timely diagnosis is critical for successful management during the course of the illness. While spontaneous remission occurs in most cases, BECTS patients may develop behavioral or cognitive problems [4–7]. Furthermore, atypical features such as status epilepticus, developmental delay, daytime-only seizures, screaming during seizures, and postictal Todd's paresis may occur [2,8].

There is limited clinical data on BECTS in Tunisian children, so prognoses and treatment strategies are based on clinical studies of other populations. We conducted a retrospective review of 24 local cases of BECTS in order to describe the specific clinical characteristics and outcomes in our area. Furthermore, we compared our results to earlier studies and to the conclusions of a previous meta-analysis.

## METHODS :

We conducted a retrospective study of all cases of BECTS treated by our department from January 2010 to December 2017. During this period, 24 children aged 2 to 16 years of age were diagnosed with BECTS and enrolled for long-term follow-up. This case series study was approved by the institutional board of research ethics and informed written consent was obtained from all parents or guardians. The diagnosis was based on characteristic seizure manifestations, including the typical EEG with spikes or sharp waves in the centrotemporal area that may or may not lead to secondary generalized seizures. Aside from seizure history and these EEG findings, all patients were normal as assessed by neurological examination or neuroimaging (including cranial computed tomography [CT] and/or magnetic resonance imaging [MRI]).

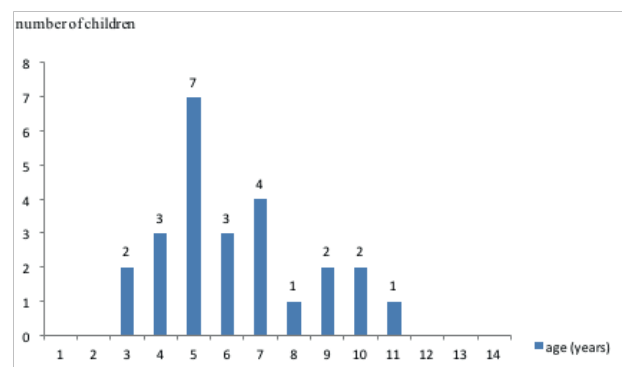
We distinguished atypical from typical BECTS by the criteria of Datta and Sinclair [2]. Patients exhibiting earlier onset of epilepsy (before the age of 4 years), learning problems, abnormal neurological examination at onset, other seizure types, or atypical EEG abnormalities were classified as having atypical BECTS. The information obtained from each patient also included family history of epilepsy, history of febrile convulsions, age at onset and recovery, disease duration, seizure frequency, features of individual seizure episodes, and the occurrence of secondary generalized seizures. Finally, we determined long-term outcome, focusing on the presence of developmental delay and learning difficulties.

## RESULTS :

### Epidemiology

Over a 8-year period, 24 children (14 boys and 10 girls) out of the 571 cases of child epilepsy treated by our department met the inclusion criteria of BECTS. During the same period, we also registered 2 children with Panayiotopoulos syndrome and 8 children with idiopathic childhood occipital epilepsy of Gastaut. The incidence of partial idiopathic epilepsy was 5.9% (34/571); BECTS represented 4.2% of all child epilepsy cases and 70% (24/34) of all partial idiopathic epilepsy cases treated.

Age at first seizure ranged from 3 to 11 years (mean age, 6 years and 8 months) but a large fractions (14/24, 58%) had their first seizure between the ages of 5 and 7 years (Figure 1).



**figure 1:** Distribution of age at onset of seizures

A family history of epilepsy was found in 3 cases (12.5%) and febrile seizures were reported in 2 cases (8%). Three patients (12.5%) had febrile seizures before the onset of BECTS.

### Clinical features

Most patients (16/24 or 66%) had simple partial seizures, 6 patients (25%) developed secondary generalized seizures, and two patients (8.3 %) had primary generalized seizures (Table 1).

**Table 1 :** Clinical information of patients

Characteristics	Number of cases(%)
<b>Sex</b>	
Male	14 (58,3)
Female	10 (41,6)
<b>Types of seizures</b>	
Partial	16(66)
Primary generalized	2 (8,3)
Secondary generalized	6(25)
<b>Time of seizures</b>	
Sleeping	18 (75)
Waking	2 (8,3)
Both	4 (16,6)
<b>Number of seizures before enrollment</b>	
1	7 (29)
2-3	13 (54)
>3	4 (16,6)
<b>Treatment</b>	22(91,6)
VPA	21 (87,5)
CBZ	1 (4)
<b>Number of seizures at the end of the study</b>	
1	2 (8,3)
2-5	16 (66)
6 -10	5 (20)
>10	1 (4)

During seizures, most patients exhibited unilateral facial sensory-motor and oropharyngolaryngeal symptoms, hyper-salivation, and speech arrest (75%). Loss of consciousness occurred in 8 patients (33%). Eighteen patients (75%) had seizures only during sleep, while 2 patients (8.3%) had seizures while awake and 4 patients (16.6%) had seizures in both the sleeping and waking states. Before clinical intervention, 7 patients (29%) had only one seizure, 13 (54%) had two or three seizures, and 4 (16.6%) had more than three seizures. Individual seizure episodes were brief, lasting 1 to 3 minutes in 42.6% of the cases. However, in 11 cases (46%), seizures lasted from 10 to 15 minutes. Most patients underwent cranial CT (75%) or MRI examinations (8%); these tests revealed no CNS abnormalities.

### **Electroencephalographic findings**

In all cases, the interictal EEG had a normal background with high amplitude, repetitive, diphasic spikes. The spikes were confined to one hemisphere in 20 cases (83%) and occurred bilaterally in 4 cases (17%). When unilateral, spikes were more frequent in the right hemisphere (60%). These interictal spikes were more frequent during sleep in all patients, and 30% of patients showed interictal spikes only during sleep.

Two patients had brief generalized spike-and-wave discharges, but with no concurrent absence seizures. These discharges were present in the awakening state.

### **Subtype of BECT**

Based on the criteria of Datta and Sinclair [2], twenty children had typical BECTS and four had atypical BECTS, including 2 cases with age at onset younger than 4 years and 2 cases with atypical EEG abnormalities.

### **Treatment**

Twenty-two patients (91.6%) received anti-epileptic drugs (AEDs) after recurrent seizures. The mean number of seizures before drug treatment was 2.28. Among AED-treated patients, 21 (87.5%) were prescribed valproic acid and one was given carbamazepine. One patient with atypical BECTS was treated with more than one drug due to incomplete seizure control. The mean duration of drug treatment was 2.9 years and 10 patients were still under treatment at the end of the study. For those children no longer taking AEDs, two experienced relapse, at four and six months after treatment ceased.

### **Outcome**

All BECTS patients were monitored for at least 3 years and 48% were still receiving follow-up care at the end of this study. The mean duration of follow-up was 4.05 years after the initial seizure.

Two patients experience only one seizure (8.3%), 16 (66%) experienced 2 to 5 seizures, 5 patients had 6 to 10 seizures, and only one (4%) experienced more than 10. In total, 74% of the patients had fewer than five seizures.

The average age at seizure remission for patients taken off AEDs was 9.3 years. The mean time to seizure-free status in this group was approximately 2 years.

Nineteen children (79%) attended regular school classes and all maintained average or above average grades. However, five patients (20.8%) exhibited major behavioral problems at school and deficits in concentration. Three of these children (12.5% of the total patient group) were no longer in regular school, while two (8.3%) attended but with poor results.

We tested sex, age at onset, diurnal pattern, seizure type, seizure duration, the time interval between the first and second seizures, and EEG spike frequency as candidate prognostic indices of seizure frequency to define risk factors for recurrence. However, seizure frequency was not significantly different between sexes or other defined subgroups ( $P > 0.05$  by Chi-square test). Furthermore, the outcome of the four patients with atypical BECTS was similar to those with typical BECTS. In fact, among these four patients, three were free of seizures before the end of the study (at 7, 9, and 10 years of age) and none of the three exhibited learning difficulties or any other behavioral problems. Only one atypical BECTS patient, with an earlier age at onset than the other three, still had seizures (2/year) at the end of the 4 year follow-up.

## **DISCUSSION :**

In this study, benign childhood epilepsy with centro-temporal spikes (BECTS) exhibited a male predominance (58.3%), consisted with similar case series reported from other countries [9-12]. The age at onset ranges from 3 and 13 years, with most patients experiencing their first seizure at 7-8 years of age and recovering by the age of 16 [8, 12-16]. In the current study, the age at onset was between 3 and 11 years and the majority of initial seizures (58%) occurred between 5 and 7 years of age, in general accord with previous studies.

BECTS is characterized by partial or secondary generalized seizures, most often during sleep. Previous studies reported that only 5-20% of patients had seizures during the waking state only, whereas 15% had seizures during both sleep and waking states [10, 17]. We found that 75% of Tunisian children with BECTS experienced seizures during sleep, especially soon after falling asleep and shortly before waking, while only 8.3% had seizures only while awake, and 16.6% had seizures in both the sleeping and waking states. Seizures in BECTS patients are typically partial with parasthesias and tonic or clonic activity of the lower face associated with drooling and dysarthria. In our study, 91% of patients presented with partial seizures, while only 8.3% had primary generalized seizures.

The classical EEG presentation of BECTS shows normal background with high-voltage diphasic spikes

or sharp waves in the centrotemporal area. These discharges may be seen individually, or in clusters, with individual spikes repeating at 2 Hz [2, 9, 10]. Spikes or sharp waves most commonly originate in the central or centrotemporal area. They may be synchronous, or spread to frontal, parietal, or occipital regions, and can sometimes spread from one hemisphere to the other. Again, most of our cases shared these general characteristics. Lerman [10] reported that approximately 60% of seizures had a unilateral focus, whereas 40% showed bilateral lesions. In addition, the spikes or sharp waves could be synchronous or asynchronous, symmetrical or asymmetrical. However, we found that the spikes were confined to one hemisphere in most (83%) of patients and occurred bilaterally in only 17%.

Massa et al. [5] monitored 60 patients with BECTS and concluded that patients at greater risk for neuropsychological impairments had at least three of six distinct interictal EEG patterns: intermittent slow-wave focus, multiple asynchronous spike-wave foci, long spike-wave clusters, generalized 3 Hz spike wave discharges, conjunction of interictal paroxysms with negative or positive myoclonia, and/or frequent interictal abnormalities during both wakefulness and sleep.

BECTS is considered benign because it is usually well controlled by anti-epileptic drugs (AEDs) and demonstrates spontaneous remission. It has even been proposed that patients with BECTS do not require antiepileptic drugs or should receive only low doses [9, 11]. However, Blom et al. [18] reported that a few patients were refractory to AEDs. In our study, 91% required AED treatment (mean of 2.9 years) for adequate seizure control, but only two relapsed once AED treatment was stopped.

Bouma et al. [13] conducted a meta-analysis of 20 publications that examined a total of 794 patients with BECTS. In this large patient sample, seizures occurred only once in 15.6% of patients, 2 to 5 times in 62.1%, 6 to 15 times in 17.3%, and more than 15 times in 5.3%. Thus, 77% of the patients had less than five seizures, similar to the proportion found in our study. In the meta-analysis, secondary generalized seizures occurred in 43.5% of patients, significantly higher than found in the current study. Follow-up was successfully conducted without AED in 18.4% of these patients. Anti-epileptic drug treatment was successfully discontinued in 87.8% of these patients and only 14.2% experienced seizure recurrence after termination of AED therapy. Finally, seizure remission was confirmed in 97.7% of all patients. The authors concluded that future seizures cannot be determined with certainty at first presentation. In other words, it is difficult to predict at the time of onset whether a patient will require prolonged AED treatment to suppress subsequent seizures. On the contrary, several risk factors have been identified that suggest a longer duration of the active seizure period and more frequent recurrence. Shorter intervals between the first three sei-

zures, a younger age at onset (less than 4 years), the presence of recurrent generalized tonic-clinic seizures (GTCS), and seizures in both sleep and waking states suggest a longer and more severe peak period requiring early AED treatment [19].

There are no case-control studies to guide the choice of AEDs for BECTS patients, so treatment is based on experience and known drug efficacy and tolerability. Thus, CBZ or VPA are the best choice for BECTS patients. Sulthiame and GBP are good second options for CBZ- and VPA-refractory cases. In all cases, however, AED treatment should be as brief as possible. Usually the treatment lasts for 1-2 years after the last seizure, and then treatment is discontinued without waiting for the disappearance of centrotemporal (Rolandic) spikes [19].

Although the ultimate prognosis for BECTS is excellent, recent neuropsychological studies using more sophisticated tests demonstrated that Rolandic spikes could interfere with specific cognitive and behavioral functions. Between 28% and 53% of children with BECTS displayed neuropsychological abnormalities during the active phase of epilepsy, including difficulties with auditory-verbal and visuospatial memory tasks, deficits in test of executive function, language impairments, attention disorders, learning disabilities, and behavioral disturbances [20]. Similarly, 20.8% of our patients exhibited major behavioral problems at school and impaired concentration. However, we do not know whether these neuropsychological abnormalities are a consequence of persistent Rolandic spikes or if cognitive deficits preceded the onset of epilepsy. Furthermore, it remains uncertain whether chronic AED treatment can prevent neuropsychological dysfunction in this subgroup of BECTS patients [19].

## CONCLUSION :

BECTS is a benign childhood epilepsy with generally favorable prognosis. However, a fraction of patients show learning disabilities and behavioral disturbances, particularly during the most active phase, and may require additional or continued therapy.

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