Vol. 48 (2023) No. 4 TIMOK MEDICAL GAZETTE Review article

Self-limited epilepsy with centrotemporal spikes - an old acquaintance in a new guise

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Summary: The International League Against Epilepsy (ILAE) in 2017, in its latest classification, lists Self-limited epilepsy with centrotemporal spikes (SeLECTS) among childhood focal epilepsies. The cardinal feature of rolandic epilepsy is focal epileptic seizures. Seizures can manifest in various ways, usually classified into groups of symptoms: 1) unilateral facial sensory-motor symptoms (30% of patients); 2) oro-pharyngo-laryngeal symptoms (53% of patients); 3) speech impairment (40%); 4) hypersalivation (30%). There is a clear influence of sleep, drowsiness, and sleep deprivation on seizure frequency. Three-quarters of seizures occur during nonREM sleep, mostly at the beginning of sleep or just before waking up. Febrile convulsions are often encountered in personal history (5-15%). A positive family history is often found in SeLECTS, indicating a genetic etiology. EEG findings: High-voltage spike-wave complexes activated during drowsiness and sleep are a striking feature of this entity (essential for diagnosis). The initial part of the graph element is usually described as a spike, although precise measurements often show it to be a sharp wave. The site of occurrence is typical, and most earlier names for this syndrome referred to that site. Furthermore, it has been shown that the frequency of spike-wave complexes depends on the state of wakefulness, i.e., they occur more often during sleep. Moreover, in repeated EEG registrations, the site of occurrence can change, so the epileptic focus often appeared in a different location compared to previous registrations ("spike migration"). This also involved a change of hemisphere, which was strong evidence against a structural lesion, i.e., indirect evidence that this is the entity in question. With the expansion of knowledge about benign childhood epilepsy with centrotemporal spikes, it is generally accepted that there are small but statistically significant abnormalities in the cognitive, behavioral, and emotional fields of children with this type of epilepsy.
Keywords: epilepsy/classification; self-limited epilepsy with centrotemporal spikes, electroencephalogram, high-voltage spike-wave complexes, focal epileptic seizures

INTRODUCTION

The International League Against Epilepsy (ILAE) in its 2017 classification includes Self-Limited Epilepsy with Centrotemporal Spikes among pediatric focal epilepsies [1].

The clinical manifestation typical of Self-limited epilepsy with centrotemporal spikes (SeLECTS) according to van Hufflen was first described by Martinus Rulandus in the 17th century (639/1989) [2].

In mid-20th century the first descriptions of epilepsy specific to children emerged, characterized by certain types of seizures and identifiable findings in EEG [3]. This type of epilepsy has proven to have an excellent prognosis, adding a third key characteristic to the clinical and neurophysiological findings: a benign course. In attempts to make the name as precise as possible, authors included three or four terms in the name, each individually describing the key characteristics of this entity.

In early works addressing this issue, the emphasis was placed on distinguishing this from other types of epilepsies. This approach led to the formation of a unique entity that clearly stands apart from other epilepsies [3].

With the increasing adoption of knowledge, this epilepsy became more recognizable in clinical practice and better described. Initially, authors gave various names to this type of epilepsy, namely there was not a single term used by all authors.

Problems with determining the name of the syndrome

Different names have been used for this type of childhood focal epilepsy. One group of authors used the eponym "Rolandic," while others employed a descriptive term, aiming to encapsulate the main characteristics of this entity and provide a more precise definition of this type of epilepsy. In their attempts to be more precise, authors included three or four terms in the name, individually describing the key features of this entity:

1) The most important characteristic is a benign prognosis, so the term "Benign" is usually placed first in the name.

2) The determining point related to the time of onset of this syndrome is child's age. In the names, "children's or "childhood" is used.

3) In the third position is the determining point related to focal occurrence (focal, partial). Some authors omit this determining point, assuming it is implied when specifying the location of interictal epileptiform graphoelements in EEG.

4) The next determining point is the location of interictal specific graphoelements (spike, EEG focus). The location is determined in two ways: by neurophysiological criteria (centrotemporal, based on electrodes placed according to the international 10-20 system in EEG) or by an anatomical model, i.e., the part of the brain where epileptic discharge is presumed to occur – the Rolandic region, around the Rolandic fissure. American authors used the term "mid-temporal" to describe these discharges [4,5], while French authors preferred "Rolandic spikes" [6,7,8,9].

It has been observed that an identical EEG finding characteristic of this type of childhood epilepsy also occurs in children without seizures. In such cases, terms like BFEDCs (Benign Focal Epileptiform Discharges of Childhood) [10,11,12], or BEDs (Benign Epileptiform Discharges) [13] are commonly used.

Childhood benign focal epilepsies form a group of epilepsies or epileptic syndromes sharing common features. According to the ILAE recommendation [14], these epilepsies are collectively termed Self-limited focal epilepsies of childhood (SeLFE), previously known as BCFE - Benign Childhood Focal Epilepsy [12] or Idiopathic focal epileptic syndromes (IFE) [15].

Self-limited epilepsy with centrotemporal spikes (SeLECTS) is the most common syndrome in this group, and this term was recommended by the ILAE in its new nomenclature in 2017 (275-2022). Throughout history, this type of epilepsy has had various names and abbreviations. The used names, abbreviations, authors, and publication years are listed in Table 1.

Table 1. The used names, abbreviations and publication years for Childhood epilepsy with centrotemporal spikes

BECCT	**B**enign Epilepsy of Children with Centro-Temporal EEG Foci[17]	1972
BFEC	**B**enign Focal Epilepsy of Childhood[16]	1975
BECT	**B**enign Partial Epilepsy with Eentrotemporal Spikes [18,19]	1988
BERS	**B**enign Childhood Epilepsy with Rolandic Spikes[20]	1990
BECCT	**B**enign Epilepsy of Chidhood with Centrotemporal Spikes[21]	1991
BECTS	**B**enign Epilepsy with Centrotemporal Spikes[22,23,24,25]	1992
BECCTS	**B**enign Epilepsy of Childhood with Centrotemporal Spikes[26]	1994
BECRS	**B**enign Epilepsy of Childhood with Rolandic Spikes[27]	1996
BREC	**B**enign Rolandic Epilepsy of Childhood[29]	1996
BCECTS	**B**enign Rolandic Epilepsy[28]	1997
BCSSS	Benign Childhood Seizure Susceptibility Syndrome[30]	2008
BRE	Benign Rolandic Epilepsy [31]	2009
ECTS	Epilepsy with CentroTemporal Spikes[32]	2019
CECTS	**C**hildhood Epilepsy with Centrotemporal Spikes[33]	2021

The three main characteristics that constitute this entity (SeLECTS) are: Clinical manifestation, specific EEG findings, and a favorable prognosis, i.e., a benign course.

Clinical manifestation

The cardinal feature of Rolandic epilepsy is focal epileptic seizures, which can manifest in various ways typically categorized into symptom groups [34]:

(1) Unilateral facial sensory-motor symptoms (30% of patients),

(2) Oro-pharyngeal-laryngeal symptoms (53% of patients),

(3) Speech impairment (40%),

(4) Hypersalivation (30%) [30].
In addition to focal seizures, generalized tonic-clonic seizures also occur, commonly considered secondary generalized.
Beyond the seizure semiology and classification in this syndrome, anamnesis can provide other relevant data. There is a clear influence of sleep, drowsiness, and sleep deprivation on the frequency of seizures. Three-quarters of seizures occur during non-REM sleep, mainly at the onset of sleep or just before waking up [30].
Febrile seizures are often encountered in personal history (5-15%) [1,35].
A positive family history is also frequently found in children with BECT, indicating a genetic etiology [36].

Specific EEG findings

High-voltage spike-wave complexes activated during drowsiness and sleep constitute a distinctive finding in this entity (essential for diagnosis) [1].
The initial part of the graphoelement is commonly described as a spike, although precise measurements often reveal a sharp wave.
The location is typically specific, and most of the earlier names of this syndrome were related to this location.
Furthermore, the frequency of spike-wave complexes has been shown to depend on the wakefulness state, occurring more frequently during sleep [34].
In repeated EEG recordings, the location of occurrence can change, so the epileptic focus often appeared in a different place compared to previous registrations ("spike migration") [37]. This included a change in the hemisphere, a strong indication that it wasn't a structural lesion, providing indirect evidence of this entity.
The frequency of spikes in the EEG was not related to the frequency of seizures, which was a perplexing factor for clinicians. On the other hand, it was observed that some children with such EEG findings during nocturnal sleep exhibited almost continuous discharges. This led to the formation of a new entity (Epilepsy with continuous spike-and-waves during slow-wave sleep), separating this type of epilepsy from BECT (216/2001).
Regarding the location, most spikes are found in centro-temporal regions, but spikes in BECT can also be found outside these regions. Even though, in some cases, spikes in this entity may appear in other regions, it is not sufficient reason to exclude it from this syndrome ([38].
Many researchers have attempted to demonstrate different subtypes of this syndrome, but over time, this has been established only for spikes located in the occipital region. Only in correlation with the clinical description of seizures, two new types of epilepsy with clear clinical-neurophysiological distinctions were recognized: Gastaut's type and Panayiotopoulos' type of childhood occipital epilepsy. According to the ILAE definition from 2022 [39], Panayiotopoulos syndrome is called Self-limited epilepsy with autonomic seizures, and Gastaut's type of occipital epilepsy is called Childhood occipital visual epilepsy (COVE).
Panayiotopoulos then introduced the concept of the susceptibility syndrome [35], a continuum of childhood benign focal epilepsies. The concept consists of a unique nosological entity with phenotypic variations. According to this concept, the central and largest part is BECT, while at the milder end is Panayiotopoulos syndrome, and at the other end is epilepsy with continuous discharges during sleep.
When it comes to the EEG findings, it has been observed that identical spike-wave complexes seen in BECT also appear in children without seizures. Genetic studies have shown that this trait is inherited, but the type of inheritance and the responsible gene (or genes) remain unknown. Many genes have been associated with this trait [40], but there is no consensus on the inheritance pattern. Inheritance has been found not to be gender-related since such discharges in healthy children (children without seizures) occur equally in boys and girls, unlike in BECT where there is a clear male predisposition. It can be concluded that BECT discharges are a necessary but not sufficient condition for the development of BECT. Only the second one (gender-related inherited condition) allows seizures to occur in children with predisposition (i.e. spike-wave complexes in EEG).
The nature of the spike in EEG remains unknown. Despite advances in medicine and science in general, it is still unclear which neurophysiological processes in the brain lead to the appearance of spikes in EEG.

Benign course

The third key characteristic of this syndrome is a favorable prognosis, i.e., the resolution of seizures during development [16]. While crucial for the entity, from a clinician's perspective, this characteristic lacks significant diagnostic value. It requires a sufficiently long period to confirm the benign nature of the epilepsy. Consequently, a definitive diagnosis can only be made retrospectively, once the child outgrows the age when this epilepsy occurs, and since this period is defined differently in the literature, the final diagnosis can only be established after a prolonged, vaguely defined period.
On the other hand, the favorable prognosis holds significant prognostic value, for it reassures parents that their child's epilepsy will likely resolve over time, making it crucial for clinicians to have the first two elements present (clinical and EEG findings) to determine the third (favorable course), similar to how, in mathematics, two angles in a triangle can determine the third one.
However, the concept of benignity has been reevaluated and has been completely removed from the name following the ILAE recommendation [39]. This action is based on numerous studies indicating various changes in these children, mainly on a cognitive, behavioral, and psychological level. These changes were detected through carefully designed and precisely conducted studies, reaching statistical significance. Since the term benignity could imply "insignificance" across all aspects of this entity due to its broadness, it has been replaced with the term "self-limited," indicating a time-limited occurrence of seizures. In other words, by removing the term "benign" from the name, the favorable course of epilepsy remains acknowledged.
The term "benign" is eliminated from the title while retaining the concept of a favorable course.

Classification

International League Against Epilepsy (ILAE) provided a classification of epileptic seizures in 1981 [41], and in 1989, they published a classification of epilepsies and epileptic syndromes [42]. Both classifications proved to be highly valuable for both practitioners and researchers, operating at both clinical and scientific levels.
The 1989 classification of epilepsies and epileptic syndromes [42] lists two entities among idiopathic focal epilepsies of childhood:
Benign childhood epilepsy with centro-temporal spike
Childhood epilepsy with occipital paroxysms
In the report of the ILAE Commission on Classification and Terminology in 2001 [38], presented by Engel, five axes were proposed for diagnosing patients with epilepsy.
1. The first axis involves the description of seizures (ictal semiology).
2. The second axis involves the type of epileptic seizure. The ILAE Commission provided a list of accepted seizure types, categorized into self-limited seizures, continuous seizures, further divided into generalized and focal seizures.
3. The third axis is the syndromic diagnosis, including a list of accepted epileptic syndromes.
4. The fourth axis consists of specific etiology when known.
5. The fifth axis is optional and relates to the degree of impairment resulting from epilepsy.
Idiopathic childhood epilepsies (Axis 3), besides Benign Childhood Epilepsy with Centrotemporal Spikes, recognize two additional syndromes: Benign Childhood Occipital Epilepsy with Early Onset (Panayiotopoulos type) and Childhood Occipital Epilepsy with Late Onset (Gastaut type). It's notable that the term "benign" remains in the name of two syndromes in this group of epilepsies.
In 2010, ILAE issued a revision of terminology and the concept of organizing seizures and epilepsies [43]. The concept of electroclinical syndrome was introduced, referring to complex clinical data, signs, and symptoms that together define a distinct and recognizable clinical disorder. There are specific disorders identified by features such as the age of onset, specific EEG findings, types of seizures, and other characteristics that, when considered together, allow a specific diagnosis. A syndromic diagnosis, in turn, impacts the treatment, management, and prognosis of epilepsy.
The recommendation related to Rolandic epilepsy in this revision pertains to the use of the term "Benign Epilepsy." The recommendation is not to use the term "benign." The reasons are manifold. Firstly, it has been shown that childhood focal benign epilepsies are not as "benign" as initially thought. Increased knowledge indicates a connection between epilepsy and a broad spectrum of brain disorders such as cognitive, behavioral, and psychiatric disorders. The term "benign" may mislead both professionals and patients and their families to underestimate and neglect these associated conditions. On the other hand, the

term "benign" has not been completely eliminated from the names of these epileptic syndromes, so in the category of childhood electroclinical syndromes, the following names have remained:
Panayiotopoulos syndromeBenign epilepsy with centrotemporal spikes (BECTS)
Late onset childhood occipital epilepsy (Gastaut type)
Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS)
Landau-Kleffner syndrome (LKS)
In 2017, the ILAE introduced a new classification of epileptic seizures [44] with an attempt to facilitate its use in clinical practice [45]. This classification is operational (practical) and is based on the 1981 classification and its expansion in 2010.
Significant progress in understanding epilepsy and its mechanisms was summarized in a noteworthy classification, the first after the one in 1989.. This classification provides diagnostic guidelines for clinicians divided into three steps: First, the diagnosis of the type of epileptic seizure. The second step is determining the type of epilepsy, including focal epilepsies, generalized epilepsies, combined generalized and focal epilepsies, and the unknown epilepsy group. The third step is determining the epileptic syndrome, where a syndromic diagnosis can be established. Regarding the cause, instead of the terms idiopathic, cryptogenic, and symptomatic, the etiology of epilepsy can be (1) genetic, (2) structural, (3) metabolic, (4) immunological, (5) infectious, and (6) unknown.
The term "benign" has been replaced with "self-limited" or "pharmacoresponsive." This recommendation also extends to the name of the electroclinical syndrome, so "Benign epilepsy with centrotemporal spikes" is now called "self-limited epilepsy with centrotemporal spikes."
The change in the name of the most common childhood epilepsy after decades of using the word "benign" as a key element in the name stems from the imprecision of the term "benign." With the increased knowledge about benign childhood epilepsy with centrotemporal spikes (BECT), it has been widely accepted that there are small but statistically significant abnormalities in the cognitive, behavioral, and emotional areas in children with this type of epilepsy. Consequently, BECT is no longer entirely "benign," leading to the replacement of the term "benign" with "self-limited." This new term is more precise and clearly indicates one of the main characteristics of this electroclinical syndrome, namely the mandatory cessation of seizures upon entering adolescence (i.e., with the completion of nervous system maturation).
However, while gaining precision, there is a loss on the other side. The name of this syndrome was already awkward and often replaced with abbreviations, which, on the other hand, were not always standardized. The term "self-limited" is not commonly used in everyday language, requiring additional mental effort to understand its meaning. Instead of one widely accepted word ("benign"), a compound term ("self-limited") is introduced, usually requiring further explanation. In the end, instead of a name consisting of five words, we now have a name with six words. In the professional community, confusion may arise, leading to the perception of a new entity when encountering this term. The key word in the old name ("benign") is now missing and replaced by a new compound term ("self-limited").
Attempts to precisely define an entity in its name inevitably lead to a name that can be awkward and unwieldy can create difficulties in its acceptance in clinical practice.

CONCLUSION

The concept of epileptic syndromes and the dynamics of renaming certain diseases depend on the rapid progress of scientific knowledge in medicine. Recommendations from ILAE contribute to terminology standardization and a better understanding of the essence of epilepsy. Given the dynamic nature of this field, ILAE will continue to monitor new achievements in epileptology and update classifications to reflect the latest knowledge. Clinicians are urged to not only formally but also substantively follow developments in their medical field to provide the best and most contemporary assistance to their patients.

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