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Epileptic Disorders

CLINICAL COMMENTARY

Electroclinical features of myoclonic-tonic and spasm-tonic seizures in childhood

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Abstract

Myoclonic-tonic (MT) and spasm-tonic (ST) seizures represent distinctive features in late infantile epileptic encephalopathy (LIEE). This commentary aims to delineate the electroclinical characteristics of MT and ST seizures, setting them apart from other seizure types. Our analysis encompasses 211 ST and MT seizures observed in 31 patients diagnosed with LIEE, providing a comprehensive overview of video-EEG features and polygraphic signatures. In MT seizures, EEG findings reveal a high-voltage diffuse spike/polyspike and wave discharge, often succeeded by diffuse electrodecrements. The amplitude-integrated EEG (aEEG) signature is described as a "reversed checkmark." Conversely, ST seizures exhibit EEG findings such as a vertex positive deflection after a slow-wave and relative electrodecrement, with intermixed epileptiform discharges. In comparison to MT seizures, polygraphic characteristics in ST seizures appear more distinct, featuring a brief rhomboid shape corresponding to the spasm, followed by a lengthier rectangular shape indicative of the tonic phase of the ST seizure. While the pathophysiology of ST and MT seizures remains inadequately understood, their concurrent occurrence and association with other seizure types (tonic, epileptic spasm, myoclonic) within the temporal context of LIEE and other epileptic encephalopathies prompt us to anticipate advancements in our understanding through future research. We hope that this study serves as a foundation for unraveling these complexities in the times to come.

KEYWORDS

late-onset infantile epileptic encephalopathy, late-onset spasm, myoclonic-tonic, spasm-tonic

1 | INTRODUCTION

Before the advent of electroencephalography (EEG), physicians had already started recognizing distinct seizure types and their potential occurrence in isolation or combination. The evolution of technologies such as video EEG and polygraphy has significantly advanced our contemporary understanding of epilepsy syndromes, enabling researchers to precisely characterize the features of seizures and their associated electroclinical syndromes. This article specifically delves into the features of myoclonic-tonic (MT) and spasm-tonic seizures (ST), recognized as

characteristic of late infantile epileptic encephalopathy (LIEE).[1]

Although MT seizures are acknowledged in the International League Against Epilepsy (ILAE) 2010 Revised Terminology for Organization of Seizures and are referenced in the 2017 operational classification, the existing literature providing a detailed delineation of its features is limited.[2,3] Notably, Beniczky et al. list tonic spasm as a seizure type in their Standardized Computer-based Organized Reporting of EEG (SCORE) report, yet the specifics of this entity were not expounded upon.[4] Various reports in the literature align with ST seizures, though an

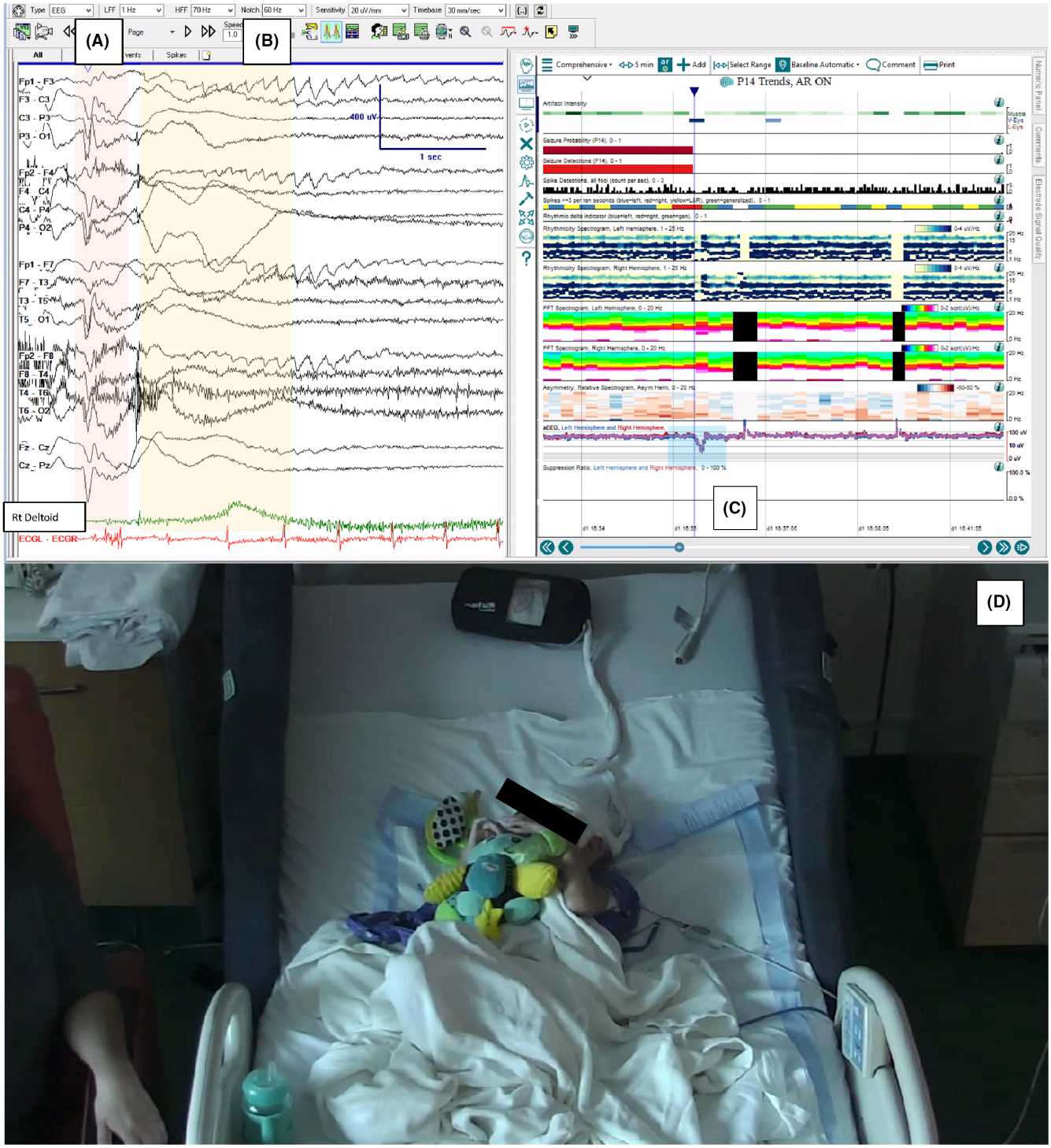


FIGURE 1 Myoclonic-tonic seizure. (A) Diffuse spike and wave discharge during the myoclonic phase of seizure. (B) Profound electrodecrement and relatively bland polygraphic channel during tonic phase of MT seizure with myoclonic seizure phase evident in ECG channel. (C) Reversed checkmark seen on aEEG trend. (D) Video of clinical MT seizure.

array of terminologies is employed, including late-onset epileptic spasms (ES), periodic spasms, and ES without hypsarhythmia or with modified hypsarhythmia.[5–10]

Well-established seizure types exhibit distinct clinical, electrographic, and electromyographic signatures. Myoclonic seizures (MS) are characterized by involuntary, exceedingly brief contractions of muscle group(s), typically lasting less than 150 ms, manifesting as body jerks or twitches. The EEG during MSs reveals a diffuse negative spike–wave discharge preceding the myoclonus, often succeeded by a period of electrodecrement. On the other hand, tonic seizures (TS) involve sustained contractions lasting at least a few seconds, presenting as abnormal positioning of involved body parts. The EEG in TSs displays relative attenuation and low-voltage fast activity with superimposed electromyographic artifacts. In contrast, ES typically manifest as sudden flexion and/or extension of proximal limb and trunk muscles, lasting a second or less, occurring in clusters. ES can be asymmetric and as subtle as head nodding, eye movement, grimacing, and paraspinal stiffening. The EEG in ES reveals a diffuse high-voltage slow wave followed by diffuse electrodecrement and often includes low-voltage rhythmic fast activity. Characteristic EMG/polygraphic features include a brief rhomboid shape for ES, a sustained rectangular shape for TS, and a time-locked burst of activity in MS. In more sustained or successive MS, the polygraphic signature may resemble that of ES.[11]

This commentary aims to elucidate the electroclinical and polygraphic features of MT and ST seizures, distinguishing them from each other and other co-occurring seizure types.

2 | METHODS

In this study, 31 patients with LIEE were identified and their seizure types (MT and ST) were closely analyzed with video EEG, polygraphy, and amplitude-aEEG. A total of 211 seizures were reviewed from ictal EEG capture in 22 of the patients. However, 89 ST seizures were reviewed from 12 patients and 122 MT seizures were reviewed from 17 patients. Distinguishing features of both seizure types were synthesized from this comprehensive review as below.

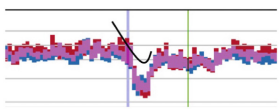
2.1 | Late infantile epileptic encephalopathy background EEG features

Both seizure types occurred in children with diagnosed LIEE. The background EEG in LIEE reveals a diffusely slow, disorganized, and discontinuous background with superimposed multifocal epileptiform discharges.[1]

2.2 | MT seizures

Core features of MT seizures were ascertained from 122 examples of MT seizure in 17 patients. MT seizures have high-voltage diffuse spikes or polyspike and wave discharges on EEG(A) followed by 2–3 s of diffuse and profound electrodecrement (B). The polygraphic channel does not deliver a clear high-amplitude signal. A characteristic "reversed checkmark" is seen on aEEG in the

TABLE 1 Summary table of features of myoclonic-tonic and spasm-tonic seizures.

Seizure type (number of reviewed seizures)	Myoclonic-tonic (122)	Spasm-tonic (89)
EEG	Diffuse spike and wave often followed by electrodecrement	Vertex positive deflection, after going slow wave and relative electrodecrement with intermixed epileptiform discharges
Typical/ideal surface EMG pattern	Brief burst/deflection (myoclonus) followed by incremental tonic discharge 	Brief rhomboid shape discharge (spasm) followed by an incremental tonic discharge 
aEEG	Reversed checkmark 	No clear change
Clinical	Body twitch/jerk and tonic seizure, sometimes with eyelid fluttering	Body epileptic spasm and tonic seizure

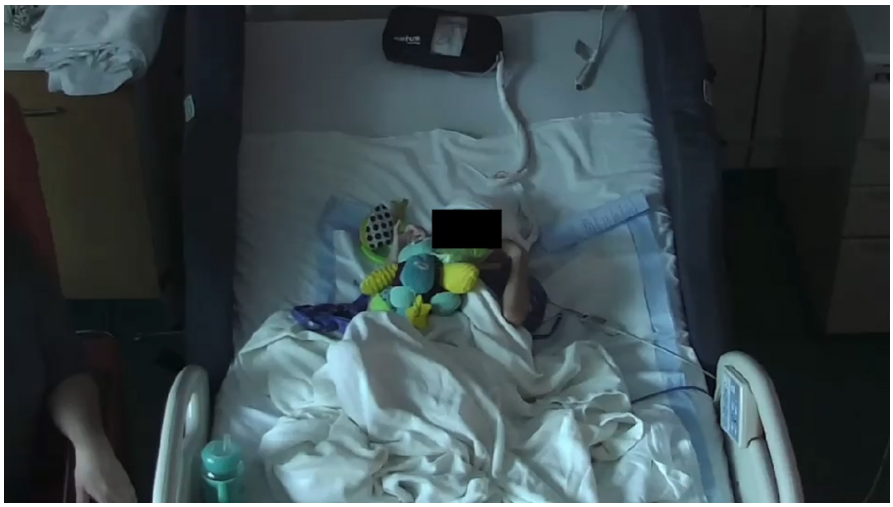
quantitative spectral array software *Persyst* (C). Clinically, patients with MT seizures have a myoclonic component followed by a brief TS component in the seizure. A clinical example of a patient experiencing an MT seizure is shown (D) (Figure 1).

2.3 | ST seizures

A total of 89 ST seizures were thoroughly examined within the patient cohort diagnosed with LIEE. The ST seizures exhibit an initial high-voltage slow wave with vertex positivity on bipolar montage (A). Subsequently, there is an electrodecrement with an overriding beta rhythm lasting between 2 and 3 s (B). Within this relative electrodecrement, interictal discharges persist. The EMG polygraphic leads showcase a distinct and easily recognizable rhomboid shape during the spasm phase (C), followed by a longer rectangular, lower-amplitude contraction representing the tonic component of this seizure. Clinically, there is a hallmark spasm component lasting about 1 s, followed by a TS lasting 2–3 s (E). Notably, there is no reversed checkmark sign observed on aEEG (D). When TSs are weak, the EMG pattern is generally less incremental and resembles the shape of a rectangle (Table 1; Videos 1 and 2). When TSs are forceful, the EMG pattern becomes more incremental and resembles a horizontal triangle (Figure 2).

3 | DISCUSSION

MT and ST seizures are observed in patients diagnosed with LIEE. Frequently, this pattern emerges within the context of an evolution from Early Infantile Epileptic



VIDEO 1 Myoclonic-tonic seizure.

VIDEO 2 Spasm-tonic seizure.

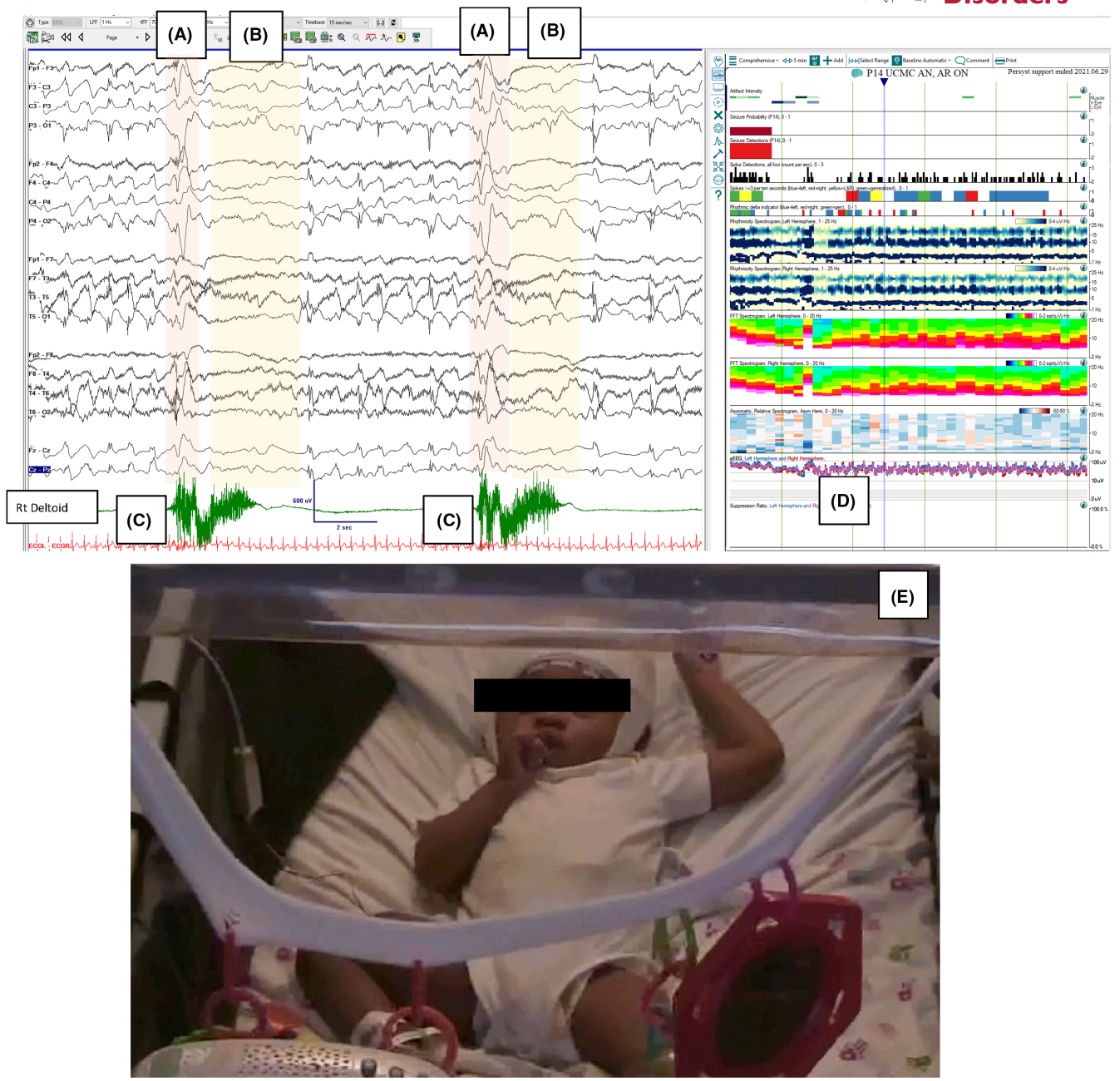


FIGURE 2 Spasm-tonic (ST) seizures. (A) High-voltage slow wave (B) relative electrodecrement with persistence of interictal discharges (C) rhomboid shape EMG signature in right deltoid (D) aEEG without the presence of reversed checkmark (E) clinical video of ST seizure.

Encephalopathy (EIEE) to Lennox–Gastaut syndrome (LGS). Intriguingly, a substantial number of LIEE patients experience both MT and ST simultaneously, with 32% of patients in our cohort demonstrating electroclinically confirmed co-occurrence. Nevertheless, in most cases, one seizure type tends to be more predominant.

LIEE was designated to encompass the spectrum of epileptic encephalopathies and recognize the existence of a distinct form characterized by the onset of MT and ST seizures occurring after 1 year of age.[12] This distinction is particularly significant as some patients with LIEE lack a history of preceding infantile spasms and/or EIEE, and they may not necessarily progress to LGS. Expert experience and reports consistently demonstrate a robust response to specific therapies such as the classic ketogenic diet (CKD) and felbamate.[1]

The pathophysiology of MT and ST has not been independently studied, but it is suspected to involve both cortical and subcortical structures, similar to what is observed in the spectrum of TSs and ES. An important caveat is that, even with video EEG–EMG, there were instances where making a clear electroclinical distinction between MT and ST posed challenges, leaving uncertainty about whether the origin of these seizures lies on a continuum.

4 | CONCLUSION

MT and ST represent seizure types with distinct electroclinical and polygraphic signatures, though these classifications have yet to be formally defined and remain relatively underrecognized. Recently, both MT and ST seizures have been identified as characteristic in LIEE. In MT seizures, polyspike-wave discharges and subsequent electrodecrement are accompanied by an aEEG deflection exhibiting a distinctive "reversed checkmark" appearance. Conversely, ST seizures display a positive vertex deflection and subsequent electrodecrement on EEG, coupled with a rhomboid-rectangular polygraphic signature.

As our understanding of epilepsy evolves and its phenotypes become clearer, this commentary aims to assist healthcare providers in identifying patients with MT and ST seizures, ultimately aiding in the diagnosis of LIEE. The ability to recognize these seizure types has significant therapeutic and prognostic implications, such as the potential for early treatment with a ketogenic diet. Conducting higher-powered and blinded future studies would be valuable in assessing the onset of these seizures, understanding their origin, and identifying the factors contributing to their predominant phenotype in LIEE.

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CONFLICT OF INTEREST STATEMENT

Mohamed Taha, Douglas R. Nordli, III, Shawn Kacker, Audrey Oetomo, Chalongchai Phitsanuwong, and Douglas R. Nordli, Jr. report no financial disclosures or conflicts of interest.

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REFERENCES

1. Kacker S, Phitsanuwong C, Oetomo A, Nordli DR Jr. Late infantile epileptic encephalopathy: a distinct developmental and epileptic encephalopathy syndrome. Epileptic Disord. 2023;26:98–108. https://doi.org/10.1002/epd2.20185
2. Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, Van Emde Boas W, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE commission on classification and terminology, 2005–2009. Epilepsia. 2010;51:676–85. https://doi.org/10.1111/j.1528-1167.2010.02522.x
3. Fisher RS, Cross JH, D'Souza C, French JA, Haut SR, Higurashi N, et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia. 2017;58(4):531–42. https://doi.org/10.1111/epi.13671
4. Beniczky S, Aurlien H, Brøgger JC, Hirsch LJ, Schomer DL, Trinka E, et al. Standardized computer-based organized reporting of EEG: SCORE—second version. Clin Neurophysiol. 2017;128(11):2334–46. https://doi.org/10.1016/j.clinph.2017.07.418
5. Caraballo RH, Fejerman N, Bernardina BD, Ruggieri V, Cersósimo R, Medina C, et al. Epileptic spasms in clusters without hypsarrhythmia in infancy. Epileptic Disord. 2003;5(2):109–13.
6. Korff CM, Nordli DR Jr. The clinical-electrographic expression of infantile seizures. Epilepsy Res. 2006;70(Suppl 1):S116–S131. https://doi.org/10.1016/j.eplepsyres.2005.11.016
7. Eisermann MM, Ville D, Soufflet C, Plouin P, Chiron C, Dulac O, et al. Cryptogenic late-onset epileptic spasms: an overlooked syndrome of early childhood? Epilepsia. 2006;47:1035–42. https://doi.org/10.1111/j.1528-1167.2006.00518.x
8. Nordli DR Jr, Korff CM, Goldstein J, Koh S, Laux L, Kelley KR. Cryptogenic late-onset epileptic spasms or late infantile epileptogenic encephalopathy? Epilepsia. 2007;48:206–8. https://doi.org/10.1111/j.1528-1167.2007.00978_2.x
9. Auvin S, Lamblin MD, Pandit F, Vallée L, Bouvet-Mourcia A. Infantile epileptic encephalopathy with late-onset spasms: report of 19 patients. Epilepsia. 2010;51(7):1290–6. https://doi.org/10.1111/j.1528-1167.2010.02534.x
10. De Marchi LR, Seraphim EA, Corso JT, Naves PVF, de Carvalho KC, Ramirez MDH, et al. Epileptic spasms without hypsarrhythmia in infancy and childhood: tonic spasms as a seizure type (WITH VIDEO). Epileptic Disord. 2015;17(2):188–93. https://doi.org/10.1684/epd.2015.0738
11. Hirano Y, Oguni H, Funatsuka M, Imai K, Osawa M. Differentiation of myoclonic seizures in epileptic syndromes: a video-polygraphic study of 26 patients. Epilepsia. 2009;50(6):1525–35. https://doi.org/10.1111/j.1528-1167.2008.01859.x
12. Nordli DR Jr. Epileptic encephalopathies in infants and children. J Clin Neurophysiol. 2012;29(5):420–4. https://doi.org/10.1097/WNP.0b013e31826bd961

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