Clinical commentary

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Benign spasms of infancy: a mimicker of infantile epileptic disorders*

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ABSTRACT – Benign spasms of infancy (BSI), previously described as benign non-epileptic infantile spasms or benign myoclonus of early infancy, are non-epileptic movements manifesting during the first year of life and spontaneously resolving in the second year of life. BSI are characterized by spasms typically lasting 1-2 seconds, involving, to varying degrees, the head, neck, trunk, shoulders and upper extremities. Ictal and interictal EEG recordings are normal. BSI are not associated with developmental regression and do not require treatment. Distinction between BSI and infantile epileptic disorders, such as epileptic spasms or myoclonic epilepsy of infancy, can be challenging given the clinical similarities. Moreover, interictal EEGs can be normal in all conditions. Epileptic spasms and myoclonic epilepsy require timely treatment to improve neurodevelopmental outcomes. We describe a six-month-old infant presenting with spasm-like movements. His paroxysms as well as a positive family history for epileptic spasms were in keeping with a likely diagnosis of West syndrome. Surprisingly, ictal video-EEG did not reveal epileptiform activity, and suggested a diagnosis of BSI. We emphasize that ictal video-EEG is the gold standard for classification of infantile paroxysms as epileptic or non-epileptic, thereby avoiding over-treatment for BSI and facilitating timely targeted treatment of infantile epilepsies. [*Published with video sequences*]

Key words: infantile spasms, West syndrome, benign myoclonus of early infancy, myoclonic epilepsy of infancy, epileptic spasms

VIDEOS ONLINE

Infantile movements are often non-voluntary and at times difficult to classify as epileptic or non-epileptic, and may include spasm-like paroxysms. Non-epileptic spasms have been reported as "benign myoclonus of early infancy" or "benign non-epileptic infantile spasms" (Dravet *et al.*, 1986; Maydell *et al.*, 2001; Caraballo *et al.*, 2009).

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*The work has not been previously published but has been presented at the 2019 Canadian Neurological Sciences Federation (CNSF) conference as an e-poster presentation. In this poster, video-EEG of the spasms was displayed, however, the details of the case and diagnostic pathway were not discussed.

We suggest the simplified and descriptive term "benign spasms of infancy" (BSI).
BSI is a non-epileptic motor phenomenon manifesting in the first year of life (Dravet *et al*., 1986; Maydell *et al*., 2001; Caraballo *et al*., 2009). The condition is self-limiting, requiring no treatment (Caraballo *et al*., 2009). BSI can mimic epileptic disorders such as West syndrome, and distinguishing BSI from epileptic seizures is crucial to inform treatment decisions (Maydell *et al*., 2001; Caraballo *et al*., 2009). We describe an infant with recurrent clusters of spasms, diagnosed with BSI via video-EEG monitoring. Clinical features and differential diagnosis of BSI are discussed along with a diagnostic pathway to classify infantile paroxysmal movements as either epileptic or non-epileptic.

Case study

A six-month-old boy presents to the emergency department with a one-week history of sudden brief contractions involving the shoulders and upper extremities, sometimes associated with head drop and truncal flexion. The episodes occur multiple times per day in clusters during wakefulness. There is no obvious trigger and the boy immediately resumes his activities following a paroxysm. The parents share a video (*video sequence 1*). On physical exam, the boy is healthy with a normal neurological and developmental status.
The patient was born after an uneventful pregnancy via emergency Caesarean section due to a non-reassuring fetal heart rate. His Apgar scores were nine (one minute) and nine (five minutes). Starting on his first day of life, he was noted to have twitching movements during sleep. EEG recordings of these paroxysms on day 3 of life did not reveal epileptiform activity, and he was diagnosed with benign neonatal sleep myoclonus.
Family history reveals seizures and West syndrome: the patient's maternal aunt had therapy-refractory epileptic spasms diagnosed at three months of age, developed Lennox-Gastaut syndrome, and passed away at the age of 22 years in the context of status epilepticus. The patient's father had one tonic-clonic seizure at the age of three years, and the patient's paternal aunt had multiple febrile seizures; both have remained seizure-free since childhood.
Suspecting a diagnosis of epileptic spasms in our patient, video-EEG monitoring is performed for 48 hours. Surprisingly, EEG background and interictal activity are normal. Thirty events are captured; none with electrographic epileptiform correlate (*video sequence 2*). The paroxysms consist of a combination of shoulder shrugging and head drop with occasional truncal flexion, usually lasting 1-2 seconds, occurring during wakefulness. Based on his clinical presentation and the EEG findings, the patient is diagnosed with BSI and discharged from hospital. Follow-up visits, including several sleep-deprived EEGs, reveal normal development and EEGs. The spasms decrease in frequency at 12 months of age and cease at 18 months of age.

Discussion

History and clinical features of BSI

BSI was first described as "benign myoclonus of early infancy" by Lombroso and Fejerman in 1977 (Lombroso and Fejerman, 1977). It was renamed "benign non-epileptic infantile spasms" by Dravet in 1986, due to the clinical resemblance of the paroxysms (Dravet *et al*., 1986). Considering the fact that the term "infantile spasms" has recently been changed to "epileptic spasms" by the International League Against Epilepsy, we suggest the simplified and descriptive term "benign spasms of infancy" (BSI). Benign myoclonus of early infancy is a misnomer, since typical spells of BSI are longer than myoclonic jerks, and the usual age of BSI occurrence is not early but rather mid-to-late infancy.
BSI manifest within the first year of life, mainly between four and seven months of age, in normally developed infants (Maydell *et al*., 2001; Caraballo *et al*., 2009; Fernández-Alvarez, 2018). Sudden paroxysmal movements typically present in clusters during wakefulness and are characterized as spasms involving, to varying degrees, the head, neck, trunk, shoulders and upper extremities, but not the lower limbs (Caraballo *et al*., 2009; Fernández-Alvarez, 2018). The duration of an attack is usually 1-2 seconds. In addition, movements that are shorter in duration and myoclonus-like as well as atonic paroxysms have been described in infants with BSI. The events do not cause any distress or impairment in consciousness and there is no postictal period (Caraballo *et al*., 2009; Fernández-Alvarez, 2018).
EEG is normal during and in-between spells. The condition is self-limiting and infants will continue to develop normally. The spasms typically decrease in frequency within three months of onset and cease in the second year of life with no treatment required (Maydell *et al*., 2001; Caraballo *et al*., 2009; Fernández-Alvarez, 2018).

Differential diagnosis

Non-epileptic conditions

Shuddering attacks are characterized by shiver-like movements typically involving the head, trunk and

arms, with no impairment of consciousness or distress to the infant, lasting several seconds (Fernández-Alvarez, 2018; Tibussek *et al*., 2008). They are regarded as a variant of normal behavior, and spontaneously resolve within the first few years of life (Tibussek *et al*., 2008). As infantile epileptic conditions do not usually present as shuddering, a video of an event may be sufficient to diagnose this benign infantile motor phenomenon.

Non-epileptic head drops and myoclonus are also benign paroxysmal movements of infancy, typically manifesting at around 4-7 months of age, and resolving in the second year of life. They may clinically be indistinguishable from epileptic disorders and will therefore require ictal EEG recordings to exclude epileptiform activity (Caraballo *et al*., 2009; Capovilla *et al*., 2013).

BSI, shuddering attacks, benign non-epileptic head drops and myoclonus have previously been reported as one nosological entity: a case series of 102 patients with "benign myoclonus of early infancy" included 35 infants presenting with shuddering attacks, 23 with myoclonus, and four patients with atonic events (Caraballo *et al*., 2009). In the absence of a genetic marker or a known common etiology, it is however currently still unclear if those paroxysms represent different manifestations of the same entity.

Other self-limiting infantile movement disorders include benign neonatal sleep myoclonus, benign paroxysmal tonic upgaze, Sandifer syndrome, spasmus nutans, and benign paroxysmal torticollis. These non-epileptic conditions are all clinically distinct from BSI, but are also often reported as epilepsy mimickers.

Epileptic conditions

West syndrome or epileptic spasms, formerly known as infantile spasms, is an epileptic encephalopathy associated with developmental arrest or regression which may improve with timely anticonvulsant therapy (Maydell *et al*., 2001; Pavone *et al*., 2014). Epileptic spasms typically present in the first year of life (Maydell *et al*., 2001; Caraballo *et al*., 2009; Pavone *et al*., 2014). Seizures consist of brief contractions involving the muscles of the neck, trunk and extremities, lasting up to two seconds, and commonly occurring in clusters. Interictal EEG typically reveals hypsarrhythmia, a highly disorganized background activity, with high-voltage irregular slow waves intermixed with multifocal spikes and polyspikes (Maydell *et al*., 2001; Pavone *et al*., 2014). However, a recent study demonstrates that up to 18% of patients with epileptic spasms may present without hypsarrhythmia and still require standard West syndrome anticonvulsant treatment (Demarest *et al*., 2017). Although these patients' interictal EEGs were abnormal, even in the absence of hypsarrhythmia, patients with epileptic spasms and normal interictal EEGs have previously been reported (Caraballo *et al*., 2003). Hence, the clinical and interictal EEG presentation of epileptic spasms may be indistinguishable from BSI. We suggest that ictal EEG recordings, commonly demonstrating high-voltage sharp or slow waves followed by low-amplitude fast activity and voltage attenuation during epileptic spasms (Caraballo *et al*., 2003), are required to differentiate West syndrome from BSI.

Myoclonic epilepsy of infancy is another differential diagnosis for BSI and can also present in the first year of

Table 1. Characteristics of benign spasms of infancy and epileptic disorders presenting with similar features.

	Benign spasms of infancy	Epileptic spasms with hypsarrhythmia	Epileptic spasms without hypsarrhythmia	Myoclonic epilepsy of infancy
Typical age at onset	1st year of life	1st year of life	1st year of life	1st year of life
Typical neurodevelopment prior to onset	Normal	Normal	Normal	Normal
Typical semiology	Spasms	Spasms	Spasms	Myoclonus
Frequency	Multiple daily	Multiple daily	Multiple daily	Multiple daily
Clusters	+	+	+	-
Psychomotor retardation	No	Yes, improves with timely treatment	Yes, improves with timely treatment	Rarely, may improve with treatment
Interictal EEG	Normal	Hypsarrhythmia	Abnormal; rarely normal	Often normal
EEG ictal epileptiform activity	-	+	+	+

life in typically normally developed children. Seizures may occur several times per day during wakefulness and are characterized by brief myoclonic jerks. Ictal EEG is abnormal, but patients may have normal interictal EEGs, representing a challenge when distinguishing the condition from BSI. Cognitive, motor and behavioral difficulties have been reported particularly in children with uncontrolled seizures. Therefore, timely and targeted anticonvulsant treatment is recommended (Korff and Nordli, 2006).

Severe myoclonic epilepsy of infancy, or Dravet syndrome, differs from the other epileptic conditions discussed as it typically presents initially as generalized or unilateral clonic or tonic-clonic seizures, often in the context of fever, and myoclonic seizures generally occur only later, between the age of one and four years (Korff and Nordli, 2006). In view of the different semiology of seizures in infancy, Dravet syndrome is not to be considered as a major differential diagnosis for BSI.

Characteristics of BSI and epileptic disorders presenting with similar features are summarized in *table 1*.

Suggested diagnostic pathway

A detailed history and neurological examination revealing abnormalities in neurodevelopment, or a positive personal or family history of seizures, raises suspicion of an epileptic condition. A routine EEG may demonstrate epileptiform activity or hypsarrhythmia and be already diagnostic for West syndrome or other infantile epileptic disorders. However, in case of a normal routine EEG not capturing ictal events, a prolonged EEG (preferably with video and EMG), recording paroxysmal events, should be obtained to assess for ictal EEG correlates.

It has been reported that a normal interictal EEG may be sufficient for the diagnosis of BSI (Maydell *et al*., 2001; Fernández-Alvarez, 2018). However, we would like to strongly emphasize that a normal interictal EEG is not sufficient to diagnose BSI, as epileptic conditions closely resembling BSI can also present with normal interictal EEGs. Video-EEG monitoring of the spasms in order to capture ictal epileptiform activity on EEG is the gold standard for the classification of infantile paroxysmal movements and reliably informs treatment decisions. □

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None of the authors have any conflict of interest to declare.

Legend for video sequences

Video sequence 1.

Home video of a spasm at six months of age, obtained prior to hospitalization.

Video sequence 2.

Video-EEG recording of multiple spasms at six months of age during inpatient hospitalization.

Key words for video research on www.epilepticdisorders.com

Phenomenology: myoclonic tonic, myoclonus (non-epileptic), non-epileptic paroxysmal event
Localisation: not applicable
Syndrome: non-epileptic paroxysmal disorder
Aetiology: unknown

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TEST YOURSELF

(1) Which epileptic disorders present similarly to benign spasms of infancy?

(2) What is the most accurate diagnostic approach to an infant presenting with spasms, with suspicion of having benign spasms of infancy?

(3) What is the treatment for benign spasms of infancy?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".