Original article

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Nocturnal variant of benign myoclonic epilepsy of infancy: a case series

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ABSTRACT – Myoclonus is a brief, rapid, involuntary muscle jerk originating in the central nervous system that can be physiological or a symptom of disease. We report a group of five children with excessive myoclonic jerks, only during sleep, and abnormal EEG during the events. Although only one third of the events had EEG epileptiform correlate, the presence of myoclonus without epileptiform EEG correlate has been described in patients with benign myoclonic epilepsy of infancy. We hypothesize that these findings may represent a variant of benign myoclonic epilepsy of infancy.

Key words: benign myoclonic epilepsy of infancy, nocturnal myoclonus, hypnic jerk

Myoclonus is a brief, rapid, involuntary muscle jerk originating in the central nervous system (Marsden *et al*., 1982). This paroxysmal event may be physiological or a symptom of underlying disease. Pathological myoclonus may be non-epileptic or epileptic, depending on whether there is an abnormal electrical discharge in the cortex at the time of the jerk.

Isolated jerks during sleep in infants and toddlers are common and are usually attributed to benign sleep myoclonus or hypnic jerks (Vendrame and Kothare, 2011). Excessive jerking during sleep is unusual and can be a cause to seek medical attention.

We report a group of five children with excessive myoclonic jerks, only during sleep, and abnormal EEG. We hypothesize that these findings may represent a variant of benign myoclonic epilepsy of infancy.

Case studies

We describe a series of five children who presented to St. Christopher's Hospital for Children with a history of exclusively nocturnal myoclonic jerks. These patients had myoclonic events that were frequent enough to seek medical attention.

We included patients without any history of daytime myoclonus or other types of seizures. Each patient had an EEG recorded during the typical event. The median age of onset was 12 months (range: 3-22

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months). All were males. All but one were born at 40 weeks of gestation (one was born at 31 weeks gestation; Patient 2). All infants had a normal neurological examination and psychomotor development. All patients described episodic or continuous bilateral upper and lower extremity jerks which occurred during sleep. Movements were more frequent at the initiation of sleep and continued throughout the night. The patients had no problems with excessive daytime fatigue, and no abnormal movements during the day. There were no symptoms of bruxism, night terrors, nightmares, sleepwalking, hallucinations, or apnoea. Two of the six patients had a history of febrile seizures. *Table 1* shows the baseline characteristics as well as the distinctive features of the clinical presentation.

Twenty-four-hour video or ambulatory EEG monitoring was performed and this was reviewed independently by three board-certified paediatric neurologists (DK, KC, and IV). Four of the patients had 24-hour video EEGs and one had an extended routine video-EEG. We reviewed 51 events, of which 15 (29.41%) demonstrated epileptiform discharges on EEG. They showed high-amplitude generalised delta slowing, intermixed with spikes lasting less than three seconds (see *figures 1, 2 and 3*). One patient (Patient 5) had an additional parasagittal spike-and-slow-wave pattern. In four patients, the events occurred during stage II or slow-wave sleep, and in one (Patient 3) during stage 1. *Table 2* shows the electrographic changes. The remaining 36 (70.59%) events were associated with non-epileptic EEG findings, such as sharp vertex transients, K complexes, or other features of sleep.

Four children were followed for neuro-developmental assessment. The mean period of follow-up was 46 months after the initial event. One patient was lost to follow-up. Two patients had mild speech delay.

Two children were treated at onset, each with clonazepam and levetiracetam. At follow-up, they were no longer taking antiepileptic drugs (AEDs) and were free of events. The other three remained untreated since the initial evaluation was based on individual parental decision. At follow-up, one patient continued to have exclusively nocturnal events and one had nocturnal myoclonus only in the setting of fever. No patient progressed or evolved to develop other forms of epilepsy.

Table 1. Clinical features of patients.

Patient	Gender	Description of event	Age at onset of symptoms	Family history of epilepsy/ febrile seizures	Months of follow-up after initial event	Neurological examination at follow-up	Treatment
1	Male	Nocturnal myoclonic jerks involving both arms and legs, longest episode lasted two minutes.	22 months	Febrile seizures	86	Normal	Clonazepam at diagnosis, none currently
2	Male	Nocturnal myoclonic jerks involving both arms and legs	16 months	Febrile seizures	30	Mild speech delay, nocturnal myoclonus when febrile	Levetiracetam at diagnosis, none currently
3	Male	Nocturnal myoclonic jerks involving both arms and legs	12 months	Epilepsy	33	Mild speech delay, occasional nocturnal myoclonic jerks	None
4	Male	Nocturnal myoclonic jerks involving both arms and legs, sleep tremors episodically	8 months	None	40	Normal	None
5	Male	Nocturnal myoclonic jerks involving both arms and legs, longest episode lasted seconds	3 months	None	Unknown	No follow-up information	No follow up information

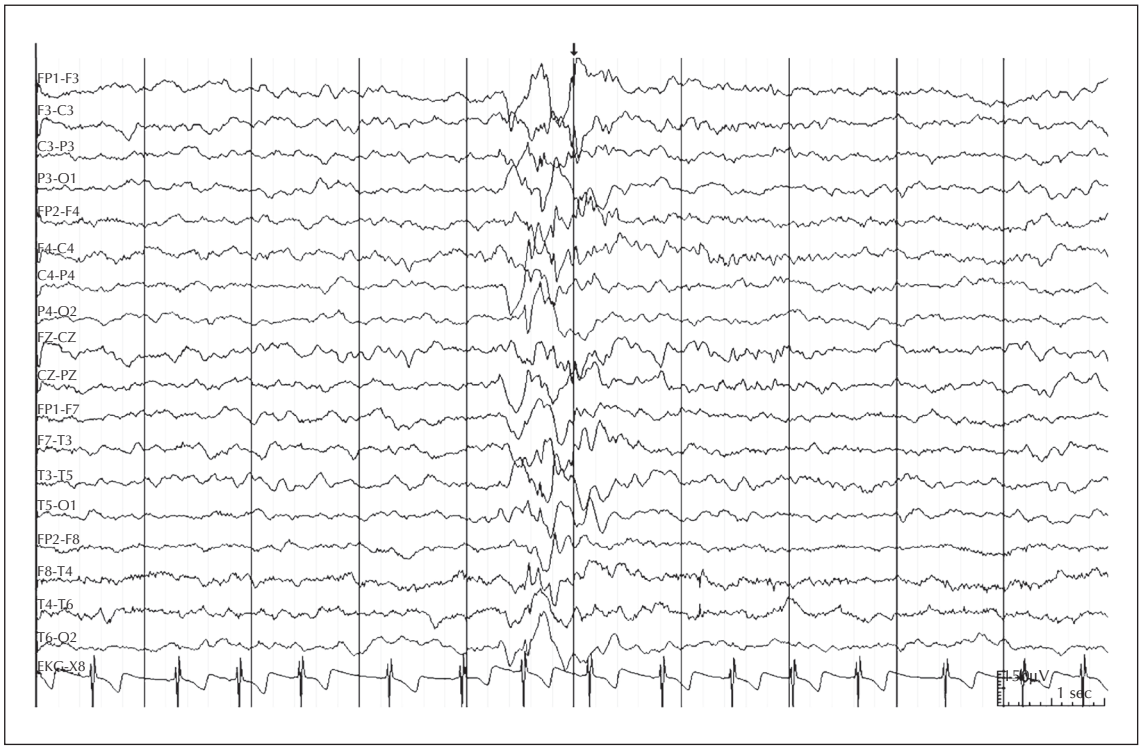

Figure 1. Generalised burst of delta wave activity with intermixed spikes.

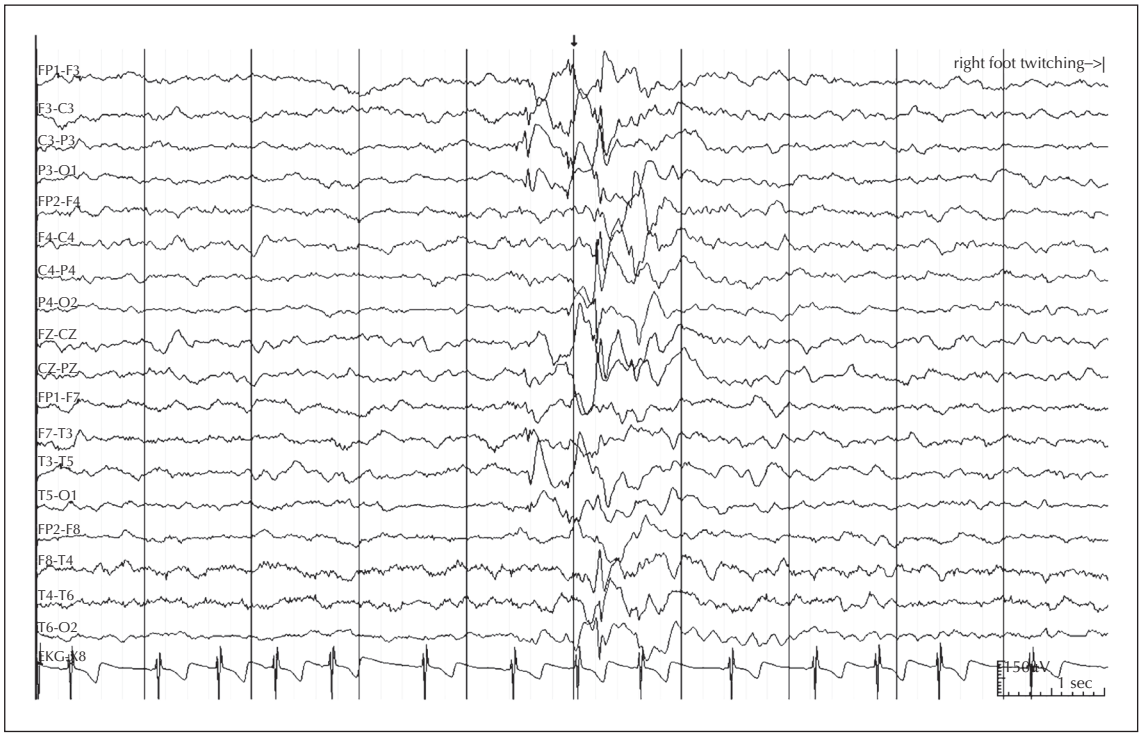

Figure 2. Generalised burst of delta waves interspersed with spikes, greater on the left than the right. The patient had right foot myoclonus followed by bilateral lower and upper extremity myoclonus.

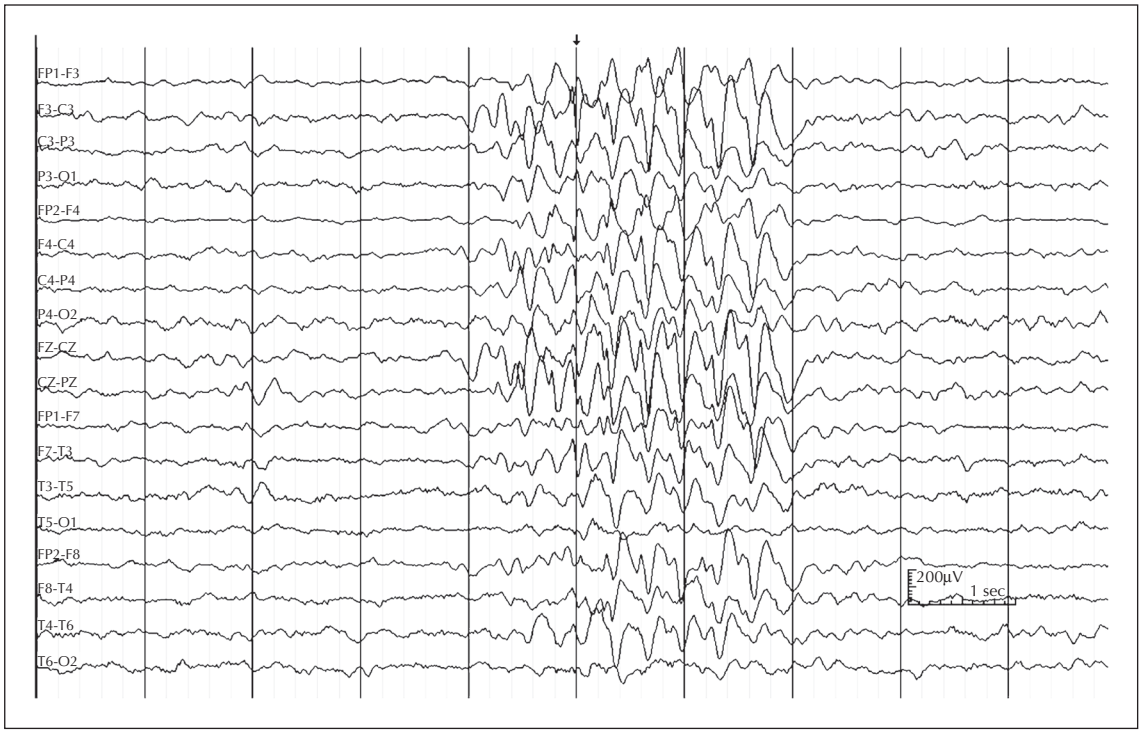

Figure 3. Generalised spike-and-wave activity at a frequency of 3 Hz, corresponding to the myoclonic episode.

Table 2. Electrographic features of patients.

Patient	Hours of EEG reviewed	Number of events	Number of events with EEG correlate (%)	EEG features	Phase of sleep
1	24	8	3 (38)	Bilateral burst of delta or theta activity, high-amplitude intermixed with spikes.	II
2	24	15	2 (13)	High amplitude of generalised delta slow activity, intermixed with spikes.	II, Slow-wave sleep
3	24	2	1 (50)	High amplitude of generalised delta slow activity, intermixed with spikes.	I
4	1	9	2 (10)	High amplitude of generalised delta slow activity, intermixed with spikes.	II
5	24	17	7 (41)	High amplitude of generalised delta slow activity, intermixed with spikes; para-saggital spike and slow wave pattern.	II, Slow-wave sleep

Discussion

We report a group of five children with excessive myoclonic jerks only during sleep and abnormal EEG. The movements, in all of the cases, involved both upper and lower extremities and were terminated upon waking the child. There was no daytime myoclonus or other seizures. In about a third of the

myoclonic jerks noted, there was associated epileptiform activity on the EEG. We believe that our patients might be best classified under the spectrum of benign myoclonic epilepsy of infancy, but only presenting with nocturnal seizures. The lack of EEG seizure correlate and presence of normal sleep architecture in some of the myoclonic jerks is a well-described phenomenon in benign myoclonic epilepsy of infancy, which is found in more than 50% of the patients (Rossi *et al.,* 1997).

Benign myoclonic epilepsy of infancy, described by Fejerman in 1997, is an epilepsy syndrome characterised by myoclonic seizures that manifest in young children with normal development (Fejerman, 1997). The brief myoclonic attacks occur in otherwise normal infants from 6 months to 3 years of age, involving the upper limbs, head, and rarely the lower limbs. The movements are repetitive and occur in clusters of two or three. The attacks are present during wakefulness and sleep. Benign myoclonic epilepsy of infancy may show normal interictal EEGs (Auvin *et al.,* 2006; Caraballo *et al.,* 2009). Patients exhibit diffuse polyspike waves which are synchronous with myoclonic jerks, although asynchronous discharges have also been seen. These discharges involve the fronto-central and vertex areas. The discharges can be seen during wakefulness, drowsiness, and slow-wave sleep (Kellaway, 2003; Darra *et al.,* 2006; Caraballo *et al.,* 2009). Patients with benign myoclonic epilepsy of infancy have been treated to varying degrees of success with multiple antiepileptic medications, including valproate, ethosuximide, clonazepam, and clobazam.

The primary differentiating feature between the patients in our series and the patients with typical benign myoclonic epilepsy of infancy, is the timing of the events. The patients described by us had exclusively nocturnal events. In benign myoclonic epilepsy of infancy, the EEG changes are seen in the drowsy state (stage 1) or wakefulness, or slow-wave sleep, however, 80% of the events in our series were captured in stage 2 and slow-wave sleep, and only 20% in stage 1. None were captured during wakefulness. There were no interictal EEG changes.

In a young child with abnormal paroxysms or body jerking, it is important to classify the behaviour, as this may have significant implications for treatment and prognosis. Although it was initially thought that patients with benign myoclonic epilepsy of infancy always have a good outcome, there are reports showing that it can evolve into other epilepsies (Moutaouakil *et al.*, 2010). The differential diagnosis for paroxysmal movements during sleep is very broad and includes non-epileptic conditions such as hypnic jerks, benign neonatal myoclonus, periodic limb movement disorder, Sandifer syndrome, hyperekplexia, and epileptic syndromes such as benign myoclonic epilepsy of infancy, and infantile spasms (Vendrame and Kothare, 2011).

We hypothesize that these findings may represent a variant of the benign myoclonic epilepsy of infancy, which has not been previously described.

The limitations of the study include its retrospective nature, a lack of accuracy with regards to the definition of excessive myoclonic jerks, and the small number of patients included. Further prospective descriptions of the EEG correlate of children with isolated excessive myoclonic jerks during sleep might corroborate our hypothesis. □

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