Benign Neonatal Sleep Myoclonus

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Montida Veeravigrom and Tayard Desudchit

A term male newborn GA 38 weeks by date, Birth weight 2800 m. AGA. He was born by vaginal delivery with APGAR score 9 and 10 at 1 and 5 min respectively. No complication was noted during peri or postnatal delivery. At day 10 of life, the baby had brief jerks of arms and legs during sleep for 2–3 s. The cessation of the jerk occurred spontaneously. During the event, there was no changes in vital signs. The patient remained active and alert when he woke up. Physical examination and neurological examination were unremarkable.

18.1 Epidemiology

Three infants with sleep myoclonus were first reported by Coulter and Allen with the term "benign neonatal myoclonus" [1]. Benign neonatal sleep myoclonus (BNSM) is characterized by myoclonic jerks occurred exclusively during sleep at neonatal onset. Myoclonic jerks were abrupt and consistently cessation with arousals. Electroencephalogram is normal during the event with excellent prognosis [2].

The syndrome was underrecognized or unfamiliarity by pediatricians or neonatologists for 25 years and often remain misdiagnosis. This syndrome is a non-epileptic movement disorder that sometime mimic neonatal seizure. After it has been recognized, the syndrome was not a rare disorder. The incidence varies between 0.8 and 3 cases per 1000 birth [3]. This condition is more common in male. The ratio of male to female was 2: 1 in the largest study [4].

18.2 Etiology

Even the syndrome is usually sporadic, genetic factors may contribute to the etiology of BNSM. Some familial cases have been reported [5–9]. Afawi et al. reported that BNSM showed autosomal dominant inheritance and is not allelic with KCNQ2 and KCNQ3 gene [10]. KCNQ2 and KCNQ3 genes were found in benign familial neonatal seizure, one of differential diagnoses of BNSM.

The pathophysiology of BNSM is not fully understood. Two hypotheses were reported. The study of BNSM with combined EEG-polymyography suggested a generator in cervical spinal cord, not in reticular activation system in the brain stem [11]. Another study postulated

M. Veeravigrom (✉)
Section of Neurology and Sleep Medicine, Department of Pediatrics, The University of Chicago, Chicago, IL, USA
e-mail: mveeravigrom@uchicago.edu; Montida.V@chula.ac.th

T. Desudchit
Division of Pediatric Neurology, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

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A. M. Li, K. C. Chan (eds.), *Paediatric Sleep Disorders*,
https://doi.org/10.1007/978-981-19-5791-8_18

immature or imbalance of serotoninergic system [12]. In neonate, the corticospinal tract is a descending inhibitory pathway and myelination develops in rostro-caudal direction. Immature myelination leads to incomplete control movement which resulted in myoclonic jerks. Myelination increases most at 6–7 months of age coincides with spontaneous resolution of BNSM. The rare presentation of facial involvement is due to the immature myelination of corticobulbar tract. Normally corticobulbar tract is myelinated before the corticospinal tract [11, 13].

18.3 Presentation and Diagnosis

Myoclonus manifested by sudden, brief, shock-like involuntary movement caused by muscle contraction which was called positive myoclonus. It also caused by lapse of contraction which was known as negative myoclonus [14]. BNSM is one of benign self-limiting positive myoclonus that occurred exclusively during sleep. BNSM was observed in term newborn infants during first week of life. From Kaddurah A, et al. eighteen case series, the mean age of onset was 9.6 days ± 8.8 days., with a median onset of 7.5 days (range,1–35 days) [15]. The earliest onset has been reported at 5 h of age [1].

The majority of myoclonus involves bilateral upper and lower extremities. However, unilateral myoclonus has been reported and around one third of the patients had lateralized features. The myoclonus jerks were irregular in frequency with two to three rapid abduction-adduction bilateral jerks followed by short pause. Head and facial myoclonus was rare to be seen in BNMS, however about 11% in the series were reported. Myoclonic jerks typically appear during quiet sleep. They may present in the transition from sleep to wakefulness [15]. Simple maneuvers such as repetitive sound, tactile stimuli or rocking provoke BNSM [16]. Benzodiazepines worsen or exacerbate myoclonic jerks in BNSM [17]. Restraint does not stop myoclonic jerks [18]. The differential diagnosis of BNMS is summarized in Table 18.1.

Table 18.1 Differential diagnosis of benign neonatal sleep myoclonus (BNMS)

Differential diagnosis of BNMS
Neonatal jitteriness
Neonatal drug withdrawal
Physiologic hypnic myoclonus
Benign myoclonus of early infancy
Neonatal seizure • Benign familial neonatal seizure
Neonatal status epilepticus

There are variabilities of case presentation of BNSM. The syndrome appears exclusive during sleep especially quiet sleep. Some cases have been reported during wakefulness at the awakening. The frequency of myoclonic jerks was also variable with median of 1/day (range 0.5–4). This condition was lasted with a mean duration of 11.8 ± 6.2 weeks (median 12 weeks; range 3–24 weeks) [15].

There are several case reports that BNSM was misdiagnosis as neonatal seizure or status epilepticus [19–21]. The misdiagnosis was from variability of the presentation such as focal features, head and face involvement and prolong duration. There is another case series about BNSM evokes somatosensory response. Somatosensory response was seen in EEG as theta band slow waves on vertex and central electrodes concomitant with myoclonic jerks and jerk-locked back-averaging revealed a sequence of deflections following myoclonus [22]. This EEG changes may mimic epileptiform discharges. This resulted in unnecessary diagnostic studies and inappropriate antiepileptic drug therapy (Table 18.2).

Table 18.2 How to differentiate Benign neonatal sleep myoclonus and neonatal seizure

	BNSM	Neonatal seizure
Onset	Commonly in the first 2 weeks of life	Variable depend on causes
Semiology	Myoclonic, majority symmetric, irregular Rare, asymmetric. Head and facial involvement.	Variable; tonic, subtle, clonic, multifocal clonic and myoclonic. Often with facial involvement
Eye characteristic	Persistent eye close	Eye usually open
Provocation	Repetitive sound, tactile stimulus, rocking	Occurs abruptly, spontaneously
Sleep/wake	Appears exclusively during sleep	Occurs in sleep and wakefulness
Terminated by	Arousals, wakefulness	Antiepileptic drug or spontaneously ended.
EEG during the event	Normal	Abnormal
Cause	Healthy term or near-term infant, Normal neurological infant, unknown cause.	Multiple causes; congenital brain malformation, hypoxic ischemic encephalopathy, stroke, metabolic, infection
Outcome	Excellent	Depend on underlying causes.

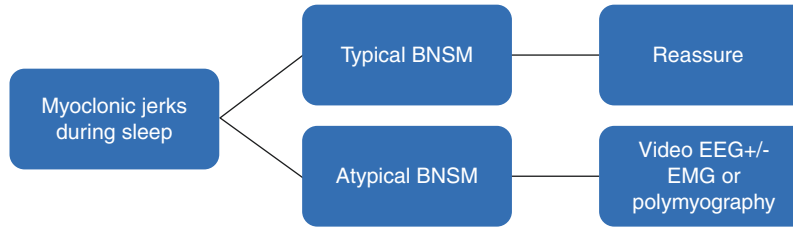

Fig. 18.1 Flow algorithms for management of BNSM

18.4 Management

BNMS is self-limited condition. It is important for pediatrician, neonatologist, and pediatric neurologist to recognize variability of clinical presentation. The correct diagnosis of BNMS will prevent unnecessary diagnostic procedure and unwarranted antiepileptic therapy. Antiepileptic medication does not treat myoclonic jerks and sometimes exacerbate them. The reassurance of this diagnosis will relieve parental anxiety.

There are atypical features of BNMS that sometimes make it is uncertain to diagnose from clinical standpoints. The atypical features were as the followings: prolong duration, head and face involvement, consistent focal features, occurred during wakefulness. These events may need to reconfirm with video EEG with or without EMG/polymyography (Fig. 18.1).

18.5 Cross Cultural Perspective

There are Few researches about BNMS in Asia Pacific region. Case series of 15 patients in Japan showed similar clinical manifestation with previous reported in western countries. BNSM was also misdiagnosed as neonatal seizure. Two patients received antiepileptic drug and three infants underwent lumbar puncture. In this study, there was a link between BNSM and migraine. Long term follow-up, 3 children had migraine

after 5 year of age and 42% of parents in this study had migraine. The link was hypothesized from serotoninergic pathway [23]. Two other papers were from India as a case report and eighteen case series of BNMS that mimics neonatal seizure [21, 24].

18.6 Summary of Key-Take-Home Messages and Research Gaps

1. Benign neonatal sleep myoclonus is a self-limited condition with variability in presentation.
2. The correct diagnosis of BNMS will prevent unnecessary diagnostic procedure and unwarranted antiepileptic therapy.
3. Further research needed regarding of pathophysiology and genetics.

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