Clinical commentary

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Paroxysmal non-epileptic events in infancy: five cases with typical features

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ABSTRACT – The differential diagnosis of paroxysmal non-epileptic events in early childhood is one of the most challenging tasks in paediatrics, and may be difficult even for specialized child neurologists. Parents are usually concerned by every unusual movement of their children and consult paediatric general practitioners immediately. We investigated five infants/toddlers (aged 1-30 months) referred by their general practitioners with a suspicion of epilepsy. None of them were ultimately shown to have epilepsy. Our aim was to determine the main reasons for referral and describe, through images and video, the typical features of five non-epileptic paroxysmal events (benign neonatal sleep myoclonus, jitteriness, shuddering attack, paroxysmal tonic upgaze, and infantile masturbation). The review of these events reveals the significance of the circumstances within the history of the patients. A detailed history is of considerable help in the differentiation of epileptic paroxysmal events from non-epileptic events, avoiding unnecessary investigations. Video-EEG examination is necessary only in cases when epilepsy is strongly suspected. [*Published with video sequences*].

Key words: benign neonatal sleep myoclonus, jitteriness, shuddering, upgaze, gratification, non-epileptic paroxysmal events, infant

Seizure or seizure-like episodes are among the most concerning symptoms during childhood, especially in very young children, and therefore parents are usually scared and visit paediatric emergency care units or general practitioners (GPs). The majority of these seizure-like episodes are benign movements occurring as paroxysms and there is no need for further investigations besides reassuring and informing parents.

The incidence of paroxysmal movements is 8.9% in the first year of life, but only a small proportion of infants has epilepsy (Visser *et al*., 2010). Neither parents of healthy children, nor those of children with epilepsy are able to clearly judge the precise nature of a particular movement. Paroxysmal events are correctly judged by parents of epileptic children in 44.5% cases (Nagy *et al*., 2017).

Without knowing the detailed history of the paroxysmal events, the differentiation between epileptic seizures and other harmless movements, especially in the neonatal and infantile periods, is extremely hard. Parents can help in the assessments by making home video recordings. The videos may reveal

VIDEOS ONLINE

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very important clinical features which can be crucial in the diagnostic work-up. But even for trained specialists, the differentiation based solely on video recording and some medical history details can be challenging. Moreover, even physicians working in a neonatal intensive care unit were able to recognize these events correctly in only 54% cases (Malone *et al*., 2009).

The differential diagnosis is not simple, not only in the very young infant population, but sometimes also in the case of older children as well. Uldall *et al*. (2006) revealed that 30% of patients (aged from eight months to 17 years, eight months) referred to their tertiary epilepsy centre with a firm epilepsy diagnosis turned out not to have epilepsy.

In each case, when there is any doubt of the origin of the unusual movement, long-term video-EEG examination/monitoring should be performed and an evaluation of the EEG by an expert is mandatory.

Our objective was to investigate typical histories and symptoms/signs of infants with non-epileptic paroxysmal events, based on our database, with an aim to demonstrate the typical features of these events and help paediatricians and paediatric neurologists in decision-making. For three typical paroxysmal non-epileptic events, we were able to capture photographs and video recordings which clearly confirm the benign nature of extra movements in children.

Benign neonatal/infantile sleep myoclonus

History: The mother noticed jerking of the limbs of her three-week-old baby twice. Both times this occurred during sleep. On the first occasion, the infant was in supine position and all his limbs were twitching. The second time, the baby was in prone position and his left leg started to twitch and twitching spread to the other limbs. No similar movements were observed when the baby was awake.

Benign neonatal/infantile sleep myoclonus occurs only during sleep and ceases after awakening. The incidence of the only neonatal form is about 0.8-3/1,000 newborns (Maurer *et al*., 2010). The typical age ranges from a few days to six months; it mostly disappears at the age of three months (Orivoli *et al*., 2015). Myocloni can be symmetric or asymmetric and can involve one or more limbs. The EEG shows normal brain activity. Although the word "benign" forms part of its name, Paro-Panjan and Neubauer (2008) found mild abnormalities in axial muscle tone in 8/38 children with sleep myoclonus. Suzuki *et al*. (2015) suspected a connection with the later occurrence of migraine: 3/12 children with sleep myoclonus had migraine at the age of five years, and 5/12 of their parents also had migraine. Sleep myoclonus can be clearly differentiated from epileptic myoclonus which is more severe, symmetric or asymmetric, and occurs even during wakefulness. This type of myoclonus may refer, for example, to a severe metabolic disorder such as non-ketotic hyperglycinaemia or hypoxic-ischaemic encephalopathy.

Jitteriness

History: The parents of a two-week-old baby noticed shaking of his limbs (mainly the lower extremities) from birth. This shaking lasted a few seconds, and occurred 10-15 times a day, only when awake. They were not able to relate this shaking to anything, but could stop it by grasping the limb.

This description is typical of jitteriness (or recurrent tremor): rhythmic, involuntary, oscillatory movements. This event can be considered physiological in healthy newborns (there is no other neurological symptom). Parker *et al*. (1990) found jitteriness in 44% of healthy full-term neonates. However, we found data suggesting that tremor, shuddering, and shiver can be seen as the earliest signs of vitamin D deficiency in healthy-appearing neonates as well (Collins and Young, 2017). Several theories exist about the development of jitteriness, and it has been suggested to be involved in the maturation process of the central nervous system. Coarse tremor (with higher amplitude and lower frequency) usually refers to a pathological condition (hypoxic-ischaemic encephalopathy, intracranial bleeding, metabolic or electrolyte disturbances, drug withdrawal, etc.). The differentiation of tremor from epileptic phenomena may be helped by the following:

– tremor can be stopped by touching or flexion of the involved limbs;
– tremor can be induced by certain types of stimuli;
– ocular movements and autonomic symptoms do not accompany the tremor (Orivoli *et al*., 2015).

Shuddering attack

History: The one-year-old girl was referred by her GP with a three-month history of "weird" grimaces on her face, several times per week, often during eating. These sometimes co-occurred with moderate shivering (figure 1 and video sequence 1).

Shuddering attacks usually occur in the first year of life. These may recur several times a day. The movements resemble the reaction a child would have if an ice cube slid down his/her back, leading to shaking and grimacing. During this event, the patient's reactions remain intact, and the EEG is normal. Shuddering attacks disappear spontaneously within the first decade of life. The pathophysiology of these events is still unknown (Jan, 2010).

Figure 1. Shuddering attack.

Figure 2. Paroxysmal tonic upgaze.

Paroxysmal tonic upgaze

History: The nine-month-old child was referred by the paediatric GP with a two-day history of upward fixation of his eyes lasting for a few seconds, 3-5 times a day. His parents were very concerned by these symptoms because of positive family history; the boy's cousin had epilepsy starting at the age of two years (figure 2 and video sequence 2).

Spontaneous paroxysmal tonic upgaze can be similar to absence seizures, where the eye balls slide upwards and the gaze of the child becomes vacant. Paroxysmal tonic upgaze is a completely benign phenomenon in the majority of cases, and it remits spontaneously in an otherwise healthy child. However, patients should be examined thoroughly and followed, as learning difficulties occur in 40% of cases and moderate or severe cognitive deficit in 10% cases, later on. In about a quarter of children, residual ataxia and ocular motility anomalies may be present (Ouvrier and Billson, 2005). To date, the pathophysiology has not been identified. Ouvrier and Billson (2005) suspected involvement of structural lesions of the upper dorsal brainstem, but the intermittent nature refers to a functional problem. Kartal (2019) reported a case caused by vitamin B12 deficiency.

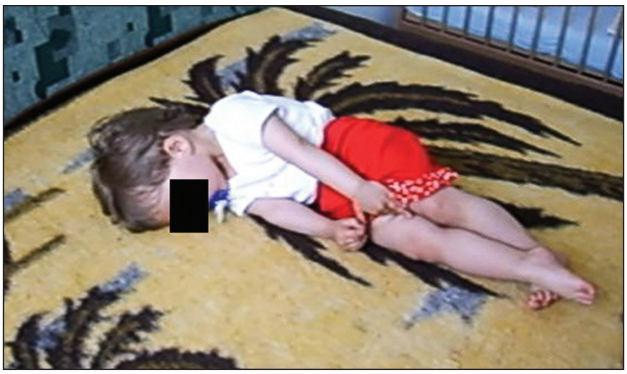

Figure 3. Infantile gratification (masturbation).

Infantile gratification (masturbation)

History: The paediatric GP referred the two-and-half-year-old child to our university hospital with a two-week history of "weird" movements. During sleep, she turned to her side, tensed and crossed her lower extremities, and made scissor-like movements which lasted usually 20-30 minutes. She repeated these movements 2-3 times a day. During these particular movements, her face became hyperaemic and sweaty. She was reactive, but no gaze fixation was observed and she did not like to be disturbed while doing these movements (figure 3 and video sequence 3).

Infantile masturbation or gratification is a stereotypic movement that may last even hours. Manual stimulation is usually not involved. The typical age ranges from three months to three years and occurs mainly in girls. It may be accompanied by sounds, wheezing, flushing, and sweating. Consciousness is not altered (Mallants and Casteels, 2008). The parents should be reassured that this is normal behaviour and part of the child's psychomotor development. It causes a pleasing sensation for the child similar to thumb sucking. No further investigation is needed. Yang *et al*. (2005) presented

12 cases with infantile masturbation. Before the diagnosis, four of 12 children had invasive diagnostic tests including lumbar puncture or muscle biopsy, and eight of the 12 had been treated previously with antiepileptic medication without any reason.

Conclusion

The differential diagnosis of paroxysmal movements in infancy and in early childhood seems to be clear when we have a very thorough history and we know the circumstances. Home videos taken by parents can be of considerable help in the differential diagnosis. In the majority of cases, there is no need to perform any extra examinations, *e.g.* EEG or MRI.

Parents usually suspect an epileptic seizure when they notice their children doing such movements. The assessment of myocloni can sometimes be challenging. Based on our previous study, nystagmus and more severe myoclonus may be considered as "red flags" for epileptic seizures for specialists (paediatric neurologists), while other specific features (for example: cessation on touching) characterize only non-epileptic events (Nagy *et al*., 2017).

In our study, we present five patients with non-epileptic paroxysmal events without other neurological signs. During the two-year follow-up period, none of these children developed epilepsy and no other neurological abnormality was revealed. Our aim is to bring these commonly occurring phenomena, based on typical photographs and videos, to the attention of paediatric GPs and child neurologists, in order to assist them with decision-making. □

Legends for video sequences

Video sequence 1.

Shuddering attack.

Video sequence 2.

Paroxysmal tonic upgaze.

Video sequence 3.

Infantile gratification (masturbation).

Key words for video research on www.epilepticdisorders.com

Phenomenology: non-epileptic paroxysmal event (videos 1 and 3); eye deviation (video 2)
Localization: not applicable
Syndrome: non-epileptic paroxysmal disorder
Aetiology: non-epileptic paroxysmal disorder

Supplementary data.
Summary didactic slides are available on the www.epilepticdisorders.com website.

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We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines. Parents give their permission to present the photographs. Eszter Nagy was supported by the ÚNKP-18-3-I, New National Excellence Program of the Ministry of Human Capacities.

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TEST YOURSELF

(1) What are the most common paroxysmal non-epileptic events in infancy?

(2) List the three most typical features of jitteriness that can help in differentiating between non-epileptic events and epilepsy?

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".