Child Neurology: Benign nocturnal alternating hemiplegia of childhood

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Alternating hemiplegia of childhood (AHC) is a disorder of recurrent hemiplegia beginning before age 18 months and is associated with dystonia, nystagmus, and progressive cognitive and motor impairment. This disorder was first recognized by Verret and Steele¹ in 1971. Benign nocturnal alternating hemiplegia of childhood, which differs from AHC by its absence of decline in neurologic or cognitive impairment, is very rare or possibly only rarely recognized. We describe 2 children diagnosed with this syndrome and review the literature published. In contrast to the severe prognosis of the much more known syndrome of AHC,^{1,2} the prognosis of benign nocturnal alternating hemiplegia of childhood is excellent.

CASE REPORTS In August 2008, a 2-year-old boy visited our outpatient department because of possible psychomotor delay. He had started walking at age 23 months and was only talking in single words. He was the second child of healthy, nonrelated parents. His paternal grandmother had migraine without aura. Neurologic examination revealed no abnormalities. We diagnosed benign delay in gross motor function and advised no further analysis. Just by chance, his parents mentioned that a few weeks earlier, they had noted that their son cried loudly while asleep. When they arrived, they found him in bed. He was unable to lift his head. When his parents took him out of bed, he seemed to be completely flaccid. In their opinion, he was fully conscious during this attack. After 20–30 minutes the symptoms gradually disappeared. According to his parents, the left side of his body recovered earlier than the right side.

MRI of the brain was performed, which was normal. Furthermore, we asked the parents to make a home video in case this phenomenon would reoccur. The parents recorded 2 further episodes of a right-sided paresis. Both occurred around 3:00 AM and lasted several minutes. On basis of the video recording, we made the diagnosis of benign nocturnal alternating hemiplegia of childhood. We reassured the

parents and told them about the benign and self-limiting course of this disorder. No specific genetic analysis was performed. There has been 1 more attack, making a total of 4 episodes. Motor development at the age of 5 years is normal, and he is visiting the regular primary school although there is concern about some possible autistic features. Psychiatric evaluation will start in the next months.

The second boy visited our outpatient department for the first time at age 20 months. He is the first son of nonrelated parents and has normal psychomotor development. His parents have noted periods in which he wakes up crying with a left-sided paresis of his face and arm since the age of 6 months. They were not sure whether the leg was involved. They told that they found it difficult to evaluate the responsiveness of their child during an attack, because of the continuous crying. After about 5 minutes, the symptoms gradually disappear. When waking up the next morning, all symptoms and signs have resolved completely. The frequency of these attacks changed between 2 times a month and every 2 months. There was no family history of migraine.

Investigations were done to exclude other possible causes. MRI showed a minor area of left-sided periventricular gliosis. This was considered a coincidence and not responsible for his symptoms. Magnetic resonance angiography showed no abnormalities. A regular daytime EEG did not show any abnormalities. A 24-hour EEG showed 2 right frontal sharp waves, no spike or spike-wave activity, and insufficient to diagnose epilepsy. Genetic analysis of the *CACNA1S* gene (hypokalemic periodic paralysis type 1) and *ATP1A2* (AHC) showed no mutations. Recently he has had 2 daytime attacks with right-sided facial paresis that lasted approximately 30 seconds and were triggered by stress and lack of sleep.

DISCUSSION A recent article about AHC published in the Resident & Fellow section gives an extensive differential diagnosis of acute focal weakness

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in childhood.² A very large spectrum of disorders (stroke, metabolic and neuromuscular disorders, head trauma, radiculopathy, seizures with postictal paralysis, familial hemiplegic migraine, and AHC) is mentioned.² Benign nocturnal alternating hemiplegia of childhood was not included in this list, indicating the fact that it is a relatively unknown disorder.

Benign nocturnal alternating hemiplegia of childhood was first described by Andermann et al.³ in 1994. Since then, only 4 more articles have been published.^{4–7} The syndrome is characterized by the occurrence of flaccid hemiparesis arising from sleep or within seconds after awakening³ and has only been described in boys.^{3–7} The diagnosis is purely descriptive. No additional analysis to confirm this diagnosis is available, only to exclude other etiologies. Age at onset is between 3 months⁶ and 3½ years.⁵ Commonly, these attacks last between 5 and 20 minutes,⁵ although attacks lasted up to 7 hours in 1 case.⁵ The reported frequency is between several attacks per year⁴ to 3 attacks per week³ and become less frequent with increasing age.⁴

In general, 1 or 2 hours after the child has gone to sleep, the parents are alerted by screaming, crying, or moaning.^{3,7} Some children have early attacks after 10–30 minutes of sleep⁴; others have attacks later in the night.⁴ When they arrive, the child has a half-sided paralysis involving the face, arm, and leg. Unilateral attacks can involve the same side of the body for many years.⁴ Attacks with bilateral paresis have also been described,^{3–5} as was the case in our first patient. In case of bilateral attacks, the weakness seems to be less severe.^{3,4} Coexisting aphasia,^{3,5} headache,⁵ vomiting,⁵ eye deviation,⁶ and breathing difficulties^{3,4,6} and hemi-dystonia^{4,5} and hemi-ataxia⁴ on the hemiparetic side have been reported. Interestingly, the attacks seem to occur mainly during nighttime sleep, rarely during daytime naps.^{3,4,7}

In all children, symptoms had disappeared the next morning when the child woke up. Some children were able to recall their attacks the next morning^{5,6}; some did not remember anything.^{4,7} One article described the occurrence of daytime attacks in one child. Those attacks appeared after the nocturnal attacks had ceased.⁴

The attacks can be misdiagnosed as AHC,^{1,3} migraine,⁷ benign focal epilepsy of childhood,⁷ nocturnal frontal lobe epilepsy,⁷ infantile colic,⁶ pavor nocturnus,⁶ or other sleep-related movement disorders.⁷ Interestingly, the first cases were described in the series described by Vernet and Steele¹ and both diagnosed as AHC (cases 6 and 7). These 2 brothers had nocturnal attacks of hemiplegia, and a normal development. By 4 years of age, the attacks ceased spontaneously.¹

The early sign to distinguish benign nocturnal alternating hemiplegia of childhood from AHC is the absence of paroxysmal eye movements.⁷ Besides, none of the children described with benign nocturnal alternating hemiplegia of childhood had hypotonia.⁷ It is stated that dystonic attacks do not occur in benign nocturnal alternating hemiplegia of childhood.⁷ However, that seems untrue because hemidystonic attacks have been reported in benign nocturnal alternating hemiplegia of childhood.^{4,5} Neurologic disability is present in all patients with AHC,⁸ not in benign nocturnal alternating hemiplegia of childhood, although the presence of hyperactivity, clumsiness, and motor tics has been described.⁴

Only a few EEG recordings of children during a nocturnal hemiplegic attack have been published. All reported slowing of background activity of the contralateral hemisphere during and after an episode.^{3–5,7} Slowing of background activity is not specific; it is also observed during episodes of migraine.⁷ The attacks that were observed occurred in sleep stage IV.^{3,4} Transcranial Doppler,⁵ cerebral angiography,^{3,5} CT,^{3,6} MRI^{3–7} and magnetic resonance angiography,⁵ and SPECT^{3,6,7} have been performed in some children; the results were normal in all of them. Interictal fluorodeoxyglucose PET scan showed normal results in several children, except for 1 child in whom the PET scan showed cerebellar hypometabolism.⁴

Many authors have tried prophylactic treatment during a certain period. Flunarizine,^{4,5} nifedipine,⁵ phenytoin,^{3–5} sodium valproate,⁵ carbamazepine,^{4,5} topiramate,⁷ ibuprofen,⁵ pizotyline,³ and propranolol³ had no effect on the occurrence of attacks. In one boy, flunarizine reduced the duration of the attacks and clonazepam reduced the frequency of episodes.^{3,4}

In contrast to the less favorable prognosis of the much more known AHC,^{1,2,8} the prognosis of benign nocturnal alternating hemiplegia of childhood is excellent.^{3–7} Psychomotor development, neurologic examination, and intelligence in the older children are normal.^{3–7} Besides, attacks cease spontaneously when the child grows older.^{3,4,6,7} In one article, it is described that a boy still had attacks at age 8 years.⁵ One boy had a few mild and short episodes a year until age 10 years.⁴

Concerning the etiology, an X-linked inheritance is suggested because of the fact that it only occurs in boys,^{4,7} although an autosomal recessive inheritance is possible.⁴ Extensive metabolic evaluation did not show any abnormalities.⁷ Most cases are sporadic, although 2 pair of siblings with this disorder have been reported.^{1,3} There is often a family history of migraine^{4,5} or migraine with aura.^{3,4} A channelopathy has been suggested because of the paroxysmal character and the observation that stress, excitement, and

sleep deprivation trigger attacks.^{3–5} Until now, no pathologic mutation in the *CACNA1A*, *ATP1A2*, or *SCN1A* genes and in mitochondrial DNA have been identified.⁷

The differential diagnosis of acute focal weakness is extensive. Benign nocturnal alternating hemiplegia of childhood should be considered in young boys (between 3 months and 3½ years) with attacks of hemiparesis or bilateral paresis occurring in sleep.

AUTHOR CONTRIBUTIONS

Dr. Wagener-Schimmel participated in drafting or revising the manuscript. Dr. Nicolai designed the study and participated in drafting or revising the manuscript.

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DISCLOSURE

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