ELSEVIER

Seminars in
Pediatric
Neurology

The Episodic Syndromes That Maybe Associated with Migraines

Diana Lebron, MD,[*] and Elza Vasconcellos, MD[†]

The "childhood periodic syndromes" have been renamed "the episodic syndromes that maybe associated with migraines". These syndromes were initially considered precursors of migraines that only occurred in childhood; however recent literature suggests that the episodic syndromes can occur in adults with known migraine and does not necessarily present as a precursor. This review article discusses the recent literature regarding the episodic syndromes and potential treatments. These disorders are seen by multiple subspecialists, therefore it is important to recognize and use the same definitions, criteria and nomenclature. A collaborative and multidisciplinary approach is critical to characterize, manage and potentially improve outcomes.
Semin Pediatr Neurol 23:6-10

Introduction

The "childhood periodic syndromes" were renamed by the International Classification of Headache Disorders (ICHD-III beta) as the "episodic syndromes that may be associated with migraines." They were historically described in children and were thought to be the precursors of migraines. However, recent literature has shown that these disorders are also seen in adults, can occur in patients with migraines, and are not always precursors.[1-4] These individuals may also experience motion sickness, sleep walking, sleep talking, night terrors, and bruxism.[5]

There is abundant literature regarding childhood migraine. Migraine headaches cause severe disability, lost days of school or work, and it interferes with social activities. The episodic syndromes are equally disabling, may at times be difficult to recognize and can be challenging to treat.[6-9] These patients often undergo an extensive work-up, have multiple emergency department visits, and require frequent hospital admissions. The diagnosis is usually delayed by years, causing severe anxiety to the patient and families.[10]

This review article discusses the recent literature regarding the episodic syndromes that often start in childhood, and their association with migraine and potential treatments. Some of the episodic syndromes begin in early infancy while others occur during childhood; therefore, the conditions will be discussed in chronological order.

From the *Department of Pediatrics, University of Tennessee Health Science Center, Memphis, TN.
†WeMind Institute, Miami Children's Hospital, Miami, FL.
Address reprint requests to Diana Lebron, MD, Department of Pediatrics, University of Tennessee Health Science Center, 920 Court Ave, Memphis, TN 38163. E-mail: diana.lebron@ttuhsc.edu

Migraine and the Episodic Syndromes

The migraineur has a hypersensitive pain pathway. Stress, dehydration, lack of sleep, and weather changes can potentially activate the pain pathway and trigger an attack. The autonomic dysfunction (photophobia, phonophobia, nausea, vomiting, abdominal pain, and vertigo) that accompanies the headache is the key that distinguishes migraines from other headache types.

Like migraine, the episodic syndromes are intermittent, disabling attacks that have an abrupt onset, stereotypic behavior, and are followed by complete resolution of the symptoms. In between attacks, the patient is healthy. Migraines can evolve with age and time. Individuals with migraines can experience autonomic dysfunction without the headache. Migraines and the episodic syndromes share autonomic dysfunction as part of the clinical manifestations. Infantile colic, benign paroxysmal torticollis (BPT), benign paroxysmal vertigo (BPV), cyclical vomiting syndrome (CVS), abdominal migraines, and vestibular migraines (VMs) are examples of the episodic syndromes.

Prevalence of the Episodic Syndromes

The prevalence of the episodic syndromes is believed to be 1.8%-4% of the pediatric population. In patients with

1071-9091/16/$-see front matter
http://dx.doi.org/10.1016/j.spen.2016.01.003

known migraines, it is as high as 9.8%.[11] A retrospective chart review at an outpatient pediatric neurology clinic in Brazil found that of the 674 children with headache, 5.6% presented with some type of episodic syndrome.[11]

A retrospective cohort study of 1134 Italian children with primary headaches (migraine and tension type) found that the episodic syndromes were reported in 70.3% of the children irrespective of the primary headache type. The children with an episodic syndrome had a higher headache frequency. Abdominal pain, motion sickness, and leg pain were the most common complaints. More than one type of episodic syndrome occurred in some individuals.[12]

Infantile Colic [A1.6.4]

Infantile colic was first described by Dr Wessel in 1954. This syndrome typically begins at 3 months of age and is characterized by abrupt onset, paroxysmal inconsolable crying, (fussiness) for more than 3 hours a day, and occurs more than 3 times a week. To make the diagnosis the symptoms must be present for at least 3 weeks. Infantile colic is a self-limited condition, which spontaneously resolves at approximately 9 months of age. The infants tend to cry more often in late-afternoon and evening, suggesting a temporal pattern.

The incidence ranges between 5% and 19%.[7,13] A recent multicenter, case-control study performed in Europe showed that children with migraine were more likely to have experienced infantile colic compared to controls.[13] A cross-sectional observational study suggested that infants with a maternal history of migraine were 2.6 times more likely to have colic than infants without a maternal history of migraine.[7]

Infantile colic is currently in the ICHD-III beta Appendix as the literature suggests that it is likely a precursor to migraines. It is believed to be an "early-life expression of migrainous tendencies."[7]

Although common, benign and self-limiting, the crying and fussiness is stressful for parents and a potential global health hazard as this condition has been associated with shaken baby syndrome.[14-17]

Behavioral strategies for treatment, such as placing the infant in a dark, quiet room, and minimizing sensory stimulation, may be beneficial. Dietary changes and Simethicone have not been shown to be beneficial.[18] In a small study, there was a suggestion that probiotics may have benefits, yet a larger study was not able to confirm the response.[19,20] There is insufficient data to make any evidence-based recommendation regarding treatment at this time. Early recognition and understanding of the biology of this condition may help to determine more effective therapies in the future.

BPT Benign Paroxysmal Torticollis [1.6.3]

Formally known as BPT of infancy, is a condition that was first described by Dr Snyder in 1969. The average age of onset is approximately at 6 months of life. It is characterized by abrupt onset of head or trunk tilt (tortipelvis) lasting anywhere from minutes to 30 days. Nausea, irritability, vomiting, pallor, drowsiness, ataxia, gaze abnormalities, limb dystonia, or nystagmus may be associated clinical manifestations. The frequency of attacks varies from once in a week to 1 episode in every 5 months. In between attacks, the neurologic examination is normal. BPT typically resolves by 4 years of age.[21] The symptoms must not be attributable to any other medical condition. Some of these babies develop childhood migraines or other episodic syndromes (ie, cyclical vomiting, BPV, abdominal migraine, VM, and motion sickness).[21-23]

Mutations of the CACNA1A have been identified in some patients with BPT.[24-26] This same mutation has been linked to patients with familial hemiplegic migraine type 1, episodic ataxia type 2, and a variant of alternating hemiplegia. A PRRT2 mutation was described in a family with BPT, paroxysmal kinesigenic dystonia, and hemiplegic migraine.[27] This suggests that some cases of BPT may be due to a channelopathy.

There are currently no evidence-based studies available to suggest treatment. However, if the child appears to be in pain, some authors recommend a trial of cyproheptadine.[28] The treatment is essentially managed by reassurance and supportive care.

BPV Benign Paroxysmal Vertigo [1.6.2]

First recognized in 1964 by Basser, this condition was formally known as Benign Paroxysmal Vertigo of Childhood. BPV usually occurs between 1 and 4 years of age.[29-33] The prevalence is reported to be 2.6% of children between the ages 5 and 15 years.[30-32] It is characterized by recurrent episodes of vertigo, lasting minutes to hours with spontaneous resolution. It may be associated with nystagmus, ataxia, vomiting, pallor, or fearfulness. These patients often initially present to ear, nose, and throat physicians. A retrospective chart review of 100 children that presented to a neurology clinic in Turkey with vertigo showed that 39% had BPV.[33] In between the episodes the neurologic examination, audiometric and vestibular function is normal.[5] BPV usually spontaneously resolves by 10-12 years of age.[30] It is believed to be a precursor of migraines, and according to the study by Batu et al,[33] 20% of the children diagnosed with BPV ultimately developed migraines.

CVS Cyclical Vomiting Syndrome [1.1.6.1]

CVS was initially described in 1882 by Samuel Gee, who reported a cohort of 9 children between the ages of 4 and 8 years.[34,35] This condition can occur in all age groups, from 6 months of age to adulthood.[1,35-37] A retrospective study of a cohort of adults with CVS determined that the age of onset in that particular group was anywhere from 2-49 years of age.[1]

The prominent clinical features are severe nausea and intense vomiting. Headaches can be mild or severe and may or may not be present. The vomiting must occur at least 4 times in an hour for at least an hour. The duration varies from an hour to 5 days.[5] There are typically 4 phases