WriteClick: Editor's Choice

Editors' Note: WriteClick submissions this week all reference the article by Dr. Polvi et al., "Shared loci for migraine and epilepsy on chromosome 14q12-q23 and 12q24.2-q24.3." Drs. Millichap and Nordli suggest that the syndrome described by the authors could be consistent with the benign childhood epilepsy disorder Panayiotopoulos syndrome (PS), which is characterized by syncope-like autonomic seizures. The authors respond that the patients in their series lacked the most typical clinical symptoms of PS, nausea, retching, and vomiting, as well as the prerequisite occipital interictal spikes on EEG. Dr. Panayiotopoulos and colleagues weigh in, commenting that the clinical and EEG findings in PS are more varied than currently acknowledged and that the diagnosis should remain open. The authors reply that, as a relatively new entity, PS is likely underdiagnosed, and refer to an upcoming article that may shine more light on the topic.

Megan Alcauskas, MD, and Robert C. Griggs, MD

SHARED LOCI FOR MIGRAINE AND EPILEPSY ON CHROMOSOMES 14q12-q23 AND 12q24.2-q24.3

John J. Millichap, Douglas R. Nordli, Jr., Chicago: We read with interest the recent article by Polvi et al.,[1] who described shared loci on chromosomes 14q and 12q for migraine and epilepsy in a large Finnish family. Ten of the 60 family members had clinical events that were unclassified by the authors and characterized by "sudden somnolence leading to transient unconsciousness and inability to be awoken" (SUA). Individuals with SUA also had onset of epilepsy from 1 to 5 years old, EEG foci in the centrotemporal and other localizations often changing with age, and cessation of symptoms in later childhood. This constellation of findings suggests a common benign childhood epilepsy called Panayiotopoulos syndrome (PS), as recognized in the International League Against Epilepsy classification system.[2] PS is marked by a susceptibility to syncope-like autonomic seizures (the child becomes unresponsive and flaccid) which are strikingly similar to the SUA.[3] The epileptiform EEG discharges in PS are often multifocal and increase in frequency during sleep. Although occipital localization is most common, the epileptiform activity may be seen in any region and often shifts with age. If the authors would elaborate on the clinical and electrographic presentation, the diagnosis of PS could likely be confirmed. The prospect of a novel causative gene would be an exciting development in the characterization of this epilepsy syndrome.

Author Response: Auli L.M. Siren, Helsinki; Heikki Rantala, Oulu; Anne Polvi, Helsinki; Maija Wessman, Helsinki; Anna-Elina Lehesjoki, Helsinki, Finland: We thank Drs. Millichap and Nordli for their interest in our article.[1] We investigated and discussed the clinical features and classification of the SUA attacks. Three reasons led us to use the term SUA. First, review of medical files and EEG reports and interviews of parents and family members revealed no other signs than unconsciousness resembling autonomic seizures or autonomic status epilepticus.[3] Second, no EEG was recorded during any of the SUA events, so we cannot be definitive about the nature of the events. Occipital interictal spikes are a hallmark of PS and were the prerequisite for diagnosis in the original series,[4,5] although some children had spikes also in other brain areas. None of the children in our series had occipital spikes. Third, it is possible that other autonomic signs or symptoms had occurred but were not recorded. However, the most typical symptoms of PS—nausea, retching, and vomiting—are not easily overlooked[6] and none of our patients had these symptoms. Since the most typical clinical and EEG findings of PS were lacking in our patients with SUA, we think it is very improbable that they had PS.

1. Polvi A, Siren A, Kallela M, et al. Shared loci for migraine and epilepsy on chromosomes 14q12-q23 and 12q24.2-q24.3. Neurology 2012;78:202–209.
2. Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. Epilepsia 2010;51:676–685.

3. Ferrie C, Caraballo R, Covanis A, et al. Panayiotopoulos syndrome: a consensus view. Dev Med Child Neurol 2006; 48:236–240.
4. Panayiotopoulos CP. Vomiting as an ictal manifestation of epileptic seizures and syndromes. J Neurol Neurosurg Psychiatry 1988;51:1448–1451.
5. Panayiotopoulos CP. Benign childhood epilepsy with occipital paroxysms: a 15-year prospective study. Ann Neurol 1989;26:51–56.
6. Covanis A. Panayiotopoulos syndrome: a benign childhood autonomic epilepsy frequently imitating encephalitis, syncope, migraine, sleep disorder, or gastroenteritis. Pediatrics 2006;118:1237–1243.

Chrysostomos P. Panayiotopoulos, Oxford; Michael Koutroumanidis, London; Colin D. Ferrie, Leeds, UK: Polvi et al.[1] should be commended for their meticulous study of a 5-generation Finnish family with epileptic seizures, migraine, or both. Drs. Millichap and Nordli[2] correctly point out that certain clinico-EEG features favor Panayiotopoulos syndrome (PS). Nearly all patients had childhood-related seizures. These were usually prolonged and consisted of a variety of visual elementary, motor, and autonomic manifestations. The authors also reported tonic-clonic convulsions that could have been of focal onset. EEGs showed frequent sharp wave multiple foci, changing localization before normalization with age. Furthermore, the episodes of sudden somnolence leading to transient unconsciousness and inability to be awoken (SUA) are similar to syncope-like epileptic seizures (SL-ES) that are common in PS.[3–5] In SL-ES, the child becomes flaccid and unresponsive for brief or commonly prolonged periods, can occur alone—pure SL-ES—as in SUA, or concurrently with other autonomic manifestations.

In their response, the authors consider that "most typical clinical and EEG findings of PS were lacking" in their patients. However, the clinico-EEG range of PS is much wider than previous recognized[3,5]; vomiting and occipital spikes may not happen in one-fourth of patients. The possibility of a spectrum of benign childhood focal epilepsies including rolandic epilepsy, PS, and idiopathic and photosensitive childhood occipital epilepsy of Gastaut[5] should be considered particularly when prospectively examining the newer generation of this family.

Author response: Auli L.M. Siren, Helsinki; Heikki Rantala, Oulu; Anne Polvi, Helsinki; Maija Wessman, Helsinki; Anna-Elina Lehesjoki, Helsinki, Finland: We thank Dr. Panayiotopoulos et al. for their letter and expert opinion on the nature of SUA being similar to SL-PS in PS.[1]

We adopted a conservative view on the SUA events due to lack of EEG data and the narrow spectrum of autonomic features during the events reported in our patients. PS, as a recently acknowledged entity, is most likely underdiagnosed[6] and this might have happened in our study. The upcoming article by Koutroumanidis et al.[4] will hopefully further clarify this topic.

Although this family is a gem for genetic studies on epilepsy and migraine, to our knowledge no affected individuals with epilepsy or SUA exist in the next generation (descendants of individuals 17–29). When new data on the genetics of PS become available, we are ready to study the SUA/SL-PS patients.

1. Polvi A, Siren A, Kallela M, et al. Shared loci for migraine and epilepsy on chromosomes 14q12-q23 and 12q24.2-q24.3. Neurology 2012;78:202–209.
2. Millichap JJ, Nordli DR Jr. Shared loci for migraine and epilepsy on chromosomes 14q12-q23 and 12q24.2-q24.3. Neurology Epub 2012 Feb 9. Letter.
3. Panayiotopoulos CP. Panayiotopoulos Syndrome: A Common and Benign Childhood Epileptic Syndrome. London: John Libbey & Company; 2002.
4. Koutroumanidis M, Ferrie CD, Valeta T, et al. Syncope-like epileptic seizures in Panayiotopoulos syndrome. Neurology (in press 2012).
5. Panayiotopoulos CP, Michael M, Sanders S, Valeta T, Koutroumanidis M. Benign childhood focal epilepsies: assessment of established and newly recognized syndromes. Brain 2008;131:2264–2286.
6. Panayiotopoulos CP. The birth and evolution of the concept of Panayiotopoulos syndrome. Epilepsia 2007;48:1041–1043.

Author disclosures are available upon request (journal@neurology.org).

Shared Loci for Migraine and Epilepsy on Chromosomes 14q12-q23 and 12q24.2-q24.3

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