PEDIATRIC NEUROLOGY BRIEFS
A MONTHLY JOURNAL REVIEW

J. GORDON MILLICHAP, MD. EDITOR
JOHN J. MILLICHAP, MD. ASSOCIATE EDITOR

Vol. 28, No. 8 August 2014

SEIZURE DISORDERS

CHROMOSOMAL MICROARRAY TESTING AND EPILEPSY

Investigators at the Boston Children's Hospital, MA, and other centers evaluated the role of copy number variants (CNVs) detected using chromosomal microarray (CMA) testing in 805 patients seen between 2006 and 2011 and having ICD-9 codes for epilepsy or seizures. They observed 437 CNVs in 323 patients (1-4 per patient), including 185 (42%) deletions and 252 (58%) duplications. Forty (9%) were confirmed de novo, 186 (43%) were inherited, and parental data were unavailable for 211 (48%). CNV size ranged from 18kb to 142Mb (excluding full trisomies), and 34% were >500kb. The epilepsy phenotype was explained by a CNV in at least 40 cases (5%), including 29 patients with epilepsy associated syndromes and 11 with likely disease-associated CNVs involving epilepsy genes or "hotspots" (e.g., 1q21.1, 15q11.2, 16p13.11) that predispose to epilepsy.

Genetic syndromes associated with epilepsy and confirmed by CNV testing included 22q11 duplication (4 cases), Mowat-Wilson (3 cases), Wolf-Hirschhorn (3 cases), Dravet (2), Williams (2), Kleefstra (2), Angelman (2), Phelan-McDermid (2), and benign familial neonatal convulsions, totalling 3.6%. CMA is recommended in the diagnosis of unexplained epilepsy. (Olson H, Shen Y, Avallone J, et al. Copy number variation plays an important role in clinical epilepsy. **Ann Neurol** 2014 Jun;75(6):943-58).

COMMENTARY. The advantages of the CNV to the patient with an unexplained epilepsy, parents, and clinician include an earlier more definitive diagnosis, an estimate

PEDIATRIC NEUROLOGY BRIEFS © 1987-2014, ISSN 1043-3155 (print) 2166-6482 (online), is published monthly and covers selected articles from the world literature. The Editor is Pediatric Neurologist and the Associate Editor, Pediatric Epileptologist and Neurologist at the Ann & Robert H. Lurie Children's Hospital of Chicago; Northwestern University Feinberg School of Medicine, Chicago, IL. PNB is a continuing education service designed to expedite and facilitate the review of current scientific information for physicians and other health professionals. Apply to PediatricNeurologyBriefs.com for Subscriptions (12 issues, January-December). Digital Edition PDF: $72; Print + Free Digital: $96 within US/UK, $128 outside US/UK. Institutions: Digital Edition IP Access $188, Print + Free Digital $228. Mailing address for subscription: Pediatric Neurology Briefs Publishers, PO Box 11391, Chicago, IL 60611

of prognosis, and in some cases, more specific treatment. Screening for rare CNVs is a valuable routine diagnostic workup in patients with unclassified epilepsies and complex phenotypes; 88 rare CNVs were discovered in 71 of 222 patients (31.9%) [1]. A chromosomal microarray (CMA) screen of 215 patients with a broad range of neurological phenotypes of unknown etiology found 30 (14%) were abnormal; phenotypes included infantile spasms, other epilepsies, and cortical malformations [2].

CMA is recommended especially in unclassified epilepsy patients with dysmorphic features, developmental delay, autistic spectrum disorder, family history of epilepsy, or parental consanguinity. More directed genetic testing for specific epilepsy genes or genetic neurological syndromes is indicated for patients with a characteristic phenotype [3].

References.
1. Helbig I, et al. Eur J Hum Genet. 2014 Jul;22(7):896-901.
2. Howell KB, et al. J Paediatr Child Health. 2013 Sep;49(9):716-24.
3. Millichap JG. Neurological Syndromes : A Clinical Guide to Symptoms and Diagnosis. New York: Springer; 2013:279.

COMPARISON OF 5- AND 30-MINUTE STATUS EPILEPTICUS

Investigators at Boston Children's Hospital and other centers compared the characteristics of patients with status epilepticus (SE) lasting 5-29 min with those with SE lasting >30 min. Of a total 445 patients with a median age at SE of 5.5 (2.8-10.5) years, 296 (66.5%) had SE lasting 5-29 min, and in 149 (33.5%) SE lasted >30 min. Patients with SE >30 min were younger than those with SE 5-29 min at time of seizure onset (median 1 vs 2.1 years, p=0.0007). SE as the first seizure presentation was more frequent in patients with SE >30 min (24.2% vs 12.2%, p=0.002). MRI abnormalities tended to be more frequent in patients with SE >30 min (70.5% vs 57.1%, p=0.061). Shorter vs longer SE cases showed no differences in seizure frequency, seizure types (febrile vs nonfebrile), developmental delay, and EEG abnormalities at baseline. At a median follow-up of 3.7 years after SE, 21 patients (4.7%) had died (median time of 3.1 years after SE), mostly unrelated to epilepsy. The odds of dying showed an increase of 0.005 per min of SE duration. SE thresholds of either 5 or 30 min identify groups of patient with similar electroclinical characteristics. (Fernandez IS, Vendrame M, Kapur K, et al. Comparison of pediatric patients with status epilepticus lasting 5-29 min versus >30 min. **Epilepsy Behav** 2014 Jun 17;37C:1-6).

COMMENTARY. Longer SE duration (>30 min) probably reflects a more severe underlying cause for SE, but patients with shorter (5-29 min) SE have comparable electroclinical characteristics to those with longer SE duration. Since seizures are more difficult to treat and carry a poorer outcome the longer they last [1][2], seizures lasting 5 min or longer are treated as aggressively as those > 30 min duration. Seizures (5-29 min) are considered as "impending" SE and those > 30 min as "established" SE.

References.
1. Eriksson K, et al. Neurology. 2005 Oct 25;65(8):1316-8.
2. Seinfeld S, et al. Epilepsia. 2014 Mar;55(3):388-95.