

SEIZURE DISORDERS

AUTOIMMUNE EPILEPSY GUIDELINES FOR DIAGNOSIS

Investigators at the Children's Hospital at Westmead, University of Sydney, Australia, and John Radcliffe Hospital, Oxford, UK, describe 13 children (11 female; mean age 6 years, range 1-13 years) seen over a period of 3.5 years with suspected autoimmune epilepsy. Using modified adult guidelines (Zuliani L, et al. **J Neurol Neurosurg Psychiatry** 2012 Jun;83(6):638-45), patients were classified as having definite autoimmune epilepsy in 5, probable in 1, possible in 3, unlikely in 2, and unknown in 2 patients, according to the neuronal surface or GAD antibodies, and response to immune therapy. Classical NMDAR encephalitis was diagnosed in 3 patients, VGKC in 2, limbic encephalitis with negative antibodies in 2, epilepsy with other autoimmune diseases in 3 (1 with GAD antibodies), fever-induced refractory epileptic encephalopathy in school-aged children (FIRES) in 2, and epileptic encephalopathy associated with VGKC antibodies in 1. Seven with suspected autoimmune epilepsy were positive for neuronal surface antibodies (NMDAR, VGKC-complex, and GAD). Immunotherapy used in 9 cases had a positive response in patients with positive neuronal surface antibodies (5/5) and less commonly in those with negative antibodies (2/4). (Suleiman J, Brillot F, Lang B, Vincent A, Dale RC. Autoimmune epilepsy in children: Case series and proposed guidelines for identification. **Epilepsia** 2013 Jun;54(6):1036-45). (Response: Dr Russell C Dale. E-mail: Russell.dale@health.nsw.gov.au).

COMMENT. Of children with suspected autoimmune epilepsy, those with neuronal surface antibodies and GAD antibodies frequently respond to immunotherapy. Guidelines may be useful in the diagnosis of seizures of autoimmune etiology. CNS disorders, some without associated tumors, may be antibody mediated and may benefit from immunomodulatory therapies.

Prevalence of autoantibodies in patients with epilepsy. In two large cohorts of adult patients with new untreated and established epilepsy screened for the multiple autoantibodies tested positive in 11% (VGKC in 5%), glycine receptors (3%), GAD (1.7%), and NMDA (1.7%). The prevalence of antibodies was the same in patients with established or newly diagnosed epilepsy. There was a significantly higher prevalence of positive antibody titers in patients with focal epilepsy of unknown cause than in those with structural/metabolic focal epilepsy (14.8% vs 6.3%; $p < 0.02$) (Brenner T, Sills GJ, Hart Y, et al. **Epilepsia** 2013 Jun;54(6):1028-35). VGKC complex antibodies in pediatric severe acute encephalitis are uncommon with only one (2.2%) of 46 children affected, a 4-year-old girl presenting with influenza A infection in Taiwan (Lin J-J, et al. **Brain Dev** 2013 Aug;35(7):630-635).

PROLONGED FEBRILE SEIZURES AND THEIR MANAGEMENT

Investigators at Tel-Aviv Sourasky Medical Center, and three other medical centers in Israel, obtained data, prospectively, on all children presenting in the emergency departments from January 2008 to March 2010 with prolonged febrile seizures. Information related to seizure semiology, treatment, and outcome was collected and

reviewed centrally on a total of 60 children, median age 18.3 months (range 12-28), with a median seizure duration of 35 min (range 26-60), 43 (71.7%) lasting >30 min. Seizures had focal onset in 34 infants (57%). Ambulance service activated by 54 families (90%) had a median arrival time of 8 min (range 5-10). Of 33 (61%) children treated with AEDs by the ambulance paramedics, only 15 (45%) responded. Children treated with rectal diazepam were less likely to respond: Only 1 (11%) of 9 children receiving rectal diazepam responded compared with 11 (58%) of 19 who received intravenous diazepam. Thirty-one children (52%) were still seizing on arrival in the ED, and 38 were admitted to hospital. EEG in 37 (61.7%) was abnormal in 17, but referral for EEG was independent of age, seizure duration, focality, and multiple seizure type. Lumbar puncture (LP) was performed in 12 patients (20%), ages 3-35 months, and none showed bacterial meningitis. Of children undergoing LP, 50% were <18 months of age, seizures had longer mean duration (73.8 vs 42.4 min ($p=0.001$), and most had active seizures in ED. Focality of seizure was not associated with performance of LP. Predictors of prolonged FS (> 30 min) were an independent effect of intermittent seizure semiology and initial treatment with rectal diazepam ($p=0.001$). (Bassan H, Barzilay M, Shinnar S, Shorer Z, Matoth I, Gross-Tsur V. Prolonged febrile seizures, clinical characteristics, and acute management. **Epilepsia** 2013 Jun;54(6):1092-8). (Response: Dr Haim Bassan, Dana Children's Hospital, Tel Aviv Sourasky Medical Center, Tel Aviv 64239, Israel. E-mail: bassan@post.tau.ac.il).

COMMENT. A prolonged febrile seizure (PFS), as defined in this study, is a subtype of the complex febrile seizure and one lasting >15 minutes. More recent data suggest that 10 minutes may be a more appropriate cutoff between the simple and complex FS (Hesdorffer DC, et al. **Ann Neurol** 2011 Jul;70(1):93-100). A febrile seizure lasting >30 min is classified as febrile status epilepticus (FSE), accounting for 5-9% of febrile seizure patients (Berg AT, Shinnar S. **Epilepsia** 1996 Feb;37(2):126-33).

PFS and FSE may be associated with hippocampal injury, subsequent mesial temporal sclerosis, and temporal lobe epilepsy (Hesdorffer DC, et al. **Epilepsia** 2012 Sep;53(9):1471-80) (Shinnar S, et al. **Neurology** 2012 Aug 28;79(9):871-7). In light of the increased risk of subsequent epilepsy, the acute management and prevention of PFS and FSE become highly important.

Rectal versus Intravenous Diazepam Treatment. The ineffectiveness of rectal diazepam in management of PFS reported in the Israel study is consistent with the findings in the UK, that control of status epilepticus with intravenous lorazepam was significantly superior to that with rectal diazepam (Chin RF, et al. **Lancet Neurol** 2008 Aug;7(8):696-703). In contrast, a retrospective analysis of a 30-month consecutive sample of ambulance-transported children in a large urban emergency medical service in San Francisco found rectal diazepam to be a simple, effective, and safe method of pre-hospital management of pediatric status epilepticus (Dieckmann RA. **Ann Emerg Med** 1994 Feb;23(2):216-24). Compared with IV diazepam, rectal diazepam is easier to administer, and is equally efficacious and less likely to produce respiratory depression. Short duration of action is an important limitation of both treatments.