

# PEDIATRIC NEUROLOGY BRIEFS

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J. GORDON MILLICHAP, M.D., F.R.C.P., EDITOR

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### SEIZURE DISORDERS

#### SEIZURES AND ANTI-NMDA-RECEPTOR ENCEPHALITIS

The clinical and immunological features of 100 patients with encephalitis associated with antibodies against NR1-NR2 heteromers of the NMDA receptor were analyzed in a study at the Children's Hospital of Philadelphia, and University of Pennsylvania. Median age was 23 years (range 5-76 years), and 91 were female. One boy (11 years old, without tumor) and 21 girls (12 with ovarian tumor) were a median age of 15 years (range 5-18 years). Prodromal symptoms in 86% consisted of headache, low-grade fever, or a non-specific viral-like illness within 2 weeks before hospital admission. Presenting symptoms were psychiatric or memory problems in 100%, seizures in 76%, decreased consciousness in 88%, dyskinesias, chiefly orofacial (86%), autonomic instability (69%), and hypoventilation (59%). Seizures were generalized tonic-clonic in 45 and partial complex in 10. EEG was abnormal in 92, and showed slow activity in 71 and epileptic activity in 21. Brain MRI was abnormal in 55, with increased FLAIR or T2 signal, and limited to the medial temporal lobes in 16. CSF was abnormal in 95, with pleocytosis in 91, increased protein in 32, and oligoclonal bands positive in 26 of 39 tested. Brain biopsy in 14 patients was nonspecific. Ovarian teratoma or other tumors were associated in 59%. Seventy-five patients recovered or had mild deficits, and 25 had severe deficits or died. Among those who recovered with mild deficits, 64 (85%) had signs of frontal lobe dysfunction including poor attention, impulsivity, and behavioral disinhibition. Patients with better outcomes and fewer neurological relapses had received early tumor treatment, usually with immunotherapy (P=0.04). Improvement was associated with a decrease of serum antibody titers. The effect of antibodies on neuronal cultures was determined by quantitative analysis of NMDA-receptor clusters. Patients' antibodies decreased the numbers of cell-surface NMDA receptors and clusters in postsynaptic dendrites. (Dalmau J, Gleichman AJ, Hughes EG, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *Lancet Neuro*

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Dec 2008;7:1091-1098). (Respond: Dr Josep Dalmau, Division of Neuro-Oncology, Department of Neurology, 3 W Gates, University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104; E-mail: [josep.dalmau@uphs.upenn.edu](mailto:josep.dalmau@uphs.upenn.edu)).

COMMENT. Anti-NMDA-receptor encephalitis is a new category of immune-mediated disorders of adolescents or young adults, often paraneoplastic (60%), diagnosed serologically, and amenable to surgical and/or immunotherapy. This disorder is not uncommon, almost 100 cases identified at the Univ Pennsylvania in 2 years. CSF findings are helpful in diagnosis but MRI abnormalities are nonspecific. Seizures, attention and behavior disorders are common sequelae in the 75% patients who recover. The role of prodromal viral infection or other event in triggering the immune response requires further study. The antibody-induced modulation of the target antigens is similar to the Lambert-Eaton myasthenic syndrome that occurs with or without tumor association. In Lambert-Eaton syndrome the presence of small-cell lung cancer confers a poor neurological outcome, whereas in anti-NMDA-receptor encephalitis, cases associated with teratoma of the ovary or testis and treated early have a good prognosis. (see Reflection and Reaction. Vincent A, Bien CG. *Lancet Neurol* 2008;7:1074-1075).

## HEAD NODDING SEIZURES AND *O.VOLVULUS* INFESTATION

Head nodding (HN) syndrome, a new epilepsy disorder in sub-Sahara Africa, is described in 62 patients studied prospectively at the University of Ulm, Germany; Haydom Lutheran Hospital, Tanzania; and other centers in Austria, Tanzania, and Canada. The onset of HN attacks was at 6 to 10 years in 50% cases, and at 11-15 years in 37%. At the time of diagnosis and evaluation, most patients were between 11 and 15 years of age. Twenty-eight (45%) patients had only HN attacks, and 28 had HN plus one other type of seizure, usually generalized or partial complex. HN was associated with loss of neck tone, and 37 (60%) patients had additional loss of tone of upper extremities. Consciousness was impaired in 11 (18%). Food was a provoking factor in 9 patients, and bathing in cold water caused HN in 2. A family history of epilepsy was present in 90%. EEGs in 10 patients were normal in 4 and showed abnormal slowing in 6, with sharp waves in 2. MRIs in 12 patients were normal in 4, and showed hippocampal sclerosis in 5 and gliotic changes in 5. Thirty-one (61%) of 51 patients had microfilariae visible on microscopic examination of the skin. Traces of *Onchocerca volvulus* DNA in the skin were identified by PCR in 12 of 20 without microscopically visible microfilariae. Skin PCR positivity was significantly associated with MRI abnormalities. Neutrophil counts were elevated in 14 (27%) patients and eosinophils in 28 (55%). *O. volvulus* serum ELISA test was positive in 44 (86%). CSF PCR was negative in all patients. HN seizures were 50% controlled by conventional antiepileptic drugs. (Winkler AS, Friedrich K, König R, et al. The head nodding syndrome – clinical classification and possible causes. *Epilepsia* Dec 2008;49:2008-2015). (Respond: Dr Andrea S Winkler, Department of Neurology, University of Ulm, Oberer Eselsberg 45, 89081 Ulm, Germany. E-mail: [drawinkler@yahoo.com.au](mailto:drawinkler@yahoo.com.au)).

COMMENT. The prevalence of epilepsy is reportedly higher in areas where onchocerciasis is endemic, eg Mexico, Sudan, Uganda, Tanzania, and S America, but meta-analysis fails to show a significant association between *O. volvulus* and epilepsy (Druet-