INFECTIOUS DISORDERS

N-METHYL-D-ASPARTATE RECEPTOR ANTIBODIES IN HERPES SIMPLEX ENCEPHALITIS

Researchers at Charite University Medicine Berlin, and other centers in Germany, Spain and the US performed a retrospective analysis of 44 patients with polymerase chain reaction-proven herpes simplex encephalitis (HSE) for the presence of onconeuronal and synaptic receptor antibodies. N-methyl-D-aspartate receptor (NMDAR) antibodies of the immunoglobulin (Ig) subtypes IgA, IgG, or IgM were detected in 13 of 44 (30%) patients, suggesting secondary autoimmune mechanisms. Antibodies were often present at hospital admission, but sometimes developed after the first week of HSE. Antibody-positive sera resulted in downregulation of synaptic marker proteins in hippocampal neurons. These findings have implications for the diagnosis and treatment of HSE. (Pruss H, Finke C, Holtje M, et al. N-methyl-D-aspartate receptor antibodies in herpes simplex encephalitis. **Ann Neurol** 2012 Dec;72(6):902-11). (Response: Dr Pruss. E-mail: harald.pruess@charite.de).

COMMENT. A subgroup of patients with HSE and NMDAR antibodies may benefit from immunotherapy. NMDAR antibodies (IgG, IgA and IgM) should be determined in patients with HSE. According to an article just published online, NMDA-R antibodies should also be determined in patients acutely ill with a diagnosis of schizophrenia.

N-methyl-D-aspartate glutamate receptor antibodies and schizophrenia. Diverse NMDA-R antibodies were identified in 15 subjects, primarily those with an initial schizophrenia diagnosis (9.9%), contrasted with 2.8% in patients with major depression, and 0.4% in controls. Two patients initially classified as catatonic schizophrenia were reclassified as having NMDA-R encephalitis with specific serum and CSF IgG NR1a antibodies. All other seropositive cases had IgA or IgM antibodies. Acutely ill patients with an initial diagnosis of schizophrenia show an increased prevalence of NMDA-R antibodies. The antibody subtypes in schizophrenia, depression and HSE are different from the repertoire with NMDA-R encephalitis. NMDA-R encephalitis should be considered as a differential diagnosis, especially in young females with acute disorganized behavior or catatonia. (Steiner J, Walter M, Glanz W, et al. **JAMA Psychiatry** 2013 Jan 23:1-8).

UNUSUAL ONSET OF ANTI-NMDA-RECEPTOR ENCEPHALITIS

A 19-year-old female presented with vomiting, diarrhea, emotional lability, auditory hallucinations, expressive dysphasia, and delirium. Atypically, she had no dyskinesia, movement disorder, central hypoventilation or autonomic instability, and she had only one seizure. CSF showed 129 nucleated cells primarily lymphocytic; PCR for HSE was unremarkable, and immunofluorescence of serum and CSF was positive for anti-NMDA-R antibodies. Brain MRI showed a left temporal T2 hyperintensity. CT scan

of chest, abdomen and pelvis revealed a 1.9 cm right ovarian dermoid and mycoplasma pneumonia opacities in the lungs. Paraneoplastic limbic encephalitis was suspected, and recovery followed removal of the teratoma and 5 plasmapheresis treatments. (Reid DK, Clardy SL. Anti-NMDA-receptor encephalitis: unusual presentation of an uncommon condition. **J Neurol Neurosurg Psychiatry** 2013 Jan;84(1):69-70). (Response: Dr Stacey L Clardy, Penn State MS Hershey Medical Center, Department of Neurology, EC037, PO Box 859, Hershey, PA 17033. E-mail: staceylynnclardy@yahoo.com).

COMMENT. The authors considered this case to be a less severe phenotype in the clinical spectrum of anti-NMDA-receptor encephalitis. They refer to cases presenting with new-onset epilepsy and psychosis. (Niehusmann P, Dalmau J, Rudlowski C, et al. **Arch Neurol** 2009 Apr;66(4):458-64).

INFANTILE SEIZURES

PRRT2, INFANTILE CONVULSIONS, PAROXYSMAL DYSKINESIA, AND MIGRAINE

Researchers at the Institut de Neurobiologie de la Mediterranee (INMED), Marseille, and other centers in France have extended the spectrum of PRRT2 mutations and phenotypes to hemiplegic migraine and other types of migraine. Previously, they and others had identified PRRT2 (proline-rich-transmembrane protein) as the gene causing infantile convulsions with paroxysmal kinesigenic dyskinesia syndrome (IC/PKD). Thirty-four additional families with either typical IC/PKD or IC/PKD with migraine were analyzed, and 2 known and 2 novel PRRT2 mutations were detected in 18 families. The proportion of migraineurs among PRRT2 mutation carriers (10/37) was significantly increased as compared with the overall migraine prevalence (~12%)(p=0.02). (Cloarec R, Bruneau N, Rudolf G, et al. PRRT2 links infantile convulsions and paroxysmal dyskinesia with migraine. **Neurology** 2012 Nov 20;79(21):2097-103). (Response and reprints: Dr Pierre Szepetowski. E-mail: szepetowski@inmed.univ-mrs.fr).

COMMENT. No less than 6 articles and one editorial in the Nov 20, 2012 issue of Neurology are devoted to PRRT2 gene mutations and their link to infantile convulsions, paroxysmal dyskinesia, ataxia, and hemiplegic migraine. PRRT2 gene mutations are also occasionally reported in patients with febrile seizures, febrile seizures plus, and absence epilepsy (Scheffer IE, et al. PRRT2 phenotypic spectrum includes sporadic and fever-related infantile seizures. **Neurology** 2012 Nov 20;79(21):2104-8).

The increasing number of reports on phenotypes associated with PRRT2 mutations emphasizes the role of non-ion channel genes in the pathogenesis of various paroxysmal neurologic disorders. (Guerrini R, Mink JW. Editorial. **Neurology** 2012 Nov 20;79(21):2086-8). Confirmation of PRRT2 mutations in patients with infantile seizures, paroxysmal dyskinesia, or both provides reassurance that the seizures are likely to be benign and self-limited but the risk of dyskinesia during childhood is increased. An increased risk of PRRT2-related hemiplegic migraine, migraine, or episodic ataxia requires further study.