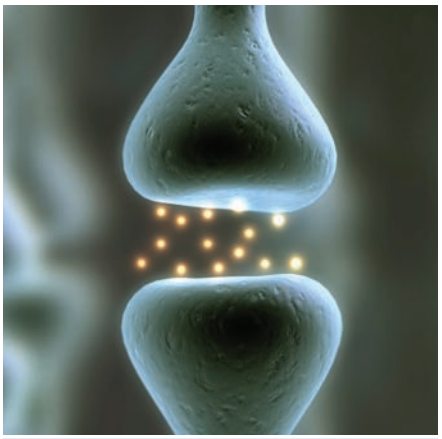

BRIEF REPORT

Anti-N-methyl-D-aspartate Receptor Encephalitis

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Innov Clin Neurosci. 2011;8(9):24–25

FUNDING: There was no funding for the development and writing of this article.

FINANCIAL DISCLOSURES: The authors report no conflicts of interest relevant to the content of this article.

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KEY WORDS: Anti-N-methyl-D-aspartate receptor encephalitis, limbic encephalitis, NMDA receptors, NMDA antibodies, paraneoplastic syndrome, autoimmune disorder

ABSTRACT

Anti-N-methyl-D-aspartate receptor encephalitis is a rare and serious autoimmune disorder, usually part of a paraneoplastic syndrome. Patients present with a change in mental status, bizarre behavior, and seizures. There are many neoplastic and infectious etiologies, with 90 percent of documented cases in young women, frequently with an ovarian teratoma. Damage to limbic brain receptors is most often induced by teratoma cell-produced anti-N-methyl-D-aspartate antibodies. Treatment targets the specific oncologic or infectious cause and/or employs steroids, plasmapheresis, or other anti-inflammatory therapies. Neurological sequelae persist 75 percent of the time, relapse occurs in 20 percent of cases, and the mortality rate is 25 percent.

INTRODUCTION

Anti-N-methyl-D-aspartate (NMDA) receptor encephalitis is a newly described autoimmune condition that is frequently part of a paraneoplastic syndrome.[1–5] Its pathology is centered at NMDA receptors. Nearly 90 percent of anti-NMDA receptor encephalitis cases occur in women, with a median age of 23. Ovarian teratoma in one or both ovaries is the most frequent etiology, present in approximately half of women with anti-NMDA; however, other sources of neoplasia include testis, lung, thymus, or breast. Infectious etiologies exist as well. The initial evaluation includes a global workup, which prioritizes an oncological assessment and rules out infection.

At illness onset, behavior is often bizarre and restless with psychotic thought processes. Patients initially appear to have a mental illness, but they soon exhibit recurrent seizures and movement disorders, such as myoclonus or orofacial dyskinesias.[1–5]. They may also develop fever and delirium. Approximately 85 percent of patients exhibit decreased responsiveness and become comatose. Difficulty breathing is documented in 65 percent of cases, with oxygen saturations that frequently demand respiratory support.

CLINICAL VIGNETTE

A 22-year-old Caucasian woman presented with seizures, psychosis, and bizarre behavior. Her past medical history was unremarkable. Initial vital signs, physical and mental status examinations, magnetic resonance imaging (MRI), several

electroencephalograms (EEGs), and cerebrospinal fluid analysis were all within normal limits. She soon developed a fever, became comatose, and required intubation for respiratory failure. A repeat MRI revealed brain enhancement foci in limbic subcortical areas, and a subsequent EEG illustrated an ictal tracing pattern. An anti-NMDA antibody test was positive. Despite three months of anti-inflammatory therapy, she remains comatose with seizures and without sign of recovery.

DISCUSSION

The pathology of anti-NMDA is inflammatory limbic encephalitis.[6] Typically, the teratoma cells produce anti-NMDA antibodies, which result in severe damage to limbic brain NR1 and NR2 glutamate NMDA receptors.

Diagnosis may be difficult to determine.[1–6] Routine examinations, laboratory tests, brain imaging, electroencephalography (EEG), and cerebrospinal fluid studies can initially be unremarkable, but help to rule out other pathology. Repeat examinations might reveal subcortical enhancement on magnetic resonance imaging (MRI) as evidence of limbic brain disease, and an EEG may confirm ictal activity, slowing, or disorganization. Positive results on an anti-NMDA antibody test help to confirm the diagnosis.

Every suspected case requires a total body evaluation, particularly an oncology assessment, with special emphasis on teratoma detection. Infectious etiologies should also be ruled out. A delirium workup is performed to exclude metabolic, toxic, or other pathologic etiologies.

The primary initial intervention is reducing inflammation using intravenous steroids. Definitive treatment targets the specific etiology, such as removing a tumor or prescribing therapy for an infection. If these measures are not productive, parenteral immunoglobulin, plasmapheresis, plasma exchange, and hydration may at least diminish the illness severity.

In treating anti-NMDA, the physician should always provide seizure control, respiratory care, and supportive measures.[1–6] Slow but incomplete recoveries with neuropsychiatric sequelae are documented 75 percent of the time. About 20 percent of patients experience a relapse, often associated with an ovarian teratoma recurrence, and death occurs in 25 percent of patients.

REFERENCES

1. Anti-NMDA receptor encephalitis. http://en.wikipedia.org/wiki/Anti-NMDA_receptor_encephalitis Accessed August 27, 2011.
2. Vitaliani R, Mason W, Ances B, et al. Paraneoplastic encephalitis, psychiatric symptoms, and hypoventilation in ovarian teratoma. *Ann Neurol*. 2005;58(4):594–604.
3. Sansing L, Tüzün E, Ko M, et al. A patient with encephalitis associated with NMDA receptor antibodies. *Nat Clin Pract Neurol*. 2007;3(5):291–296.
4. Vincent A, Bien CG. Anti-NMDA-receptor encephalitis: a cause of psychiatric, seizure, and movement disorders in young adults. *Lancet Neurol*. 2008;7(12):1074–1075.
5. Dalmau J, Gleichman A, Hughes E, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *Lancet Neurol*. 2008;7(12):1091–1098.
6. Lancaster E, Hernandez M, Dalmau J. Encephalitis and antibodies to synaptic and neuronal cell surface proteins. *Neurology*. 2011; 77:179–189.