**INTRODUCTION**

Anti-N-methyl-d-aspartate (NMDA) receptor encephalitis results from an immune response against extracellular epitopes of the NR1 subunit of the NMDA receptor. The disorder was first described in 2005 and is becoming recognized as an important cause of encephalitis.

**CASE DESCRIPTION**

**INITIAL PRESENTATION**

HPI: A 20 year-old woman with no significant past medical history presented after a generalized seizure in the setting of a 10-day history of headache, neck stiffness, nausea, vomiting, and confusion with intermittent word finding difficulty. Her symptoms were preceded by a week of diarrheal illness during which multiple family members and her pet dogs were also ill. Her exposure history was otherwise unremarkable, and she had received all usual childhood vaccines.

- PE: Notable for tachycardia, disorientation, and slowed speech.
- Labs: CBC and BMP unremarkable. CSF with WBC 185 (98% lymphocytes), glucose 62, and protein 32.
- Imaging/Studies: Brain MRI was normal. EEG had diffuse slowing.

She was treated empirically for herpes encephalitis with six days of acyclovir IV followed by two days of oral valacyclovir and started on antiepileptic drugs. She was discharged to home.

**INTERVAL HISTORY**

She presented four days later for waxing and waning altered mental status, behavioral disturbances, visual hallucinations, and increased seizure activity.

Infectious workup included the following:

- HIV antibody and PCR
- Serum RPR
- Serum RPR
- CSF VDRL
- CSF Cryptococcal antigen
- CSF Herpes Simplex virus PCR
- CSF Epstein-Barr virus PCR

Serum anti-NMDA receptor antibody titer was 1:160 (normal <1:10). CSF anti-NMDA receptor antibody titer was 1:20 (normal <1:1). She was diagnosed with anti-NMDA receptor encephalitis.

**TREATMENT & OUTCOME**

She received a five-day course of methylprednisolone IV and immune globulin IV, but continued to experience episodes of extreme agitation, intermittent disorientation, and seizures. Her symptoms began to improve after two doses of rituximab 1g given a week apart. At clinic follow-up two months after her initial presentation, she complained of insomnia and increased anxiety, but was otherwise feeling like her usual self. She will be followed with serial imaging to evaluate for malignancy every six months.

**DIFFERENTIAL DIAGNOSIS**

- **Viral encephalitides**
  - Herpes simplex virus
  - Enterovirus
  - Arbovirus
  - Rabies
- **Autoimmune encephalitides**
  - Acute disseminated encephalomyelitis
  - Paraneoplastic limbic encephalitis
  - Systemic lupus erythematosus cerebritis
  - Hashimoto's encephalopathy
- **Psychiatric disorders:**
  - Psychosis
  - Schizophreniform disorder
  - Neuroleptic malignant syndrome
  - Serotonin syndrome
- **Toxic and metabolic disorders:**
  - Toxic ingestion
  - Porphyria
  - Mitochondrial disorders

**TREATMENT**

**First-line:**
- Steroids, IVIG, plasmapheresis
- tumor removal if present

**Second-line:**
- Rituximab, Cyclophosphamide

**DISCUSSION**

Anti-NMDA receptor encephalitis is an important, yet under-recognized, cause of encephalitis with incidence rates rivaling viral encephalitides. The disorder is characterized by acute behavioral change, psychosis, and catatonia and can evolve to include seizures, memory deficits, dyskinesias, and autonomic dysregulation. Most cases occur in young individuals with a strong female predominance. Diagnosis is confirmed by the finding of elevated anti-NMDA receptor antibody titers. The disorder can be associated with underlying malignancy, most commonly ovarian teratoma, or may be preceded by an infection. As the disorder has become more recognized, more cases are being identified without underlying malignancy. Treatment includes immunotherapy and removal of the underlying tumor, if present. Most patients have a good outcome, although recovery can be prolonged and some individuals experience relapse.

Improved recognition of this disorder may lead to earlier initiation of treatment with improved clinical outcomes and may prevent patients from being subjected to expensive diagnostic testing and unnecessary antimicrobial treatment.

**REFERENCES**