Thinking Outside the Box About Young Female Patients With Sudden-Onset Bizarre Behavior: A Case of Anti–*N*-Methyl-D-Aspartate Receptor Encephalitis

To the Editor: My colleagues and I believe that anti–*N*-methyl-D-aspartate receptor (NMDAR) encephalitis should be considered in the differential diagnosis of acute psychosis with neuropsychiatric features in a young population because early diagnosis and therapy are crucial to achieve the best possible outcome. We thus present this brief case presentation to communicate with colleagues who practice medicine, especially in the field of neuroscience and psychiatry.

Until recently, patients presenting to their primary care physicians with memory deficits and acute psychiatric symptoms have been treated like many other psychiatric patients. Unfortunately, in some cases the patient's condition can deteriorate rapidly, resulting in severely decreased consciousness, seizures, dyskinetic movements, and eventual hypoventilation. This constellation of symptoms, especially in young women, can represent a severe form of encephalitis mediated by immunologic attack upon the NMDAR.[1,2]

Case report. Ms A, a 19-year-old African American woman with no significant past medical history, developed acute-onset psychosis 6 days prior to hospitalization. Initially, she exhibited auditory hallucinations, labile mood, paranoia, retrograde amnesia, and anorexia. Urine drug screen was negative. She received treatment with haloperidol, lorazepam, and diphenhydramine for agitation and risperidone for psychosis. Soon after presentation, she became febrile to 101.1°F, tachycardic, and hypertensive. Creatine phosphokinase was measured at > 6,000 IU/L, although this was attributed to antipsychotic medications. She remained stuporous and developed choreoathetoid movements of the hands as well as orofacial dyskinesias. She was intubated on the second day of admission for airway protection.

Lumbar puncture showed a glucose level of 72 mg/dL, a protein level of 10 mg/dL, a white blood cell count of 47/mm^3 with 98% lymphocytes, a red blood cell count of 118/mm^3, and negative cultures/assays for herpes simplex virus, varicella-zoster virus, Lyme disease, Epstein-Barr virus, rapid plasma reagin, and bacteria. Blood cultures showed no growth. Electroencephalogram showed diffuse slowing without overt epileptiform discharges. Magnetic resonance imaging of the brain showed restricted diffusion in the splenium of the corpus callosum. The patient showed no response to empiric antibiotics, and no source of infection was identified. A cerebrospinal fluid (CSF) paraneoplastic neurologic syndrome antibody panel (ANNA, Purkinje, amphiphysin, voltage-gated calcium channel, voltage-gated potassium channel) proved negative. Computed tomography of the chest, abdomen, and pelvis revealed a left adnexal mass compatible with dermoid cyst. Pursuant to this finding, in conjunction with the patient's presentation and examination, an assay for CSF anti-NMDAR immunoglobulin G antibody was obtained and found to be positive in an indirect immunofluorescence assay (ARUP Laboratories, Salt Lake City, Utah). The patient underwent a laparoscopic left salpingo-oophorectomy on day 16, with pathology confirming a mature cystic teratoma. Post-surgery, she received methylprednisolone 1,000 mg daily for 5 days followed by intravenous immunoglobulin 10% 45 g daily for 5 days.

Ms A ultimately demonstrated neurologic improvement and was successfully weaned from ventilator support on day 20, and she was able to follow simple commands the next day. She remained febrile throughout much of her hospitalization; however, central fever is a prominent feature of anti-NMDAR encephalitis, and her infectious workup was otherwise negative. She was referred for inpatient rehabilitation once medically stable for transfer. She had a gradual recovery and returned to an independent life with her family after 90 days.

From the time of the initial description of anti-NMDAR encephalitis, reported cases have increased exponentially worldwide. Anti-NMDAR encephalitis produces antibodies that target NMDARs in the forebrain, limbic system, and hypothalamus.[3] This disease is most commonly found in young women and often is associated with ovarian teratoma.[4] It is an acute, potentially lethal encephalitis from which recovery is possible given appropriate support. Long-term impairment of attention, short-term memory, episodic memory, and executive function may result from misdiagnosis or delayed diagnosis.[2] The available evidence suggests that deficits of executive function and memory can be diminished with immunotherapy and prompt removal of the teratoma.[5] If clinicians consider this devastating disease in their differential diagnosis, timely treatment can be initiated and life-altering residual deficits can be avoided.

Since most of these patients present first with neuropsychiatric symptoms, the recognition by mental health professionals is key to early diagnosis. The fact that some of these patients with anti-NMDAR antibodies may have isolated psychiatric symptoms makes the diagnosis difficult for health care providers. Physicians should consider anti-NMDAR encephalitis in the differential diagnosis of acute psychosis and dyskinesia, particularly in patients with no prior mental health issues.

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Ali Seifi, MD, FACP
seifi@uthscsa.edu
Brent T. Xia, MD
Robert F. Felte, MD

Author affiliation: Department of Neurosurgery, Neuro Critical Care, University of Texas Health Science Center San Antonio (Dr Seifi); Department of Surgery, University of Cincinnati, Cincinnati, Ohio (Dr Xia); and Department of Surgery, Christina Care Health System, Newark, Delaware (Dr Felte).

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