Neuropsychiatric Presentation of Anti–*N*-Methyl-D-Aspartate Receptor Encephalitis With Comorbid Sinus Venous Thrombosis

To the Editor: Anti–*N*-methyl-D-aspartate (NMDA) encephalitis is an autoimmune disorder in which antibodies are formed against NMDA receptors.[1] Anti-NMDA is associated with neurologic deficits, autonomic dysfunction, range of prominent psychiatric symptoms, and fluctuations in consciousness.[2–4] The disorder commonly affects young women and in some cases is associated with ovarian teratomas.[4] Due to its relatively rare incidence and complex neuropsychiatric sequelae, diagnosis is often difficult and frequently delayed given the time taken to rule out more common psychiatric and neurologic conditions. Appropriate and timely diagnosis may lead to definitive treatment associated with favorable outcomes.

Case report. A 23-year-old woman with a history of anxiety presented to her primary care provider with complaints of headaches, vertigo, and tinnitus. She was prescribed meclizine for her symptoms. A few days later, the patient presented with worsening headaches and anxiety, and she was also noted to have a nonlinear thought process. At this point, she was given clonazepam for her symptoms. Over the next 2 weeks, the patient exhibited pressured speech, became aggressive toward her family, and was reported to be threatening her mother and children. Subsequently, she was admitted to a psychiatric facility and was administered antipsychotics due to severe agitation and symptoms of psychosis. However, she developed muscle rigidity and altered mental status with unstable vital signs, and her creatine phosphokinase level was found to be < 10,000 U/L. Her presentation was found to be consistent with neuroleptic malignant syndrome and she was transferred to the intensive care unit.

Later, she developed episodic seizures and amnesia and was noted to be paranoid with intermittent agitation. At this point, the differential diagnosis included paraneoplastic syndrome, autoimmune encephalitis, and an acute psychotic episode. Infectious etiologies were ruled out by otherwise normal blood cultures and urinalysis; the electroencephalogram was negative for seizures; computed tomography (CT) (thorax, abdomen, and pelvis) scans were negative; and magnetic resonance imaging of the head was significant for a right transverse thrombus. Cerebrospinal fluid analysis was significant for lymphocytic pleocytosis. The patient had minimal improvement on antipsychotics. However, these medications were used to manage episodes of extreme agitation and aggression. At this point, autoimmune encephalitis was high on the differential, and the right sinus venous thrombosis further complicated the clinical presentation. Prior to initiating therapy, a comprehensive panel was drawn for coagulopathies and autoimmune etiologies. These analyses included antiphospholipid antibodies, factor VIII levels, factor V Leiden, prothrombin G20210A, antiribosomal antibodies, antinuclear antibody, and protein C and S concentrations. Due to high clinical suspicion, the patient was started on intravenous (IV) steroid and IV heparin. Over the next 3 days, the patient failed to show improvements, and, subsequently, IV steroids were stopped. Results from the diagnostic workup revealed anti-NMDA receptor antibodies and elevated factor VIII levels. The patient continued to exhibit altered mental status, refractory tachycardia, paranoid delusions, and aggression, and she remained nonverbal. A chest CT ruled out pulmonary embolism, and a pelvic ultrasound ruled out ovarian teratomas. At this time, plasmapheresis was initiated, and the patient was continued on IV heparin. There was progressive improvement in mentation; she was able to follow 2-step commands, showed insight into her condition, and no longer displayed symptoms of psychosis. At discharge, the patient had word-finding difficulty and gait instability, which was attributed to central sinus venous thrombosis, and she was referred to a rehabilitation facility for further care.

Autoimmune encephalitis is more common in women with a median age of 21 years, and in many cases is associated with ovarian teratomas. This case illustrates the complexities associated with diagnosing and treating anti-NMDA receptor encephalitis. Clinical presentation was further complicated by comorbid sinus venous thrombosis, which can be associated with neurologic symptoms such as seizures and altered mental status. The clinician must have a high degree of suspicion and should always include this diagnosis in the differential when a patient presents with neuropsychiatric symptoms with progressive unremitting deteriorating clinical course.

References

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