The Horse With Stripes: A Case of Anti–NMDA Receptor Encephalitis

To the Editor: Anti–*N*-methyl-D-aspartate (NMDA) receptor encephalitis, although rare, is an emerging cause of catatonia.[1] We describe a 22-year-old male patient whose akinetic catatonia responded to intravenous immunoglobulin therapy and steroid therapy after his cerebrospinal fluid and serum samples tested positive for the anti-NMDA antibody.

Case report. Mr A, a 22-year-old white male veteran with a history of posttraumatic stress disorder (PTSD), initially presented to a Veteran Affairs urgent care center in 2010. He described recurrent periods of anxiety and confusion, recent binge-drinking activity, and a week of persistent cough. On examination, he had a mild fever of 100°F, new-onset tachycardia, and hypertension. Chest radiograph revealed no abnormalities, and his cough symptoms were felt to be secondary to a viral upper respiratory infection. The urgent care center discharged him with symptomatic management and referred him to outpatient psychiatric services for his anxiety symptoms.

Three days later at an outpatient psychiatric clinic, Mr A described worsening confusion and episodic emesis. He reported "choppy vision" with horizontal visual tracking and occasionally felt that his "right side was the left side."[2] On examination, he was flushed and diaphoretic, with persistent tachycardia and hypertension. Despite concern for an infectious process, the provider noted the unremarkable urgent care center evaluation with negative blood cultures. Mr A was sent home on treatment with sertraline 50 mg/d and lorazepam 0.5 mg orally 3 times daily as needed for anxiety related to PTSD (*DSM-IV* criteria), diagnosed previously on disability compensation evaluation. Mr A's treatment was switched to quetiapine 25 mg 4 times daily as needed for anxiety 1 week later, after which time his condition continued to deteriorate. He called his mother continually for reassurance, seeking verbal instruction for meal preparation and for bathing. He experienced visual hallucinations of his brother taunting him at home while his brother was actually at work. Finally, his mother found him immobile, staring at the sky, and repetitively saying "I'm dying." She brought him back to the urgent care center, where he was disoriented and confused, requiring physical guidance to follow most verbal commands. He had persistent tachycardia and hypertension, and his temperature was 100°F. He was given lorazepam 2 mg and haloperidol 5 mg orally in the emergency department, after which occurred some improvement in his confusion. The inpatient psychiatric unit admitted him with a provisional diagnosis of psychotic disorder not otherwise specified with catatonia (*DSM-IV* criteria).

The following day, Mr A was catatonic, staring at the ceiling for hours with echopraxia, mutism, posturing, withdrawal, catalepsy, and stereotypy, but without waxy flexibility or rigidity. He was treated with oral haloperidol 5 mg twice daily and lorazepam, the latter of which was titrated to 20 mg daily. He was predominantly sedentary with persistent drooling, hypertension, and tachycardia as well as recurrent apneic behaviors. As lorazepam dosages increased, he became lucid for increasingly longer periods, but also began to exhibit hebephrenic, charging behaviors.

Findings of an extensive medical workup were negative for abnormalities. Cerebrospinal fluid analysis was significant for lymphocytic predominance at 94% with white blood cell count at 4/mm^3 and protein at 1 mg/dL. Magnetic resonance imaging (MRI) revealed no abnormalities. Electroencephalogram revealed nonspecific right temporal lobe abnormality without epileptiform spikes: frequent slowing in the theta range over the right occipital region and 2 Hz moderate voltage slowing over the right temporal lobe region, occasionally rhythmic. The right temporal lobe abnormality was suggestive of a seizure focus, but lorazepam may have been suppressing any seizures.

Three weeks after admission, the patient was started on oral valproate 500 mg for possible partial complex seizures. With this addition, he became heavily sedated and suffered from dehydration, requiring intravenous fluid treatment in the hospital medical unit. Valproate was discontinued, and he now received intravenous lorazepam 10 mg daily and intravenous haloperidol 5 mg daily, but he failed to recover to his baseline condition prior to the initiation of valproate.

Just as the psychiatry unit arranged for electroconvulsive therapy for his refractory catatonia, serum and cerebrospinal fluid samples returned positive for NMDA-receptor antibody. Electroconvulsive therapy was cancelled, and Mr A completed 5 days of intravenous immunoglobulin followed by 3 separate courses of methylprednisolone, each lasting 5 days. Video electroencephalography revealed recurrent tonic-clonic seizures with central vertex epileptogenic disturbance, and he was treated with levetiracetam and phenytoin. Two months after admission, the patient was discharged home with outpatient neurocognitive rehabilitation. He demonstrated persistent deficits in memory and impulse control. Magnetic resonance imaging now revealed focal areas of T2 prolongation within the subcortical white matter most evident within the right parietal region. Six months after discharge, Mr A was caring for himself independently without further seizure episodes. He continued to receive outpatient neurocognitive rehabilitation for mild deficits in complex psychomotor processing, verbal learning, and executive functioning.

Limbic encephalitis often presents with sudden behavioral disturbances associated with neurologic symptoms,[1] and, historically, encephalitis lethargica has been the most described cause for organic catatonia.[3] Mr A's rapid evolution of catatonic symptoms and sudden deterioration prompted his early neurologic investigation. Various viral causes for infectious encephalitides were investigated, including rabies, West Nile virus, herpes, and influenza. Neoplastic process was considered, but unlike other forms of paraneoplastic encephalitis that show bilateral temporal hyperintensities, anti–NMDA receptor encephalitis rarely presents with abnormal MRI findings.[1] The patient's unremarkable MRI and cerebrospinal fluid findings delayed diagnosis and treatment. Mr A's personality changes were initially misdiagnosed as alcohol abuse and factitious disorder, highlighting a subacute clinical course with an atypical constellation of symptoms that has also been incorrectly diagnosed as malingering, acute psychosis, or drug abuse in other cases of paraneoplastic encephalitis.[4] The lack of psychiatric history in this patient led to an extensive medical workup. His presentation of catatonia contrasts with the majority of the catatonia literature, which focuses on patients in psychiatric settings. Of the few recent studies applied to nonpsychiatric populations, there is a higher percentage of organic catatonia in patients presenting to a nonpsychiatric emergency department than in patients presenting to psychiatric emergency departments.[5] Organic catatonia presents more acutely (10 days) in comparison with schizophrenia (7 weeks), with a higher incidence of akinetic symptoms.

Mr A's symptoms and outcomes are similar to those reported in a few case series in the literature. Studies have frequently observed prodromal upper respiratory symptoms, and authors have speculated pathogens such as *Mycoplasma pneumoniae* or various viruses leading to the condition.[1,6] Other characteristic features included oral dyskinesias, central hypoventilation, and a rapidly evolving catatonia.[1] Teratomas have been commonly associated with anti-NMDA encephalitis,[1] but our patient was similar to those in the case series from the California Encephalitis Project, with no identified tumors.[6]

Anti–NMDA receptor encephalitis is a challenging diagnosis presenting with neurologic and psychiatric symptoms that can be potentially lethal but treatable if recognized promptly.

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