

Acute Psychosis Associated With Anti-NMDA-Receptor Antibodies and Bilateral Ovarian Teratomas: A Case Report

To the Editor: Paraneoplastic limbic encephalopathy, initially described in 1968, is a rare disorder associated with neoplasms and characterized by symptoms and signs of limbic system disorder.¹ A subtype of limbic encephalopathy with autoantibodies to the NR1 subunit of the *N*-methyl-D-aspartate (NMDA) receptor has been described by Dalmau et al.² Of 100 patients, 77 presented first to a psychiatrist with anxiety, agitation, bizarre behavior, or psychotic symptoms. The other 23 first presented with a seizure or memory impairment. Within a few weeks, patients typically manifested serious neurologic impairment with alterations of consciousness. A majority showed dyskinesias and central hypoventilation requiring a ventilator along with autonomic instability. Electroencephalograms (EEGs) universally showed abnormalities, with slow waves and sometimes spikes; brain magnetic resonance imaging (MRI) showed abnormalities about half the time; and cerebrospinal fluid (CSF) analyses showed pleocytosis in 91% of patients. Fifty-eight of the 100 had tumors, including 53 with ovarian teratomas. NMDA receptors were present in all 25 teratomas evaluated for them. Autoimmune encephalopathies also occur in the absence of neoplasms, and given the rapidly increasing reports may not be as rare as first believed.³ I present here a case of acute psychosis associated with anti-NMDA-receptor antibodies and bilateral ovarian teratomas.

Case report. Ms A, a 28-year-old Jamaican woman, presented in August 2006 to an emergency department with friends who described hyperactivity; hypergraphia and loquaciousness; speaking in English, pidgin, and gibberish; and making religious references. Her friends described loss of appetite and 14 kg of weight loss. They said she abused neither alcohol nor drugs. In the emergency department, she was chanting, singing, and speaking in gibberish. She could follow some commands. She was disoriented in 3 spheres with impaired memory and disorganized thoughts. Her physical examination was significant only for a pulse of 117 bpm and blood pressure of 144/102 mm Hg. Serum potassium level was 3.2 mg/dL, and whole blood hemoglobin concentration was 11.1 g/dL. Urinalysis showed 3+ ketones. A brain computed tomography (CT) scan revealed no abnormalities. When admitted involuntarily to a psychiatric unit, where she received a DSM-IV diagnosis of psychotic disorder not otherwise specified, she was oriented to month, year, and "being at a hospital."

Over the next 3 days, she fluctuated from confusion with passive cooperation to extreme agitation. She received lorazepam, haloperidol, lithium carbonate, and benztropine and, because of elevated blood pressure, metoprolol and clonidine. On the third day of admission, although somnolent, she met with an attorney and consented to a psychiatric treatment plan. Her serum potassium level was 3.2 mg/dL, her pulse 39 bpm, and regular, and her blood pressure 119/100 mm Hg. Because she was refusing oral potassium, she was transferred to a medical floor. Upon transfer, she had a tonic-clonic seizure and became obtunded, staring into space. An MRI revealed no abnormalities, as did 3 subsequent ones. Lumbar puncture showed pressure within normal limits; CSF protein level was 29 mg/dL, and CSF glucose level was 71 mg/dL. She had a red blood cell (rbc) count of 1 rbc/mm³ and a white blood cell (wbc) count of 60 wbc/mm³, 88% of which were lymphocytes. She developed flaccid paralysis, hypothermia requiring a warming blanket, and heavy drooling and was no longer responsive.

Four days after her first seizure, she required a ventilator and a percutaneous endoscopic gastrostomy tube for nutrition. An EEG showed 7-Hz waves with a single left temporal spike. Extensive

testing of serum and CSF for viral, bacterial, and fungal infection or toxic-metabolic causes was negative. A brain biopsy reported nonspecific mild microglial activation. Serum CA-125 level was elevated at 58 U/mL. After an abdominal CT scan revealed a right ovarian mass, the patient underwent bilateral salpingo-oophorectomy for bilateral mature teratomas. Serum and CSF were positive for autoantibodies to the NMDA receptor, but negative for other paraneoplastic autoantibodies.

Post-surgically, the patient received intravenous methylprednisolone, immune globulin, cyclophosphamide, and rituximab. One week after cyclophosphamide treatment, the patient opened her eyes, moved her left hand on command, nodded her head in assent, and sat up. She improved with weaning from the ventilator 37 days after cyclophosphamide was administered. By discharge, she spoke in full sentences and used her upper extremities. A year later, her sister reported her doing well but still getting some physical therapy.

Psychiatrists should be aware of the syndrome of autoimmune limbic encephalitis and its association with undiagnosed ovarian teratoma because a psychiatrist is often the first physician to see these patients. Despite the severity of the illness (patients averaged 8 weeks on a ventilator), 47 of the 100 patients in the study by Dalmau et al² made a full recovery. Early diagnosis and treatment with surgery and immunologic treatments improve outcomes. This syndrome may also provide better understanding of the function of NMDA receptors.

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