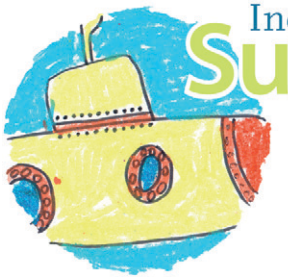

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1 Acute Psychosis in a 16-year-old Girl with an Ovarian Teratoma

Thuthu Aung, MD,* Neha Ahuja, MD,* Joan Graziano, MD,* Melissa Grageda, MD*

**Department of Pediatrics, Richmond University Medical Center, Staten Island, NY*

PRESENTATION

A 16-year-old girl presents to the psychiatric emergency department with acute worsening aggression, auditory hallucinations, and suicidal thoughts for the past 10 days. Her medical history is significant for a resected right ovarian teratoma 7 years earlier. Due to escalating combativeness in the emergency department, the psychiatrist administers antipsychotics and anxiolytics, including haloperidol, chlorpromazine, and lorazepam. She is admitted to the psychiatric unit with a diagnosis of acute psychosis and depression.

A few hours later, her neurologic examination findings worsen, with fluctuating mental status and profuse drooling. She is tachycardic (heart rate, 110 beats/min) and hypertensive (blood pressure, 136/81 mm Hg). Her temperature is 98.6°F (37.0°C), respirations are 17 breaths/min, and oxygen saturation is 97%. The rest of her physical examination findings are normal. She is transferred to the medical unit for further evaluation.

Head computed tomography, drug screening, and video electroencephalography results are normal. Cerebrospinal fluid (CSF) analysis reveals an elevated opening pressure of 31 cm H_2O (normal, <25 cm H_2O), no red blood cells, an elevated white blood cell count of 36/μL (0.036 × 10^9/L), and 100% lymphocytes. Her CSF protein level is 23 mg/dL (0.23 g/L) (normal, 15-45 mg/dL [0.15-0.45 g/L]), and her glucose level is 63 mg/dL (3.5 mmol/L). The CSF analysis is positive for oligoclonal bands. Additional evaluation leads to the diagnosis.

The Case Discussion and Suggested Readings appear with the online version of this article at http://pedsinreview.aappublications.org/content/38/10/487.

EDITOR'S NOTE

We invite readers to contribute Index of Suspicion cases through the PIR manuscript submission system at: https://mc.manuscriptcentral.com/pir.

AUTHOR DISCLOSURE Drs Aung, Ahuja, Graziano, and Grageda have disclosed no financial relationships relevant to this article. Dr Aung is currently a pediatric allergy fellow for the Section of Clinical Immunology, Allergy and Rheumatology, Department of Medicine, Tulane University School of Medicine, New Orleans, LA. Dr Ahuja is currently a pediatric gastroenterology fellow for the Division of Pediatric Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, State University of New York Downstate Medical Center, Brooklyn, NY. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product/device.

DISCUSSION

Consideration of a paraneoplastic process prompted an evaluation for a recurrent ovarian teratoma. An abdominal magnetic resonance image revealed a left adnexal mass consistent with a teratoma measuring 6.6 × 4.9 cm (Fig), and it was promptly resected. Due to the acute psychosis, CSF lymphocytic pleocytosis with oligoclonal banding, and recurrent ovarian teratoma, this patient was highly suspected of having an antibody-mediated autoimmune encephalitis, such as anti–*N*-methyl-D-aspartate (NMDA) receptor encephalitis. Her CSF and serum samples both tested positive for the presence of antibodies against the GluN1 (NR1) unit of the NMDA receptor, thereby confirming the diagnosis.

The patient's neurologic status continued to worsen after hospital admission, and she was transferred to the PICU. She exhibited echolalia, orofacial dyskinesias, and choreoathetosis and eventually became catatonic. Due to the high suspicion of antibody-mediated encephalitis, the patient was promptly started on pulse corticosteroid, intravenous immunoglobulin, and plasmapheresis therapies after sending the diagnostic tests to the laboratory. By the time the test results were available and the diagnosis was confirmed, the patient was about to complete her fifth and final round of plasmapheresis. She began to show signs of improvement approximately 1 week after the conclusion of immunotherapy. Supportive management was provided with anxiolytics and antipsychotics, as well as physical and occupational rehabilitation. Her emotional and cognitive functioning gradually improved. She completely recovered without any cognitive or physical deficits, and she was discharged home in stable condition. Corticosteroid, anxiolytic, and antipyschotic medications were tapered over the next few months. One year later, she remains asymptomatic and tumor free; she is off all medications and is performing well in school.

The Condition

Antibody-mediated encephalitis of childhood presents with a broad spectrum of symptoms, such as psychosis, catatonia, autonomic dysregulation, seizures, and choreoathetosis. Several pathogenic autoantibodies have been identified, such as anti-NMDA, anti-glycine receptor, anti–metabotropic glutamine receptor 5, anti–γ-aminobutyric acid type A, anti–γ-aminobutyric acid type B, anti–dopamine D2 receptor, and voltage-gated potassium channel complex antibodies.

Anti-NMDA receptor encephalitis was first described as a paraneoplastic autoimmune syndrome in previously healthy young female patients with acute psychosis and ovarian teratomas; however, it is now known to occur in males and females of all ages, with and without tumors. Multiple stages characterize this illness. Symptoms may begin with a self-limited viral-like prodrome period. After approximately 2 weeks, neuropsychiatric symptoms manifest. Most patients are initially seen and diagnosed by a mental health professional. Worsening neurologic symptoms eventually prompt medical evaluation and may require management in an intensive care setting.

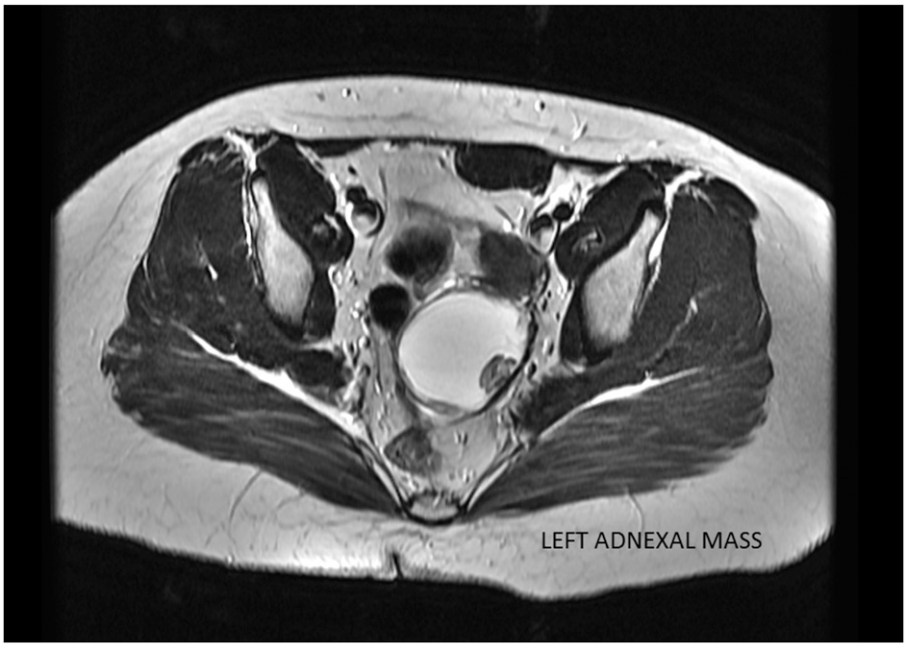

Figure. Abdominal magnetic resonance image revealed a left adnexal mass consistent with a teratoma measuring 6.6 × 4.9 cm.

The NMDA receptors are ligand-gated cation channels that play a role in synaptic transmission, plasticity, and memory. They are highly expressed in the forebrain limbic system and hypothalamus. Abnormal production of antibodies against the NMDA receptor, therefore, affects behavioral, cognitive, and memory skills. As levels of NMDA receptor activity decrease, patients begin to manifest with neuropsychiatric symptoms, such as mood changes, impulsivity, aggression, and visual/auditory hallucinations. Later clinical presentations include worsening neurologic abnormalities, such as decreased level of consciousness, increased oral secretions, hypoventilation, catatonia, echolalia, involuntary movements (eg, oro-lingual-facial dyskinesias, choreoathetosis, elaborate motions of extremities), and seizures. Dysautonomic symptoms, such as dysrhythmias, breathing, and temperature dysregulation, occur in the last and most severe phase of this condition.

Differential Diagnoses

Other causes of acute fluctuating mental status in an adolescent patient include drug or alcohol intoxication, malingering, trauma, psychosis, intermittent prolonged complex partial seizures, and encephalopathy from an underlying systemic autoimmune disease, such as systemic lupus erythematosus.

Diagnosis

An elevated lumbar puncture opening pressure, lymphocytic pleocytosis, and oligoclonal banding in the CSF support the diagnosis of antibody-mediated encephalitis. Definitive diagnosis is established by detection of IgG NMDA antibodies in the CSF and/or serum. Results of electroencephalography and brain magnetic resonance imaging are variable and may indicate the stage or duration of the ongoing inflammatory process. Screening for an associated teratoma or other tumor is recommended.

Management

Urgent resection of the tumor (if identified), followed by immunotherapy, is associated with improved outcomes. First-line immunotherapy includes pulse corticosteroid therapy, plasma exchange, and γ-globulin therapy (given alone or combined). Early initiation of therapy is highly recommended and should not be delayed (ie, while waiting for diagnostic confirmation). Second-line therapy involves the use of immunosuppressants such as rituximab, cyclophosphamide, and methotrexate.

Psychiatric symptoms may be treated with anxiolytics and antipsychotics. Patients requiring intensive care may undergo endotracheal intubation, assisted ventilation, pacemaker placement, and assisted enteral feeding. Comprehensive rehabilitation leads to more favorable outcomes for patients with residual neurologic and cognitive deficits.

The Prognosis

Prompt recognition and therapy have rendered this condition treatable. Complete recovery occurs in most patients, although there remains a low mortality risk from multiorgan failure, especially with a late diagnosis. Close surveillance is warranted for relapse of the teratoma and/or encephalitis.

Lessons for the Clinician

- Anti–*N*-methyl-D-aspartate (NMDA) receptor encephalitis should be highly considered as a differential diagnosis in adolescent females presenting with acute psychosis, and they should be evaluated for a teratoma.
- Anti-NMDA receptor encephalitis is treatable but can progress to a devastating disease if there is a delay in diagnosis and treatment.
- Prompt resection of the tumor (if identified) and autoimmune therapy are associated with improved outcomes.

Note: This case was based on a manuscript submitted by the authors and awarded second prize at the 2016 Annual Residents' and Fellows' Research Paper Competition sponsored by the Academy of Medicine of Richmond, Staten Island, New York. Award Date: June 14, 2016.

Suggested Readings

Bigi S, Hladio M, Twilt M, Dalmau J, Benseler S. The growing spectrum of antibody-associated inflammatory brain diseases in children. *Neurol Neuroimmunol Neuroinflamm*. 2015;2(3):e92

Brenton JN, Goodkin HP. Antibody-mediated autoimmune encephalitis in childhood. *Pediatr Neurol*. 2016;60:13–23

Dalmau J, Gleichman AJ, Hughes EG, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *Lancet Neurol*. 2008;7(12):1091–1098

Additional Resources for Pediatricians

AAP Textbook of Pediatric Care, 2nd Edition

- Chapter 290: Meningoencephalitis - https://pediatriccare.solutions.aap.org/chapter.aspx?sectionId=136093777&bookId=1626

Point-of-Care Quick Reference

- Meningoencephalitis - https://pediatriccare.solutions.aap.org/content.aspx?gbosid=165541

For a comprehensive library of AAP parent handouts, please go to the *Pediatric Patient Education* site at http://patiented.aap.org.

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