Abstract:
Children presenting to the emergency department with an acutely altered mental state require a thoughtful systematic approach to accurately identify the underlying disease process. We present a case of anti–*N*-methyl-D-aspartate receptor encephalitis that initially presented to our emergency department with acute confusion. With increasing recognition of this form of encephalitis, emergency physicians will benefit from understanding the salient neuropsychiatric features, disease progression, diagnostic options, management, and prognostic outcome of these patients.

Keywords:
Anti–N-methyl-D-aspartate receptor antibody encephalitis; anti-NMDAR encephalitis; encephalitis; altered mental state; confusion; psychosis

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A Confused Child

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A 12-year-old girl was brought to the emergency department (ED) in June for evaluation of sexual assault. The girl had arrived home late that evening and, upon questioning by her parents, stated that she was taken off the school bus and raped in a subway station by the bus driver. Upon hearing this, the parents immediately called the police and emergency medical services.

In the ED, upon further police questioning, she recanted her story. She admitted fabricating her story to avoid punishment for returning home late. During evaluation by the pediatric ED physician and social worker, it became clear that the patient's behavior was not normal. She had intermittent bouts of loud laughter between periods of barely audible monosyllable answers. Despite her odd behavior, it was ascertained that she had been feeling helpless, fatigued, and depressed in mood with anhedonia for the past 3 weeks. Even more concerning, however, was her admission that for the past 2 weeks she had been hearing voices instructing her to commit suicide.

The parents denied their daughter had any recent illness, fever, headache, or other complaints. She was known to have simple headaches in the past and had a history of cutting her wrists, but neither of these had occurred recently. She had not seen any mental health provider previously, was not on any medication, and had no allergies.

She had a normal term birth, reached all her milestones as expected, and was doing well in seventh grade. She achieved menarche at age 11, and her last menstrual period was 4 days before presentation. Her immunizations were up to date. She lived with both her parents and 2 older brothers. Everyone in the family was healthy with no family history of psychiatric or neurologic disorders. She denied any form of abuse.

Her vital signs included a heart rate of 80 beats per minute, respiratory rate of 20 breaths per minute, blood pressure of 123/76 mm Hg, a temperature of 37.4°C, and she had an oxygen saturation of 100% in room air. On physical examination, she was a well appearing, well-nourished child. She had no evidence of trauma to her head; a supple neck; and a normal eye, ear, nose, and throat examination. She had good pulses and perfusion, and her heart and lung examinations were normal. Her abdomen was soft and

nontender, with normal bowel sounds, and no masses were appreciated. The external genitourinary examination was normal, with no signs of trauma, and a pelvic examination was deferred. Her neurologic examination revealed an alert and oriented individual, with a Glasgow Coma Score of 15, with normal-sized, equal and reactive pupils, normal muscle tone, strength, reflexes, sensation, and coordination in upper and lower limbs. She had a normal cranial nerve examination and was compliant enough to stand and walk with a normal gait. Her mental status examination was significant for avoidant eye contact and seeming indifferent to her surroundings. Her speech was slow and halting. Her mood appeared depressed with a blunt affect, but, at times, she burst out in bouts of laughter. She could not identify a reason for feeling sad but acknowledged auditory hallucinations that were telling her to kill herself.

On laboratory evaluation, she had a normal complete blood count (white blood cell count, 7.5; hemoglobin level, 13.7; hematocrit, 42.6, and platelets, 259) and a normal comprehensive metabolic panel (sodium, 143; potassium, 4.3; chloride, 106; carbon dioxide, 22; serum urea nitrogen, 9; creatinine, 0.46; glucose, 93; calcium, 9.7; aspartate aminotransferase, 27; alanine transaminase, 16; alkaline phosphatase, 187; albumin, 4.7; and total bilirubin, 0.2). In addition, her blood ethanol, salicylate, and acetaminophen levels and her urine toxicology screen were all negative. She also had a normal urinalysis, normal thyroid stimulating hormone level, and a negative urine pregnancy test.

Given the current lack of an organic cause for her altered behavior, history of depressed mood, and auditory hallucinations, the psychiatry service was consulted. On their assessment, she was deemed to be a danger to herself and was unable to engage in a contract for safety. She was admitted to the inpatient psychiatric unit with a 1:1 nursing sitter to ensure her safety.

Upon admission to the psychiatry unit, she was started on the antipsychotic, olanzapine. During the first 3 days of her inpatient stay, she displayed increasingly bizarre activity including use of profanity, frequent touching of her genitalia and mouth, and constant rubbing of her buttock on the unit floor. She also had new onset hypertension with blood pressures ranging from 130/80 up to 160/90 mm Hg. During episodes of agitation, she was given lorazepam and haloperidol to calm her down. On her fourth day on the unit, her mental status was noted to be waxing and waning; and she experienced an observed, self-limited, 2-minute, tonic-clonic seizure. She also started to drool and exhibit frequent orofacial movements resembling grimacing and pouting. She remained afebrile. The pediatric neurology service was consulted. On their examination, she was found to have a Glasgow Coma Score of 9 (E1, V3, and M5). She had normal-sized equal and reactive pupils, new onset increased tone of her right upper extremity, normal reflexes, and the rest of the examination was deferred given her mental status. They recommended transfer to the pediatric intensive care unit (PICU) and further investigations that led to the definitive diagnosis in this acutely encephalopathic 12-year-old girl.

DIFFERENTIAL DIAGNOSIS

Children who present with an acutely altered mental state are a diagnostic challenge given the extensive number of potential diagnoses. Infections, intracranial lesions, drugs, psychiatric conditions, epileptic syndromes, and autoimmune diseases are broad differential groups that warrant consideration. Emergency physicians need to obtain a detailed history of symptoms to narrow the differential. The presence of fevers, prodromal illness, neurologic impairments, use of recreational drugs, medical history of an autoimmune, epileptic or headache syndrome, or a family history of any of these is a potential lead to a diagnosis. The examination needs to be systematic and thorough, observing the patient's vital signs, mental status, and stigmata of autoimmune or malignant diseases and eliciting any focal neurologic deficits. The use of appropriate investigative imaging and laboratory data is crucial in aiding the clinician to make a diagnosis and plan management.

Immediate life-threatening conditions need to be screened for initially. Glucose and thyroid function tests are easily obtained to detect hypoglycemia and thyroid storm. A child with a fever and an altered mental state needs to be investigated expeditiously for infectious encephalitis or meningitis, and these should be high on the ED clinician's differential. Bacterial or viral pathogens like mycoplasma, herpes simplex virus (HSV) 1 or 2, enteroviruses, and arboviruses are conceivable causative agents. With infections, a lumbar puncture generally shows cerebrospinal fluid (CSF) pleocytosis and may reveal a deranged CSF glucose and protein value.

Intracranial pathology, including mass lesions and strokes, can present with psychosis and altered behavior, albeit rarely. More commonly, there is a depressed mental state associated with other signs of increasing intracranial pressure, such as headache, nausea, and vomiting. Imaging is the most sensitive method to diagnose these conditions.

Ingested drugs, such as anticholinergics, hallucinogens, and sympathomimetics need to be investigated for in a previously well child that develops a