Acute confusional states represent neurologic emergencies with broad differential diagnoses, including toxic ingestions, subarachnoid hemorrhage, stroke, encephalitis, and confusional migraine. Particularly in the adolescent period and in children with Lennox-Gastaut, nonconvulsive status epilepticus is a relatively uncommon but well-described clinical entity. Clinical hallmarks include a dazed affect, limited or monosyllabic verbal responses, difficulty following commands, occasional automatisms, but normal vital signs and no tonic clonic movements. Nonconvulsive status epilepticus encompasses absence status epilepticus as well as other forms of status epilepticus. Clinical recognition of absence status epilepticus in the emergency department can be difficult, but early confirmation can promote early resolution, prevent unwarranted investigation, and avoid unnecessary treatment for unrelated conditions. We discuss 2 cases of absence status, with a review of the literature and a proposed algorithm for acute confusional state.

Clin Ped Emerg Med 4:215-220. © 2003 Elsevier Inc. All rights reserved.

Acute Confusional State in the Emergency Department: Consider a Common Zebra

By Amy Baxter, MD

NORFOLK, VIRGINIA

A 11-YEAR-OLD WHITE MALE presented to the emergency department (ED) after being referred by his private pediatrician for an urgent urine drug screen. He had been quiet that morning before school, then was given lunchtime detention for “goofing around” and not responding appropriately to a spelling test. The teachers became concerned when he was unable to read aloud in class. When his parents retrieved him from school, he could walk but was “completely dazed,” distant, and unable to recognize his surroundings. His pediatrician noted confusion but an “intact neurological exam,” and referred him for further testing.

The patient had no recent head trauma history. He had been diagnosed 4 days earlier with otitis media and sinusitis for which he was being treated with amoxicillin/clavulanate. In addition, he had been prescribed an over-the-counter decongestant and a codeine-containing cough suppressant which he had used once the evening before. His parents noted he had slept less than usual the previous night, but said he had not complained of headaches, fever, nausea, vomiting, or dizziness in the days immediately preceding the visit. Review of systems was otherwise benign. The family denied knowledge of illicit drug use and noted there were no prescription pills, marijuana, or other CNS-active medications available at home. He had a past history of allergies to cefaclor and morphine, both of which caused a mild rash.

Physical examination revealed a quiet, well-developed, early adolescent. Vital signs included temperature 36.8°C, blood pressure 109/72 mmHg, pulse 68 beats per minute, respiratory rate 26 breaths per minute, weight 33.5 kg, and oxygen saturation 98% on room air. The general physical examination was signifi-
cant only for mild erythema without effusion in the left tympanic membrane. His neck was supple without lymphadenopathy. He had no rashes and his cardiovascular, gastrointestinal, and respiratory exams were benign.

His pupils were both 5mm, round, and reactive to light, with prominent hippus. Fundi were normal with intact venous pulsations, and extraocular movements were full without nystagmus. He had no tics, blinking, facial grimacing, or myoclonic jerks. Initially, he appeared alert and oriented to name but not to time or place. His mental state seemed to vacillate from attentive to confused, with a generally flat affect devoid of facial expression. He did not answer most questions or follow one-step commands. Brief periods of increased lucidity were noted but his confusional state never fully resolved. His neurological exam was also significant for severely decreased short-term memory: he could repeat 2 of 3 objects immediately, but recalled none of 3 objects at 2 minutes. His speech was slightly slurred, he cried easily, and he had occasional echolalia. While compliant with the exam, he responded slowly. When asked to draw a clock, he instead spelled “CLOCKK,” crossing out the final K when he looked at the word he’d written. After being asked to copy a drawing of a clock, he drew appropriately spaced hatches counterclockwise from 11 to 6 o’clock, and then perseverated, drawing small, closely spaced hatches from 6 to 1 o’clock. He orally spelled the word “WORLD” “F-O-R-L-O-D,” and could not spell it backwards. Strength was 5/5 in upper and lower extremities, gait was slow but symmetrical, Romberg absent, heel toe walk normal, and he had no intention tremor. A slight bilateral pronator drift corresponded with his waxing and waning confusional state. Cranial nerves were intact. His deep tendon reflexes were 2+ throughout, and his Babinski was equivocal.

Laboratory findings included a normal computed tomography (CT) of the head, except for mucosal thickening within the sphenoid sinus. Urine drug screen was negative and electrolytes were normal, as was an LP. At this time a neurologist was consulted, and a definitive test was done.

**Case 1: ED Course**

Electroencephalogram (EEG) conducted during his ED visit was positive for continuous 3 to 4 Hz generalized slow spike-wave pattern consistent with non-convulsive status epilepticus. During the EEG the patient received a slow infusion of 2 mg of lorazepam intravenously with prompt return to a normal mental state and a resolution of the slow spike-wave abnormalities. Twenty minutes later his mental status reverted to his previous confusional state, so a repeat dose was given with similar improvement. He was started on valproic acid 250 mg by mouth twice a day, and was admitted for observation. A third 2-mg dose of lorazepam was given when symptoms reemerged later that night. His EEG was repeated the following day and was normal. He was discharged with valproate 250 mg bid. Outpatient MRI was normal, and the patient has remained seizure-free for 2 years on this regimen.

**Discussion**

The differential diagnosis of acute confusional state is broad, with potential outcomes ranging from complete resolution to severe brain damage. Nonconvulsive status epilepticus (NCSE) is a relatively uncommon but well described clinical entity, encompassing absence status epilepticus (ASE) as well as other forms of status epilepticus. Clinical recognition of ASE in the ED can be difficult, but early confirmation can promote early resolution, prevent unwarranted investigation, and avoid unnecessary treatment for unrelated conditions.

Acute mental status changes should prompt immediate action in the ED. While acute delirium states are frequent adult ED diagnoses, they occur uncommonly in children. These changes are frightening for parents, and typically lead to a compre-
hensive investigation to rule out a life-threatening infection or other intracranial process.

The differential diagnosis of altered mental status in children is extensive (Table 1). A diagnosis of nonconvulsive status epilepticus is often only entertained when the child is unresponsive and rigid or has a known seizure disorder. Both partial complex status epilepticus (PCSE) and ASE, however, can present with subtle findings erroneously ascribed to other etiologies, and may occur in patients without a known seizure history.

ASE appears in the literature under many names, from “petit mal status” to “spike-and-wave stupor” to “status pyknolepticus.” Status epilepticus without convulsions was well described in the 19th century, with Lennox first correlating the electrical with the clinical aspects of ASE in 1945. Confounding the literature are the multitude of clinical and electroencephalographic (EEG) presentations which have been reported together labeled less specifically than ASE, NCSE, or PCSE. A schematic of NCSE shows etiologic distinctions between subtypes (Fig 1). Taken together, NCSE accounts for almost 20% of status epileptics.

In PCSE, as in generalized tonic clonic seizures, excessive excitatory neurotransmitter release leads to depolarization and increased intracellular calcium. When gamma-aminobutyric acid (GABA) inhibition is overwhelmed, calcium-triggered proteases and lipases lead to cell injury and death. PCSE has been associated with neuronal damage and stroke and is more likely to be caused by primary pathology of the cortex, such as an infection or bleed. In contrast, ASE probably has a different and less harmful origin, seemingly resulting from vacillating thalamocortical excitation and excessive synchronous neuronal inhibition, which could explain the absence of tissue injury following its resolution.

There are often clinical differences that can help distinguish ASE from PCSE. While both may produce acute confusional states, PCSE is often distinguished by a heralding aura and more pronounced postictal lethargy. Waxing and waning alertness, complex automatisms, and more antagonistic behavior have been reported with PCSE. ASE clinically spans the behavioral spectrum from minimally affected to catatonic, but typically retains approximately the same degree of confusion throughout the seizure. Simple automatisms such as eye blinking or lip smacking suggest the epileptic nature of the confusion but do not distinguish between PCSE and ASE.

In practice, the overlap of presentations is such that even when a seizure is suspected, an EEG is needed to definitively categorize the seizure subtype. The diagnostic EEG feature of ASE is a bilaterally synchronous and rhythmic 1.5 to 4 Hz slow spike-wave discharge. Atypical ASE is associated with a slower, still generalized, 1 to 2.5 Hz spike-wave pattern, while PCSE has focal or asymmetric cycling of 8 to 20 Hz spikes with variable background activity.

ASE and PCSE are particularly relevant entities in the pediatric patient. It is not uncommon to have a patient’s initial presentation of seizure disorder to be ASE. The reported frequency of ASE ranges from 3% to 10% in patients with primary generalized epilepsy, with 75% of ASE occurring before the age of 20. In addition, ASE is quite common in children with developmental delay or Lennox-Gastaut syndrome, though their EEG patterns will reveal the slower atypical generalized spike and wave.

Typical isolated absence seizures account for 13% to 24% of all epilepsy in children and are more commonly a daytime phenomenon. These brief absence seizures present in patients between the ages of 4 years and adolescence. Absence seizures or status may occur spontaneously or may be precipitated. Triggers include recent illness or surgery, sleep deprivation, intermittent photic stimulation,
extreme excitement, or hyperventilation (the mechanism by which absence seizures are often induced in a controlled clinical setting for confirmation diagnosis). Hypocalcemia, hyponatremia, hyperthyroidism, antidepressant or benzodiazepine withdrawal, paraneoplastic syndrome, or occult brain metastases must also be suspected.

Particularly with Juvenile Absence and Juvenile Myoclonic Epilepsy, the pubertal timing of the seizure’s onset adds drug ingestion, psychosis, and sports-related head injuries as diagnostic categories. With Lennox-Gastaut, the patient’s baseline deficits may cause their change in mental status to be overlooked, especially if in concert with a mild intercurrent illness.

Case 2

A 14-year-old black male with a history of Lennox-Gastaut syndrome presented to the ED after a one-week history of decreased activity level and decreased oral intake. The day of presentation he had had an increased number of head drop attacks, 2 short generalized tonic clonic (GTC) seizures, followed by increased sleepiness, “not wanting to drink,” and persistent rubbing of his stomach. At baseline, he was able to communicate basic needs with gestures or smiles and was usually aware of his surroundings. He did not have a gastrostomy tube and typically tolerated and enjoyed oral feedings. His baseline seizure frequency was 1 to 2 GTC seizures per month. His medications included valproic acid 250 mg twice a day, topiramate 50 mg twice a day, and diazepam 0.5 ml once a day for the preceding 10 days, increased to twice a day the day before presentation.

Physical examination revealed a thin early adolescent with some contractures, leaning forward in a wheelchair. He was sleeping but easily arousable; when awake, his eyes were open and he maintained his posture, but he reacted to stimulation with only occasional low grunts and minimal movement. No stomach rubbing or other automatisms were noted. Vital signs were normal. The physical examination was significant for 1 episode of head drop. Pupils were equal, round, and reactive to light. Fundi were cant for symmetric quadriparesis and visual field defects. The patient was discussed at this time with his neurologist. His antiepileptics were increased, diazepam was held and an EEG was scheduled for the following morning.

Discussion

Current ED practice for a confused patient includes initial investigation for metabolic derangement and screening for toxins. As in our first patient, when initial lab work fails to reveal a source, a head CT and lumbar puncture are often obtained to rule out life-threatening processes such as acute trauma or CNS infection. In a hemodynamically stable patient with a nonfocal neurologic examination and no history of trauma, fever, or headache, a reasonable alternative might be to check a blood glucose level, perform electrolyte and urine drug screens, and then arrange an EEG if head CT is negative (Fig 2).

The availability of this test is typically limited by the availability of both EEG technicians and a neurologist, thus putting it out of practical bounds for many EDs. However, patients with ASE often present during regular daytime hours, rendering an EEG feasible if the process is initiated early and the neurologist is willing. In addition to identifying seizures, the EEG may be helpful in identifying other CNS conditions such as slowing or paroxysmal lateralizing epileptiform discharges (PLEDs) which can be associated with cerebral infection, tumor, or stroke. Early in the course of afebrile encephalitis, the EEG may actually point to the correct diagnosis (especially HSV encephalitis) before the CT, MRI, or LP results are abnormal.

When ASE has been diagnosed, the benzodiazepine of choice for treatment is lorazepam. As
Comatose patients with nonconvulsive status may worsen with benzodiazepines, this should not be attempted in obtunded patients. Injectable valproic acid has been reported in the acute setting with good results in a small series. While phenytoin has been used as a second line treatment to terminate generalized convulsive SE, therapeutic doses of phenytoin or carbamazepine may actually result in refractory ASE or increased frequency of ASE in patients previously under good control. Long-term therapeutic options for ASE include ethosuximide and valproate. Lamotrigine has recently been found to be an effective monotherapy for absence seizures and may have future application for prevention of ASE.

A few historical features should alert the practitioner for increased risk of NCSE. Clearly, a child who has had absence seizures in the past is more likely to present in ASE. In children with developmental delay or Lennox-Gastaut syndrome, a new onset of decreased responsiveness or mental status changes without obtundation may point to ASE. In a patient with known cerebral injury, PCSE is the more likely diagnosis. Finally, the patient with a history of idiopathic generalized epilepsy who is given phenytoin or carbamazepine may respond paradoxically with refractory ASE.

When the EEG is pursued and is nonspecific or normal, a head CT and CSF should be obtained to rule out occult trauma, neoplasm, or encephalitis. If these are normal, ingestion, confusional migraine, or vascular etiologies may still be entertained.

As ASE is unlikely to lead to irreversible neuronal damage, hyperkalemia, acidosis, hyperthermia,
or other sequelae of convulsive status, the argument has been made that pursuing emergent diagnosis is not appropriate.\textsuperscript{14} When feasible, however, there is a strong rationale that an EEG may be clinically and practically indicated in the acute confusional state. The difficulty of reliably distinguishing between PCSE and ASE supports early identification. In addition, a number of misdiagnoses or prolonged NCSE with undesirable outcomes have been reported in the literature,\textsuperscript{3} including memory loss\textsuperscript{15} and significantly delayed diagnoses. One 17-year-old was misdiagnosed with a psychiatric disorder for 10 years.\textsuperscript{16} Finally, the current progressive work-ups often take considerable time in the ED; if NCSE is diagnosed, a head CT and LP are no longer needed emergently and more rapid disposition may be made.

Summary

In conclusion, earlier application of the EEG in the ED for the acutely confused patient may be warranted. The algorithm proposed in Figure 2 utilizes the EEG as an important test in the diagnosis of acute confusional state. Alternately, after discussion with a neurologist, a trial of an antiepileptic may be warranted when an EEG cannot be readily obtained.

References