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Foundation for Education and Research in Neurological Emergencies

An Elderly Woman who has Stopped Seizing…or has she?

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A 72-year old woman is brought to the ED by EMS with altered behavior and unusual movements. She was preparing for bed when she was noted to be acting in a peculiar manner. The patient is unable to speak and is having jerking muscular movements.

The patient has no history of seizures. There is a history of stroke two years previously with residual mild right-sided hemiparesis. There is no history of trauma. The patient has a history of hypertension and takes a diuretic.

Physical examination reveals vital signs of blood pressure 120/80, pulse 90, respiratory rate 14, temperature 99, pulse oximetry 98% saturated on supplemental oxygen. She appears alert with her eyes open but is unable to speak. She does appear to look towards the examiner when questions are asked but is unable to follow commands and gives no clear sign of understanding the commands. The right side of the patient's face and her right upper extremity are having a continuous rhythmic motion and the eyes are deviated to the right.

Cranial nerves appear intact with the exception of facial twitching. Deep tendon reflexes are difficult to obtain because of movements.

The obvious twitching stops after intravenous administration of lorazepam. Eyes remain open and deviated to the right with fine nystagmoid movements. Examination was otherwise unremarkable.

What might be your next management or diagnostic steps?

Key Clinical Questions

What is a basic classification of seizures?

What is status epilepticus and when is status epilepticus a medical emergency?

When is an EEG indicated in the emergency department?

Key Learning Points

- **What is a basic classification of seizures?**

  The basic classification of seizures uses the concept of generalized at onset versus partial onset of the seizure.

- **What is status epilepticus and when is status epilepticus a medical emergency?**

  Status epilepticus refers to any seizure type that is enduring. Recent proposals call for treating generalized tonic-clonic status epilepticus as an emergency when the duration of the seizure activity is greater than 5 minutes of continuous activity.

- **When is an EEG indicated in the emergency department?**

  Indications for emergency EEG vary but one compelling argument is when a patient with ongoing seizure activity requires neuromuscular blockade or if the possibility of subtle status epilepticus exists.

Status Epilepticus: Classification and Indications for Urgent EEG

What is a basic classification of seizure types?

Clear classification schemes for seizures exist. The current preferred terminology makes use of several key words and modifiers and is based on video-EEG documentation. "Partial" is used to describe isolated phenomena that reflect focal cortical activity, either evident clinically or by electroencephalogram (EEG). The term "simple" indicates that consciousness is not impaired. For example, a seizure visible as a momentarily twitching upper extremity that subsides would be termed a simple partial seizure with motor activity. Additional modifiers are added to note the specific area of the body involved, for example, upper extremity or lower extremity. Partial seizures may have motor, somatosensory, psychic, or autonomic symptoms.

The term "complex" denotes an alteration of consciousness associated with the seizure. "Generalization" is a term used to denote spread from a focal area of the cortex, either evident clinically or by EEG, to involve all areas of the cortex with resulting generalized motor convulsion. From careful studies, it is known that in adults the most common seizure type is that of initial activation of one area of the cortex with subsequent spread to all areas of the cortex; frequently this occurs too quickly to be appreciated by bedside observation.

The other major grouping of seizure types is for generalized seizures which may be termed convulsive or nonconvulsive. On EEG, all areas of the cortex are activated at once with generalized seizures. This is seen with absence seizures, myoclonic seizures, and some other seizure types.

Sometimes physicians are so focused on the common tonic-clonic seizure type that other types of seizures are misdiagnosed. The fundamental definition of a seizure is abnormal motor, sensory, or psychic phenomena caused by abnormal cerebral electrical activity. It is possible that almost any type of behavior may represent seizure activity. Fairly commonly encountered are seizures of frontal or temporal cortical origin with non-classical motor movements. The patient may show some seemingly organized motor activity without the usually in-phase jerking movements more typical of generalized seizures. Also complicating the problem is that clouding or alteration of consciousness may occur without complete loss of consciousness. Again, these have been exhaustively documented by video-EEG techniques.

The emergency physician must avoid being too rigid in his definition of seizures; the axiom that "not all seizures shake" needs to be remembered. The emergency physician must play probabilities in an educated manner --this behavior is likely a seizure, this behavior is unlikely to be a seizure-- and may at times be unable to diagnose some unusual events.

Accurate description of a seizure should include any aura reported by the patient, any specific initial motor manifestations, a description of the tonic phase, if present, and a description of the clonic phase with duration. Post-ictal characteristics, including duration, should be documented as well. An accurate description is preferable to using jargon.

What is status epilepticus and when is status epilepticus a medical emergency?

A publication by the World Health Organization defined status epilepticus as, "a condition characterized by an epileptic seizure that is sufficiently prolonged or repeated at sufficiently brief intervals so as to produce an unvarying and enduring epileptic condition." Typically, status epilepticus is defined as 30 minutes of continuous seizure activity or a series of seizures without return to full consciousness between the seizures. This definition is imprecise and investigators in the area often use their own criteria. Note that these definitions are based on clinical observations rather than EEG or any other physiologic monitoring. Many feel that pathophysiologic studies suggest that a shorter period of seizure activity causes neuronal injury and makes seizure self- termination unlikely and suggest 5 minutes or briefer times define status epilepticus. A series of patients with frequent secondarily generalized tonic-clonic seizures documented by video-EEG monitoring revealed that the mean duration of seizures was 1 minute and that seizures that stopped spontaneously terminated within 2 minutes; they urged intravenous anticonvulsant drug administration for generalized tonic-clonic seizures lasting greater than 2 minutes. The implications of this shortened time definition are great for emergency services; most dispatches for seizures should be treated as status epilepticus if the patient is continuing to seize at the time of EMS arrival. Current recommendations are that status epilepticus be considered when one seizure lasts 5 minutes or there are sequential seizures without full return of consciousness between seizures.

One useful way to sort status epilepticus (SE) is to divide SE into a classifications similar to seizures. The term "simple" in this scheme implies that an isolated area of the cortex is involved with resulting focal motor, sensory, special sensory, or other phenomena with full consciousness preserved. Again, the term "complex" in seizure classification means that consciousness is altered. The term "generalized" means that the abnormal electrical activity involves all areas of the cortex; motor movements are typically seen but notable exceptions exist as describe below.

One seizure type may evolve into another seizure type. For example, a simple motor seizure may evolve into a complex partial seizure with altered consciousness; at times this state may persist for hours or days with minimal or no associated motor activity; the terminology for this would be "partial complex status epilepticus."

Absence seizures (also known as petit mal) are a primarily generalized seizure type involving all cortical areas at once; this is typically a seizure disorder of childhood with a characteristic EEG pattern. At times, absence seizures may persist with minimal motor movements and altered consciousness for hours or days. Absence status epilepticus and complex partial status epilepticus are often grouped under the term "nonconvulsive status epilepticus" and are referred to at times as twilight or fugue states.

There is controversy in the term "nonconvulsive status epilepticus (NCSE)." NCSE has been used to describe the absence of convulsive seizures with EEG activity indicating that electrical generalized seizures were continuing diffusely throughout the cortex as well as the twilight states described above. Currently, nonconvulsive status epilepticus is best reserved for absence status epilepticus and partial complex status epilepticus. The term "subtle status epilepticus" is more

correctly used to indicate patients that have evolved from generalized convulsive status epilepticus or are in a comatose state with epileptiform activity.

Table-Clinical classification of status epilepticus (including both primary and secondarily generalized seizures)

overt generalized convulsive status epilepticus (continuous convulsive activity and intermittent convulsive activity without regaining full consciousness)
- convulsive (tonic-clonic)
- tonic
- clonic
- myoclonic

subtle generalized convulsive status epilepticus following generalized convulsive status epilepticus with or without motor activity

simple status epilepticus (consciousness preserved)
- simple motor status epilepticus
- sensory status epilepticus
- aphasic status epilepticus

nonconvulsive status epilepticus (consciousness impaired; twilight or fugue state)
- petit mal status
- complex partial status epilepticus

Extensive animal studies and more limited pathologic work in humans following generalized tonic-clonic status epilepticus (GCSE) consistently demonstrate neuronal damage. Significant physiologic changes accompany GCSE. Temperature varies in patients with status epilepticus, but there is a tendency for hyperpyrexia (infectious causes excluded) which is thought to follow the vigorous muscle activity of status epilepticus; this may be greater than 41 C. Hypertension, tachycardia, cardiac arrhythmias, and hyperglycemia are among the systemic effects caused by the marked increase in catecholamines that accompany GCSE. Lactic acidosis is common after a single generalized motor seizure and resolves with termination of the seizure. Many of these systemic responses are thought to result from the catecholamine surge that follows a seizure and accompanies generalized convulsive status epilepticus; the above effects are seen early in the course. Increased pulmonary transcapillary fluid flux may lead to pulmonary edema. With prolonged generalized convulsive status epilepticus, a variety of clinical responses including hypotension, hypoglycemia, rhabdomyolysis, and CNS damage from ischemia and other process occurs. Cerebral metabolic demand increases greatly with GCSE; however, cerebral blood flow and oxygenation are thought to be preserved or even elevated early in the course of GCSE. In an experimental model, a divergence between sympathetic activity and cardiovascular response was noted when catecholamine levels remained elevated for hours but hypotension developed. Systemic hypotension that occurs with prolonged generalized convulsive status epilepticus may

contribute to the late development of cerebral ischemia as perfusion diminishes but cellular energy demand remains high.

Experiments in paralyzed and artificially ventilated animals with many of the systemic metabolic changes manipulated and controlled yielded the conclusion that neuronal loss after focal or generalized status epilepticus is linked to the abnormal neuronal discharges and not simply to the systemic effects of GCSE.

Table-RATIONALE FOR AGGRESSIVE TREATMENT IN STATUS EPILEPTICUS

1. The longer generalized convulsive status epilepticus persists, the harder it is to control

2. Neuronal damage is primarily caused by continuous excitatory activity, not systemic complications of generalized convulsive status epilepticus.

3. Systemic complications of seizure activity, particularly hyperpyrexia, may exacerbate neuronal damage.

4. Every seizure counts in terms of making generalized convulsive status epilepticus more difficult to control and for causing neuronal damage.

Table-Classification of status epilepticus according to need for aggressive treatment

STATUS EPILEPTICUS REQUIRING IMMEDIATE, AGGRESSIVE TREATMENT
Continuous generalized convulsive activity with impaired consciousness lasting greater than 5 minutes*

Serial seizures without return to full consciousness between seizures

Subtle generalized convulsive status epilepticus- coma with minimal or no associated motor activity †
-consider if post-ictal state is not improving in 20 minutes*
-may evolve from generalized convulsive status epilepticus

STATUS EPILEPTICUS THAT POSSIBLY BENEFITS FROM AGGRESSIVE TREATMENT (evidence of CNS injury from seizures is not as clear)
complex partial status epilepticus (twilight or fugue state)†

STATUS EPILEPTICUS REQUIRING TREATMENT, TIME INDETERMINATE
(no data to suggest that rapid cessation of seizures is necessary to prevent neuronal injury)
Absence status epilepticus (spike-wave status epilepticus)†
simple motor status epilepticus (epilepsia partialis continua)†

*time is arbitrary; see text for details
†EEG may be required for diagnosis

When is an EEG indicated in the emergency department?

Recommendations have been made to obtain emergency EEG for persistent altered consciousness, refractory status epilepticus, pharmacologically managed sedation and coma, and for the diagnosis of viral encephalitis as well as for a variety of other clinical conditions including coma and brain death.

The most compelling argument for emergent EEG is for the detection of generalized convulsive status epilepticus that may have evolved into subtle status epilepticus with continuing abnormal electroencephalograhic discharges. A sequence of EEG evolution has been observed by some investigators in clinical and experimental studies of GCSE progressing from discrete EEG seizure activity to periodic epileptiform discharges on a flat background; these changes seem to parallel bedside observations of continuous seizure activity evolving into subtle GCSE. The concern is that the ongoing electrical seizure activity may cause cell injury even in the absence of convulsive movements and with conventional advanced live support. A recent trial examining treatments for generalized convulsive status epilepticus employed EEG early in the clinical course and found that 26% of patients had evidence of continuing electrical seizures when generalized convulsions were thought to have been terminated by bedside observation.(Treiman)

This "subtle status epilepticus" was regarded as an evolution of suboptimally treated or nonterminated convulsive status epilepticus. Others have noted that nonconvulsive status epilepticus may persist after control of generalized convulsive status epilepticus and suggest that EEG monitoring be immediately available after the control of convulsive status epilepticus.(DeLorenzo) Continuous EEG monitoring for patients with status epilepticus that is refractory to optimal doses of a benzodiazepine and phenytoin is recommended as well.

The detection of nonconvulsive status epilepticus in comatose patients in intensive care units is another area of active research. In comatose patients without clinical signs of seizure activity, up to 8% met criteria for nonconvulsive status epilepticus in one study. These studies were performed on patients in intensive care units with continuous EEG-monitoring techniques. The application of these studies to patients in emergency departments and impact of any treatment on patient outcome remains unclear.

In spite of recommendations, a recently published multicenter survey of management of patients with seizures revealed that EEG was uncommonly performed in ED's and only rarely in the ED for the indication of status epilepticus. Most EEG's were performed at one institution in the study likely reflecting local practice pattern.

A survey of medical directors of accredited North American clinical EEG laboratories and directors of facilities offering accredited EEG fellowships revealed that the majority of facilities required neurologic consultation or other specialized consultation before emergent EEG could be obtained. The survey revealed no clear consistency between centers regarding which clinical syndromes were appropriate for emergent EEG study. Furthermore, a response time from request of approximately 3 hours stands beyond ideal availability for treatment of time-critical conditions.

Local access to neurologic and electroencephalographic expertise, access to technical personnel and equipment, other technical considerations, and local practice patterns limit performance of EEG's in the emergency departments. The widespread practice of neurologic consultation prior to obtaining an EEG seems reasonable and is likely to continue given that EEG interpretation is a specialized province within the specialty of neurology. Emergency physicians should be encouraged to seek prompt neurologic consultation including possible performance of an EEG in patients without improving consciousness after termination of generalized convulsive status epilepticus, in seizing patients requiring neuromuscular blockade for critical care management, in patients with refractory status epilepticus, when suspicion of subtle status epilepticus exists, or in patients with persistent altered mental status or coma when nonconvulsive status epilepticus is prominent in the differentiable diagnosis.

Patient Outcome

Lorazepam 2 mg intravenously did not result in a change in the patient's condition. The patient was administered fosphenytoin with resolution of the abnormal eye movements but persistence of the eye deviation. An EEG was obtained approximately four hours later and did not show any periodic epileptiform activity. The eye deviation resolved over several hours and was thought to be a post-ictal phenomenon. The patient returned to baseline state.

CT and MRI imaging did not reveal any acute CNS lesions. The previous stroke the patient had suffered was thought to be the nidus of the seizures and she was discharged on phenytoin.

Annotated Bibliography

1. Fountain NB, Lothman EW: Pathophysiology of status epilepticus. *Journal of Clinical Neurophysiology* 1995; 12:326-342. Classic review article of pathophysiology and status epilepticus.

2. Kaplan PW: Nonconvulsive status epilepticus in the emergency room. *Epilepsia* 1996;37:643-650. There was considerable overlap in clinical features of patients with complex partial SE (CPSE) and generalized nonconvulsive SE. Delays in seeking medical attention were common. Diagnosis was significantly delayed in 10 patients. The authors concluded that NCSE often goes unrecognized or is mistaken for behavioral or psychiatric disturbance. The pleomorphic clinical presentation of NCSE indicates that EEG and a therapeutic trial of AEDs afford the best diagnostic measures in acute waxing and waning confusional states associated with agitation, bizarre behavior, staring, increased tone, or mutism.

3. Bauer G, Aichner F, Mayr U: Nonconvulsive status epilepticus following generalized tonic-clonic seizures. European *Neurology* 1982;21:411-419. Early case series of 10 cases "stupor coma" following termination of GCSE; points out the differential diagnosis of post-ictal state and postconvulsive status with altered mental status.

4. Treiman DM, Meyers PD, Walton NY, Collins JF, et al: A comparison of four treatments for generalized convulsive status epilepticus. *New Engl J Med* 1998; 339:792-8. Although generalized convulsive status epilepticus is a life-threatening emergency, the best initial drug treatment is uncertain. The investigators conducted a five-year randomized, double- blind, multicenter trial of four intravenous regimens: diazepam (0.15 mg per kilogram of body weight) followed by phenytoin (18 mg per kilogram), lorazepam (0.1 mg per kilogram), phenobarbital (15 mg per kilogram), and phenytoin (18 mg per kilogram). Patients were classified as having either overt generalized status epilepticus (defined as easily visible generalized convulsions) or subtle status epilepticus (indicated by coma and ictal discharges on the electroencephalogram, with or without subtle convulsive movements such as rhythmic muscle twitches or tonic eye deviation). Treatment was considered successful when all motor and electroencephalographic seizure activity ceased within 20 minutes after the beginning of the drug infusion and there was no return of seizure activity during the next 40 minutes. Lorazepam was successful in 64.9 percent of those assigned to receive it, phenobarbital in 58.2 percent, diazepam plus phenytoin in 55.8 percent, and phenytoin in 43.6 percent. Lorazepam was significantly superior to phenytoin in a pairwise comparison (P=0.002). Bottom line: benzodiazepines are good; phenytoin alone less good. There were a surprising number of patients with “subtle” status epilepticus--electrical storm by EEG without clinical manifestations. Is this group comparable to the ED population*?*

5. Towne AR; Waterhouse EJ; Boggs JG; Garnett LK; Brown AJ; Smith JR Jr; DeLorenzo RJ: Prevalence of nonconvulsive status epilepticus in comatose patients. ***Neurology*** **2000 Jan 25;54(2):340-5.** Status epilepticus (NCSE) is a form of status epilepticus (SE) that is an often unrecognized cause of coma. A total of 236 patients with coma and no overt clinical seizure activity were monitored with EEG as part of their coma evaluation. EEG demonstrated that 8% of these patients met the criteria for the diagnosis of NCSE. The study included an age range from 1 month to 87 years. NCSE is an under recognized cause of coma in the ICU, occurring in 8% of all comatose patients without signs of seizure activity. EEG should be considered in the routine evaluation of comatose patients even if clinical seizure activity is not apparent.

6. Privitera MD, Strawsburg RH: Electroencephalographic monitoring in the emergency department. ***Emergency Medical Clinics of North America*** **1994;12:1089-1100.** The authors urge immediate EEG for patients with persistent, unexplained, altered consciousness. In their prospective study, 37% of patients referred for emergency EEG had combined EEG and clinical evidence of seizures that were not tonic-clonic that would have gone undetected without EEG.

7. Quigg M, Shneker B, Domer P: Current practice in administration and clinical criteria of emergent EEG. ***Journal of Clinical Neurophysiology*** **2001;18:162-164.** The authors surveyed medical directors of accredited EEG laboratories (n = 84) to determine the ranges of availability and clinical indications for approval of continuously available emergent EEG (E-EEG). The mean estimated response time from request to expert interpretation was 3 +/- 4 hours (range, 1-24 hours). The five clinical indications for which most respondents approved E-EEGs were possible nonconvulsive status epilepticus (100%), treatment of status epilepticus (84%), cerebral death exam (81%), diagnosis of convulsive status epilepticus (79%), and diagnosis of coma or encephalopathy (70%). Respondents disagreed widely when asked which clinical situations merited E-EEG, with some approving all requests and others denying all except for nonconvulsive status epilepticus. The wide range of current practice suggests that research focused on outcomes of aggressive, EEG-aided patient evaluation and treatment are needed to define better the costs and benefits of a continuously available EEG service.

8. Jordan GB: Continuous EEG monitoring in the neuroscience intensive care unit and emergency department. ***Journal of Clinical Neurophysiology*** 1999;16:14-39. This is the report of an institution's experience with continuous EEG monitoring. In the diagnosis and management of convulsive and nonconvulsive status epilepticus, CEEG value appears established. It is finding benefit in the early diagnosis and management of precarious cerebral ischemia, including severe acute cerebral infarctions and post-SAH vasospasms. In comatose patients, it may provide diagnostic and prognostic information that is otherwise unobtainable.

Questions

1. **What does the world "complex" mean in seizure classification?**
    a. Difficult to control
    b. Difficult to categorize
    c. Combined seizure types
    d. Impairment of consciousness during the seizure

2. **Why is status epilepticus a medical emergency?**
    a. Hypoxemia
    b. Hypotension
    c. Ongoing electrical activity is damaging to brain
    d. All of the above

3. **Nonconvulsive status epilepticus has been used to describe which of the following?**
    a. Absence status epilepticus
    b. Subtle status epilepticus following generalized convulsive status epilepticus
    c. Complex partial twilight state
    d. All of the above

4. **Status epilepticus should be considered to exist when a generalized convulsive seizure lasts how long?**
    a. 5 minutes
    b. 15 minutes
    c. 30 minutes
    d. 1 hour

5. **The most accepted indication for an emergency EEG in the emergency department is which of the following?**
    a. New onset seizure
    b. Possibility of subtle status epilepticus in unresponsive patient following generalized seizures
    c. Brain death
    d. Non-convulsive status epilepticus-complex partial seizures

Answers

1. Answer d.
"Complex" means that consciousness is impaired during the seizure.

2. Answer d.
Status epilepticus is a medical emergency for all of these reasons but remember that the abnormal electrical activity alone is damaging to the brain.

3. Answer d.
Nonconvulsive status epilepticus has been used to describe all of these conditions.

4. Answer a.
Status epilepticus should be considered to exist when a generalized convulsive seizure lasts 5 minutes according to recent recommendations.

5. Answer b.
Possibility of subtle status epilepticus in unresponsive patient following generalized seizures is the probably the best indication for emergency EEG according to current recommendations.