

Epilepsy

CASE 1

A 32-year-old man was observed to suddenly become unresponsive followed by four episodes of generalized tonic-clonic convulsions of the upper and lower extremities while at work. Each episode lasted about 5–10 minutes and he failed to regain awareness after each episode. He was brought to the ER about 30 minutes after his first convulsion. Clinical examination revealed unresponsiveness to external stimuli, deep sighing breaths with respiratory rate of 24 per minute, BP of 155/100 mmHg, and HR of 118 per minute. Left lateral tonic head deviation and flexor contraction of the left upper extremity were observed before another episode of generalized convulsions in the ER.

Localization

Generalized convulsions suggest a global increase in cerebral activity, however, forced tonic head deviation to the left and flexor contraction of the left upper extremity prior to convulsions suggest a right frontal focus of cortical irritability.

Differential Diagnosis

Generalized convulsive SE is most likely. This is defined as a single generalized seizure lasting 5 minutes or more in adults, 10 minutes or more in children, or two or more seizures without fully regaining consciousness in between episodes. Etiologies include *abrupt AED withdrawal/noncompliance*, *alcohol withdrawal*, *metabolic derangement* (low/high Na^+ , glucose, low Ca^{2+} , low magnesium [Mg^{2+}], uremia), *trauma*, *hypoxia*, *infection* (cerebral abscess, encephalitis), *neoplasms*, *vascular malformations*, *congenital malformations*, *genetic diseases* (children), *drug intoxication*, or *idiopathic*. Other diagnostic considerations include *anoxic encephalopathy with post-anoxic myoclonus*, *Wernicke's encephalopathy*, *malinger*, and *pseudoseizures*. However, the clinical presentation makes these differentials highly unlikely.

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Investigations

Investigations should include capillary (finger stick) glucose, CBC with differential, comprehensive metabolic profile, PT/PTT/INR (prior to LP if needed for septic work-up), thyroid function test (TFT), Mg^{2+} , phosphate (PO_4^{3-}), serum/urine toxicology, AED levels, and ABG (to assess for respiratory alkalotic compensation for metabolic acidosis). Lactate and prolactin levels may help differentiate SE from pseudoseizures. If convulsions are prolonged, creatine kinase (CK) is useful for assessing rhabdomyolysis. EKG (arrhythmias can occur during prolonged seizure or with treatment) should be performed.

Electroencephalogram (EEG) may also localize seizure focus post- or inter-ictally; continuous EEG monitoring may be necessary if the patient does not regain consciousness despite treatment (to evaluate for nonconvulsive SE) or to monitor comatose patient for electrographic seizure control. CT scan of the head without contrast should be performed when stable to exclude ICH. MRI of the brain with and without gadolinium (seizure protocol: thin cuts through temporal lobes) should be performed for a structural etiology.

Management

Generalized convulsive SE is a neurological emergency. The airways should be secured and adequate oxygenation provided. Intubation and mechanical ventilation in poorly responsive/comatose patients or if significant respiratory depression occurs is required. Adequate hydration with i.v. normal saline is necessary. Electrolyte abnormalities should be corrected. Give thiamine and glucose i.v. (can omit glucose if capillary or serum level is normal) in comatose patients of undetermined etiology.

Pharmacological treatment is as follows:

Lorazepam 0.05–0.20 mg/kg at 1–2 mg i.v. every 2 minutes (maximum about 8 mg in adults and 4 mg in children) or **diazepam** i.v. 0.15–0.25 mg/kg (adults) or 0.1–1.0 mg/kg (children) at maximum rate of 5 mg per minute. Maximum dose is 10 mg in adults and children.

Rectal diazepam 0.5 mg/kg (maximum dose 20 mg) can be given to children. There is a risk of SE recurrence approximately 30 minutes after administration, despite early onset of action with diazepam.

Phenytoin 20 mg/kg at 50 mg per minute (adults) or 1 mg/kg per minute (children) or **fosphenytoin** 20 mg/kg phenytoin equivalents at 150 mg per minute (adults) or 3 mg/kg per minute (children) should be given, even with SE cessation with lorazepam. Can give additional **phenytoin** 5–10 mg/kg at the same infusion rates for refractory cases (defined clinically as failure to respond to first and second-line agents), up to a total of 30 mg/kg. **Phenobarbital** (especially in children)

20 mg/kg at 50–100 mg per minute or **valproate** i.v. (in adults) 20–25 mg/kg over 60 minutes loading dose, then start at 10–15 mg/kg per day every 6 hours in divided doses can be used in addition to phenytoin in refractory cases.

If SE remains refractory, pharmacological coma with electrographic seizure cessation or “burst suppression” should be induced with anesthetics: **propofol** 1–2 mg/kg i.v. loading dose, then 2–10 mg/kg per hour, **midazolam** 0.2 mg/kg slow bolus, then 1–10 µg/kg per minute or **pentobarbital** (more commonly used in children) 5–15 mg/kg i.v. bolus over 1 hour, then 0.5–3.0 mg/kg per hour. Vasopressors may be required to maintain BP and cerebral perfusion while on these drugs. Maintenance doses of AEDs (e.g., phenytoin 3–5 mg/kg per day i.v. divided every 8 hours) should be instituted on cessation of SE. Check levels and titrate AED dose accordingly.

Hypotension, cardiac arrhythmias (particularly with phenytoin, less so with fosphenytoin), and respiratory depression (particularly with benzodiazepines and barbiturates) are common side effects of drug therapy in SE. There is an increased risk of infections with propofol (owing to its lipophilic nature). An “infusion syndrome” (rhabdomyolysis, severe metabolic acidosis, and cardiovascular collapse) rarely occurs in children treated with propofol, so it is contraindicated in this age group. Central nervous system (CNS) depression or paradoxical agitation is common in children treated with barbiturates. Midazolam undergoes tachyphylaxis after 24–48 hours, resulting in progressively increased doses for seizure control.

Prognosis

Prognosis after generalized convulsive SE depends on age of patient, duration (>30 minutes), and cause for SE. Mortality rates vary from 3 to 35% (average 25%), with children having lower mortality rates than adults. Morbidity is more difficult to estimate because of a lack of studies with neuropsychological evaluation. In SE, subtle-to-adverse effects on intellectual development in children and memory/cognitive deficits in adults may occur. Drugs used in treating SE may have toxic side effects that may influence morbidity.

Counseling

Patients should be counseled about AED compliance, alcohol and drug avoidance, and about the cognitive consequences of this disorder. Seizure triggers such as sleep deprivation or stress should be avoided. Long-term AEDs are not needed for SE secondary to metabolic etiologies. Structural and idiopathic etiologies require long-term management, with eventual AED cessation more likely in idiopathic cases. Having a medical alert bracelet should be suggested.

SUMMARY

- **Generalized convulsive SE** is a neurological emergency because outcomes are dependent on duration of seizures; with irreversible sequelae and death more likely for seizures **lasting more than 30 minutes**.
- **Cardiopulmonary support** may be required during treatment.
- Drug treatment may include the following:
 - First line: **lorazepam** 0.05–0.20 mg/kg at 1–2 mg i.v. every 2 minutes (preferred) or **diazepam** 0.15–0.25 mg/kg (adults) or 0.1–1.0 mg/kg (children) at a maximum rate of 5 mg per minute.
 - Second line: **Phenytoin** 20 mg/kg at 50 mg per minute (adults) or 1 mg/kg per minute (children) or **fosphenytoin** 20 mg/kg phenytoin equivalents at 150 mg per minute (adults) or 3 mg/kg per minute (children).
 - Third line: **Phenobarbital** (children/adults) 20 mg/kg at 50–100 mg per minute or **Valproate** i.v.(in adults) 20–25 mg/kg over 60 minutes.
 - Anesthetics: **propofol** 1–2 mg/kg i.v bolus, then 2–10 mg/kg per hour; **midazolam** 0.2 mg/kg bolus, then 1–10 µg/kg per minute or **pentobarbital** 5–15 mg/kg i.v. bolus over 1 hour, then 0.5–3.0 mg/kg per hour.
- Mortality is **3–35%**: depends on **age**, **cause**, and **duration** of SE.

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