First Generalized Tonic-Clonic Seizure

Background
1. Definition
   o Paroxysmal clinical event resulting from abnormal and excessive cortical neuronal discharge leading to impaired consciousness and motor, sensory, autonomic, or psychic events\textsuperscript{1,2} May be single or multiple within 24 hour period with recovery of consciousness between seizures\textsuperscript{1,2}
   o Generally has 6 properties
     ▪ Abrupt onset, usually without aura
     ▪ Brief duration
       • Usually < 90-120 seconds, average of 30 seconds
       • Witnesses often overestimate
     ▪ Altered mental status or cognition
     ▪ Purposeless activity, eg, automatisms and tonic-clonic movements
     ▪ Unprovoked
     ▪ Post-ictal state
     ▪ Status epilepticus 5 – 30 min.
2. General info
   o Prognosis & treatment depend upon distinguishing epileptic vs. non-epileptic events, type of epilepsy, and identifiable causes of epilepsy
   o Classification of seizures\textsuperscript{1}
     ▪ Partial
       • Simple partial – no loss of consciousness
         1. motor
         2. sensory
         3. autonomic
         4. psychic
       • Complex partial – impaired consciousness
         1. simple partial progressing to impaired conciousness
         2. No other feature
         3. Feature as in simple partial
     ▪ With automatism
     ▪ Generalized
       • Absence
       • Myoclonic
       • Clonic
       • Tonic
       • Tonic-Clonic
       • Atonic
     ▪ Unclassified

Pathophysiology
1. Pathology of Disease
   o Multiple hypothesis
   o Susceptibility to seizure is often multifactorial, idiopathic vs secondary
     ▪ Genetic predisposition
     ▪ Acquired brain disorders
     ▪ Metabolic derangements
1. Incidence, prevalence
   - 1.5 – 5% experience one seizure in a lifetime\(^1,3\)
   - Prevalence = 4 - 57/10000\(^1\)
   - Men approximately equal Women in prevalence (men 1.0-2.4 time the incidence of women)\(^1,4\)

2. Risk factors
   - Central Nervous System infection
   - Cerebral Vascular Accident
   - CNS trauma, CNS mass lesion, Arterial-Venous Malformation
   - Medication toxicity
   - Alcohol withdrawal
   - Drug withdrawal (benzodiazepines, barbiturates)

3. Morbidity, mortality
   - No difference compared to pts without established diagnosis of epilepsy

**Diagnostics**

1. History
   - Accurate description from witnesses
     - Setting
     - Initial behavior, preceding symptoms
     - Eye movements
     - Limb movements
     - Onset (focal vs generalized)
       - Focal onset suggests structural brain disease
     - Pattern of progression
       - Tonic followed by clonic movements
     - Duration
     - Tongue-biting
     - Incontinence
     - Loss of consciousness
     - Post-ictal state
   - Patient Hx
     - Aura, preceding symptoms
       - N/V, odd smells, tastes
       - Abdominal pain
       - Déjà vu, staring
       - Behavioral changes, sleep deprivation
     - Fever
     - HA
     - Neurologic and cardiovascular symptoms
     - HTN, DM, renal or hepatic failure
     - Endocrine abnormalities
     - Alcohol or substance use
     - Meds
     - Hx of head injury
     - Hx of perinatal complications
• Consider cysticercosis if recent travel to endemic areas such as:
  Latin America, Africa, or Asia.
  • CAT Scan with cystic lesions

2. Physical exam
   o Must include full neurologic exam, cardiovascular exam, and
     neuropsychological evaluation
   o Signs of seizures
     ▪ Tongue/ oral lacerations
     ▪ Posterior shoulder dislocations
     ▪ Bladder incontinence
   o R/o hepatomegaly, ascites, telangiectasias
   o Assess fundi, nystagmus, TM, pharynx, dentition
   o Check for meningeal signs
   o Signs of trauma
   o Neurologic exam
     ▪ Mental status
     ▪ Cranial nerves & deep tendon reflexes
     ▪ Motor, sensory, gait
     ▪ Evaluate focal deficits, increased intracranial pressure

3. Diagnostic testing
   o Laboratory evaluation
     ▪ Glucose, sodium, potassium, calcium, phosphorus, magnesium,
       BUN, ammonia (if indicated), alcohol level, CBC, pregnancy test –
       (SOR:C)\textsuperscript{2,5}
     ▪ urine drug screen – (SOR:C)\textsuperscript{5}
   o Diagnostic imaging
     ▪ MRI preferred over CT (if available without delay) – (SOR:B)\textsuperscript{4,5,6,7}
     ▪ CT scan may be performed emergently to r/o bleed – (SOR:B)\textsuperscript{4,5,6,7}
     ▪ Neuroimaging recommended for symptoms/signs of intracranial
       pathology (SOR:C)\textsuperscript{2,5,6,7}
   o Other studies
     ▪ Electroencephalogram – (SOR C)\textsuperscript{2,5,6}
       • Electroencephalogram most sensitive when performed within
         24 hr of Sz (29% sensitivity), 12 – 70% positive, average
         51%
       • If Electroencephalogram normal, perform sleep-deprived
         study (48% sensitive) a normal electroencephalogram does
         not exclude seizure disorder
       • If Dx still in doubt, consider 24-hour ambulatory
         electroencephalogram or video electroencephalogram
       • Electroencephalogram with generalized spikes and wave
         discharge or focal spikes are associated with a greater risk of
         seizure recurrence.
     ▪ Consider lumbar puncture if any suspicion of meningitis, sub-
       arachnoid hemorrhage, or if patient is immunocompromised,
       (SOR:C)\textsuperscript{2,5,6}

4. Diagnostic criteria
   o Diagnosis of epilepsy is based upon a history of recurrent Seizures
- Should not be made after single episode, even if anticonvulsant therapy is initiated
  - There may be serious medical, social, economic, and legal consequences associated with a diagnosis of epilepsy

**Differential Diagnosis**

1. Key differential diagnosis
   - Perinatal complications
   - Febrile seizure
   - CVA
     - >50% of elderly patients with new onset Sz
   - Head trauma
     - If loss of consciousness > 30 min, post-traumatic amnesia > 30 min, or focal neuro findings)
   - CNS infection
     - Meningitis
     - Encephalitis
     - Cerebral abscess
     - Cerebral parasitosis (esp neurocysticercosis)
     - HIV with toxoplasmosis
   - Neurodegenerative diseases
     - Multiple Sclerosis
     - Alzheimer's
     - Neurofibromatosis
     - Tuberosclerosis
     - Sturge-Weber
     - CNS vasculitis
     - Systemic Lupus Erythematosus
     - Polyarteritis nodosum
   - CNS neoplasm
   - Arterial-Venous Malformation
   - Hypertensive encephalopathy
   - Intoxication
     - Amphetamines, cocaine, Phencyclidine Theophyllin, Isoniazide, Tricyclic Antidepressants, lithium, lead, strychnine, camphor
   - Drug withdrawal
     - Alcohol, barbiturates, benzodiazepines
   - Metabolic disorders
     - Uremia
     - Hypoglycemia (if < 45 mg/dl)
     - Hyponatremia (if < 120 mEq/L)
     - Hypernatremia (if > 160 mEq/L)
     - Hypocalcemia (if < 7.5 mEq/L)
       - Hypoparathyroidism, renal failure, acute pancreatitis
     - Hypomagnesemia (esp if < 1 mEq/L)
       - Consider alcoholism or diuretic use
     - Hypothyroidism
     - Hepatic encephalopathy
   - Eclampsia
2. Extensive Differential Diagnosis
   o Must differentiate Sz from non-epileptic events
   o Transient Ischemic Attack
   o Complicated migraine
   o Sleep disorders
   o Transient global amnesia
   o Convulsive syncope
   o Pseudoseizure
   o Malingering

Therapeutics
1. Acute treatment – Medication used for status epilepticus or recurrent seizures. Prophylaxis for first uncomplicated idiopathic seizure is not recommended. No difference in outcome treated versus non-treated\(^2,10\)
   o See Seizures: General Approach
   o CVA (Insufficient evidence)
   o Tumor (Insufficient evidence)\(^9\)
2. Status epilepticus
   o See Status Epilepticus
3. Further management (24 hrs)
   o Postictal state may last for minutes to hours
     - Decreased level of arousal and responsiveness
     - Disorientation
     - Amnesia
     - Headache (HA)
   o Two unusual postictal manifestations
     - Todd's paralysis
     - Neurogenic pulmonary edema
       - May respond to Positive Pressure Ventilation
       - May be confused with aspiration pneumonitis
   o No need for hospitalization if labs normal and no signs of intracranial pathology. -- (SOR C)\(^2,4,5,6\)
   o Each state has different regulations regarding driving restrictions in patients with seizure disorder
     - Many states require mandatory physician notification to the Division of Motor Vehicles
4. Long-term care
   o Neurologists do not recommend anticonvulsant therapy after a first Idiopathic seizure\(^2,10\)
     - If pt has a normal neurologic exam and preliminary tests are negative -- (SOR:C)\(^2,5,6,10\)
     - 50% risk of recurrence
   o Risk for recurrent Sz
     - Age < 16
     - Sz occurring at bedtime/sleep
     -Sibling with epilepsy
     - Partial Sz
     - Episode of Todd's paralysis
     - Hx of cerebral palsy or mental retardation
- Focal abnormality on neuro exam
- CNS tumor seen on imaging
- EEG findings
  - If EEG with epileptiform discharge, 2-year cumulative risk of recurrence is 83%\(^1,5,10\)
  - If EEG with non-epileptiform abnormality, 2-year risk is 41%\(^1,5,10\)
  - If EEG nl, 2-year risk is 12%\(^1,5,10\)

  o Need for anticonvulsant therapy after second seizure is generally agreed upon
    - Phenytoin, carbamazepine, valproate, and Phenobarbital are equally effective
    - Lamotrigine, Levitiracetam, and other newer anticonvulsants are alternative choices to first line medications
    - Phenobarbital has more side effects
  o Consider patient's occupation and public safety
    - crane operators, bus drivers, ability to work on ladders or scaffolds, etc.
  o Consider Medic Alert bracelet (800-736-3342)
  o Know your state laws about reporting seizures for Vehicle Operator’s License

**Prognosis**

1. Risk of recurrence after initial Sz in adult without correctable predisposing factor is 50%.
2. 10-15% of patients with significant head injury will develop epilepsy
3. 4-9% of stroke patients will develop epilepsy

**References**

1. Bradley: Neurology in Clinical Practice. 5\(^{th}\) ed. 2008

Evidence-Based Inquiry

1. What physical exam techniques are useful to detect malingering?

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