

First Generalized Tonic-Clonic Seizure

Background

1. Definition

- Paroxysmal clinical event resulting from abnormal and excessive cortical neuronal discharge leading to impaired consciousness and motor, sensory, autonomic, or psychic events^{1,2} May be single or multiple within 24 hour period with recovery of consciousness between seizures^{1,2}
- 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

- Prognosis & treatment depend upon distinguishing epileptic vs. non-epileptic events, type of epilepsy, and identifiable causes of epilepsy
- Classification of seizures¹
 - 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 consciousness
 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

- Multiple hypothesis
- Susceptibility to seizure is often multifactorial, idiopathic vs secondary
 - Genetic predisposition
 - Acquired brain disorders
 - Metabolic derangements

- Cerebral hypoxia
 - Drug or alcohol withdrawal, intoxication
 - See also Seizures: General Approach
- 2. Incidence, prevalence
 - 1.5 – 5 % experience one seizure in a lifetime^{1,3}
 - Prevalence = 4 - 57/10000¹
 - Men approximately equal Women in prevalence (men 1.0-2.4 time the incidence of women)^{1,4}
- 3. 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)
- 4. 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
- Must include full neurologic exam, cardiovascular exam, and neuropsychological evaluation
 - Signs of seizures
 - Tongue/ oral lacerations
 - Posterior shoulder dislocations
 - Bladder incontinence
 - R/o hepatomegaly, ascites, telangiectasias
 - Assess fundi, nystagmus, TMs, pharynx, dentition
 - Check for meningeal signs
 - Signs of trauma
 - Neurologic exam
 - Mental status
 - Cranial nerves & deep tendon reflexes
 - Motor, sensory, gait
 - Evaluate focal deficits, increased intracranial pressure
3. Diagnostic testing
- Laboratory evaluation
 - Glucose, sodium, potassium, calcium, phosphorus, magnesium, BUN, ammonia (if indicated), alcohol level, CBC, pregnancy test – (SOR:C)^{2,5}
 - urine drug screen – (SOR:C)⁵
 - Diagnostic imaging
 - MRI preferred over CT (if available without delay) – (SOR:B)^{2,4,5,6,7}
 - CT scan may be performed emergently to r/o bleed – (SOR:B)^{4,5,6,7}
 - Neuroimaging recommended for symptoms/signs of intracranial pathology (SOR:C)^{2,5,6,7}
 - Other studies
 - Electroencephalogram– (SOR C)^{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)^{2,5,6}
4. Diagnostic criteria
- 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
 - Tuberous sclerosis
 - Sturge-Weber
 - CNS vasculitis
 - Systemic Lupus Erythematosus
 - Polyarteritis nodosum
- CNS neoplasm
- Arterial-Venous Malformation
- Hypertensive encephalopathy
- Intoxication⁸
 - Amphetamines, cocaine, Phencyclidine Theophyllin , Isoniazide, Tricyclic Antidepressants, lithium, lead, strychnine, camphor⁸
- 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
 - Must differentiate Sz from non-epileptic events
 - Transient Ischemic Attack
 - Complicated migraine
 - Sleep disorders
 - Transient global amnesia
 - Convulsive syncope
 - Pseudoseizure
 - 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}
 - See Seizures: General Approach
 - CVA (Insufficient evidence)
 - Tumor (Insufficient evidence)⁹
2. Status epilepticus
 - See Status Epilepticus
3. Further management (24 hrs)
 - Postictal state may last for minutes to hours
 - Decreased level of arousal and responsiveness
 - Disorientation
 - Amnesia
 - Headache (HA)
 - Two unusual postictal manifestations
 - Todd's paralysis
 - Neurogenic pulmonary edema
 - May respond to Positive Pressure Ventilation
 - May be confused with aspiration pneumonitis
 - No need for hospitalization if labs normal and no signs of intracranial pathology. -- (SOR C)^{2,4,5,6}
 - 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
 - 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
 - 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}
- Need for anticonvulsant therapy after second seizure is generally agreed upon
 - Phenytoin, carbamazepine, valproate, and Phenobarbital are equally effective
 - Lamotrigine, Levetiracetam, and other newer anticonvulsants are alternative choices to first line medications
 - Phenobarbital has more side effects
- Consider patient's occupation and public safety
 - crane operators, bus drivers, ability to work on ladders or scaffolds, etc.
 - Occupations with restrictions: Pilots, scuba diver, truck driver, etc
- Consider Medic Alert bracelet (800-736-3342)
- 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. 5th ed. 2008
2. Adams SM, Knowles PD, Evaluation of a First Seizure. American Family Physician, 75: 9, May 2007.
3. Hauser WA, Annegers JF, Rocca WA. Descriptive epidemiology of epilepsy: Contributions of population-based studies from Rochester, Minnesota. Mayo Clin Pra 1996, 71:576.
4. Sander, 2003. Sander J.W.: The epidemiology of epilepsy revisited. *Curr Opin Neurol* 2003; 16:165-170.
5. Krumholtz A, Wiebe S, Gronseth G, Shinnar S, Levison P, Ting T, Hopp J, Shafer P, Morris H, Seiden L, Barkley G, French J. Practice Parameter: Evaluating an apparent unprovoked first seizure (an evidence based review). Report of the Quality Standards Subcommittee of the Academy of Neurology and American Epilepsy Society. *Neurolog* 2007; 69 (21), 1996-2007.
6. Duvivier EH, Pollack CV Jr. Marx: Rosen's Emergency Medicine, Chapter 100-Seizures. 7th ed. 2009.
7. Algorithm for Neuroimaging (Evidence Based Medicine: neuroimaging of Seizures. *NeuroImaging Clinics O North America*, 123:2 (May 2003)
8. Dobbs: Clinical Neurotoxicology, 1st ed., 2009 Saunders

9. Glantz, MJ, Cole BF, Forsyth PA, et. al. Practice Parameter: Prophylaxis in Patients with Newly Diagnosed Brain Tumors. *Brain* 2005; 128: 1921-1930.
10. Sathasivam S, Nicolsom A. First Seizure – To treat or not to treat. *Int J Clin Prac* 2008; 62 (12), 1920-5.
11. American College of Emergency Physicians Clinical Policies Committee, Clinical Policies Subcommittee on Seizures. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with seizures. *Ann Emerg Med.* 2004;43:605–25.

Evidence-Based Inquiry

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

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