Seizures and Epilepsy: Initial Diagnosis and Management

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Definitions

Seizure = sudden involuntary burst of electrical discharges
Out of the normal rhythm of the brain
• Results in variable clinical manifestations depending
on whether the discharge is focal in origin or occurs
all over the brain at the same time

Epilepsy = the condition in which the individual has recurrent seizures

Seizure Classification

Based primarily on two features
• EEG features of the event!
• Clinical features of the event!

Generalized or Partial Seizures

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Generalized or Partial Seizures

Why Classify Seizures?

1. Determine the extent and focus of the work-up
2. Determine the likely cause of the seizure
3. Determine the most appropriate drug with which to initiate therapy
4. Determine the prognosis for;
   • Seizure control
   • Functional outcome
   • Genetic risks

Ictal EEG features

• Focal or partial seizures
  • More likely associated with lesion
  • Focal Cortical Dysplasia, Tumor, AVM, Stroke, Traumatic
    anoxia, Infarct, SITS
  • Primary localization related epilepsy (BECTS or Rolandic)
  • Different sets of drugs are more effective in control of seizures

• Generalized seizures
  • Diffuse multifocal disease
  • Primary generalized epilepsy

Often stuck with interictal EEG!
(Often helpful and occasionally diagnostic)

History of the Ictus

• "Frame by Frame" description
• The most important feature of the entire evaluation, also the most difficult to get right
  • First hand observer, don’t forget the patient
  • Aura
  • Secondary generalization
  • Rapid spread
  • Adverse seizure onset
  • Sequence of stages
  • Resolution of seizure
  • Post ictal state

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Other Methods of Classification

- Primary epilepsy
  - Code for genetic epilepsy
  - Usually no other organic brain dysfunction
- Idiopathic epilepsy
  - Cause unknown
  - Sometimes things like EEG and Infantile spasms included in this category or will go to secondary epilepsy
- Secondary epilepsy
  - Usually an identifiable cause of the organic brain dysfunction
    - Tumor, Trauma, HIE, AVM etc.

Childhood Seizure Types

- Neocortical Seizures
- Infantile Seizures
- Childhood Seizures
  - Absence Seizures
  - Lennox-Gastaut syndrome (atypical absence)
  - Juvenile Myoclonic Epilepsy
  - BECTS or Rolandic Epilepsy

Febrile Seizures

- Very Common (up to 5%)
- If typical, no increase in risk of epilepsy
- Characteristics
  - Documented fever of known origin
  - Single, brief, generalized seizure
  - Normal child before ictus
  - No family history of idiopathic epilepsy
  - ~ 50% recurrence risk
- No treatment necessary from medical standpoint
  - Therapy might be appropriate for other reasons

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Staring Spells

- 6 year-old boy
- Staring spells noted by both teacher and Mom
- Multiple spells a day
- More common with fatigue
- Last only a few seconds
- No aura or post-ictal alteration in function
- Does not fall or drop things from hands

Stops HV and “Stares into space”
Resolution

- Silly grin as he doesn’t know why he quit blowing
- No memory for the spell but the entire spell was less than 5 seconds (90% < 5 seconds)
- Frequency of automatisms and postural changes is related to the duration of spell

Typical Absence

- Normal child interictally
- Family history of similar seizures
- Does well in school
- Mother had occasional GTC seizures as child in addition to the absence seizures
- Questions?
  - Drug of choice?
  - VPA, ETX, LTG

Staring Spells

- 3 1/2 year-old
- Meningitis as infant
- Delayed development
- Drop attacks, staring spells, tonic seizures, myoclonic seizures
- Falls on face during some seizures
- Poor response to AED medications

Lennox-Gastaut Syndrome

- Underlying neurological dysfunction
- Multiple seizure types
  - tonic, Atypical absence, Atonic, Myoclonic
- Poor response to medications
- Poor outlook for function as an adult
- ~30% seizure free with any combination of therapies
Staring Spells

- 12 year-old
- Spells in school where he stares for 10-20 seconds at a time and cannot respond to questions.
- Remembers trying to speak during the spells
- Confused for moments after the event
- 4-6 spells a week

Complex Partial Absence Seizures

- May be indistinguishable from typical absence
- More likely some memory for event
- Aura
- Post-ictal state
- Infrequent occurrence
- High association with focal organic brain disease/ lesion
- EEG focal or normal
- Positive results increased by sleep deprivation, stimulants and fatigue

7 Year Old Boy

- Seizures: absence spells, myoclonic jerks in the morning, occasional generalized tonic-clonic seizures
- Normal function
- Good student
- No febrile seizures

Fp1-F7
F7-T3
T3-T5
T5-O1
Fp2-F8
F8-T4
T4-T6
T6-O2
Fp1-F3
F3-C3
C3-P3
P3-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
Fz-Cz
Cz-Pz
PG1-A1
PG2-A2
*EKG-A1

JME

- Primary generalized epilepsy
- Life long propensity to seizures
- Environmentally sensitive
  - Sleep
  - Stimulants
  - Intervernet illness
- VPA
  - Wally Pack?
- LTG
- Others?

Initial Therapy for Epilepsy

Considerations

- Choose a drug
- How to initiate therapy
- Blood level?
- Drug Failure
- Discontinuation of therapy
How do you choose a drug?

- What type of seizure are they?
- Frequency, Duration and Associated features?
- What is the psychosocial attitude regarding
  - Epilepsy
  - Drug therapy
  - Compliance
- What are the patient related factors?
  - Swallow pills?
  - Reliable supervision?
  - Other medications?
  - Pregnancy?

### Treatment Options

#### Generalized Seizures

**Drug of Choice**
- VPA (Valproic, Depakene, Depakote)

**Alternative Drugs**
- Old Drugs
  - PHT
  - ETH

- New Drugs
  - LTG (Zarontin)
  - TPM (Topamax)

**Others sometimes used**
- Pyridoxine (Folic acid)
- Carbamazepine
- Lamotrigine
- EZT (Keppra)

#### Partial Seizures

**Drug of choice**
- CBZ (Tegretol)

**Alternative Choices**
- DPL, PB
- VPA
- TPMB
- LTG
- VGB, Keppra, Zonegran, PreGabain?
- OCB (Trileptal)

### Expectations with therapy

- Goal is to have no seizures with no side effects
  - 60% of patients can expect good control
  - Significant side effects relatively common (impact quality of life)
  - If the first two drugs tried do not control the seizures, the chance of good control is not high with the next several used
  - New medications may not increase the % of patients with good control much but decrease side effects!

### Initiation of Therapy

- Calculate the "Target" dose!
  - Weight of patient
  - Begin at fraction of "Target" dose
  - Increase in increments to "Target"
  - Avoid immediate side effects
  - Usually have time
  - Loading does not shorten time to steady state
  - Blood levels?
    - At steady state!
    - Determine appropriateness of dose
      - Side effects
      - Taper to dosing
Measure Blood Levels

Control Yes!
- To know what the level is when pt. doing well
- Side effects?
  - Idiosyncratic
  - Rash, behavioral, etc.
  - Dose related?
    - Image, thinking, Plt count, etc.
    - PT/INR/Drug
- Trough Levels?
  - Dose appropriate?
  - Frequency appropriate?

Control No!
- Pt. Taking drug?
- Dose appropriate?
- Frequency appropriate?
- Side effects?
- Toxic effects

Medication Failure

- The most common reasons for failure of medication are
  - Patient not taking medications as directed
  - Side effects, education, etc
  - Incorrect classification of seizure type
- If patient has tried 2 or more medications (adequate trials, confirmed seizure type) one should evaluate the possibility of other approaches

Confirmation of Seizure Type

Possible Studies (EEG)
- Repeat EEG
- Extended EEG
- Ambulatory EEG
- Video monitoring plus EEG

Possible Imaging Studies
- High resolution MRI
- SPECT
- PET

If the drugs chosen are appropriate for the seizure type, consider other approaches

Non-medication Options

Non-medical therapies
- VNS
- Surgery
- Ketogenic Diet

Non-traditional
- "Sing", HBO, Bio-touch, Noni Juice, Acupuncture, Others
- Environmental modification?

VNS

- Stimulator implanted on chest
- Electrode on Left Vagus nerve
- Stimulation parameters
  - Voltage
  - Frequency / duration of impulse
  - Time on / off
  - Patient control
- Effectiveness?
  - 32 patients will experience improved seizure control
  - ~5% will be seizure free with the VNS
  - Statistics about the same as the “next anticonvulsant drug”

Down-side of VNS
- Must be big enough to implant device
- Mosquito skin
- Skin irritation over device
- Infection
- Battery life
- Device must be "interrogated" periodically to be sure it is functioning properly
Ketogenic Diet

- Change in calorie source toward fatty acids
  - 40-60% of calories from Fat
  - MCT oil or other
- Effectiveness
  - About 40% will have improvement in seizure frequency
  - About 5% will be seizure free
- Side effects
  - Not very palatable
  - Chronic ketosis may impact growth
  - Can be associated with liver and gall bladder problems

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Surgery

- Not new but newly improved
- Works best for "lesional epilepsy*
  - Partial seizures arising from a small lesion (cortical dysplasia, small AVM etc)
  - Expectations are that the majority will be seizure free and the final majority will have a significant improvement without significant change in function
- New techniques have improved our ability to identify the source of seizures
  - High resolution MRI (3Tesla)
  - New MRI spin echo sequences
  - Metabolic imaging
    - PET, SPECT, MRS

Epilepsy Surgery

- MTL: mesial temporal lobe sclerosis
  - Age of onset known
  - CPS, Good results
- Corpus callosotomy
  - Ordinarily limited to Pediatric Drop attacks
  - Not at all helpful for epilepsy in nature (Coffin-Lowrey Syndrome, etc)
- Multiple subpial resections
- Cerebellar stimulators
- Hemispherectomy
  - Removal of hemisphere
  - Hemimegalencephaly
- Rasmussen's Encephalitis
- Hemimegalencephaly

Discontinuation of Drug Therapy

- Age of patient
  - Just as in Cancer cure, age matters!
- Type of seizure
  - Rolandic seizures, JME
- Associated features
  - Fixed organic brain disease
  - Focal cerebral gliosis
  - Post traumatic?
    - SDH highest risk ~30%
- Rate of Taper
  - Evidence? 2 months is appropriate
  - Sedative medications much more difficult!

References

- Davis LE: Neurocysticercosis. Medlink 2005 (Online)